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A REVIEW ON PARKINSON'S DISEASE

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ABSTRACT

Parkinson's disease is a common neurodegenerative disorder that affects 1-2 out of every 1000 people at any given time. The main neuropathological finding is α-synuclein aggregation with Lewy bodies, which results in the loss of dopaminergic neurons in the substantia nigra. PD is a multifactorial disease that involves both genetic and environmental factors, and the biggest risk factor for PD is age. Other risk factors include heavy metal exposure, head injuries, exposure to toxins, gender, age, and some drugs. Parkinson's disease (PD) is characterized by stiffness, bradykinesia, postural instability, mental and emotional health issues, chewing and swallowing difficulties, skin issues, and sleep issues. The pathophysiology is concerned with how the host interacts with its surroundings. Only a small portion of the cases under study have a genetic component. The pathophysiologic alterations that result in deficits are caused by damage to the different neural systems. Alpha synuclein aggregation, oxidative stress, ferroptosis, mitochondrial failure, neuroinflammation, and other factors are among the recognized processes of Parkinson's disease. The purpose of levodopa preparations is to replenish the dopamine in the striatum. Since dopamine cannot traverse the blood-brain barrier, Parkinson's disease (PD) can be treated with levodopa, a dopamine precursor that can. Exercise and occupational therapy are examples of non-pharmacological therapy.

KEYWORDS: Parkinson's disease, dopaminergic neurons, environmental factors, caffeine, dopamine, Neurodegenerative disorder, Lewy bodies.

INTRODUCTION

One prevalent neurodegenerative condition is Parkinson's disease. Its symptoms include stiffness, resting tremor, and movement problems such bradykinesia. Although the primary origin of Parkinson's disease is unknown, several genetic variables are implicated. Additionally, environmental factors like smoking, caffeine use, and pesticide exposure have been investigated as risk factors for Parkinson's disease development. The loss of dopaminergic neurons in the substantia nigra pars compacta is the cause of many movement disorders. According to estimates, at least 1% of those over 60 have Parkinson's disease. Lewy bodies and the death of dopaminergic neurons in the substantia nigra are linked to the disorder. Idiopathic cases predominate. Just About 10% of instances, which are more common in younger people, have a hereditary basis. At any given time, 1-2 out of every 1000 people have Parkinson's disease. PD prevalence is increasing with age and PD affects 1% of the population above 60yrs. The main neuropathological finding is alpha-synuclein containing Lewy bodies and loss of dopaminergic neurons in the substantia nigra. It displays the marked diversity in time, geography, ethnicity, age and sex. The prevalence also increases over and above demographic changes. The increase has several causes as well. In many low- and middle-income nations, the incidence has increased, particularly among women. Older adults who are exposed to a variety of environmental factors are more likely to develop Parkinson's disease (PD). The reason for PD is a complex condition that involves both environmental and genetic variables. Parkinson's disease development is significantly influenced by both preventive factors (physical activity) and risk factors (pesticides). Five to ten percent of patients are genetically predisposed. As people age, both the incidence and prevalence of Parkinson's disease do rise. The number of new cases of an illness that initially appeared within a given time frame is referred to as its incidence. The overall number of individuals having the illness at a specific moment in time is referred to as prevalence.[1]

Etiolog

Cigarette smoking: PD has been researched in relation to cigarette smoking. Compared to non-smokers, heavy or chronic smokers have a lower risk of developing Parkinson's disease. Experimental models of Parkinson's disease have shown that nicotine's activation of nicotinic acetylcholine receptors on dopaminergic neurons is a protective reaction. According to a number of research, caffeine is the cause of Parkinson's disease. These studies unequivocally demonstrate that coffee consumers have a lower chance of developing Parkinson's disease.

Being an adenosine A2A receptor, caffeine has protective properties. According to certain earlier research, there is a 25% lower chance of getting prostatic dysfunction.

