ROLE OF *CENTELLA ASIATICA* PLANT'S EXTRACT IN THE PARKINSONISM: A MOLECULAR DOCKING APPROACH

A PROJECT REPORT

Submitted in partial fulfillment of the requirements for the award of the degree of

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CANDIDATE'S DECLARATION

I, **Moin Khan** hereby certify that the work which is being presented in this Major Project in the thesis entitled "**Role of Centella asiatica plant's extracts in the parkinsonism: A molecular docking approach**" in the partial fulfillment of the requirement for the award of the degree of Master of Science in Biotechnology and submitted to the Department of. Biotechnology, Delhi Technological University, Delhi is an authentic record of my own work. if is novel and my own, carried out during the period from January, 2024 to May, 2024, under the supervision of **Prof. Jai Gopal Sharma**.

The matter presented in this report has not been submitted by me for the award of any other degree from this or any other institute/University

Place: Delhi

Date:

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SUPERVISOR CERTIFICATE

Certified that **Moin Khan (2k22/mscbio/29)** has carried out their search work presented in this thesis entitled "**Role of *Centella asiatica* plant's extracts in the parkinsonism: A molecular docking approach"** for award of degree of Masters of science in Biotechnology and submitted to the Department of Biotechnology, Delhi Technological University, Delhi under my supervision. The thesis embodies result of original work, and studies are carried out by the student himself and the content of the thesis do not form the basis for the award of any other degree to the candidate or to the candidate or to anybody else for this or any other university/Institution.

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ROLE OF *CENTELLA ASIATICA* PLANT'S EXTRACTS IN THE PARKINSONISM: A MOLECULAR DOCKING APPROACH.

ABSTRACT

Parkinson disease is one of the highly prominent neurodegenerative disorders later than Alzheimer's disease, signified by the ongoing death of *dopaminergic neurons* in the central brain portion named substantia nigra pars compacta. Pathological parkinsonism is supported by the aberrant accumulation of *α-synuclein*, which the vital hallmark of Parkinson disease. Several other hall mark of Parkinson disease is chronic activation of microglia or astrocytes cell, oxidative stress, mitochondrial dysfunction, cellular cytotoxicity and brain inflammation. Parkinson is defined by motor and non-motor symptoms. Bradykinesia, resting and rhythmic tremor, rigidity and abnormal body reflexes are the motor symptoms and on the other hand non motor symptoms are pain in several areas, sleeping disorder and mental issue in some cases. Oxidative stress is one the key marker in Parkinson nowadays and generation of ROS (Reactive oxygen species) is the main cause of oxidative stress in PD. Several therapeutic techniques and medication are effective on symptoms but not all the permanent effective. *Centella asiatica* popular herbs, used in several disorder like skin issues, cancer and wound healing. With their antioxidants properties recently *C. asiatica* gained much popularity and may effective in the oxidative stress and other parkinsonism supports.

Keywords; Parkinson disease, *Centella asiatica*, oxidative stress, *Alpha synuclein*, Lewy bodies.

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LIST OF ABBREVIATIONS

S.No.	Abbreviation	Full Form
1	PD	Parkinson disease
2	C. asiatica	Centella asiatica
3	ROS	Reactive oxygen species
4	DA	dopaminergic neurons
5	LBs	Lewy Bodies
6	LBD	Lewy Body dementia
7	AD	Alzheimer’s disease
8	α-Synuclein	Alpha-synuclein
9	SOD	Superoxide dismutase’s

CHAPTER– 1

INTRODUCTION

1.1. BACKGROUND

Parkinson disease, the second most common progressive neurodegenerative disorder, effected majorly in the United States population (Beitz 2014). Age is the primary risk factor for parkinsonism, with an average starting age of 50-60 years and a rate of roughly 1% in people over 60 (Sherer et al. 2012). Parkinson disease is marked by the motor and non-motor indication like bradykinesia (slow in speed and activity), rest tremor & other tremor types, stiffness etc are motor symptoms. Sleep disorder, sensory inability like smell and taste and depression etc are the non-motor indication (Tolosa et al. 2021). The scientific community's interest in Parkinson's disease (PD) has increased due to the discovery of causative monogenetic mutations, However, these mutations are expected to account for only a small number of PD cases, and the precise pathogenetic processes leading selective dopaminergic cell death in PD remain unknown (de Lau and Breteler 2006). The progressive loss dopaminergic neurons (DA) in the substantia nigra (Portion of mid brain) is the primary cause of Parkinson's disease motor symptoms, even though various other neurotransmitter such as glutamatergic, cholinergic, tryptaminergic, noradrenergic, adrenergic, serotoninergic, and peptidergic systems are also compromised (Antony et al. 2013). α-Synuclein, a neuronal protein, serves a vital role in PD and other synuclein opathies. Aggregated α-Syn influences the creation of Lewy bodies and neurites, identified as hallmark of Parkinson's disease. Scientific indicates that α-Syn misfolding and accumulation contribute a crucial role in the growth of Parkinson's disease (PD) (Mehra, Sahay, and Maji 2019). Dopamine degradation pathway and other studies suggest that accelerated neuronal damage in the mid brain is created by the free radicals and reactive oxygen species. Therefore, Oxidative stress has become increasingly accepted as a key cause of many disorders, particularly those associated with aging, such as Parkinson's disease

(Hassanzadeh and Rahimmi 2018). C. asiatica, a versatile plant with several scientific research, is gaining popularity for its wound-healing abilities. It is recognized for its capacity to cure minor wounds, scratches, burns, and skin irritations. As technology progresses, the herb's potential is being investigated, with reported benefits including anti-inflammatory, antibacterial, antifungal, depressive, antioxidant, and anticancer characteristics in many disorders link Parkinson disease (Lokanathan et al. 2016).

1.2. LITERATURE SURVEY

Mitochondrial dysfunction is one of the crucial hallmarks in PD. PD relies on several environmental and genetic factor, Large-scale linkage analysis studies found mutations in multiple genes related with familial Parkinson's disease, including α-synuclein, parkin, PINK1, DJ-1, LRRK2, ATP13A2, and rarer genes such as PARK3. Despite in advancement of recent year of treatment, PD still remain permanent incurable because of complex dysregulation or mass dysregulation of several metabolic pathway simultaneously. Oxidative stress in parkinsonism and mitochondrial abnormalities are the major progressive pathophysiological hallmark (Subramaniam and Chesselet 2013). Several plant therapeutic approach may help of on non-motor symptoms but non completely effective in motor symptoms and completely neutralisation of ROS species.

1.3. IDENTIFICATION OF PROBLEM

Despite multiple attempts of treatment still treating of parkinsonism remains a serious difficulty because of several pathophysiological hallmark.

Parkinson's disease motor symptoms are handled predominantly with dopamine-based medications. Anticholinergic medications such as trihexyphenidyl are beneficial, although caution should be exercised owing to potential side effects. Regression of dopamine level is being the most common difficulty in PD and remain completely incurable (Armstrong and Okun 2020).

CHAPTER- 2

LITERATURE REVIEW

2.1 PARKINSON: A NUERODEGENRATIVE DISORDER

Parkinson's disease (PD) is the next prevalent neurological ailment worldwide, behind Alzheimer's disease (AD). Over more than 200 years of research on Parkinson, since James Parkinson describe the Parkinson illness in 1817 then after that several significant discoveries of several molecules and role has been made. These milestone of more than 200 years in PD research, revealed and investigate the various aspects of Parkinson disease including the clinical and pathological characteristics, anatomy of parkinsonism, environmental and genetic factor of PD and advances in diagnostics and therapy technologies. Although Jean-Martin Charcot named Parkinson disease after James Parkinson and it's been documented in ancient writings from both Western and Eastern literatures, with Parkinson first description in a monograph called "*An essay on the shaking palsy*" (Li and Le 2017). Parkinson disease is a neurodegenerative disorder marked by increasing continues loss of dopaminergic neurons in the SNPc (substantia nigra compacta) which is the portion of midbrain, linked to Lewy bodies. Lewy bodies is the main pathological hallmark of Parkinson disease, which contain the insoluble protein aggregation called α-synuclein. However, Parkinson disease having an extensive pathology in the central brain which include the other cellular component and pathways. Several motor and non-motor symptoms act as the key diagnostic criteria for Parkinson disease (PD). Motor symptoms such as resting tremor, cogwheel rigidity (potential rigidity in movement) and bradykinesia (slowness in movement and speed), On the other hand non-motor symptoms are anosmia (partial or complete loss of smell), constipation, depression (mental disorder) and sleep disorder. Non motor symptoms might appear years before the motor symptoms impairments and further during the later stages worse non-motor symptoms like pain and cognitive decline may occur (Simon, Tanner, and Brundin 2020).

Table1. Motor and non-motor symptoms occur in parkinsonism (Jankovic 2008).

S. no	Motor symptom's	Non-motor symptom's
1	Rhythmic tremor	Pain in different part of the body
2	Resting tremors	Depression
3	Bradykinesia (lack & slowness in movement)	Sleeping disorder
4	Rigidity	Anosmia (Loss of smell)
5	Hypomimia (lack of facial movement)	Ageusia (loss of taste)
6	Dysarthria (speech difficulty)	Paresthesia (especially skin)
7	Dysphagia (Difficulty in swallowing)	Apathy (motivational loss)
8	Sialorrhoea (Excessive saliva flow)	
9	Feeding issues	
10	Hygiene issue	
11	Slow activity in day-to-day life	
12	Dystonia (Involuntarily contraction)	
13	Abnormal reflex	

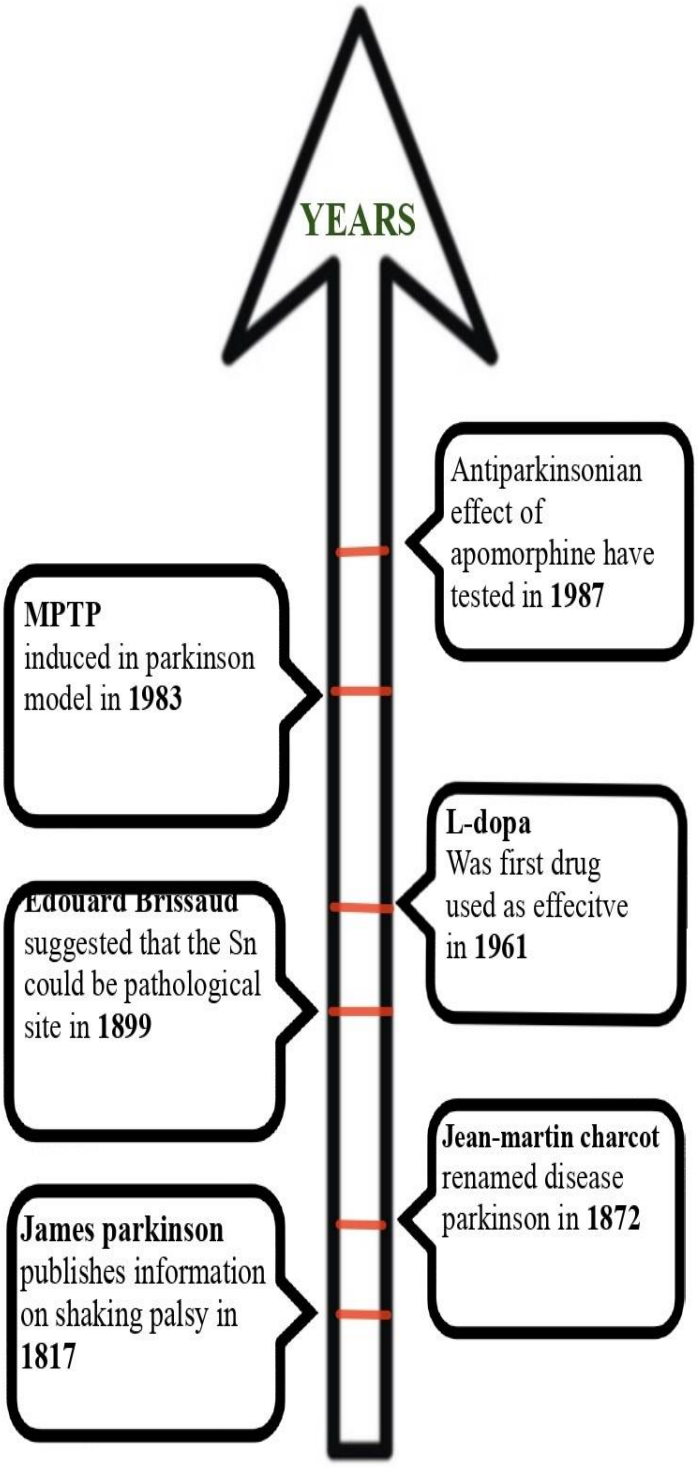

Fig 2.1. Notable History of Parkinson.

