INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Paper

A Review on Treatment of Parkinson`S Disease

Wasim Bagwan[1]*, Shivam Kumbhar[2], Aaqueeb Shaikh[3], Nilesh Shinde[4], Ayaj Pathan[5], Sohan Kotsulwar[6], Sayyed Khaled[7], Mansuri Toshib[8], Adnan Siddiqui[9]

[1,2,4,5,6]Godavari Institute of Pharmacy Kolpa, Latur-413512, Maharashtra, India.
[3,7,8,9]Ali Allana College of Pharmacy, Akkalkuwa Dis. Nandurbar 425415, Maharashtra, India.

ARTICLE INFO

Published: 28 Jan. 2025
Keywords:
Parkinson's disease, Parkinson's treatment, substantia nigra, basal ganglia, Levy bodies, α-syncline, dopamine, levodopa, gene therapy, prevention, cotinine, stem cells, precision medicine.
DOI:
10.5281/zenodo.14752422

ABSTRACT

Parkinson's disease is indeed a complex and progressive neurodegenerative disorder characterized by both motor and non-motor symptoms. Management focuses primarily on palliative care, aiming to enhance quality of life over the course of the disease, which can span several decades. Device-assisted therapies, such as deep brain stimulation, apomorphine pumps, and levodopa gel intestinal infusion, have revolutionized the treatment of advanced Parkinson's disease. These interventions can help manage motor fluctuations and improve overall function. Non-motor symptoms, including neuropsychiatric issues (like depression and anxiety), gastrointestinal problems, urogenital dysfunction, and sleep disturbances, are significant aspects of the disease. Remarkably, many of these symptoms can appear years before a formal diagnosis, underscoring the need for early recognition and comprehensive management strategies. Addressing these non-motor symptoms is crucial for improving patient care and support for those living with Parkinson's disease. Parkinson's disease (PD) is indeed a significant neurodegenerative condition, typically manifesting between ages 55 and 65. The disease leads to a gradual worsening of both motor and non-motor symptoms, profoundly impacting quality of life.

INTRODUCTION

Despite significant advances in neuroscience, the diagnosis primarily relies on clinical assessment, emphasizing the importance of recognizing motor and non-motor symptoms.1 First described by James Parkinson in his 1817 essay "An Essay on the Shaking Palsy," the condition has been the subject of extensive research and clinical observation since its inception. This review article aims to equip general neurologists and other healthcare providers with essential knowledge about Parkinson's disease, covering its pathophysiology, symptomatology, diagnostic criteria, and current management strategies.2-5 By

***Corresponding Author:** Wasim Bagwan
Address: *Godavari Institute of Pharmacy Kolpa, Latur-413512, Maharashtra, India.*
Email ✉: bwasim111@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

providing a comprehensive overview, the article seeks to enhance the understanding of Parkinson's disease, enabling healthcare professionals to deliver better patient care and improve outcomes for those affected by this challenging condition.3 Parkinson's disease (PD) is a chronic, progressive neurodegenerative disorder primarily marked by the early loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc) and the accumulation of alpha-synuclein (aSyn), an intracellular protein associated with neurodegeneration. This dopamine deficiency in the basal ganglia leads to the hallmark motor symptoms of PD, including bradykinesia, tremor, rigidity, and later, postural instabili.4-6 In addition to these motor symptoms, PD is characterized by a range of non-motor symptoms that can manifest years before the onset of motor issues. As the disease progresses, these non-motor symptoms—such as depression, anxiety, cognitive impairment, and sleep disturbances—often become more pronounced and can significantly affect quality of life.7 Currently, the primary treatment for PD is pharmacological therapy, which aims to alleviate symptoms. However, these treatments often have limitations, particularly in advanced stages of the disease, where patients may experience dopamine-resistant motor symptoms and complications related to long-term dopamine therapy.8 Despite notable advancements in both medical and surgical treatments for PD, a definitive disease-modifying therapy remains elusive. Researchers are optimistic about identifying potential targets for such therapies in the future.9 This review will cover essential aspects of PD, including its epidemiology, clinical features, pathophysiology, and diagnostic criteria, aiming to provide healthcare professionals with a comprehensive understanding of the disease to improve patient management and care. The management of Parkinson's disease (PD) involves both medical and surgical approaches, tailored to the individual needs of patients.10

