

Review Article

Parkinson Disease Pharmacological and Herbal Management: A Review

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Abstract: Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the degeneration of dopaminergic neurons in the brain. While conventional pharmacological interventions remain the primary approach to managing PD symptoms, there is a growing interest in exploring complementary strategies, including herbal remedies. This article delves into the current understanding of both pharmacological and herbal management of Parkinson's disease. The pharmacological and herbal management of Parkinson's disease (PD) presents a comprehensive exploration of treatment strategies. While pharmaceutical interventions like levodopa are widely employed, there's growing interest in the potential contributions of herbal remedies. The current review has focused on herbs such as *Mucuna pruriens*, *Ginkgo biloba*, and *Ashwagandha*, investigating their neuroprotective and antioxidant properties. However, the efficacy and safety of herbal approaches in managing PD require thorough examination and validation. Collaborative efforts between pharmaceutical and herbal approaches may hold promise in optimizing PD management, but individualized care under the guidance of healthcare professionals remains paramount.

Keywords: Parkinson, herbals, etiology, *Ashwagandha*, *Ginkgo biloba*.

INTRODUCTION

Parkinson's disease is a neurodegenerative disorder that affects movement control. It often starts with minor tremors and can progress to stiffness, slowed movement, and difficulty with balance. It is usually characterized by symptoms such as tremors, slowed movement (bradykinesia), muscle stiffness, and impaired balance. The primary cause is the loss or death of dopamine-producing neurons in the brain, however its progression can vary from person to person [1]. While there's no cure, various treatments like medications, physical therapy, and sometimes surgery can help manage symptoms. It's a complex condition, and each person's experience with Parkinson's can be unique. If you or someone you know is dealing with Parkinson's, it's important to work closely with healthcare professionals to tailor a care plan that suits individual needs [2].

Parkinson's disease was first medically described as a neurological syndrome by James Parkinson in 1817 in his essay "An Essay on the Shaking Palsy" [3]. The disease is a progressive neurological disorder caused by the loss of dopamine, leading to symptoms such as instability of posture or balance, tremors, stiffness, and slowness of movement. Since its first description, many important discoveries have been made in the 200 years of Parkinson's disease research history, revealing various aspects of the disease, including clinical and pathological characteristics, anatomy, and neurochemistry. The disease is named after English doctor James Parkinson, who published the first detailed description in 1817 [4, 5].

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Parkinson's disease is a prevalent progressive neurodegenerative disorder that leads to substantial disability and adversely affects the quality of life. While the exact cause remains unknown, the pathological aspect includes the impairment or loss of dopaminergic neurons in the substantia nigra pars compacta [6].

In the realm of Parkinson's, significant breakthroughs have occurred, paving the way for rational treatments grounded in anatomical, biochemical, and physiological investigations. For instance, the identification of dopaminergic deficiencies paved the way for the utilization of levodopa. Progress over the years has involved comprehensive exploration into clinical and pathological traits, anatomy, neurochemistry, and the staging of the disease. The comprehension of Parkinson's has advanced significantly, with notable strides in areas like functional genetics and emerging molecular mechanisms [7, 8].

Parkinson's disease typically manifests in the later stages of life, characterized by a widespread decrease in movement (bradykinesia) and, at least, one additional symptom such as resting tremor or rigidity. Additional accompanying features include a diminished sense of smell, mood disorders, disruptions in sleep, constipation, increased salivation and occasional excessive limb movements during sleep (REM behavior disorder) [9-11].

Approximately 1% of individuals aged 60 and above is believed to be affected by Parkinson's disease. However, the majority of cases are of unknown origin (idiopathic), with only around 10% having a genetic basis, typically observed in younger persons [12].

Symptoms: The most common symptoms of Parkinson's disease include.

Tremor

Characteristically, a rhythmic shaking which is known as tremor that initiates in a limb, frequently in the hand or fingers. A distinctive type is the pill-rolling tremor, where you might rub your thumb and forefinger together. Even at rest, your hand may exhibit tremors, but interestingly, the shaking may ease off when you engage in activities.