2.2 α-SYNUCLEIN AND STRUCTURE LINKED

α-syn, which include140-amino-acid in their structure protein, is prevalent in presynaptic terminals and still has an undefined physiological role. Evidence shows that its concentration can modulate the SNARE complex, hence influencing neurotransmitter release. Excessive α-syn buildup is associated with Parkinson's disease (PD), the second most prevalent neurodegenerative disorder. Triplication of the α-syn gene raises its levels, whereas mutations such as A53T and A30P impede its breakdown, resulting in Parkinson's disease (Du, Xie, and Liu 2020).

Despite intensive studies, the natural structure of alpha-synuclein is still remain uncleared characterized, with various description ranging from inherently disordered helical to a mix of both. Phospholipid membranes are more likely to include a helix-rich structure, which sheds light on the protein's functional role. Exact native state of having certain lack of understanding, determining the protein’s precise role has been difficult, specific docking partner, post translational modification. The SNCA gene and alpha-synuclein possess a crucial role in pathology of Parkinson’s disease familial cases. Several studies also confirmed that alpha-synuclein is identified as the major protein present into the Lewy bodies (Meade, Fairlie, and Mason 2019). Scientific studies suggest that hydrophobic domain of alpha-synuclein, which composed of 71-82 amino acid residues, is required for alpha-synuclein to polymerized into filaments. The study revealed that human alpha-synuclein, has an intrinsic filament-forming capacity, but on the other hand human beta-synuclein cannot polymerize into filaments even after prolonged exposure to assembly conditions. However, several reports suggest that few filaments were found of beta-synuclein after prolonged incubation (Giasson et al. 2001). About the genetic evidence, the link between genetics and Parkinson’s was first came to light in 1990. The first documented hereditary case of parkinsonism pathology was typically Lewy bodies parkinsonism (nowadays known as Parkinson disease). After the previous genetic linked and next logical steps is linkage analysis of defective genes (Golbe et al. 1990).

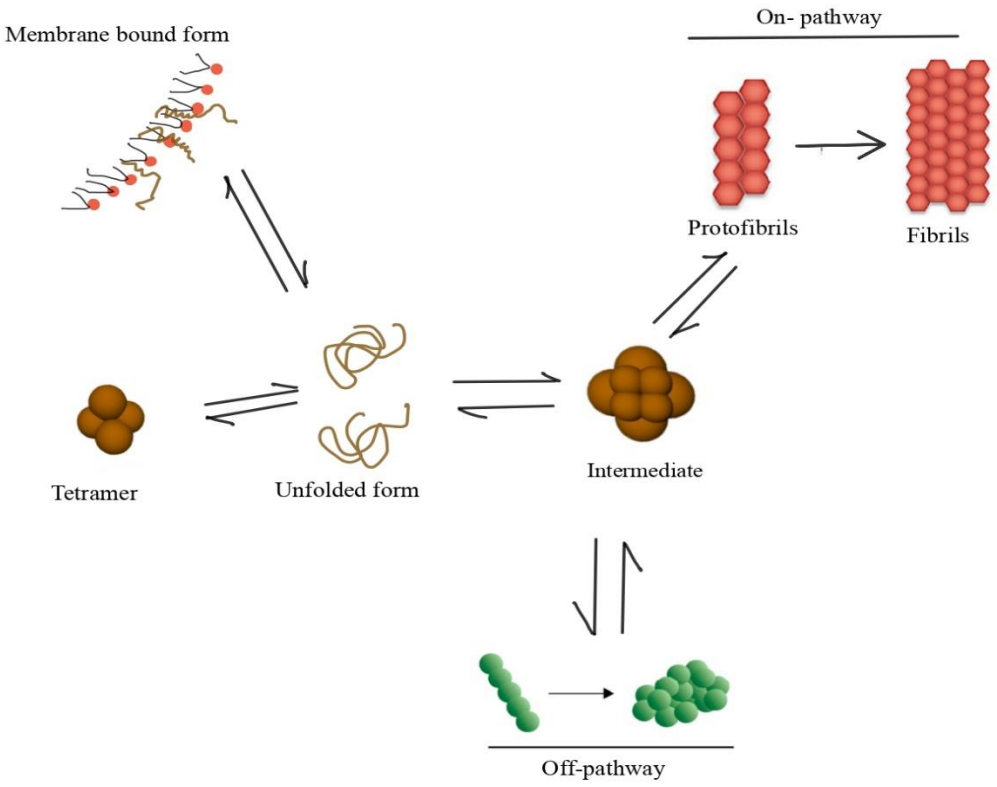

Fig 2.2. The process of accummulation and aggregation of alpha synuclein. Disrupting the balance between alpha-synuclein generation and clearance leads to the aggregation of monomers into oligomers, which can be on or off pathway oligomers.

2.3 LEWY BODY

The Lewy Bodies, published in 1912, describes Lewy's life and investigation into Parkinson's disease. Lewy was the first person to offer a detailed description of the pathological anatomy of Parkinson's disease. Lewy was named head of the Neurological Research Institute and Clinic in Berlin after seven years of hard effort in 1932 (Holdorff, Rodrigues e Silva, and Dodel 2013). There are two forms of Lewy bodies (LBs): cortical and brainstem-type. Brainstem-type LBs are abundant in eosinophils masses with a dense core and peripheral halo, whereas outer layes's LBs are irregular, poorly defined structures that lack a core. LBs are also discovered inneurons processes known as intraneuritic LB. Most LB-containing processes are axons, and both brainstem-type and cortical LBs are made up of filamentous structures (Wakabayashi et al. 2013).

Lewy bodies, a form of Parkinson's disease, are frequently studied using postmortem samples, which are static measurements of pathology. However, the use of fetal cell implants as an experimental therapy for Parkinson's disease in the 1980s and 1990s shed light on their biology. Despite variable therapeutic outcomes, several individuals treated with these cells had postmortem neuropathological examinations. Two important observations were made: a proportion of the fetal cells survived and successfully integrated into the basal ganglia, and there appeared to be Lewy body pathology in these new cells. This suggests that the aggregation of α-synuclein into Lewy bodies could spread from the aged diseased cells surrounding the implant into the newly integrated cells (Lewis and Spillane 2019), (Isacson 2003).

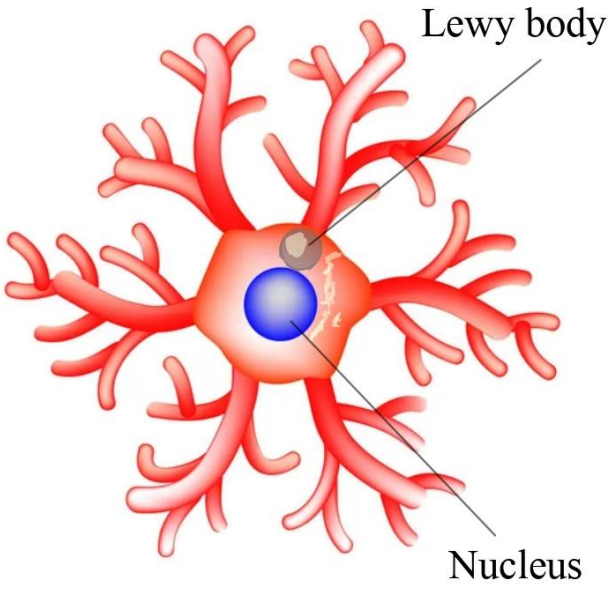

Fig. 2.3. LBL (lewy body dementia) defined into the image

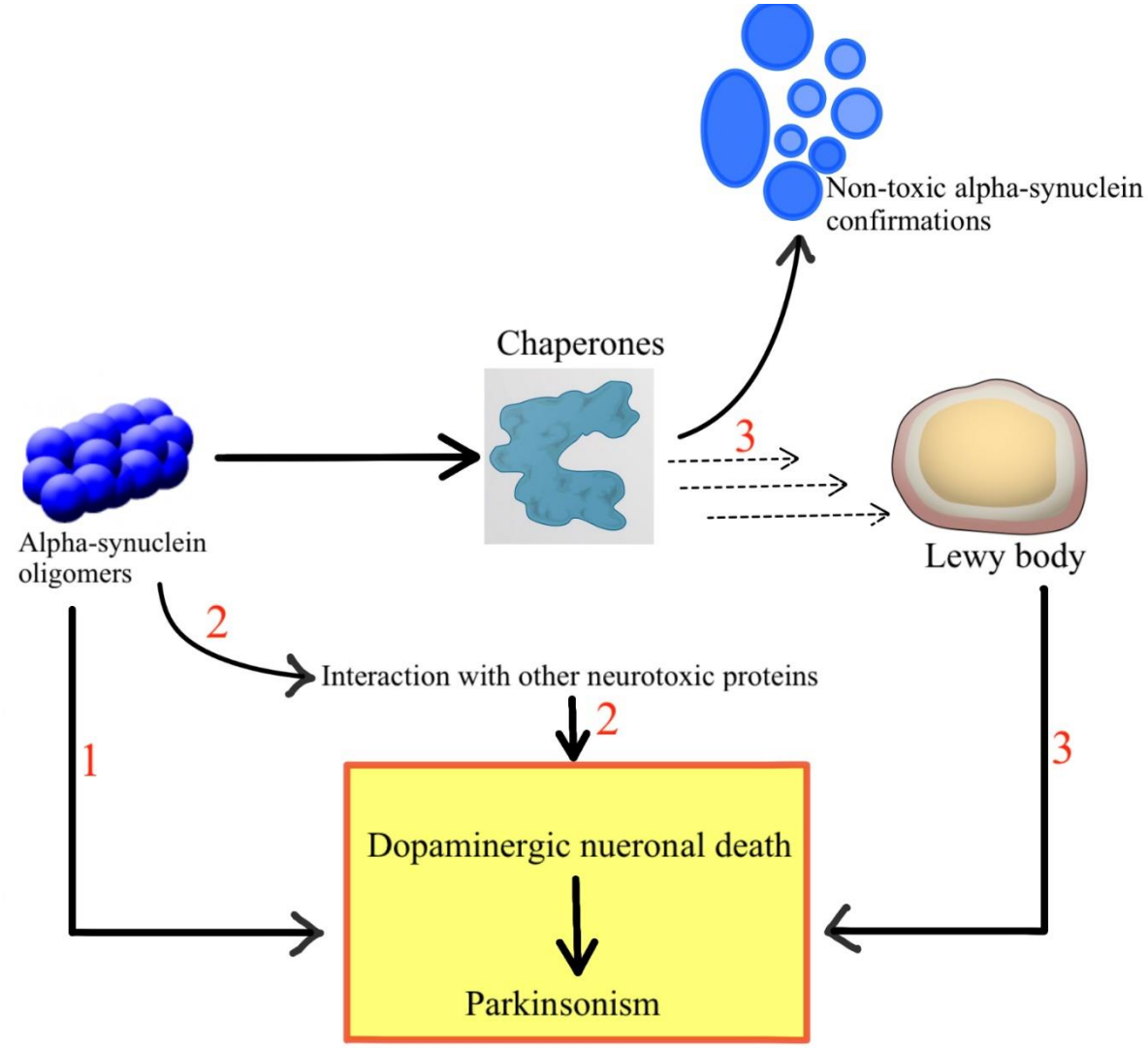

Fig 2.4. Different pathological hallmark of Parkinson disease, 1. Alpha synuclein oligomers aggregation leads to the dopaminergic neuron death, 2. α-Synuclein oligomers in mid brain interacts with other neurotoxic protein which ultimately leads to parkinsonism's, 3. Unfolded oligomers serves as Lewy body component.