Pesticides, herbicides & heavy metals

When 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine was first linked to nigrostriatal degeneration in 1983, a number of individuals experienced the classic symptoms of Parkinson's disease (PD) after injecting themselves with a medication tainted with MPTP. MPP+ is an inhibitor of mitochondrial complex-1 that specifically harms substantia nigra dopaminergic cells. PD will develop as a result of this.

Genetics

Although PD is typically an idiopathic condition, a small percentage of individuals indicate a familial history. Additionally, these have a 5% Mendelian inheritance rate. PARK genes are the ones that cause Parkinson's disease. After that, a mutation will be made to show if the inheritance is autosomal dominant or autosomal recessive.

Risk factors

Injury: Head injury from sports may increase the risk of condition.

Toxin exposure: Toxins such as pesticides, solvents, metals, pollutants.

Gender: Males are 50% more likely to develop PD than females.

Age: PD will occur at the age of 60.[2]

Drugs & medications: Some drugs can cause Parkinsonism, which is characterized by tremors and other symptoms but not Parkinson's disease.

Symptoms

P.D affects different people in different ways. The rate of progression of disease will differ in individuals.

Tremors (shaking)

Although it begins with the hand, the person's foot or mouth is impacted first. The repetitive back-and-forth motion is linked to these tremors. Later, the person will rub their thumb and fingers together, a behavior known as "pill rolling," as a result of the tremors. It occurs more frequently when a person is stressed or their hand is at rest. Later, while you sleep or move in any way you want, this tremor typically goes away.

Rigidity

Most persons with Parkinson's disease experience muscle stiffness, or reluctance to movement. The person feels stiff because their muscles remain taut and tight. The person's arm will only move in brief, jerky motions if someone else tries to move it.

Bradykinesia

It is the slowing down of an instinctive and spontaneous movement. Simple chores may become more challenging as a result.

Postural instability: Imbalance leads to problems and change in posture, it will increase the high chance of fall.

Mental & emotional health problems: It includes depression or anxiety. It occurs during early stage of disease.

Difficulty with swallowing & chewing: Chewing and swallowing issues arise later in the course of the illness. Choking or drooling may happen from food and saliva building up in the mouth and back of the throat.

Skin problems: Parkinson's patients will have more oil on their faces, especially on the sides of their nose and forehead.

Sleep problems

Drowsiness or abruptly falling asleep during the day, trouble staying asleep at night, restless sleep, nightmares, and emotional dreams are all common sleep issues in people with Parkinson's disease.

Pathophysiology

Parkinson's disease pathogenesis is still primarily regarded as idiopathic, meaning it has no identified cause. It involves how environmental and host variables interact. Genetic variables are being investigated because they are associated to a small number of instances. The symptoms of Parkinson's disease are caused by the depletion of several neurotransmitters, including dopamine. As more and more cells are impacted by the illness, the symptoms will worsen with time. As people age, some patients have very few symptoms, while others have symptoms that worsen quickly. P.D. is becoming better recognized as a complicated neurodegenerative illness with a progressive pattern. There is compelling evidence that it

affects the olfactory bulbs and nucleus, the dorsal motor nucleus of the ambiguous nerve, the locus ceruleans, and ultimately the substantia nigra. Later on, the brain's cortical regions are impacted. Pathophysiologic alterations brought on by damage to these different neural systems degrade not just the motor system but also the cognitive and neuropsychological systems. Research on transplanted neurons in Parkinson's disease patients and research using cell and animal models indicate that aberrant α-synuclein aggregation and pathology spread between the gut, brainstem, and higher brain regions probably support the growth and progression of Parkinson's disease. At a cellular level, abnormal mitochondrial, liposomal, and endosomal function can be identified in both monogenic and sporadic Parkinson's disease between the brainstem, higher brain regions, and the gut most likely underpin the onset and course of Parkinson's disease. Both monogenic and sporadic Parkinson's disease exhibit aberrant mitochondrial, liposomal, and endosomal activity at the cellular level.[3]