Parkinson's Disease (PD) often presents with tremors, a challenging symptom with varying responses to dopaminergic medication. While there is a need for a reliable, evidence-based framework for understanding PD tremor, such a framework is currently lacking, underscoring the importance of guiding future research efforts [13].

Slowed movement (Bradykinesia)

It refers to a slowness of movement, a characteristic symptom often observed in conditions like Parkinson's disease. It involves a noticeable and generalized decrease in the speed of various physical activities and is a key aspect of the clinical presentation in such neurodegenerative disorders. Bradykinesia can be translated directly as "slow movement" [14, 15].

Muscle Rigidity

Simply it is a stiffness or resistance to movement in the muscles. Rigidity stands out as a key indicator of Parkinson's disease, impacting as many as 89% of patients [16]. Clinically, rigidity denotes an elevated resistance to the passive stretching of a muscle, remaining consistent across the entire range tested [17].

Loss of Smell

It is a diminished sense of smell; however a notable trait of Parkinson's disease (PD) Recent findings suggest that over 90% of PD patients experience substantial olfactory loss. This loss is bilateral and pervasive, affecting all olfactory domains [18].

Sleep Disturbances

It is difficulties with sleep, including insomnia or disrupted sleep. Sleep disturbances are prevalent in Parkinson's disease and encompass a wide range of sleep disorders, the regulation of sleep and wakefulness is disrupted contributing to the emergence of disorders like daytime sleepiness and insomnia, as well as the control of motor activity during sleep is compromised, leading to the occurrence of parasomnias [19].

Mood Disorders

Includes; depression, anxiety, or changes in mood, however, There's a growing focus on recognizing and addressing the non-motor aspects of Parkinson's disease (PD). Mood disorders, a prevalent category of behavioral issues in PD, are among the most frequent and can manifest in both the early and advanced stages of the disease. In certain instances, these challenges may emerge before the onset of motor symptoms in PD. These disorders significantly impact the quality of life and influence daily functioning [20].

The attitude and progression of Parkinson's disease are notably affected by mood disorders and anxiety. Non-motor symptoms like, anhedonia, apathy and fatigue in Parkinson's disease often coincide with the diagnostic criteria for depression and anxiety, posing challenges in accurately diagnosing mood disorders in patients with PD [21].

Excessive Salivation (Sialorrhea)

Increased in saliva production, excessive saliva, known as sialorrhea, extends beyond the lip margin and is a prevalent issue in numerous neurological conditions. In the past, sialorrhea has not received sufficient recognition in individuals with Parkinson's disease (PD). Nevertheless, many PD patients consider sialorrhea to be one of the most challenging and debilitating aspects of the disease [22].

Constipation

Difficulty in passing stools, yet, constipation stands out as a prevalent gastrointestinal aspect of Parkinson's disease (PD), affecting over 50% of PD patients over the course of the condition. Importantly, constipation is acknowledged as a significant prodromal symptom, potentially preceding the onset of classical motor symptoms by decades. Subsequently, the prevalence and intensity of constipation in PD tend to align with the progression of both motor symptoms and nonmotor aspects, including cognitive decline and depression.

REM Behavior Disorder

Abnormal limb movements during sleep, REM (Rapid Eye Movement), and sleep behavior disorder (RBD) exhibits a preference for certain neurodegenerative disorders, particularly synucleinopathies like Parkinson's disease (PD), dementia and multiple system atrophy. The prevalence of RBD in PD has been reported to vary, ranging from 20 to 72%. RBD can either precede or follow the onset of Parkinsonism. In cases of idiopathic RBD, there's a potential link to the future development of neurodegenerative diseases, and RBD in PD patients shows associations with various clinical factors, although their causal or temporal relationships remain uncertain. Notably, RBD may be linked to the emergence of dementia and hallucinations in PD.