2.4. OXIDATIVE STRESS IN PARKINSONISM.

2.4.1. MITOCHONDRIAL MECHANISM

As we mentioned earlier, Parkinson disease cause movement impairment due to the progressive mortality of dopaminergic neurons resides in central brain portion called substantia nigra pars compacta, with the oxidative stress. Oxidative stress is a detrimental condition marked by the abnormal control of cellular redox activity, resulting to the creation of ROS. Let's enlighten the role of mitochondria in the oxidative stress and relative linked. Mitochondria are the major generators of reactive oxygen species (ROS) in the healthy aging, releasing ATP to fuel brain activity and maintain cellular homeostasis through oxidative phosphorylation (Electron transport chain) (Dröse and Brandt 2008). Improper electron transfer from Electron transport system complexes I and III to oxygen happens spontaneously in mammalian mitochondrial and producing superoxide's radicals and a by-product of energy synthesis process. Reactive oxygen species can produce hydroxyl radicals (●OH), leading neuronal oxidative injury both within and outside mitochondria. Mitochondria contains eukaryotic superoxide dismutase's (SOD), which convert superoxide radicals (O_2 −) to less damaging hydrogen peroxide (H_20_2). Manganese superoxide dismutase (SOD2) exists in the mitochondrial matrix and inner membrane; however, copper/zinc superoxide dismutase (SOD1) appears in the intermembrane space, cytosol, and other cellular compartments Weidinger & Kozlov, 2015).

The aging SNc (produces more mitochondrial ROS due to poor physiological redox management, while excessive ROS in PD SNc is affiliations. with severe ETC dysfunction, oxidative damage from environmental chemicals, pesticides, and genetic mutations. The mitochondrial ETC system is already stressed out exceeding its redox capacity due to compounding elements, high energy demands from a complex axonal arbor, and a heavy calcium-buffering burden. Environmental toxins and pesticides, such as MPTP and rotenone, can penetrate lipid membranes and accumulate in mitochondria upon inhalation or ingestion. MPTP treatment impairs mitochondrial complex 1 redox activity by limiting electron transport, raising O2− production, and decreasing ATP synthesis. However, it only leads to a transitory 20% fall in mouse

striatal and midbrain ATP levels, indicating that MPTP-induced ATP deficit may have a fundamental pathogenic function in Parkinson's disease (Chan et al. 1991). Mitochondrial dysfunction is not always associated with energy failure, but it can decrease neuron function while remain beneficial for survival, particularly when chemicals cytotoxicize nigral dopaminergic neurons. Other changes in metabolism generated by MPTP, notably considerable ROS production, are thought to clarify the selective sensitivity of a specific neuronal population to degeneration in Parkinson's disease (PD). Transgenic mice with high SOD1 antioxidant activity are resistant to dopaminergic denervation after MPTP treatment. Understanding why these chemicals are preferentially toxic to nigral dopaminergic neurons may help identify crucial processes behind particular SNc neurodegeneration in Parkinson's disease (Trist, Hare, and Double 2019).

2.4.2. ROS ACCUMULATION AND CELL DEATH PATHWAY RELATION

ROS buildup is a crucial hallmark of the initial stages Parkinson's disease (PD), which causes neuronal death. Excess ROS levels can cause a variety of cell death processes, including apoptosis, cytoplasmic cell death, and autophagic cell death. However, technical restrictions make it difficult to establish which pathways are engaged in the SNc of Parkinson's patients in vivo. The slow pace of dopamine neuron loss and the fast clearance of dead dopamine neurons make postmortem identification of cell death markers challenging and frequently incorrect. Secondary techniques have been used to study cell death processes in postmortem Parkinson's disease tissues, involving Bcl-2 family proteins, caspases, Fas, and p55. However, these procedures have produced inconsistent results and are not reproducible. Other cell death signalling pathways, such as autophagic cell death indicators, are challenging to understand since they can signal actions which encourage or decrease cell demise. Several research on cell mortality mechanisms in PD SNc has been conducted using dopaminergic cell cultures and animal models. In these models, neuronal cell death caused by PD-linked gene alterations results in different degrees of intrinsic and extrinsic apoptosis, autophagic cell death, and parthanatos. Dopamine neuronal death is also linked to the PD-mimetic

poisons MPTP, rotenone, and 6-OHDA, albeit to varying degrees (Clayton, Clark, and Sharpe 2005; David et al. 2009). Increased ROS production in primary cultures of rat mesencephalic dopamine neurons has been linked to neurodegeneration, with substantial parthanatos. Multiple scientific animal models of Parkinson's disease, ROS buildup has been linked to priming, starting, and accelerating apoptosis in SNc dopamine neurons, as opposed to parthanatos and necroptosis. Mitochondrial-driven apoptosis is notably associated with ROS-induced cell death (Venderova and Park 2012).

2.4.3. IRON ACCUMULATION IN OXIDATIVE STRESS

Iron is a contributory risk factor for Parkinson's disease (PD) because it accumulates in synaptic neoplasms (SN). However, decreasing iron concentrations in peripheral blood indicate that this buildup is not owing to iron excess, but rather to iron homeostasis imbalance. Several scientific studies suggest the significance of oxidative stress in Parkinson's disease pathogenesis, implying that FRAP, vitamin C, and glutathione may be valuable antioxidant activity markers. Inflammation is also a part of the illness process, with myeloperoxidase, NTPDase, IMA, and perhaps ecto-5'-nucleotidase serving as valid inflammatory activity indicators. The aging SNc brain region may suffer enhanced pro-oxidant interactions with dopamine as a result of labile iron buildup, which may be connected to age-dependent ferritin malfunction. This is owing to the inability to properly convert reactive ferrous iron into more stable ferric iron for storage. However, analogous experiments have not been carried out in human postmortem tissues due to challenges in maintaining iron redox state and the difficulty to reliably test ferritin iron loading in vivo. It is critical to identify the roles of microglia and astrocytes in iron accumulation in the aging SNc (Medeiros et al. 2016), (James et al. 2015).

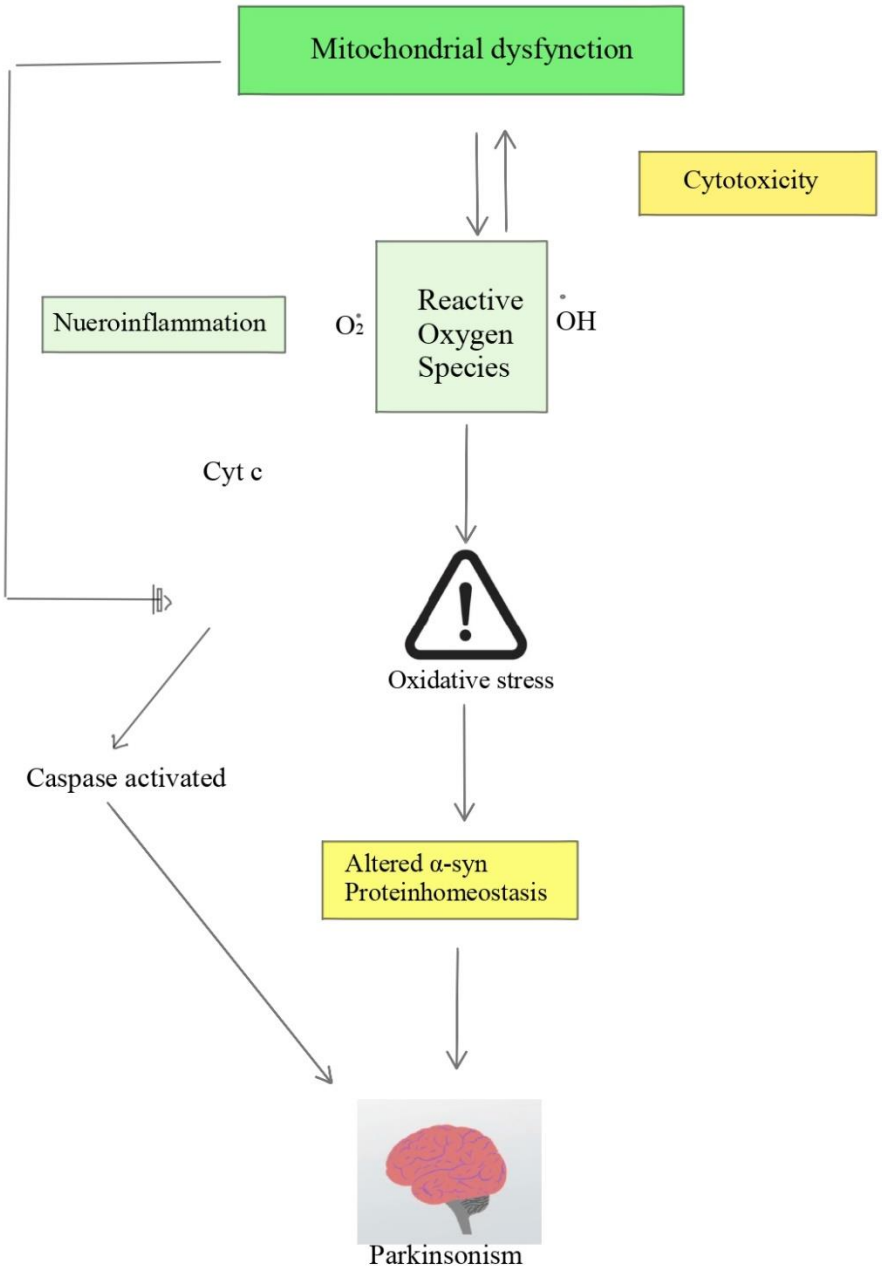

Fig 2.4.1. OS in Parkinson's disease, causes loss of DA neuron's, mitochondrial malfunction, and protein breakdown difficulties. This inhibits protein clearance, lipid peroxidation, protein oxidation, and DNA damage, resulting in neuronal death.