Etiology: - The pathogenesis of Parkinson's disease (PD) is intricate, influenced by a combination of genetic predispositions and environmental exposures. While there is ongoing debate about the precise contribution of each factor, it is widely accepted that aging is the most significant risk factor for the development of PD.11 The median age of onset typically falls between 55 and 65 years, with the risk increasing substantially after the age of 60. Additionally, PD appears to be more common in men, with studies reporting a male-to-female ratio ranging from 1.3 to 2.0. The reasons for this gender difference are not fully understood but may include biological, genetic, and lifestyle factors. For instance, lifestyle variables like cigarette smoking and postmenopausal hormone use have been shown to affect PD risk. Some research suggests that cigarette smoking may be inversely associated with PD risk, possibly due to nicotine's neuroprotective effects. Similarly, hormonal differences may contribute, as postmenopausal hormone use has been associated with a slight reduction in PD risk in some studies, although findings are mixed.12

In summary:

- Age is the most significant risk factor for PD.10
- Gender differences are observed, with men having a higher incidence, possibly due to a mix of genetic, biological, and lifestyle factors.11
- Lifestyle factors, including smoking and hormone use, may influence PD risk, but their exact effects remain under investigation.13

Caffeine intake is another lifestyle factor that may play a protective role in Parkinson's disease. Epidemiological studies have suggested an inverse association between caffeine consumption and PD risk, possibly due to caffeine's interaction with the adenosine receptors in the brain, which could help preserve dopamine neurons.14 As with other neurodegenerative diseases, PD pathogenesis is likely driven by multiple age-related biological dysfunctions that compromise cellular health and resilience. Key factors include:

- Telomere Dysfunction: Telomeres shorten with age, leading to genomic instability and cellular senescence, which could increase vulnerability to neurodegenerative changes.
- Genomic Instability: Accumulation of DNA damage over time can contribute to neuronal dysfunction and cell death.
- Epigenetic Changes: Aging brings changes in gene expression without altering the DNA sequence itself. These epigenetic modifications may exacerbate neurodegeneration by disrupting processes essential to neuronal survival.15
- Ubiquitin-Proteasome System Dysfunction: This system is responsible for degrading damaged or misfolded proteins. When it is impaired, protein aggregates, such as α-syncline in PD, can accumulate, leading to cellular stress and dysfunction.
- Autophagy-Lysosome System Impairment: Autophagy is a critical cellular mechanism for clearing damaged organelles and proteins. Deficits in this system hinder the removal of harmful cellular components, contributing to neuronal damage.
- Mitochondrial Defects: Mitochondria are essential for cellular energy production.
- Mitochondrial dysfunction, often seen in aging, reduces cellular energy levels and increases oxidative stress, both of which can drive neurodegeneration.16

Genetics of PD: Parkinson's disease (PD) is typically sporadic, the identification of several single-gene mutations has highlighted genetic contributions, particularly in familial cases. As of now, 11 genes have been mapped in relation to PD, with six—SNCA (α-syncline), UCH-L1, parkin (PRKN), LRRK2, PINK1, and DJ-1—being identified in detail. These mutations, especially those aside from LRRK2, account for only a small proportion of PD cases. However, their discovery has significantly advanced our understanding of the molecular mechanisms driving PD and related neurodegenerative diseases.17

Environmental factors: Finding specific environmental risk factors for Parkinson's disease (PD) has been challenging, though certain trends have emerged. Living in rural areas has been associated with a heightened risk, possibly linked to factors like pesticide and wood preservative exposure, though evidence is mixed across studies. Interestingly, one of the most consistent findings is an inverse association between cigarette smoking and PD risk, suggesting smoking may offer some protective effect, though the underlying mechanisms remain unclear.18 This summary highlights the complexity and variability in findings across epidemiological studies of environmental risk factors. Although some studies confirm associations (like between pesticide exposure and certain outcomes), others do not consistently find links (such as between head injury and health outcomes). The lack of robust consistency could stem from challenges in study design, measurement inaccuracies, or population differences, which are common limitations in this

research area and can lead to varying results across studies.19

Clinical diagnosis of PD: - Parkinson's disease (PD) is clinically characterized by bradykinesia, rigidity, and rest tremor, though not all these symptoms may be present in every case. Postural instability can also occur in PD, but early onset of backward instability, especially with a history of falls, is more indicative of progressive supranuclear palsy (PSP), a distinct condition. In PD, symptoms typically present asymmetrically, meaning one side of the body is usually more affected than the other, which is a useful clinical marker in differentiating PD from other movement disorders20.