Etiology

At the core of this condition is the significant loss of nerve cells, particularly dopaminergic neurons, in the substantia nigra region of the brain. This results in a decline in dopamine levels, impacting both movement and other symptomatic aspects of the disease. However, the etiology of Parkinson's disease is intricate, stemming from a combination of environmental or genetic factors or could be a combination of both of them [24].

Environmental causes

There's a thought among some researchers that environmental factors might up the chances of someone getting Parkinson's disease. It was proposed that pesticides and herbicides in agriculture, as well as pollution from industry and traffic, in addition to that, certain researches indicate that the occurrence of Parkinson's disease might be associated with exposure to chemicals and toxins in the place of work [25-27].

Genetic causes

Several genetic factors have been identified to elevate the likelihood of someone developing Parkinson's disease. While the condition can be familial, typically passed down through faulty genes from parents to children, it's uncommon for Parkinson's to be inherited in this manner. In the majority of cases, Parkinson's disease is believed to stem from an intricate interplay of various genetic and environmental elements, although there are rare instances of monogenic forms of the disease.

Definitively, mutations in six genes (LRRK2, SNCA, PRKN, PINK1, ATP13A2 and DJ1) besides (MAPT, SNCA and LRRK2) also, GBA loss-of-function mutations have been thoroughly confirmed as factors that increase susceptibility to Parkinson's disease have been established as causing familial parkinsonism [28], however, another study suggests a correlation between PD and 26 genes [29].

A study carried out in 2023 by Shrimanker *et al.*, [30] suggested another causes of PD, among them are; medications. Figure 1 shows the main causes of PD as prescribed by Dalvi *et al.*, 2014 [31].