2.5. CENTELLA ASIATICA; A BENEFECIAL PLANT FOR BRAIN

Centella asiatica is a tropical climate plant widespread in Southeast majority Asian nations. It develops in wet, gloomy places up to 7000 feet and is frequently found near river banks, streams, ponds, and irrigated fields. In India and Sri Lanka, it grows among stone walls or rocky establishes at heights of 2000 feet. C. asiatica, a herb utilized over thousands of years in India, China, Sri Lanka, Nepal, and Madagascar, is recognized for treating skin ailments, repairing wounds, and renewing nerves and brain cells, earning it the title of "Brain food" in India (Chandrika and Prasad Kumara 2015). Reactive oxygen species (ROS) serve a vital part in aging, with increased formation of ROS and a lack in antioxidant defences leading to cell death in brain diseases such as Parkinson's. Experimental studies suggest that MPTP induced mice model of Parkinson shows variance in LPO levels among brain areas might be resulting to changes in iron concentration & metabolism, which influence the formation of reactive oxygen species. The striatum and hippocampus have unusually high levels of non-heme iron, which catalyses ROS formation. MPTP exposure might have created membrane lipid peroxidation, leading in membrane loss, integrity loss, and cell death in certain brain areas. Centella asiatica, xenobiotic rich in polyphenols and triterpenes, may be an effective detoxifying agent for xenobiotics since it can reduce lipid peroxidation, boost brain antioxidants, and prevent the neurotoxic effects of MPTP, thus helping with parkinsonism care by acting as neuroprotective antioxidants (Haleagrahara and Ponnusamy 2010). Apart from the c. elegans model other model of Parkinsonism like transgenic drosophila model of Parkinson also demonstrated *that C. asiatica* component successfully limit parkinsonism in transgenic flies, with dose-dependent protection against oxidative stress at several doses capacity and C. asiatica found to be neuroprotective in MPTP toxicity in the brain model pd. Studies indicated that *C. asiatica* powder lowered low density lipoprotein levels in mice, while Asiatic acid protected SH-SY5Y cells against rotenone or H2O2-induced cell damage, indicating that it might be used as a Parkinson's disease therapeutic agent. Transgenic Drosophila model found that C. asiatica components dramatically decreased oxidative chain reaction and protein carbonyl levels in flies treated

Fig 2.5. *Centella asiatica* plant sample and also available in the several other countries (Anon n.d.).

to varying dosages. This implies that using C. asiatica extract may slow down degradation in the substantia nigra pars compacta, enhancing mobility and lowering Parkinson's disease (PD) morbidity (Siddique et al. 2014).

C. Asiatica contain multiple therapeutic component which is Widley used in research and medicine (Orhan 2012), (Harun et al. 2019). Extraction of bioactive compound form the herbs is another key important factor because bioactive chemicals are found in low quantities, developing effective and selective extraction procedures is critical for extracting them from herbal plants (Development n.d.). From past few years subcritical water method used broadly to extract bioactive compound from *C. asiatica* plant. The procedure of subcritical water method entailed collecting dried *C. asiatica* materials such as leaves, nodes, petioles, and roots, as well as acquiring *Asiatic acid, asiaticoside, acetonitrile, methanol, ethanol,* and *DI* water standard from the source and further follow standard procedure of extraction (Kim et al. 2009).

Table 2. *Centella asiatica* extract's basic characteristics.

S.no.	Extract name	Blood-brain barrier	Canonical SMILES
1	Asiatic Acid	Permeable	CC1CCC2(CCC3(C(=CCC4C3(CCC5C4(CC(C(C5(C)CO)O)O)C)C)C2C1C)C)C(=O)O
2	Asiaticoside	Non- Permeable	CC1CCC2(CCC3(C(=CCC4C3(CCC5C4(CC(C(C5(C)CO)O)O)C)C)C2C1C)C)C(=O)OC6C(C(C(C(O6)COC7C(C(C(C(O7)CO)OC8C(C(C(C(O8)C)O)O)O)O)O)O)O)O)O
3	Madecassic Acid	Permeable	CC1CCC2(CCC3(C(=CCC4C3(CC(C5C4(CC(C(C5(C)CO)O)O)C)O)C)C2C1C)C)C(=O)O
4	Madecassoside	Non- Permeable	CC1CCC2(CCC3(C(=CCC4C3(CC(C5C4(CC(C(C5(C)CO) O)O)C)O)C)C2C1C)C)C(=O)OC6C(C(C(C(O6)COC7C(C(C(C(O7)CO)OC8C(C(C(C(O8)C)O)O)O)O)O)O)O)O)O
5	Terminolic acid	Permeable	CC1(CCC2(CCC3(C(=CCC4C3(CC(C5C4(CC(C(C5(C)CO)O)O)C)O)C)C2C1)C)C(=O)O)C
6	Asiaticoside B	Non- Permeable	CC1C(C(C(C(O1)OC2C(OC(C(C2O)O)OCC3C(C(C(C(O3)OC(=O)C45CCC (CC4C6=CCC7C8(CC(C(C(C8C(CC7(C6(CC5)C)C) O) (C)CO) O) O) C) (C)C) O)O)O)CO)O)O) O

CHAPTER-3

METHODOLOGY

3.1. DATA COLLECTION

All the natural compounds taken from *Centella asiatica* plant namely *asiatic acid*, *madecassic acid* and *Terminolic acid* that have the ability to stop the progression of neurodegenerative diseases was produced by reviewing the literature. All of the compound's SMILE structures were obtained from the PubChem database. The chosen compounds were then introduced via an online Blood Brain Barrier Permeability Predictor called Light BBB. Out of all the compounds that were chosen, three compounds i.e. first one is Asiatic acid. Second one is Madecassic acid and Terminolic acid were shown to be BBB permeable.

3.2. PREPARATION OF PROTIEN

The PDB crystal 1XQ8 has only chain A and sequence with a length of 140aa. Using *BIOVIA* discovery studio, the target protein, alpha-synuclein, was created in order to dock the protein with the selected compounds. As the taken protein target 1XQ8 is human micelle-bound *alpha-synuclein,* polar hydrogen atoms were introduced after heteroatoms and crystalline water molecules were eliminated. Following its generation, the target protein's structure was saved in PDB format.

3.3. PREPARATION OF LIGAND

Each of the ligand (compound) i.e. *Asiatic acid, Madecassic acid* and *Terminolic acid* was acquired from PubChem in SDF format, and it was then required to transform them into PDB format using the Open Babel online tool. After adding *KOLLMANN*

charges, both the ligand and the receptor were transformed into a PDBQT file using the Autodock program.

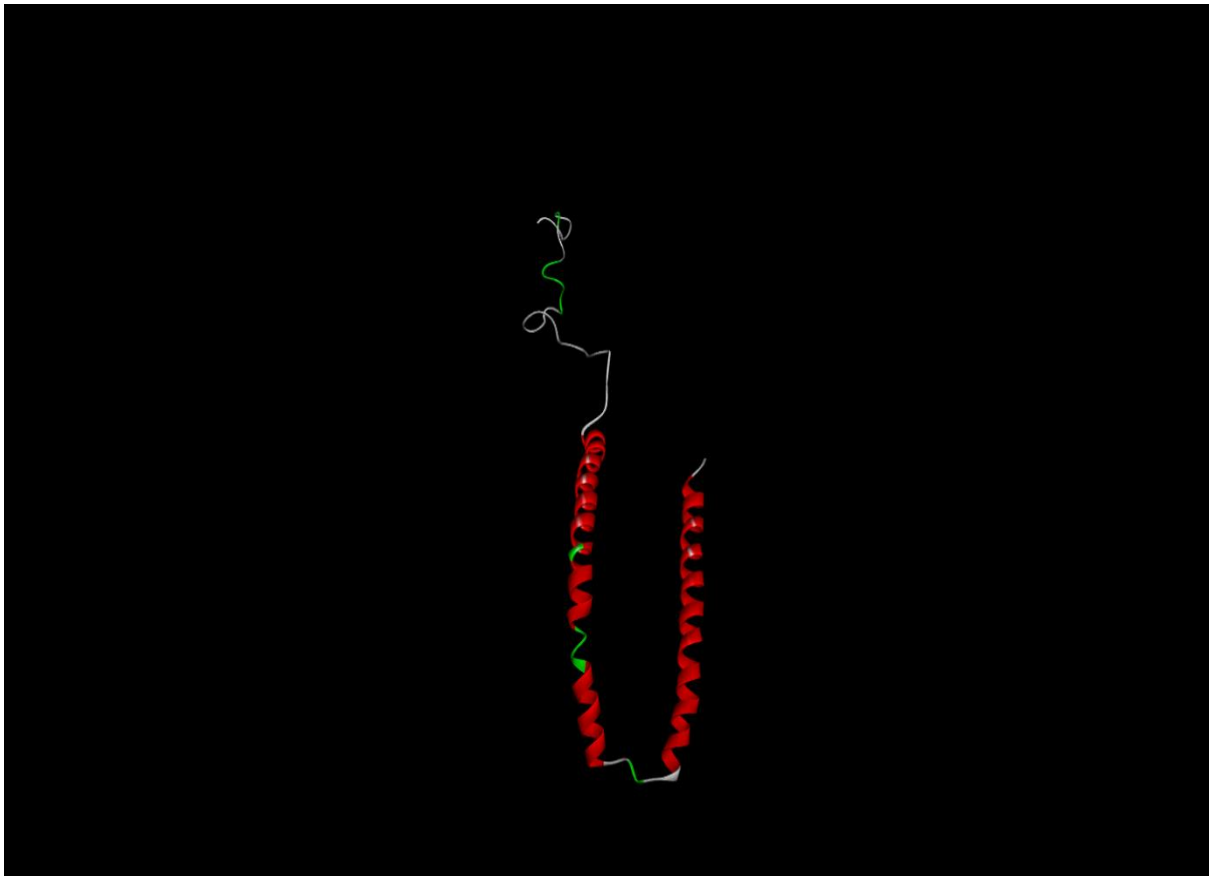

Fig 3.1. Strcuture of prepared protein of *α-Syn.*

3.4. MOLECULAR DOCKING USING AUTODOCK VINA

The virtual screening program Autodock Vina is used to examine the relationship between a ligand and a protein, or receptor. Using Autodock Vina, the protein structure was constructed and active molecules were docked. A config file was developed in order to define grid settings (Grid box centre: X-axis = 230.77; Y-axis = 27.63; Z-axis = -15.16, Coordinates: X-axis = 58.28; Y-axis = 148.22; Z axis= 25.00), ligand name, receptor name, and exhaustiveness, all of which are critical in determining the amount of conformational sampling needed in molecular docking. In this work, exhaustiveness

is used to provide enough binding choices for both the ligand and the receptor without necessitating computational exhaustiveness. To ascertain a ligand molecule's binding affinity, Vina analysis of output and log files are required, produced by Autodock. To find the interacting residues, an analysis was conducted on the compound's output file.

3.5. INTERPRETATION OF DOCKED STRUCTURE USING BIOVIA

The auto dock data was evaluated using BioVia Discovery Studio in order to regulate the structural interaction between the choosen protein and ligand. The research investigated the relationship between amino acid ligand and receptor, visualizing the two-dimensional structure of the interaction through the use of the protein-ligand complex.

3.6. INVESTIGATION TROUGH SWISS ADME

Absorption, dispersion, metabolic activity, and excretion, or ADME, is a comprehensive examination of components such as lipophilicity, pharma kinetics, water solubility, physiochemical characteristics, and medicinal chemistry to confirm a drug's effectiveness and potency. A web-based program named SWISS ADME assesses the agonist chemicals based on predetermined standards. Canonical SMILES were uploaded to the server and made them accessible for analysis.