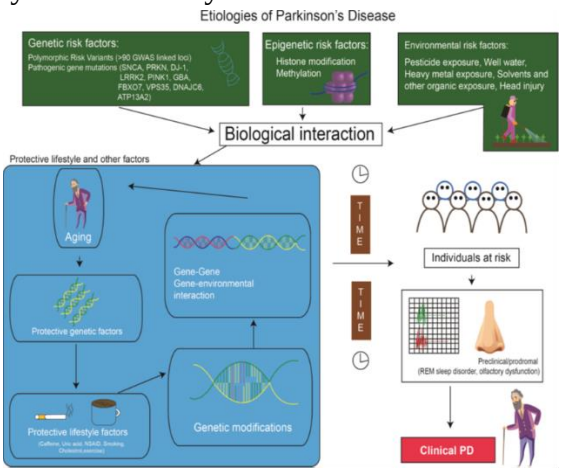

Fig No.1 Etiologies Parkinson's Disease

While Parkinson's disease (PD) diagnosis may seem straightforward, post-mortem studies have revealed that up to 25% of patients initially diagnosed with PD by general neurologists had a different condition. This diagnostic discrepancy highlights the importance of expertise in movement disorders, as diagnostic accuracy improves significantly in specialized clinics. Consequently, early referral to movement disorder specialists is recommended to ensure accurate diagnosis and appropriate management.[21] As the disease progresses, other non-motor and motor symptoms tend to develop. These include hypophonia (soft or reduced voice volume), drooling due to decreased swallowing frequency, and impaired postural reflexes, which increase the risk of falls.[22]

Motor symptoms: - Parkinson's disease (PD) is marked by a range of motor symptoms, including unilateral resting tremor, bradykinesia (slowed movements), rigidity, shuffling gait, and postural instability. These symptoms often develop gradually, with many individuals initially attributing them to normal aging. Although PD is progressive, the rate at which motor symptoms worsen varies significantly among individuals. Furthermore, there are subtypes of PD where specific symptoms like tremor, rigidity, or postural instability are more pronounced.[8] Beyond these core motor symptoms, PD can present with additional motor manifestations, such as hypomimia (reduced facial expression), a decreased blink rate, blurred vision, impaired upward gaze, dystonia, stooped posture, kyphosis or scoliosis, and difficulty turning in bed. Patients may also experience "freezing" episodes, where movement temporarily halts, and various speech

impairments, including hypophonia (soft voice) and palilalia (repetition of words or phrases).[23]

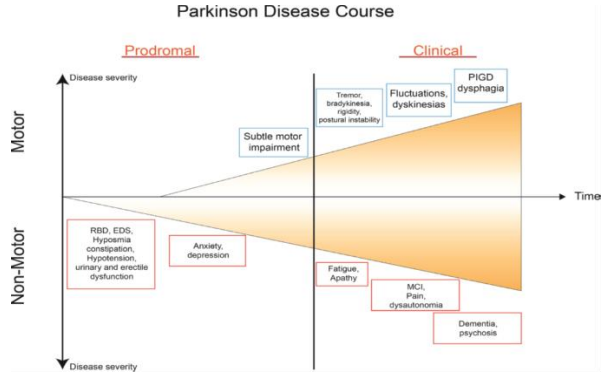

Fig No.2 Parkinson's Disease Course

Non-motor symptoms: Non-motor symptoms are a significant aspect of Parkinson's disease (PD), affecting cognitive functions, behavior, neuropsychiatric health, autonomic function, sensory perception, and sleep. These symptoms often pose some of the greatest challenges to quality of life in PD, as they generally respond less effectively to dopamine-based treatments compared to motor symptoms Interestingly, some non-motor symptoms, such as anosmia (loss of smell), sleep disturbances, and mood changes, can precede motor symptoms by many years, suggesting that non-motor symptoms might serve as early indicators of PD. [24] Nearly 90% of individuals with PD experience these non-motor symptoms during the disease course, with a substantial number developing them even before a formal diagnosis.[25] Treatment for PD, especially dopaminergic therapies like L-dopa, can also induce or worsen certain non-motor symptoms, including psychosis, orthostatic hypotension (a drop in blood pressure upon standing), and sleep attacks. Cognitive decline, particularly subcortical dementia, is common and tends to emerge as PD progresses.[26]