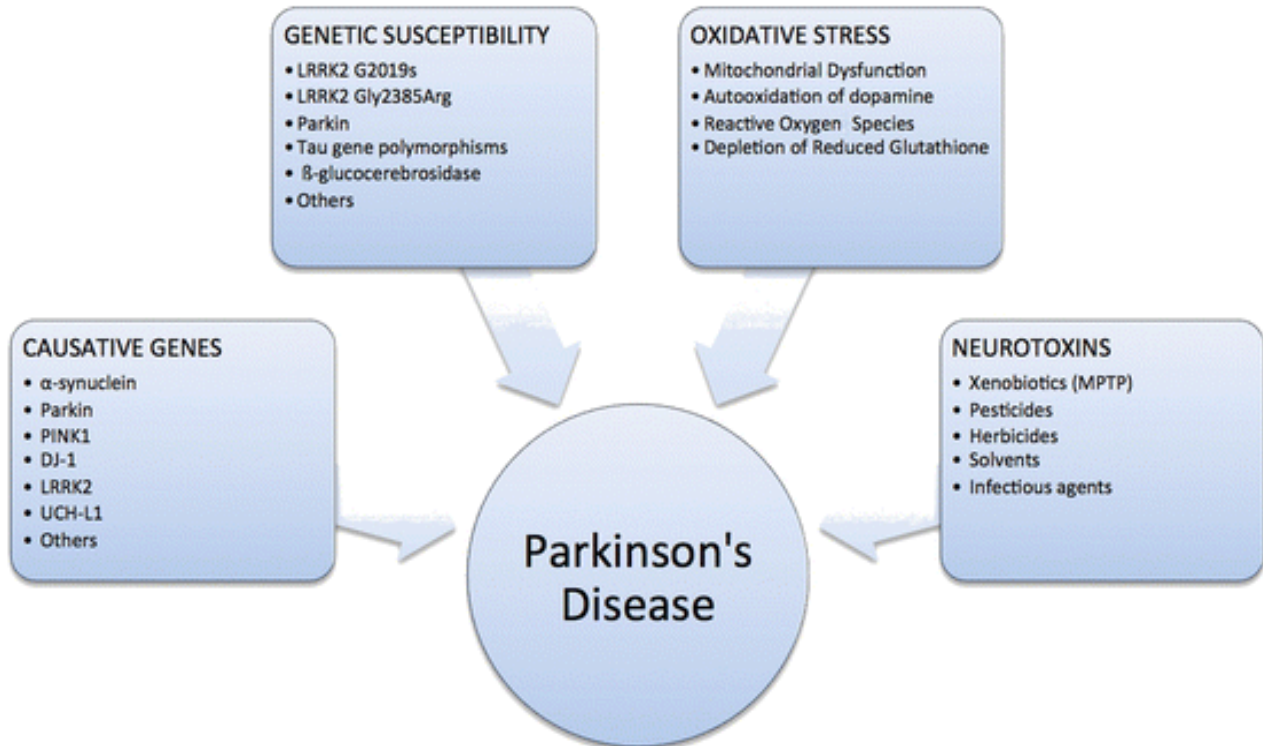


Figure 1: Main causes of PD [31]

Pathogenesis of PD

The development of Parkinson's disease is thought to encompass oxidative stress, disturbances in mitochondria, changes in the neuroinflammatory processes and protein α -synuclein [32]. Figure 2, shows a pattern of pathogenic and etiologic factors leading to cause PD [33].

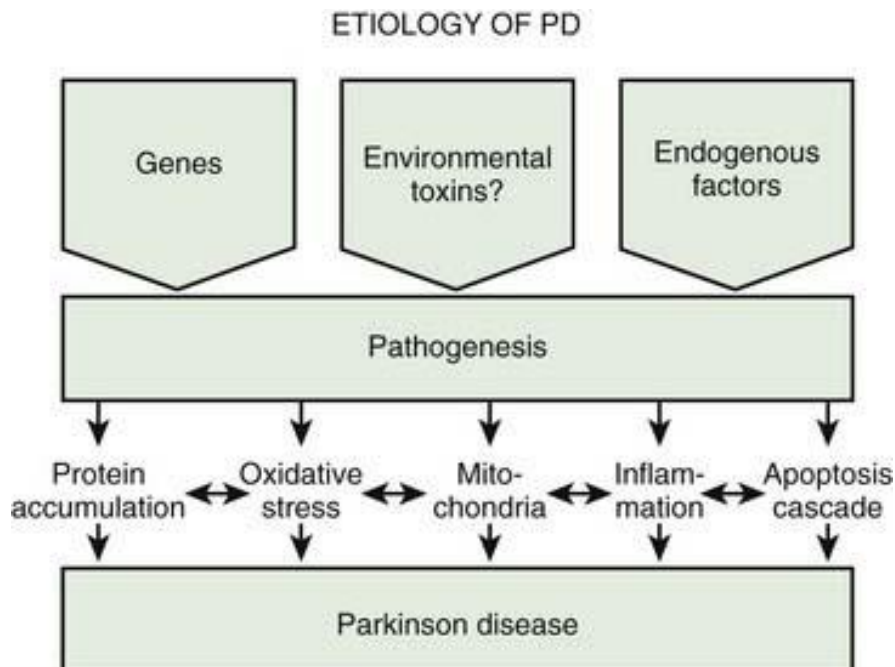


Figure 2: Scheme Pattern of pathogenic and etiologic factors leading to PD [33]

Pharmacological Management

Levodopa (L-DOPA)

Levodopa is the gold standard in PD treatment. As a precursor to dopamine, it replenishes the deficient neurotransmitter, alleviating motor symptoms. However, long-term use may lead to motor fluctuations and dyskinesias [34-37].

Dopamine Agonists:

Drugs like pramipexole and ropinirole mimic the action of dopamine, providing relief from symptoms. They are often used in conjunction with levodopa or as monotherapy in the early stages.

MAO-B Inhibitors:

Selegiline and rasagiline inhibit monoamine oxidase type B, an enzyme that breaks down dopamine. These medications help enhance dopamine levels and may delay the need for levodopa.

COMT Inhibitors

Entacapone and tolcapone prolong the effect of levodopa by inhibiting catechol-O-methyltransferase (COMT), an enzyme that breaks it down.