CHAPTER-4

RESULTS

4.1. INTERACTION BETWEEN TARGETED PROTIEN AND SELCETED LIGAND

4.1.1. ASIATIC ACID DOCKED WITH *ALPHA-SYNUCLEIN*

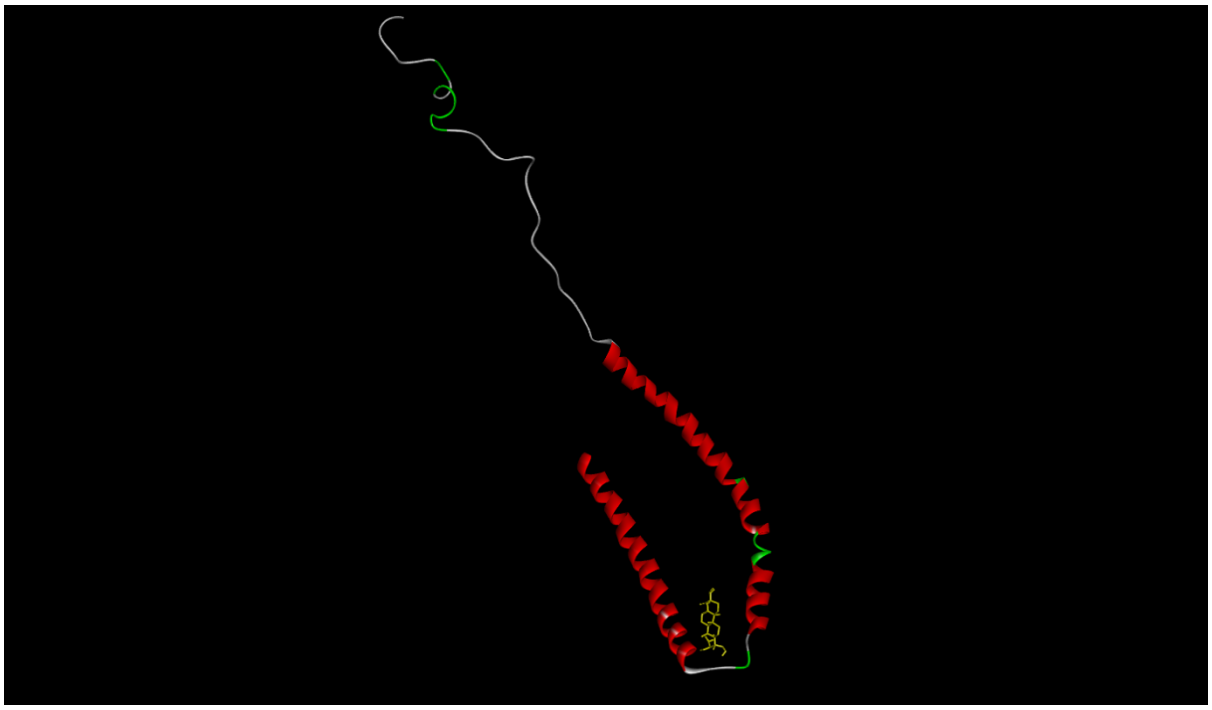

Fig 4.1. Interaction of Target protein and Asiatic acid.

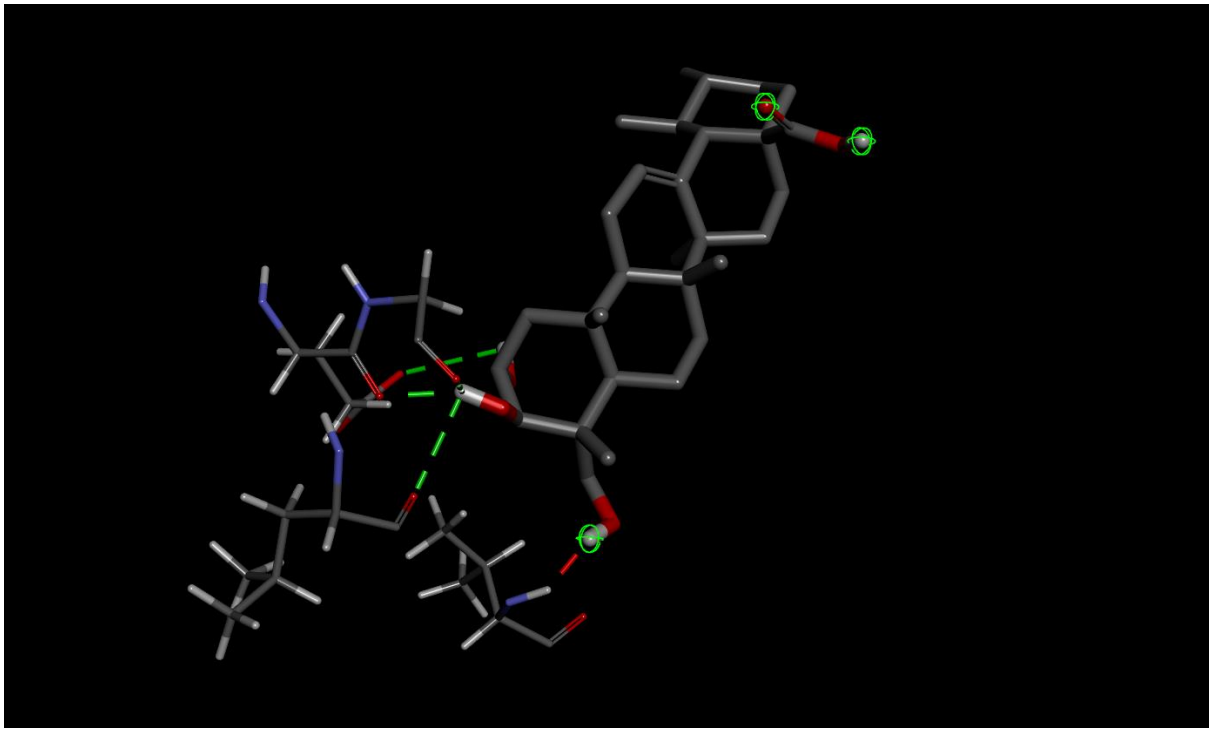

Fig 4.1.1.1. 3D-Ligand interactions with *alpha-synuclein*

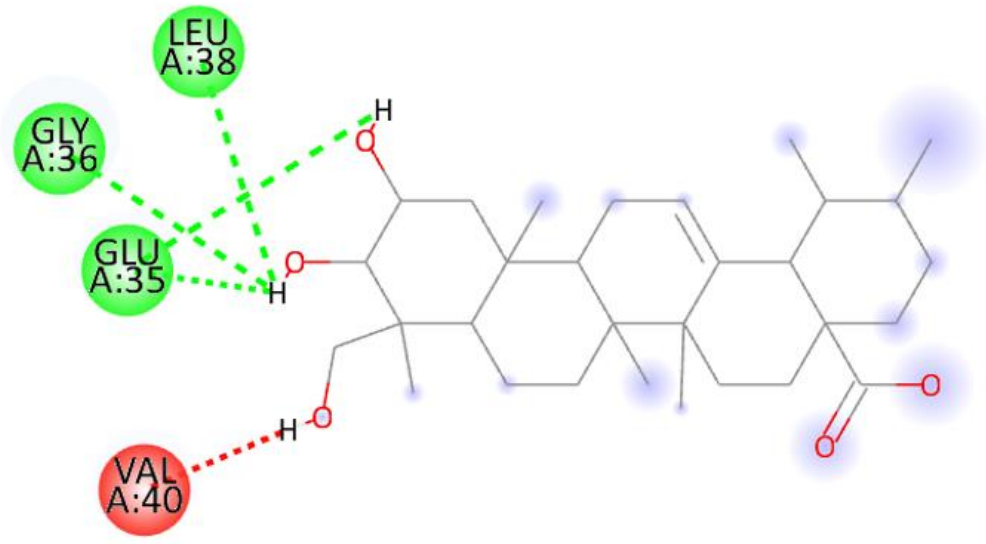

Fig 4.1.1.2 2D-Ligand interactions with targeted protein.

4.1.2. MADECASSIC ACID DOCKED WITH ALPHA-SYNUCLEIN

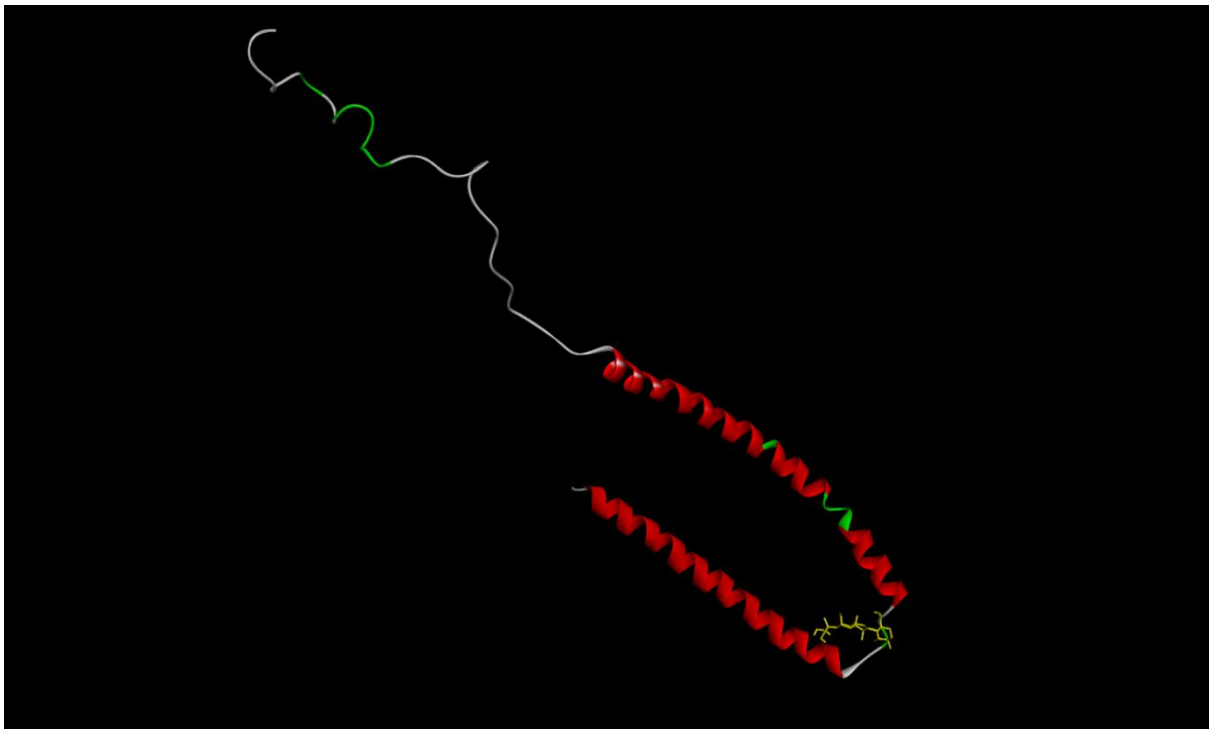

Fig 4.1.2.1 Interaction of Target protein and Madecassic acid.

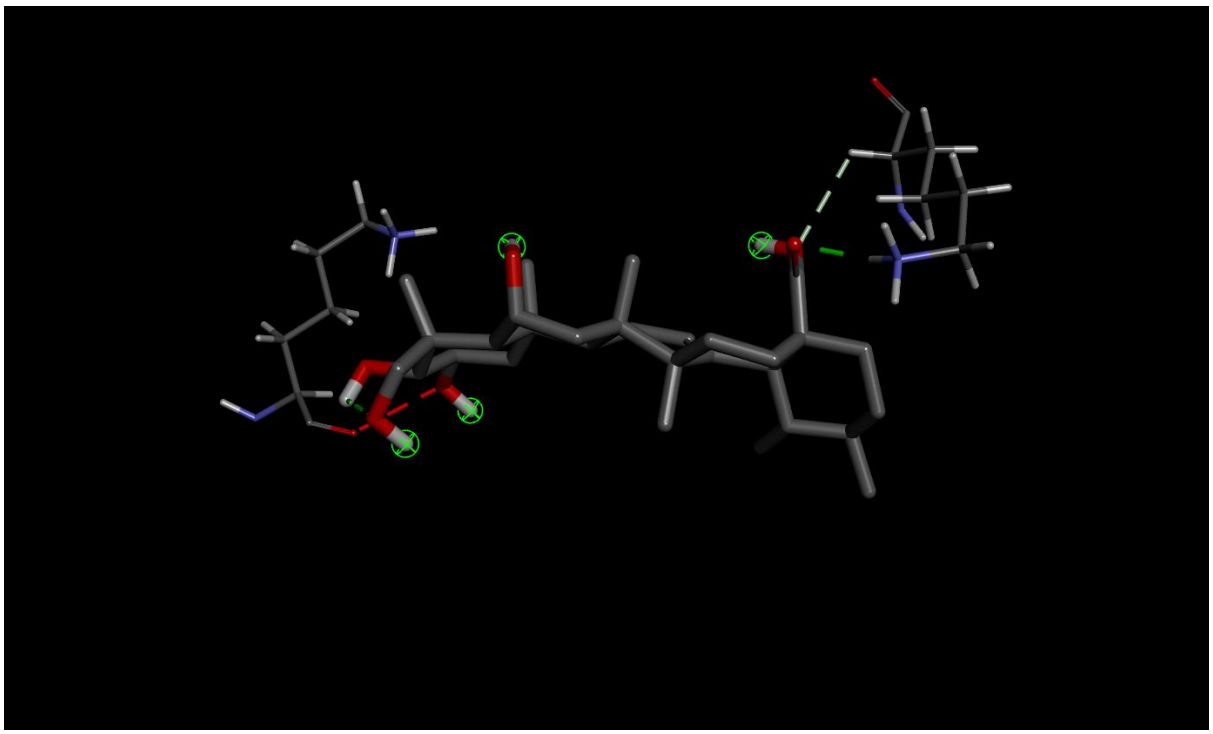

Fig. 4.1.2.2. 3D-Ligand interactions (Madecassic acid) with *alpha-synuclein*.