Table no 01. Category of Disease or Disorder and their Examples

Category	Disorders
Autonomic Dysfunction	• Sexual dysfunction (e.g., Erective Dysfunction; Vaginal Tightness) • Swallowing Disorder • Urinary Urge/Incontinence • Gastropatresis • Fecal Incontinence • Orthostatic Hypotension • Temperature Control Dysregulation Rhinorrhea
Sensory Disorders	• Pain Syndromes (Aching) • Abnormal Sensations • Olfactory dysfunction (Anosmia)

Integumentary	• Seborrhea • Malignant Melanoma • Other Skin Cancers • Drug Rashes • Amantadine (Livedo Reticularis) • Skin Denervation • Hyperhidrosis
Visual	• Diplopia • Blurred Vision • Impaired Color Discrimination
Miscellaneous	• Fatigue • Weight Gain or Loss
Neurobehavioral	• Anxiety • Depression • Psychosis/Hallucinations • Cognitive Dysfunction • Dementia • Bradyphrenia (Slowed Thinking)
Sleep Problems	• Daytime Sleepiness and Sleep Attacks • Insomnia • REM Sleep Disorder

Treatment of Parkinson's disease:

Table No 02. Treatment Of Parkinson's Disease.

Condition	Clinical features	investigations	Management
Drug-induced parkinsonism	May be associated with akathisia and Oro-mandibular dystonia	Based on history	Discontinue Offending drug. Anticholinergic drugs may be helpful for tremor
Multisystem atrophy	Orthostatic hypotension, absence of tremor, symmetrical signs, cerebellar features, erectile dysfunction, poor response to levodopa	MRI brain, sphincter EMG	Levodopa trial, amantadine measures to control postural hypotension, e.g., fludrocortisone
Progressive supranuclear palsy	Gaze palsy (down more than up), axial rigidity, frontal and pyramidal signs, poor response to levodopa	MRI brain	Levodopa trial
Normal-pressure hydrocephalus	Dementia festinating gait	CT or MRI brain, therapeutic	Evaluate for ventriculoperitoneal shunt

		lumbar puncture	
Multiple lacunar strokes	Focal findings, sensory or motor loss	CT or MRI brain	Antiplatelet treatment, control of risk factors (e.g., diabetes, hypertension, increased cholesterol)
Dementia with Lewy bodies	Visual hallucinations	MRI brain, psychometric	Consider cholinesterase inhibitor
Corticoid basal degeneration	Marked asymmetry of clinical findings, dyspraxia, cortical sensory loss, myoclonus, dystonia, alien limb phenomenon, absence of response to levodopa	EEG, psychometric	-

Drug list: -

Levodopa: - Levodopa, combined with a peripheral decarboxylase inhibitor (such as carbidopa or benserazide), has indeed been the cornerstone treatment for Parkinson's disease (PD) for over 40 years, recognized for its effectiveness in managing motor symptoms. Despite its efficacy, long-term levodopa therapy often leads to side effects that can significantly impact patients' quality of life.27 The development of levodopa-induced dyskinesia's (involuntary, erratic movements) is one of the major long-term challenges, occurring at an estimated rate of 10% annually, with younger patients being at higher risk. Motor fluctuations—such as "on" and "off" periods where the effectiveness of the medication waxes and wanes—also tend to develop with prolonged treatment, mainly influenced by the disease's duration and the cumulative exposure to levodopa.28

Despite its effectiveness, long-term use of levodopa can lead to complications, including:

- **Motor fluctuations**: Patients may experience "on" periods (when symptoms improve) and "off" periods (when symptoms return), which can become more pronounced with time.
- **Levodopa-induced dyskinesia's**: These are involuntary, erratic movements that tend to develop after years of levodopa use, especially in younger patients and those with higher doses. Dyskinesia's are believed to result from the intermittent dopamine stimulation caused by levodopa's short half-life (60–90 minutes), which leads to fluctuating dopamine levels in the brain.[29]