Molecular mechanism

The second most prevalent neurodegenerative disease is Parkinson's disease, and treating it is still quite difficult. Environmental and genetic variables are linked to the etiology of Parkinson's disease (PD), and the onset of brain lesions is caused by exposure to toxins and gene alterations. α-synuclein aggregation, oxidative stress, ferroptosis, mitochondrial failure, neuroinflammation, and gut symbiosis are the five processes of Parkinson's disease that have been found. Drug development is greatly hampered by the interconnections between these molecular pathways, which further complicate the pathophysiology of Parkinson's disease. At the same time, P.D.'s lengthy latency and intricate mechanism make diagnosis and detection challenging.

α-synuclein aggregation

One of the most significant theories explaining the death of nigrostriatal neurons in Parkinson's disease is abnormal α-synuclein aggregation. When soluble α-synuclein monomers combine to form oligomers, which then form big, insoluble fibrils and microscopic protofibrils, A-synuclein itself can turn into a neurotoxic. The ubiquitin–proteasome and liposomal autophagy mechanisms preserve α-synuclein homeostasis. Therefore, buildup of α-synuclein may result from disruption of these degradation processes.[4]

Oxidative stress

One of the main aging processes that directly damage the central nervous system is oxidative stress (OS). When ROS are unable to handle cellular antioxidant activity, OS develops. Protein collapse, enzyme failure, lipid breakdown, and cell death are all brought on by the buildup of cytotoxic chemicals. Both Parkinson's disease and Alzheimer's disease may result from the malfunction. The most significant ROS generator, NADPH oxidase (NOX), is thought to be essential in initiating OS and neurotoxicity. One electron moving from oxygen to oxygen produced the majority of the ROS produced in mitochondria. DA-quinines are easily produced by oxidizing excess cytosolic DA. Then, α-synuclein may self-assemble as a result of the DA quinine-modified α-synuclein partially inhibiting chaperone-mediated autophagy. In the meantime, mitochondrial OS will rise as an aggregate of intracellular α-synuclein forms.[5]

Ferroptosis

Ferroptosis, an iron-dependent kind of cell death, is brought on by an excessive iron metabolism and severe lipid peroxidation. This can lead to OS and cell death. In the cytosol, coenzyme A (CoA) is changed into free polyunsaturated fatty acids (PUFA) by the enzyme acetylcholine esterase synthesize long-chain family member 4 (ACSL4). Lipid peroxidation can then result from the conversion of PUFA-CoA into phospholipids, which are oxidized by lipoxygenases. Glutathione (GSH), an antioxidant produced by the body from glutamate and cytokines, can be used to inhibit ferroptosis by preventing lipid peroxidation. DJ-1, another cellular antioxidant enzyme, acts as a ferroptosis inhibitor and shields the cytokine and GSH production by preventing the destruction of the transsulfuration pathway.[6]

Mitochondrial dysfunction

Research has shown that persistent ROS production and dopaminergic neurodegeneration are caused by mitochondrial malfunction.

Pharmacological therapy

Despite the fact that there are now no such drugs to treat Parkinson's disease, current treatments can alleviate motor symptoms. In order to reduce the severity of side effects, it is common practice to start treatment.

Levodopa

In order to replenish the dopamine in the depleted striatum, levodopa-based preparations are being used to treat Parkinson's disease. Since dopamine cannot cross the blood-brain barrier, it cannot be used to treat Parkinson's disease. However, levodopa, a dopamine precursor, can cross the BBB and be used as a treatment. DOPA decarboxylase transforms it into the neurotransmitter dopamine following absorption and passage across the blood-brain barrier. The majority of people need to take 150–1000 mg each day, spread out over several doses. The chance of experiencing negative effects increases with increasing dosages. There are also certain adverse effects, some of which are brought on by DOPA decarboxylase's conversion of levodopa to dopamine outside the central nervous system. By combining levodopa with peripheral DOPA decarboxylase inhibitors (benserazide, carbidopa), these side effects are reduced. Dyskinesias, severe motor on-off swings, and motor problems can result from long-term usage of this medication.[7]