Anticholinergics

Used to manage tremors, anticholinergic medications like trihexyphenidyl can be beneficial, especially in younger patients.

Amantadine

Amantadine may provide relief from dyskinesias and improve motor function by modulating glutamate release.

Herbals

For over 5,000 years, diverse herbal remedies have been employed globally. Herbal medicines, also known as herbal supplements, encompass any products derived from plants, utilized for the preservation or restoration of health [38].

In 2023 Furhad and Bokhari [39] defined herbals as encompass items crafted from botanical wonders, aimed at addressing ailments or nurturing well-being, it can go by a variety of names such as botanical products, herbal products,, or phytomedicines, however, herbals can specifically designed for internal use, they take on the title of herbal supplements [39].

Basically, herbal remedies are comprised of plant parts or unrefined plant extracts that contain various components believed to collaborate synergistically. The renewed public fascination with herbal remedies can be linked to several factors, including [40, 41]:

- ❖ Different assertions about the efficiency or effectiveness of plant-based medicines.
- ❖ The elevated expenses and potential side effects associated with the majority of contemporary medications.
- ❖ Misguided belief in the superiority of herbal products over manufactured ones.
- ❖ Consumer inclination towards natural therapies and an increased curiosity in alternative medicines.
- ❖ Advancements in the quality, effectiveness, and safety of herbal medicines through the progress of science and technology.
- ❖ Discontent with the outcomes of conventional pharmaceuticals and the belief that herbal medicines could prove effective in treating specific diseases where traditional therapies have shown ineffectiveness or inadequacy.
- ❖ Advancements in science and technology have led to enhanced quality, efficacy, and safety of herbal medicines.
- ❖ Patients may develop a belief that their physicians haven't accurately identified the issue, leading to a sense that herbal remedies present an alternative option.
- ❖ A shift towards self-administration of medication.

Over recent years, numerous studies have delved into the potential of natural products and herbs for treating Parkinson's disease, however, certain herbs have demonstrated effectiveness surpassing conventional synthetic drugs, influencing the mechanisms involved in the development of PD [42].

Mucuna pruriens (Velvet Bean)

Velvet Bean, scientifically known as *Mucuna pruriens*, is a tropical legume recognized for its potential therapeutic attributes. With its content of L-DOPA, a dopamine precursor, this plant has sparked interest for potential applications in addressing nervous disorders, male infertility, and even as an aphrodisiac in various health contexts [43]. Research indicates that the seeds of *Mucuna pruriens* hold significant medicinal potential. The ancient Indian medical system, Ayurveda, has a historical tradition of utilizing *M. pruriens*, even for conditions like Parkinson's disease. The plant has demonstrated anti-parkinson and neuroprotective effects, potentially linked to its antioxidant activity. Moreover, in vitro studies have showcased *M. pruriens*' antioxidant capabilities by effectively scavenging DPPH radicals and reactive oxygen species. This review provides a summary of the medicinal properties of *M. pruriens*, focusing on studies employing extracts from both the seeds and leaves [44-46].

Ginkgo Biloba

Ginkgo biloba, commonly known as ginkgo or maidenhair tree, is a unique and ancient tree species with a rich history in traditional medicine. Renowned for its distinctive fan-shaped leaves, ginkgo has been used for centuries in various cultures for its potential health benefits. One of the key components in ginkgo biloba is flavonoids, which possess powerful antioxidant properties. Additionally, ginkgo contains terpenoids that may support improved blood flow by dilating blood vessels and reducing the stickiness of platelets. Research suggests that ginkgo biloba may have potential applications in cognitive function and memory enhancement. Some people also use it to alleviate symptoms associated with conditions like tinnitus (ringing in the ears) and intermittent claudication (leg pain caused by reduced blood flow) [47, 48].