Dopamine Agonist: - Dopamine agonists are a class of medications widely used in managing Parkinson's disease (PD). These drugs work by mimicking the effects of dopamine, a neurotransmitter that becomes deficient in PD due

to the loss of dopamine-producing neurons in the substantial nigra. Unlike levodopa, which is converted into dopamine in the brain, dopamine agonists directly stimulate dopamine receptors, providing an alternative to increase dopamine activity in patients with diminished dopamine levels.30

•Pramipexole (Mirapex)
•Ropinirole (Requip)
•Rotigotine (Neupro) – available as a transdermal patch
•Apomorphine – a short-acting injectable option used for sudden "off" episodes.31

Dopamine agonists have become a common choice for early treatment of Parkinson's disease (PD), especially in younger patients, with the goal of delaying the need for levodopa. By mimicking dopamine's effects in the brain, dopamine agonists can manage motor symptoms such as tremor, rigidity, and bradykinesia in the early stages of PD.32 This approach is often advantageous for younger patients, as prolonged use of levodopa, the primary treatment for PD, is associated with motor complications like dyskinesia's and motor fluctuations over time. By reducing motor complications associated with long-term levodopa use, these agonists provide a valuable option for managing PD symptoms effectively while preserving levodopa's efficacy for later stages.33

CONCLUSION: - Parkinson's disease (PD) is one of the most common neurodegenerative disorders, characterized by progressive motor and non-motor symptoms due to the loss of dopaminergic neurons, particularly in the substantial nigra. The underlying causes of PD are believed to involve a complex interplay of genetic and environmental factors, which contribute to abnormal protein aggregation (such as alpha-syncline) within specific neuron groups. In Parkinson's disease (PD), the primary protein involved in this process is alpha-syncline. Under certain conditions, alpha-syncline misfolds and forms toxic aggregates, which cluster together to create Lewy bodies within neurons. These aggregates interfere with normal cellular functions, such as protein degradation, mitochondrial function, and cellular transport. As these cellular systems become compromised, affected neurons—especially the dopamine-producing neurons in the substantial nigra—gradually lose function and die. PD remains primarily a clinical diagnosis based on characteristic motor symptoms, such as bradykinesia, rigidity, and tremor, alongside supportive findings. However, given that other conditions can cause Parkinsonism, clinicians must have a high degree of suspicion to rule out alternative causes and ensure accurate diagnosis. Current treatments primarily address symptoms without halting disease progression. Research is therefore increasingly focused on developing disease-modifying therapies that could offer neuroprotection—aiming to slow or prevent neurodegeneration rather than just manage symptoms. Advances in understanding the molecular and genetic mechanisms of PD will hopefully pave the way for new therapies that target these underlying causes.

REFERENCES

1. Parkinson, J. (1817). An Essay on the Shaking Palsy. Sherwood, Neely, and Jones.
2. Obeso, J. A., et al. (2000). "Pathophysiology of Parkinson's disease." Journal of Clinical Neuroscience, 7(5), 287-299
3. Spillantini, M. G., et al. (1997). "Alpha-synuclein in Lewy bodies." Nature, 388(6645), 839-840.