Dopamine agonist

The therapy of P.D. involves the use of dopamine agonists. Based on receptor specificities, the widely used agonists are classified as either ergot or non-ergot derived, and they all contain an ethanolamine component. In contrast to levodopa, these medications attach to dopaminergic receptors and increase dopamine system activity without requiring conversion to dopamine. When starting dopamine agonists, the dosage is often raised gradually in accordance with the patient's reaction and any adverse effects. Ropinirole dosage ranges from 9 to 16 mg (maximum 24 mg) per day. divided into three to four doses; 4–6 mg once daily for rotigotine; and up to 3.3 mg of pramipexole, divided into three doses. Compared to levodopa, treatment with dopamine agonists has been demonstrated to lessen the incidence and severity of dystopia, motor fluctuations, and dyskinesia.

Monoamine oxidise B (MAO-B) inhibitors

Reduced activity of MAO-B leads to enhanced dopaminergic activity in the striatum since it is one of the primary enzymes involved in the breakdown of dopamine. When used, they help PD patients with their motor symptoms. To lower the dosage of levodopa, MAO-B inhibitors can also be used in conjunction with levodopa-based preparations. MAO-B inhibitors such as rasagiline and selegiline are frequently utilized. In more recent times, PD has also been treated with safinamide (Xadago). It is advised to take 5–10 mg of selegiline per day and 0.5–1 mg of rasagiline once day.[8]

Anti cholinergics

Only a few medications that work through non-dopaminergic pathways are utilized to treat Parkinson's disease. The anticholinergics are one such class of medications. By functioning as antagonists at cholinergic receptors, these lessen the action of the neurotransmitter acetylcholine. They will alleviate stiffness and tremors. Anticholinergic drugs aid in the repair and maintenance of the proper balance between dopamine and acetylcholine in the brain, which is disrupted when dopaminergic neurons are lost. Trihexyphenidyl (Benzhexol), procyclidine, orphenadrine, and benztropine are a few examples of anticholinergics. Blurred vision, dry mouth, constipation, drowsiness, difficulty urinating, urine retention, confusion, cognitive impairment, hallucinations, dizziness, difficulty swallowing, dyskinetic movements, and memory issues are among the frequent side effects.

Non pharmacological therapy

These treatments' primary goal is to alleviate symptoms that medication alone is insufficient to address. However, other workouts, such as relaxation and movement, can also have beneficial psychological impacts.

Sports & exercise

As Parkinson's disease worsens, people walk more slowly. They struggle with balance and coordination, and occasionally they are completely incapable of walking. People's muscles progressively deteriorate as a result of reduced movement. Sports and exercise can aid in delaying that process. Tai chi, qigong, yoga, weighted 8 training, balancing training, music therapy, stretching, endurance training, muscular activation and relaxation, brisk walking, and jogging are a few examples.[9]

Occupational therapy

Maintaining your freedom in daily life allows you to handle things independently. This includes making adjustments at home and at work. Both fine and gross motor abilities can be enhanced by occupational therapy exercises. Occupational therapy includes tasks including dressing, cooking, and utilizing specific equipment.

Speech therapy

In addition to being immobile, many P.D. patients have a high likelihood of developing speaking difficulties. The voice sounds quieter and more monotonous as a result of the voice box, tongue, and face muscles being less flexible. Finding the correct words might also be

problematic, and it might be more difficult for others to grasp. You practice speaking louder, clearer, and more accurately in speech therapy. Your capacity to move your facial muscles, make facial expressions, and breathe can all be enhanced by a variety of speech and singing activities. Speaking to others is becoming less common as a result of self-consciousness and embarrassment. Therefore, improving communication and discourse is another goal of speech therapy.