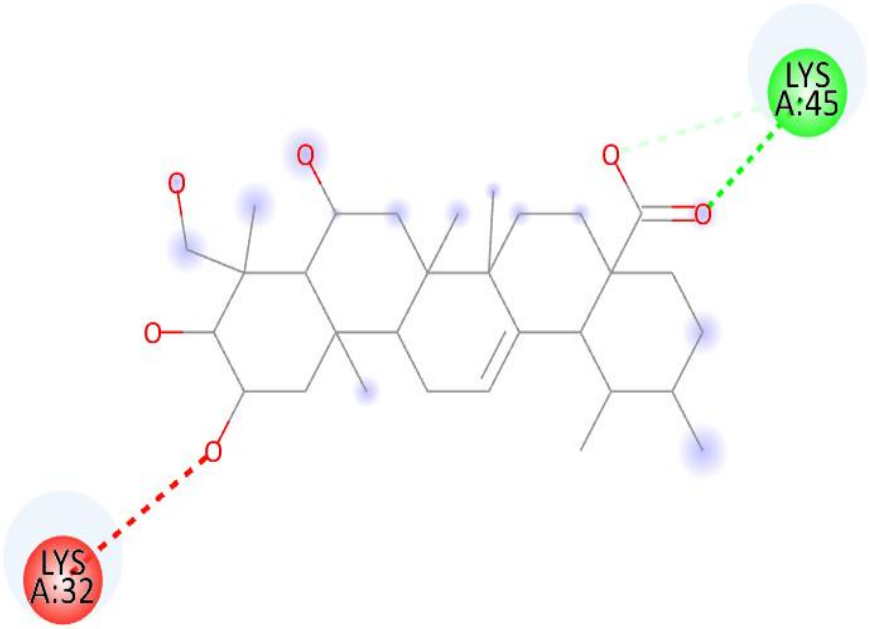

Fig. 4.1.2.3. 2D-Ligand interactions (Madecassic acid) with targeted protein**.**

4.1.3. TERMINOLIC ACID DOCKED WITH ALPHA-SYNUCLEIN

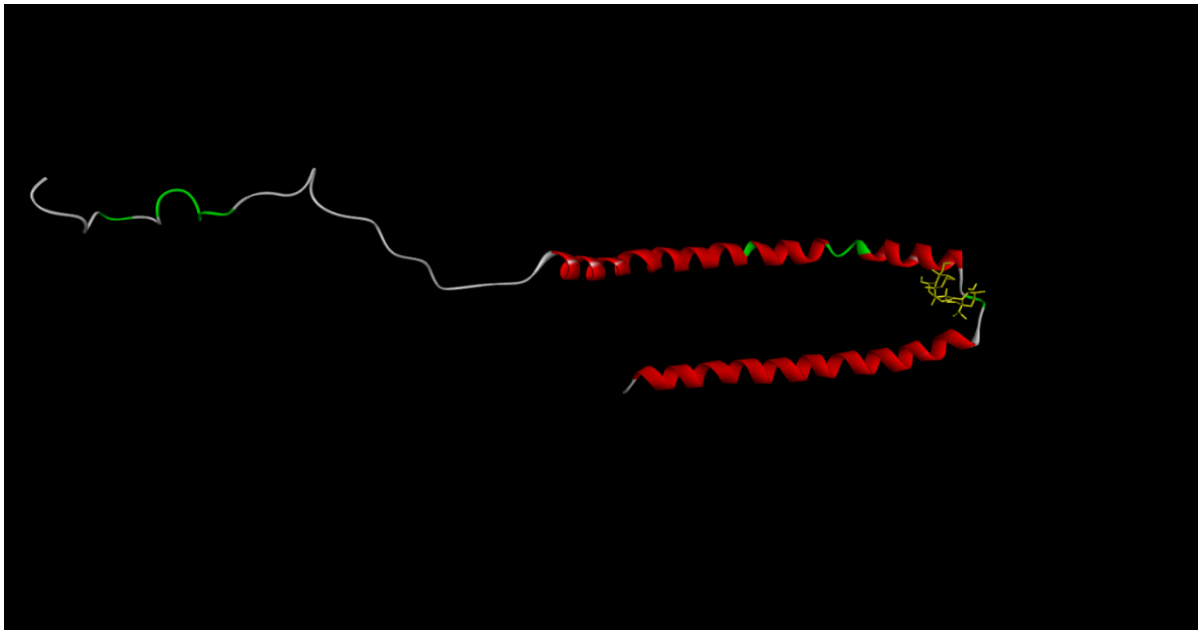

Fig. 4.1.3.1 Interaction of Target protein and Terminolic acid.

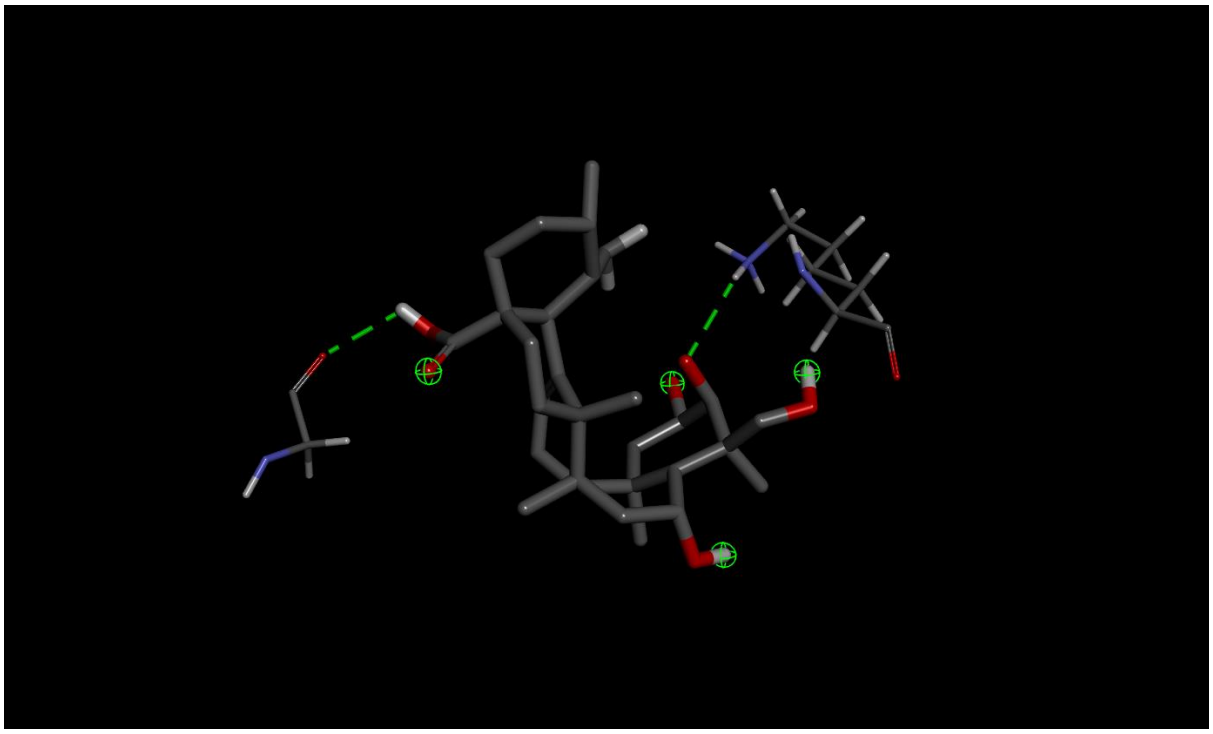

Fig. 4.3.1.2 3D-Ligand interactions (Terminolic acid) with *alpha-synuclein*.

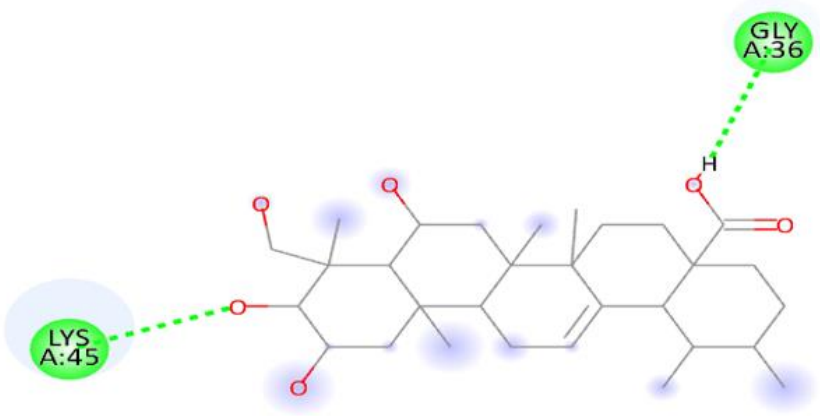

Fig. 4.9. 2D-Ligand interactions (Terminolic acid) with targeted protein**.**

The protein *alpha-synuclein* interacts with different amino acid residues, as seen below (Fig). Positive outcomes were obtained using the autodocking approach, which showed a high degree of contact between *alpha-synuclein* and ligand (Asiatic acid, Madecassic acid and Terminolic acid). According to the docking score, the ligand (Asiatic acid, Madecassic acid and Terminolic acid) efficiently binds to the *alpha-synuclein* protein. The binding energy is computed as follows: -6.3kcal/mol, -6.6 kcal/mol, -6.8 kcal/mol respectively and the Cluster RMSD value 0. Docking data was used to assess the topology of the compound's interaction with the target protein; the prospective target is represented by the spheroid and linear structure between the helical structure, whereas this interaction is represented by an A chain helical structure.

4.2. LIGAND's ADME STUDY

Determining the ADME analysis of the study's ligands. Taking Lipinski's value into consideration as required, along with its shown water solubility under logs (ESOL), logs (Ali), and logs (SILICOS-IT) segment with a value of -6.33, -7.52, -4.28; -5.58, -6.56, -3.45; -5.67, -6.70, -3.90 of Asiatic acid, Madecassic acid and Terminolic acid respectively. The values of the skin permeation value (log Kp) are less, with values of -5.23 cm/s, -6.28 cm/s, -3.81 cm/s, and -6.18 cm/s respectively. To assess the drug's lipophilicity, cast log $P_{O/W}$ (XLOGP3).

Table 3. Binding score of different confirmation *Centella asiatica* extract.