In 2020, a study carried out by Mohammed *et al.*, 2020 [49], they mentioned in their study that Ginkgo biloba extract (GbE) is recognized for its composition of various bioactive compounds and its ability to act as a scavenger for free radicals. Parkinson's Disease (PD) is a neurodegenerative condition marked by the depletion of dopaminergic neurons and linked to factors such as, apoptosis, neuroinflammation, and oxidative stress, and the study found that histological observations unequivocally verified these findings, demonstrating a clear neuroprotective effect of Ginkgo biloba extract against PD [49].

Ashwagandha (Withania somnifera):

Ashwagandha, scientifically known as *Withania somnifera*, is a revered herb in traditional Ayurvedic medicine. Commonly referred to as "Indian ginseng" or "winter cherry," Ashwagandha has a history deeply rooted in ancient healing practices. This adaptogenic herb is valued for its potential to help the body cope with stress and promote overall well-being. The active compounds in Ashwagandha, including withanolides, are believed to contribute to its therapeutic effects. Research suggests that Ashwagandha may have a range of potential benefits, such as reducing stress, improving cognitive function, and supporting immune health. While Ashwagandha is generally considered safe for many individuals, it's essential to consult with healthcare professionals, especially if you have pre-existing medical conditions or are taking medications. As with any herbal supplement, individual responses may vary, and it's crucial to use it judiciously based on personalized health considerations [50, 51].

For an extended period, *Withania somnifera* has served as a traditional Rasayana herb. Its historical applications suggest its potential benefits in alleviating various human medical conditions, including but not limited to hypertension, stress, diabetes, asthma, and cancer [52].

In 2005, a research carried out by Ahmad and his coworkers on rats with PD, the researcher gave extract of Ashwagandha and observed, after 3 weeks the improvements on rat against PD [53]. This was also confirmed by RajaSankar *et al.*, 2009 who indicates that *Withania somnifera* (Ws) holds promise as a potential therapeutic agent for addressing oxidative damage, catecholamines, and abnormalities observed in mice with Parkinson's disease [54].

Turmeric (Curcuma longa):

Turmeric, scientifically known as *Curcuma longa*, is a vibrant golden spice celebrated for both its culinary and medicinal properties. A staple in many Asian cuisines, turmeric has gained global recognition for its active compound, curcumin, which contributes to its distinct color and potential health benefits, additionally; turmeric has been used to alleviate various ailments due to its anti-inflammatory and antioxidant properties. Research suggests that curcumin may have potential applications in conditions such as arthritis, digestive issues, and even cognitive function. Moreover, turmeric has found its place in modern wellness practices, with some studies exploring its potential role in supporting heart health and managing chronic conditions [55, 57].

In 2021, Nebrisi and his coworkers mentioned in their review that curcumin has potential beneficial approach in PD [57]. However, while initial studies in animal models have hinted at a safeguarding impact of curcumin on dopaminergic neurons, the direct advantages of curcumin in the progression of Parkinson's disease (PD) are not fully comprehended [58].

Other herbals contains and active compounds that could be used in Parkinson's therapy, among them are:

- Baicalein [59].
- *Erythrina velutina* [60].
- Resveratrol [61].
- *Peganum harmala* [62].
- *Curcuma longa* (Zingiberaceae) [63].
- *Pueraria lobata* [64].
- Juglandis Semen (Walnut) [65].
- Tianma Gouteng Yin (TGY) [66].

- *Lycium barbarum* L fruit [67].

The use of herbal remedies in Parkinson's therapy is an area of ongoing research and exploration. While some herbs show potential in managing certain aspects of Parkinson's disease (PD), it's crucial to approach herbal therapies with caution and in consultation with healthcare professionals. However, it's important to note that herbal therapies should not replace conventional treatments prescribed by healthcare providers.

CONCLUSIONS

While pharmacological interventions remain the cornerstone of Parkinson's disease management, the exploration of herbal remedies offers a complementary avenue. It is crucial for individuals with PD to consult with healthcare professionals before incorporating herbal treatments into their regimen, considering potential interactions and contraindications. Ongoing research in both pharmacological and herbal approaches provides hope for a more comprehensive and personalized management of Parkinson's disease in the future.

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