Psychological therapy

Patients with Parkinson's disease will also experience psychological effects, especially if the disease is advanced. Some people experience severe depression or sadness throughout these phases. It is necessary to treat this. However, the disease will worsen over time because it can be challenging to deal with the diagnosis and treatment, particularly in the early stages. Support from a psychologist may therefore be beneficial. In order to conquer the P.D., there are several support groups and different psychological assistance alternatives from friends and family.[10]

Novel drug targets

Gene therapies

By genetically altering cells that are either directly functionally impaired or able to treat disease symptoms, gene therapy is a rapidly developing genome editing technique that aims to treat a disease. The foundation of this method is the employment of a vector to transport antisense oligonucleotides, DNA, and RNA. The safety and effectiveness of two families of viral vectors, which are distinguished by both lentiviruses (LVs) and adenoid-associated viruses (AAVs), were demonstrated by the experiments conducted on animal models. The central nervous system has made extensive use of AAVs as vectors.

Targeting alpha-synuclein

The SNCA gene encodes alpha-synuclein, a 140-amino acid protein that is abundant in the brain and, more precisely, found at the presynaptic terminals of neurons. Its role includes neurotransmitter release and synaptic vesicle recycling. The common characteristic of Parkinson's disease (PD) is the buildup of α-syn and its aggregation in cytoplasm inclusions called Lewy bodies. Current disease-modifying medicines target the formation, aggregation, degradation, and dissemination of α-syn, albeit the exact mechanism of toxicity is still understood.

Glucocerebrosidase targeting therapies

The enzyme glucocerebrosidase, which is made up of 497 amino acid liposomal hydroxyls, breaks down glucocerebroside into glucose and ceramide. The increased accumulation of glucocerebroside in the liver, spleen, bone, and bone marrow causes Gaucher's disease in individuals who are homogeneous for harmful mutations of GBA, the gene encoding GCase. Although GBA pathogenic mutations are the most prevalent known genetic cause of Parkinson's disease (PD), those who are heterozygous for them are at higher risk of developing dementia and Parkinsonism.

LRRK2 targeting therapies

Leukine-rich repeat Kinase 2 (LRRK2) belongs to the family of proteins called Ras-of-complex (ROC). Pathogenic variations of the LRRK2 gene are significant and frequently result in Parkinson's disease. Two LRRK2 Kinase inhibitors, DNL201 and DNL151, have been developed for administration to both animals after tiny molecular inhibitors that block LRRK2 activity cause α-syn aggregation and neurodegeneration to slow down in animal models.

Clinical trial participants with Parkinson's disease and healthy volunteers. A phase I, randomized research in healthy volunteers and a placebo-controlled, dose-ranging study in 29 PD patients, including subgroups with and without LRRK2 mutation, have already demonstrated the safety, tolerability, and target engagement of DNL201. Following both doses given to PD patients, there was a decrease in urine bisphosphate, a biomarker, and a more than 50% inhibition of LRRK2 and Rab10 phosphorylation in the blood.

Iron targeting therapies

PD is characterized by abnormal iron metabolism, and people with PD have been discovered to have higher iron loads in their substantia nigra. By producing reactive oxygen species (ROS), elevated iron concentrations can cause neurotoxicity and enhance the iron-buffering ability of complexes like ferritin and neuromelanin. Iron chelators that pass the blood-brain barrier, eliminate excess intraneuronal iron, and lower ROS production have been shown in preclinical research in animal models of Parkinson's disease to be therapeutically effective. This has led to improved neuron lifespan and a return to normal dopamine metabolism. Causing P. D. to be depleted.