Ligand	Binding Affinity	rmsd/ub	rmsd/lb
1xq8_119034_uff_E=876.98	-6.3	0	0
1xq8_119034_uff_E=876.98	-6.1	4.382	3.364
1xq8_119034_uff_E=876.98	-6.1	2.342	1.751
1xq8_119034_uff_E=876.98	-6	9.187	3.918
1xq8_119034_uff_E=876.98	-5.9	110.473	105.04
1xq8_119034_uff_E=876.98	-5.9	8.326	4.539
1xq8_119034_uff_E=876.98	-5.9	9.356	7.089
1xq8_119034_uff_E=876.98	-5.8	71.508	65.92
1xq8_119034_uff_E=876.98	-5.7	8.418	2.053
1xq8_73412_uff_E=769.93	-6.6	0	0
1xq8_73412_uff_E=769.93	-6.1	8.78	2.724
1xq8_73412_uff_E=769.93	-6	6.95	3.802
1xq8_73412_uff_E=769.93	-6	130	127.188
1xq8_73412_uff_E=769.93	-5.9	73.907	69.276
1xq8_73412_uff_E=769.93	-5.7	7.286	3.932
1xq8_73412_uff_E=769.93	-5.7	97.653	93.077
1xq8_73412_uff_E=769.93	-5.5	75.588	70.621
1xq8_73412_uff_E=769.93	-5.4	73.597	69.04
1xq8_12314613_uff_E=2156.24	-6.8	0	0
1xq8_12314613_uff_E=2156.24	-6.5	6.929	1.86
1xq8_12314613_uff_E=2156.24	-6.4	2.795	1.992
1xq8_12314613_uff_E=2156.24	-6.3	74.676	70.433
1xq8_12314613_uff_E=2156.24	-6.1	6.701	3.395
1xq8_12314613_uff_E=2156.24	-6	5.086	2.709
1xq8_12314613_uff_E=2156.24	-5.8	7.078	2.168
1xq8_12314613_uff_E=2156.24	-5.8	5.562	2.693
1xq8_12314613_uff_E=2156.24	-5.6	75.237	70.94

CHAPTER-5

DISCUSSION & CONCLUSION

This chapter, provides a thorough examination of a study's findings, evaluating their relevance, shortcomings, and recommendations for future research in the treatment of Parkinson disease (PD), while also addressing the study's limitations.

5.1. INTERPRETATION AND ANALYSIS OF RESULTS

Parkinsonism is a condition characterized by stiffness, tremor, and bradykinesia, with Parkinson's disease as the primary cause. It is asymmetric and responds to dopaminergic therapy, with no history or examination evidence. Pathological results show reduced nigral dopamine neurons and Lewy bodies in the surviving neurons (Samii, Nutt, and Ransom 2004). Different genetic and environmental factors which reveal the pathological hallmark of PD. Five more mutant genes associated to familial Parkinson's disease (PD), including *parkin, PTEN-induced putative kinase 1, DJ-1, HTRA2,* and *LRRK2,* have been found. These genes may contribute to mitochondrial dysfunction and oxidative stress in PD. Several scientific studies support that uncontrolled formation of ROS (reactive oxygen species) is a common feature in oxidative stress and mitochondrial dysfunction cascade (Shahrani et al. 2017). *Centella asiatica*, therapeutic and valuable herbs have several beneficial roles in the Parkinson disease and this study suggests that drugs with high binding values and permeability to the Blood Brain Barrier are more effective for treating Parkinson's disease (PD). Asiatic Acid, Madecassic Acid, Terminolic acid is the most effective ligand, according to a docking analysis. Although there is no cure X`of PD, but these discoveries may influence future research and lead to more effective treatment choices. For ligand binding stability, molecular dynamic modeling is advised, and biological activity should be assessed using both in vitro and in vivo investigations.

5.2. FUTURE SCOPE & SOCIAL IMPACT

Parkinson's disease is supported by mitochondrial impairment and oxidative stress. Rotenone, a mitochondrial complex I inhibitor, causes parkinsonism and *dopaminergic neuron* loss. *Centella asiatica* extracts reduced rotenone-prompt parkinsonism's and prevented DA neuronal death. *Centella asiatica's* neuroprotective actions include preserving mitochondrial complex I function, lowering lipid peroxidation, and upregulating antioxidant enzyme production. Consideration of several neuroprotective approach, such plant herbs could use in other hallmark of PD, which could be a revolutionary approach (Teerapattarakan et al. 2018).

Centella asiatica is a apiaceae plant, which is native to Southeast Asian countries, is a tropical medicinal plant belonging to the Apiaceae family, commonly recognised as Gotu Kola. *Centella asiatica* herb has several pharmacological benefits for human health. According to studies, the plant not only has great wound healing qualities, but it also provides considerable protection against a variety of CNS illnesses (Khazdair, Kianmehr, and Anaeigoudari 2021).

Hence this study review and analysis the neuroprotective outcomes of *Centella asiatica* plant.

REFERENCES

Anon. n.d. “Uses of Centella Asiatica (L.) Urban - National Innovation Foundation-India.” Retrieved May 20, 2024 (https://nif.org.in/CENTELLA-ASIATICA).

Antony, Paul M. A., Nico J. Diederich, Rejko Krüger, and Rudi Balling. 2013. “The Hallmarks of Parkinson’s Disease.” *The FEBS Journal* 280(23):5981–93. doi: 10.1111/FEBS.12335.

Armstrong, Melissa J., and Michael S. Okun. 2020. “Diagnosis and Treatment of Parkinson Disease: A Review.” *JAMA* 323(6):548–60. doi: 10.1001/JAMA.2019.22360.

Beitz, Janice M. 2014. “Parkinson’s Disease: A Review.” *Frontiers in Bioscience (Scholar Edition)* 6(1):65–74. doi: 10.2741/S415.

Chan, Piu, Louis E. DeLanney, Ian Irwin, J. William Langston, and Donate Di Monte. 1991. “Rapid ATP Loss Caused by 1-Methyl-4-Phenyl-1,2,3,6-Tetrahydropyridine in Mouse Brain.” *Journal of Neurochemistry* 57(1):348–51. doi: 10.1111/J.1471-4159.1991.TB02134.X.

Chandrika, Udumalagala Gamage, and Peramune A. A. S. Prasad Kumara. 2015. “Gotu Kola (Centella Asiatica): Nutritional Properties and Plausible Health Benefits.” *Advances in Food and Nutrition Research* 76:125–57. doi: 10.1016/BS.AFNR.2015.08.001.

Clayton, Rebecca, John B. Clark, and Martyn Sharpe. 2005. “Cytochrome c Release from Rat Brain Mitochondria Is Proportional to the Mitochondrial Functional Deficit: Implications for Apoptosis and Neurodegenerative Disease.” *Journal of Neurochemistry* 92(4):840–49. doi: 10.1111/J.1471-4159.2004.02918.X.

David, Karen Kate, Shaida Ahmad Andrabi, Ted Murray Dawson, and Valina Lynn Dawson. 2009. “Parthanatos, A Messenger of Death.” *Frontiers in Bioscience* 14(3):1116–28. doi: 10.2741/3297/PDF.

Development, Office of Research &. n.d. “SELECTIVE EXTRACTION OF OXYGENATES FROM SAVORY AND PEPPERMINT USING SUBCRITICAL WATER. (R825394).”

Dröse, Stefan, and Ulrich Brandt. 2008. “The Mechanism of Mitochondrial Superoxide Production by the Cytochrome Bc1 Complex.” *The Journal of Biological Chemistry* 283(31):21649–54. doi: 10.1074/JBC.M803236200.

Du, Xiao Yu, Xi Xiu Xie, and Rui Tian Liu. 2020. “The Role of α-Synuclein Oligomers in Parkinson’s Disease.” *International Journal of Molecular Sciences* 21(22):1–17. doi: 10.3390/IJMS21228645.

Giasson, Benoit I., Ian V. J. Murray, John Q. Trojanowski, and Virginia M. Y. Lee. 2001. “A Hydrophobic Stretch of 12 Amino Acid Residues in the Middle of Alpha-Synuclein Is Essential for Filament Assembly.” *The Journal of Biological Chemistry* 276(4):2380–86. doi: 10.1074/JBC.M008919200.

Golbe, Lawrence I., Giuseppe Di Iorio, Vincenzo Bonavita, Douglas C. Miller, and Roger C. Duvoisin. 1990. “A Large Kindred with Autosomal Dominant Parkinson’s Disease.” *Annals of Neurology* 27(3):276–82. doi: 10.1002/ANA.410270309.

Haleagrahara, Nagaraja, and Kumar Ponnusamy. 2010. “Neuroprotective Effect of Centella Asiatica Extract (CAE) on Experimentally Induced Parkinsonism in Aged Sprague-Dawley Rats.” *The Journal of Toxicological Sciences* 35(1):41–47. doi: 10.2131/JTS.35.41.

Harun, Nurul Hikmah, Abdi Wira Septama, Wan Amir Nizam Wan Ahmad, and Rapeah Suppian. 2019. “The Potential of Centella Asiatica (Linn.) Urban as an Anti-Microbial and Immunomodulator Agent: A Review.” *Natural Product Sciences* 25(2):92–102. doi: 10.20307/NPS.2019.25.2.92.

Hassanzadeh, Kambiz, and Arman Rahimmi. 2018. “Oxidative Stress and Neuroinflammation in the Story of Parkinson’s Disease: Could Targeting These Pathways Write a Good Ending?” *Journal of Cellular Physiology* 234(1):23–32. doi: 10.1002/JCP.26865.

Holdorff, Bernd, Antonio M. Rodrigues e Silva, and Richard Dodel. 2013. “Centenary of Lewy Bodies (1912-2012).” *Journal of Neural Transmission (Vienna, Austria : 1996)* 120(4):509–16. doi: 10.1007/S00702-013-0984-2/FIGURES/5.

Isacson, Ole. 2003. “The Production and Use of Cells as Therapeutic Agents in Neurodegenerative Diseases.” *Lancet Neurology* 2(7):417–24. doi: 10.1016/S1474-4422(03)00437-X.

James, Simon A., Blaine R. Roberts, Dominic J. Hare, Martin D. De Jonge, Ian E. Birchall, Nicole L. Jenkins, Robert A. Cherny, Ashley I. Bush, and Gawain McColl. 2015. “Direct in Vivo Imaging of Ferrous Iron Dyshomeostasis in Ageing Caenorhabditis Elegans.” *Chemical Science* 6(5):2952. doi: 10.1039/C5SC00233H.

Jankovic, J. 2008. “Parkinson’s Disease: Clinical Features and Diagnosis.” *Journal of Neurology, Neurosurgery, and Psychiatry* 79(4):368–76. doi: 10.1136/JNNP.2007.131045.

Khazdair, Mohammad Reza, Majid Kianmehr, and Akbar Anaeigoudari. 2021. “Effects of Medicinal Plants and Flavonoids on Parkinson’s Disease: A Review on Basic and Clinical Evidences.” *Advanced Pharmaceutical Bulletin* 11(2):224. doi: 10.34172/APB.2021.026.

Kim, Wan Joo, Jaehoon Kim, Bambang Veriansyah, Jae Duck Kim, Youn Woo Lee, Seong Geun Oh, and Raymond R. Tjandrawinata. 2009. “Extraction of Bioactive Components from Centella Asiatica Using Subcritical Water.” *The Journal of Supercritical Fluids* 48(3):211–16. doi: 10.1016/J.SUPFLU.2008.11.007.

de Lau, Lonneke ML, and Monique MB Breteler. 2006. “Epidemiology of Parkinson’s Disease.” *The Lancet. Neurology* 5(6):525–35. doi: 10.1016/S1474-4422(06)70471-9.

Lewis, Patrick A., and Jennifer E. Spillane. 2019. “Parkinson’s Disease.” *The Molecular and Clinical Pathology of Neurodegenerative Disease* 83–121. doi: 10.1016/B978-0-12-811069-0.00003-3.

Li, Song, and Weidong Le. 2017. “Milestones of Parkinson’s Disease Research: 200 Years of History and Beyond.” *Neuroscience Bulletin* 33(5):598–602. doi: 10.1007/S12264-017-0178-2.