4. Jankovic, J., & Tan, E. K. (2011). "Parkinson's disease: clinical aspects and management." Movement Disorders, 26(3), 395-407.
5. Jankovic, J. (2008). "Parkinson’s disease: clinical features and diagnosis." Journal of Neurology, Neurosurgery, and Psychiatry, 79(4), 368-376.
6. Stocchi, F., & Olanow, C. W. (2013). "Management of Parkinson's disease: a review of current and emerging treatment strategies." CNS Drugs, 27(11), 887-907
7. Chaudhuri, K. R., et al. (2006). "Non-motor symptoms of Parkinson's disease: Diagnosis and management." Lancet Neurology, 5(3), 235-245.
8. Poewe, W., et al. (2017). "Parkinson disease." Nature Reviews Disease Primers, 3, 17013.
9. Kalia, L. V., & Lang, A. E. (2015). "Parkinson's disease." Lancet, 386(9996), 896-912.
10. Tanner, C. M., et al. (2014). "Parkinson disease in the elderly: epidemiology and genetics." Parkinsonism & Related Disorders, 20(1), 10-16.
11. Wooten, G. F., et al. (2004). "Parkinson's disease: epidemiology." Annals of Neurology, 56(4), 491-501.
12. Tanner, C. M., et al. (2009). "Environmental factors and Parkinson’s disease: a critical review." Annual Review of Public Health, 30, 145-160.
13. Chen, H., et al. (2007). "Caffeine and the risk of Parkinson's disease." Movement Disorders, 22(13), 1947-1954
14. Tanner, C. M., et al. (2001). "Smoking, Parkinson's disease, and Parkinson's disease subtypes." Movement Disorders, 16(4), 539-546.
15. Chinta, S. J., et al. (2013). "The role of mitochondrial dysfunction and oxidative stress in Parkinson’s disease." Antioxidants & Redox Signaling, 18(7), 879-888.
16. McNaught, K. S. P., & Jenner, P. (2001). "Proteasomal function is impaired in substantia nigra in Parkinson's disease." Journal of Neurochemistry, 77(6), 1371-1378.
17. Schapira, A. H. V. (2008). "Mitochondrial dysfunction in neurodegenerative diseases." The Lancet Neurology, 7(11), 1151-1163.
18. Gorell, J. M., et al. (1998). "The risk of Parkinson's disease associated with pesticide exposure." Neurology, 50(6), 1346-1350.
19. Elbaz, A., et al. (2003). "Occupational and environmental risk factors for Parkinson's disease: a review." Current Opinion in Neurology, 16(4), 455-460.
20. Jankovic, J. (2008). "Parkinson’s disease: clinical features and diagnosis." Journal of Neurology, Neurosurgery, and Psychiatry, 79(4), 368-376.
21. Litvan, I., et al. (2003). "Diagnosis of progressive supranuclear palsy." Movement Disorders, 18(6), 552-556.
22. Hughes, A. J., et al. (1992). "Accuracy of clinical diagnosis of idiopathic Parkinson’s disease: a clinicopathological study." Journal of Neurology, Neurosurgery, and Psychiatry, 55(3), 181-184.
23. Lichter, D., & Marder, K. (2007). "Parkinson's disease: Diagnosis and clinical features." The Neurologist, 13(5), 317-322.
24. Chaudhuri, K. R., et al. (2006). "Non-motor symptoms of Parkinson's disease: Diagnosis and management." Lancet Neurology, 5(3), 235-245.

25. Sveinbjörnsdóttir, S. (2016). "The clinical symptoms of Parkinson's disease." Journal of Neurochemistry, 139(3), 318-324.
26. Schapira, A. H. V., et al. (2009). "Parkinson's disease: pathophysiology and clinical management." The Lancet Neurology, 8(7), 609-622.
27. Olanow, C. W., & Obeso, J. A. (2007). "Levodopa motor complications in Parkinson's disease: pathophysiology and management." Movement Disorders, 22(1), S329-S338.
28. Kohn, R. A., & Gurevich, E. V. (2008). "Levodopa-induced dyskinesia in Parkinson's disease: pathophysiology and management." CNS Drugs, 22(7), 569-586.
29. Coulson, N., & Lee, M. (2011). "Motor fluctuations in Parkinson's disease: Diagnosis and management." Therapeutic Advances in Neurological Disorders, 4(2), 65-74.
30. Margaritis, M., & Mertens, H. (2012). "Dopamine agonists in Parkinson's disease: Mechanisms of action and clinical uses." Current Drug Targets, 13(7), 888-897.
31. Parkinson Study Group. (2002). "Pramipexole vs levodopa as initial treatment for Parkinson disease: A randomized controlled trial." JAMA, 288(15), 1973-1983.
32. Fox, S. H., et al. (2005). "Dopamine agonists in the treatment of Parkinson's disease." Movement Disorders, 20(4), 1189-1201.
33. Rascol, O., et al. (2000). "Dopamine agonists in the treatment of Parkinson's disease: a review of their use in managing motor complications." Journal of Neurology, Neurosurgery, and Psychiatry, 68(2), 241-248.

HOW TO CITE: Wasim Bagwan*, Shivam Kumbhar, Aaqueeb Shaikh, Nilesh Shinde, Ayaj Pathan, Sohan Kotsulwar, Sayyed Khaled, Mansuri Toshib, Adnan Siddiqui, A Review on Treatment of Parkinson`S Disease, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 1, 2306-2315. https://doi.org/10.5281/zenodo.14752422