A2A receptor antagonist

One effective medication for Parkinson's disease is adenosine A2A receptor. Adenylate cyclase is stimulated by the G-protein-coupled receptor family, which includes the A2A receptor. The A2A receptor, which is involved in dopaminergic and glutamatergic neurotransmission, is expressed by a variety of cellular types, including neurons, astrocytes, oligodendrocytes, and microglia. Allosteric inhibition is caused by functional heteromeric complexes between A2A and dopamine D2 receptors, and motor inhibition is the outcome of A2A receptor activation. The mGlu5 receptor subtypes are the first glutamate receptors with which the A2A receptor interacts both physically and functionally. An increase in intracellular Ca2+ concentrations results in the suppression of A2A receptor function, while this interaction synergistically enhances glutamate release, activating NMDA receptors.[11]

Medicinal plants to treat Parkinson's disease

S. No	Plant name	Common name	Chemical constituents	Activity	Reference
1.	Bacopa monnieri	Brahmi or waterhyssop	Bacopaside Bacoside	Redox stabilization enhances mitochondrial performance.	[12]
2.	Camellia sinensis	Green tea	Polyphenols Catechins Epicatechin gallate Epigallocatechin	Redox stabilization, inhibit ROS-NO pathway, Protects DA neurons in the nigra region.	[13]
3.	Cassia obtusifolia	Java bean or sickle pod	Anthraquinones – chrysophanol, emodin, Flavonoids Terpenoids Lipids	It has multiple therapeutic actions related to the prevention of dementia and ischemia.	[14]
4.	Coffea Arabica and Coffea canephora	Arabica and Robusta coffee	Caffeine	Have neuroprotective properties.	[15]
5.	Curcuma longa	turmeric	Curcumin	Enhance dopamine levels, decrease oxidative stress, and increase mitochondrial complex-1 activity.	[16]
6.	Delphinium denudatum	Jadwar	Diterpenoids Vilmorrianone Denudatine Panicutine Condelphine Isotalatizidine	Reduced 3,4-Methylenedioxyamphetamine (MDA) levels, increased glutathione (GSH) content, Superoxide dismutase (SOD), catalase (CAT)	[17]

				activities and increased dopamine levels.	
7.	Fructus Alpinia oxyphylla	Black cardamom	Essential oils Terpinoids Flavones Steroids	Restores dopaminergic neurons.	[18]
8.	Gingko Biloba	Maidenhair tree	Ginkgolide B	Improve DA level, behavioral function and muscular coordination, Redox stabilization, boost mitochondria Function and ATP production	[19]
9.	Juglandis semen	Walnut	Caffeic acid Phenethyl ester derivative	Inhibits the MAO-B activity, Protects against 6- hydroxydopamine-induced neuronal degeneration	[20]
10.	Mucuna pruriens	Velvet bean	Glycoside Gallic acid Glutathione Levodopa	Improves locomotor & behaviour function, metal chelation, mitochondrial and Synaptic function.	[21]

REFERENCES

1. Kouli A, Torsney KM, Kuan WL. Parkinson's disease: etiology, neuropathology, and pathogenesis. Exon Publications, 2018 Dec 21; 3-26.
2. Tanner CM. Epidemiology of Parkinson's disease. Neurologic clinics, 1992 May 1; 10(2): 317-29.
3. Anantharam V, Kanthasamy A, Wang Z, Kanthasamy AG. Minhong Huang, Dan Lou 2, Adhithiya Charli1, Dehui Kong2, 3, Huajun Jin1, Gary Zenitsky1. Histone acetylation contributes to mitochondrial dysfunction and neuroinflammation in Parkinson's disease, 2022; 61.
4. Polymeropoulos MH, Lavedan C, Leroy E, Ide SE, Dehejia A, Dutra A, Pike B, Root H, Rubenstein J, Boyer R, Stenroos ES. Mutation in the α-synuclein gene identified in families with Parkinson's disease. Science, 1997 Jun 27; 276(5321): 2045-7.
5. Pizzino G, Irrera N, Cucinotta M, Pallio G, Mannino F, Arcoraci V, Squadrito F, Altavilla D, Bitto A. Oxidative stress: harms and benefits for human health. Oxidative medicine and cellular longevity, 2017; 2017(1): 8416763.
6. Tang D, Chen X, Kang R, Kroemer G. Ferroptosis: molecular mechanisms and health implications. Cell research, 2021 Feb; 31(2): 107-25.
7. Zahoor I, Shafi A, Haq E. Pharmacological treatment of Parkinson's disease. Exon Publications, 2018 Dec 21; 129-44.