Lokanathan, Yogeswaran, Norazzila Omar, Nur Nabilah Ahmad Puz, Aminuddin Saim, and Ruszymah Hj Idrus. 2016. “Recent Updates in Neuroprotective and Neuroregenerative Potential of Centella Asiatica.” *The Malaysian Journal of Medical Sciences : MJMS* 23(1):4.

Meade, Richard M., David P. Fairlie, and Jody M. Mason. 2019. “Alpha-Synuclein Structure and Parkinson’s Disease – Lessons and Emerging Principles.” *Molecular Neurodegeneration 2019 14:1* 14(1):1–14. doi: 10.1186/S13024-019-0329-1.

Medeiros, Marcio S., Arthur Schumacher-Schuh, Andreia Machado Cardoso, Guilherme Vargas Bochi, Jucimara Baldissarelli, Aline Kegler, Daniel Santana, Carolina Maria Martins Behle Soares Chaves, Maria Rosa Chitolina Schetinger, Rafael Noal Moresco, Carlos R. M. Rieder, and Michele Rechia Fighera. 2016. “Iron and Oxidative Stress in Parkinson’s Disease: An Observational Study of Injury Biomarkers.” *PLoS ONE* 11(1). doi: 10.1371/JOURNAL.PONE.0146129.

Mehra, Surabhi, Shruti Sahay, and Samir K. Maji. 2019. “α-Synuclein Misfolding and Aggregation: Implications in Parkinson’s Disease Pathogenesis.” *Biochimica et Biophysica Acta. Proteins and Proteomics* 1867(10):890–908. doi: 10.1016/J.BBAPAP.2019.03.001.

Orhan, Ilkay Erdogan. 2012. “Centella Asiatica (L.) Urban: From Traditional Medicine to Modern Medicine with Neuroprotective Potential.” *Evidence-Based Complementary and Alternative Medicine : ECAM* 2012. doi: 10.1155/2012/946259.

Samii, Ali, John G. Nutt, and Bruce R. Ransom. 2004. “Parkinson’s Disease.” *Lancet (London, England)* 363(9423):1783–93. doi: 10.1016/S0140-6736(04)16305-8.

Shahrani, Mesfer Al, Simon Heales, Iain Hargreaves, and Michael Orford. 2017. “Oxidative Stress: Mechanistic Insights into Inherited Mitochondrial Disorders and Parkinson’s Disease.” *Journal of Clinical Medicine* 6(11). doi: 10.3390/JCM6110100.

Sherer, Todd B., Sohini Chowdhury, Katherine Peabody, and Deborah W. Brooks. 2012. “Overcoming Obstacles in Parkinson’s Disease.” *Movement Disorders : Official Journal of the Movement Disorder Society* 27(13):1606–11. doi: 10.1002/MDS.25260.

Siddique, Yasir Hasan, Falaq Naz, Smita Jyoti, Ambreen Fatima, Saba Khanam, Rahul, Fahad Ali, Syed Faiz Mujtaba, and Mohammad Faisal. 2014. “Effect of Centella Asiatica Leaf Extract on the Dietary Supplementation in Transgenic Drosophila Model of Parkinson’s Disease.” *Parkinson’s Disease* 2014. doi: 10.1155/2014/262058.

Simon, David K., Caroline M. Tanner, and Patrik Brundin. 2020. “Parkinson Disease Epidemiology, Pathology, Genetics, and Pathophysiology.” *Clinics in Geriatric Medicine* 36(1):1–12. doi: 10.1016/J.CGER.2019.08.002.

Subramaniam, Sudhakar Raja, and Marie Francoise Chesselet. 2013. “Mitochondrial Dysfunction and Oxidative Stress in Parkinson’s Disease.” *Progress in Neurobiology* 106–107:17–32. doi: 10.1016/J.PNEUROBIO.2013.04.004.

Teerapattarakan, Narudol, Hattaya Benya-aphikul, Rossarin Tansawat, Oraphan Wanakhachornkrai, Mayuree H. Tantisira, and Ratchanee Rodsiri. 2018. “Neuroprotective Effect of a Standardized Extract of Centella Asiatica ECa233 in Rotenone-Induced Parkinsonism Rats.” *Phytomedicine* 44:65–73. doi: 10.1016/J.PHYMED.2018.04.028.

Tolosa, Eduardo, Alicia Garrido, Sonja W. Scholz, and Werner Poewe. 2021. “Challenges in the Diagnosis of Parkinson’s Disease.” *The Lancet. Neurology* 20(5):385–97. doi: 10.1016/S1474-4422(21)00030-2.

Trist, Benjamin G., Dominic J. Hare, and Kay L. Double. 2019. “Oxidative Stress in the Aging Substantia Nigra and the Etiology of Parkinson’s Disease.” *Aging Cell* 18(6). doi: 10.1111/ACEL.13031.

Venderova, Katerina, and David S. Park. 2012. “Programmed Cell Death in Parkinson’s Disease.” *Cold Spring Harbor Perspectives in Medicine* 2(8):a009365. doi: 10.1101/CSHPERSPECT.A009365.

Wakabayashi, Koichi, Kunikazu Tanji, Saori Odagiri, Yasuo Miki, Fumiaki Mori, and Hitoshi Takahashi. 2013. “The Lewy Body in Parkinson’s Disease and Related Neurodegenerative Disorders.” *Molecular Neurobiology* 47(2):495–508. doi: 10.1007/S12035-012-8280-Y.

Weidinger, Adelheid, and Andrey V. Kozlov. 2015. “Biological Activities of Reactive Oxygen and Nitrogen Species: Oxidative Stress versus Signal Transduction.” *Biomolecules* 5(2):472. doi: 10.3390/BIOM5020472.

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Spirulina as neuroprotective supplement in parkinsonism; A review

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ABSTRACT

Parkinson disease is a progressive disorder that impacts the central nervous system and the component that are controlled by nerves. Major pathological hallmark of Parkinsonism is the presence of anomalous aggregates of α-Synuclein protein. Several experimental and pathological studies explain the other key involvement in PD pathogenesis like; loss of dopaminergic neurons is mid brain, Chronic microglial and astrocyte's activation, mitochondrial dysfunction, brain inflammation and oxidative stress. Parkinsonism indicates the several motor and non-motor symptoms like bradykinesia (slowness and stiffness in movement), tremor and resting tremor. There is no known permanent treatment of Parkinson disease, yet certain drugs are effective on symptoms. Blue green algae such as spirulina is a unicellular species and economically distributed as nutritive food supplements. Spirulina is one the influential source of natural nutrient and many experimental studies informed about the antioxidant and anti-

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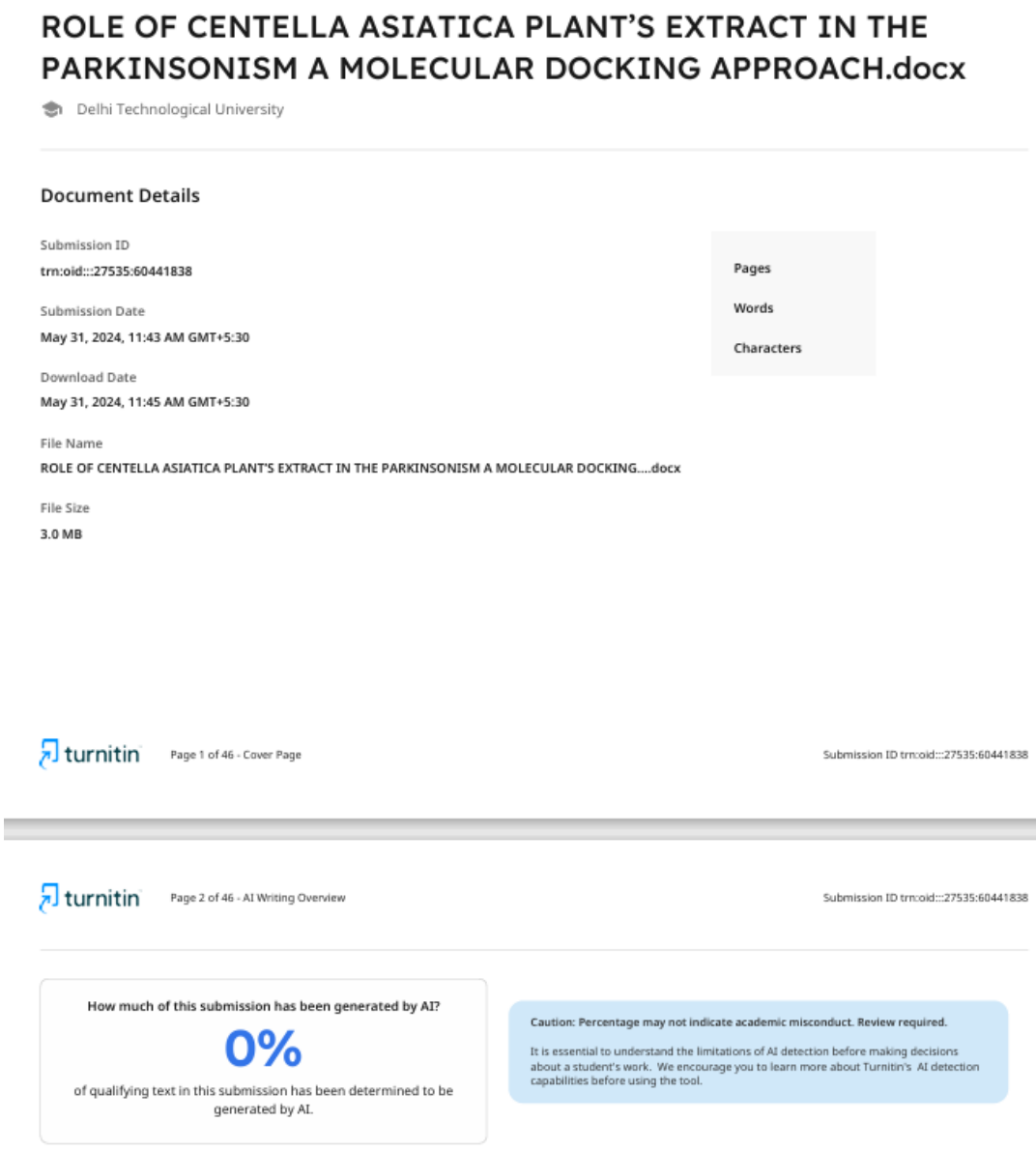

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CIRRICULUM VITAE

SUMMARY

Highly-motivated employee with desire to take on new challenges. Strong worth ethic, adaptability and exceptional interpersonal skills. Adept at working effectively unsupervised and quickly mastering new skills.

MOIN KHAN

EDUCATION

DTU (FORMERLY DCE) 2022-24
M.sc Biotechnology

MDU, ROHTAK
B.sc Biotechnology

HBSE
Senior secondary education.

MY SKILLS

Coaching and Mentoring

Escalation Matrix

Database Maintenance

Customer Service

Task Prioritization

Team Leadership

Staff Training

Customer Relationship Management

HOBBIES

- Playing cricket.
- Review research article

EXPERIENCE

ESCALATIONS MANAGER
MARCH 2021 – AUGUST 2022

TCS (CBSL) - Gurugram, India

- Developed and implemented escalations process to ensure customer satisfaction.
- Coordinated with cross-functional teams to resolve escalated issues quickly and efficiently.

ESCALATIONS MANAGER
MARCH 2021 – AUGUST 2022

AVES - Gurugram, India

- Assisted in the development of strategies for resolving complex customer issues quickly and efficiently.

SENIOR EXECUTIVE
AUGUST 2018 – MARCH 2019

One point one solution

- Ensured compliance with company policies and processes related to escalations management.

CONTACT

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