8. Brooks DJ. Dopamine agonists: their role in the treatment of Parkinson's disease. Journal of neurology, neurosurgery & psychiatry, 2000 Jun 1; 68(6): 685-9.
9. Caird FI. Non-drug therapy of Parkinson's disease.
10. Ismailova SB, Ondar VS, Prokopenko SV. The Parkinson's disease rehabilitation—non-pharmaceutical approaches. Physical and rehabilitation medicine, medical rehabilitation, 2020 Mar 31; 2(1): 57-65.
11. Fatima U, Roy S, Ahmad S, Ali S, Elkady WM, Khan I. Pharmacological attributes of Bacopa monnieri extract: Current updates and clinical manifestation. Front Nutr., 2022; 9: 972379. [Internet]. 2022.
12. Mokra D, Joskova M, Mokry J. Therapeutic effects of green tea polyphenol (–)-Epigallocatechin-3-Gallate (EGCG) in relation to molecular pathways controlling inflammation, oxidative stress, and apoptosis. International journal of molecular sciences, 2022 Dec 25; 24(1): 340.
13. Khurm M, Wang X, Zhang H, Hussain SN, Qaisar MN, Hayat K, Saqib F, Zhang X, Zhan G, Guo Z. The genus Cassia L.: Ethnopharmacological and phytochemical overview. Phytotherapy Research, 2021 May; 35(5): 2336-85.
14. Khurm M, Wang X, Zhang H, Hussain SN, Qaisar MN, Hayat K, Saqib F, Zhang X, Zhan G, Guo Z. The genus Cassia L.: Ethnopharmacological and phytochemical overview. Phytotherapy Research, 2021 May; 35(5): 2336-85.
15. Socała K, Szopa A, Serefko A, Poleszak E, Wlaź P. Neuroprotective effects of coffee bioactive compounds: a review. International journal of molecular sciences, 2020 Dec 24; 22(1): 107.
16. Silvestro S, Sindona C, Bramanti P, Mazzon E. A state of the art of antioxidant properties of curcuminoids in neurodegenerative diseases. International journal of molecular sciences, 2021 Mar 20; 22(6): 3168.
17. Khanam S, Subitsha AJ, Sabu S. Plants as a promising source for the treatment of parkinson disease: A systemic Review. IP Int J Compr Adv Pharmacol, 2021.
18. Zhang ZJ, Cheang LC, Wang MW, Li GH, Chu IK, Lin ZX, Lee SM. Ethanolic extract of fructus Alpinia oxyphylla protects against 6-hydroxydopamine-induced damage of PC12 cells in vitro and dopaminergic neurons in zebrafish. Cellular and molecular neurobiology, 2012 Jan; 32: 27-40.
19. Abdel-Kader R, Hauptmann S, Keil U, Scherping I, Leuner K, Eckert A, Müller WE. Stabilization of mitochondrial function by Ginkgo biloba extract (EGb 761). Pharmacological Research, 2007 Dec 1; 56(6): 493-502.

20. Choi JG, Park G, Kim HG, Oh DS, Kim H, Oh MS. In vitro and in vivo neuroprotective effects of walnut (Juglandis semen) in models of Parkinson's disease. International Journal of Molecular Sciences, 2016 Jan 15; 17(1): 108.
21. Giri MA, Bhalke RD, Prakash KV, Kasture SB. Antiparkinsonian and Antioxidant Effects of Hydroalcoholic Extract of Camellia sinensis, Asparagus racemosus, Mucuna pruriens and their Combination. International Journal of Pharmaceutical Investigation, 2020 Oct 1; 10(4).