



Phytotherapeutic approaches in Parkinson's disease: Bioactive Compounds, neuroprotective mechanisms, and clinical perspectives

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Abstract

Parkinson's disease and other neurological disorders are a significant public health concern, with nearly a billion people globally suffering from them. It is a progressive neurodegenerative disorder characterised by the loss of dopaminergic neurons, leading to motor and cognitive dysfunction. Current therapies relieve symptoms but do not efficiently halt disease progression and may have deleterious effects in the long term. Consequently, there has been growing interest in using medicinal plants and their bioactive phytochemicals (such as polyphenols, terpenes, and alkaloids) as possible neuroprotectants. Preclinical studies have shown that these compounds modulate dopaminergic signalling, reduce oxidative stress and neuroinflammation, improve mitochondrial function and regulate metal ion homeostasis. However, most evidence is derived from preventive studies using toxin-induced models such as MPTP (1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine), 6-hydroxydopamine (6-OHDA), and rotenone, which only partially reproduce the progressive and multifactorial pathology of idiopathic human Parkinson's Disease. Moreover, clear evidence for disease-modifying efficacy in long-term clinical investigations remains lacking. This review provides an updated synthesis of medicinal plants, phytochemicals, neuroprotective mechanisms, and growing clinical evidence while addressing obstacles relating to standardisation, safety, regulatory considerations, and translational reliability. It also outlines major knowledge gaps and future research goals to assist the clinical incorporation of evidence-based phytotherapeutic therapies for Parkinson's disease.

Keywords: α -synuclein; medicinal plants; neurological disorder; Parkinson's disease; pathophysiology; phytochemicals.

Abbreviations: PD, Parkinson's disease; MPTP, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; 6-OHDA, 6-hydroxydopamine; MPP⁺, 1-methyl-4-phenylpyridinium; UPDRS, Unified Parkinson's Disease Rating Scale; ROS, reactive oxygen species.

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1. Introduction

Parkinson's disease, or idiopathic paralysis agitans, is a common neurodegenerative condition that impacts the central nervous system (CNS). About 1% of people over 65 have Parkinson's disease. It usually starts between the ages of 40 and 70, and the onset of PD before the age of 21 years is rare. Young-onset Parkinson's disease (YOPD) is commonly used to describe PD with symptom onset between the ages of 21 and 50 years, whereas juvenile-onset Parkinsonism is defined as onset of symptoms before age 21 years. Statistics show that men are 1.5 times more likely than women to have Parkinson's disease. This shows a significant difference between the two genders in terms of risk. Wilson's disease (WD) and Huntington's disease (HD) can also cause Parkinsonian symptoms (1, 2). The Global Burden of Disease (GBD) study estimated 1.02 million incident (new) cases of Parkinson's disease worldwide in 2017 (3). In 2016, an

estimated 6.1 million people were living with Parkinson's disease globally, and the age-standardised prevalence rate increased by 21.7% between 1990 and 2016 (4). Years Lived with Disability (YLDs) serve as a prevalent metric for assessing the severity of Parkinson's disease. YLDs indicate the duration and severity of disability caused by the disease. The age-standardized rates of premature mortality attributable to PD rose by 8.9% from 1990 to 2007, with a subsequent increase of 1.0% from 2007 to 2017 (5). Right now, more than one million people in the United States have Parkinson's disease, and this number may reach about 1.2 million by 2030. Each year, over 90,000 Americans are newly diagnosed, which is much higher than earlier estimates of about 60,000 cases a year. Experts expect the number of people diagnosed with Parkinson's disease to keep rising in the coming decades (6).

Parkinson's disease is a progressive neurodegenerative disorder that is characterised by increasing degeneration

and death of dopaminergic neurons in the substantia nigra, leading to decreased motor function. Neuroinflammation and oxidative stress are the main reasons why these dopamine-producing neurons are lost in different forms of Parkinson's disease. Anticholinergic drugs may be helpful for selected patients with Parkinson's disease who have tremor and rigidity, especially in the early stages of the disease. Their use is limited by cognitive and other adverse effects, especially in the older adult (7). So, we need new medicines that don't have the side effects and restrictions of modern medicine. Recently, more research has focused on traditional medicinal herbs and their extracts. Studies suggest that phytochemicals and plant extracts may help reduce symptoms of this disease. Their anti-inflammatory and antioxidant effects support neuronal health (8). Experimental studies suggest that curcumin, thymoquinone, polyphenols, and crocin may exert neuroprotective effects by reducing oxidative stress and neuroinflammation in experimental models of Parkinson's disease (9).

Professional pharmacopoeias have existed for about 200 years, and many modern medicines still derive from plant-based sources (10). The development of clinical and fundamental pharmacology is increasingly important in medicine, and traditional medicines are being used less. Natural products to treat many ailments, especially neurological and behavioural disorders, are still under investigation by scientists (11). Researchers are exploring the use of herbal medicines for neurological problems, as the active chemicals in these medicines can act on specific receptors in the brain. This highlights the possibility of using phytochemicals to create new or adjunctive treatments for neurodegenerative diseases. Evidence from studies in people and animals supports the use of therapeutic herbs (12). They are gaining popularity because of their safety, efficacy and lower cost than standard treatments. These herbal remedies for Parkinson's disease need to be tested extensively to determine their efficacy alone and in combination with other drugs (13). The review assesses the efficacy of herbal remedies in Parkinson's disease.

Several reviews have examined the therapeutic potential of medicinal plants and phytochemicals in Parkinson's disease. However, most current reviews focus on particular herbal medicines, single phytochemicals, or isolated neuroprotective processes, and there is a lack of integration of molecular targets, endocrine modulation, translational data, and clinical applicability. Moreover, there has not been a complete synthesis of recent breakthroughs in the understanding of phytochemical-mediated control of oxidative stress, neuroinflammation, mitochondrial dysfunction, protein aggregation and developing clinical data. The present study overcomes these limitations by giving an up-to-date and integrative overview of the phytotherapeutic techniques in Parkinson's disease. The text provides a critical discussion of medicinal plants and their bioactive constituents and describes various neuroprotective mechanisms. Preclinical and clinical evidence is sum-

marised, and safety issues and combination therapy with conventional anti-Parkinsonian drugs are assessed. Finally, the present challenges and future research priorities are highlighted. This review also covers a relatively underexplored topic: the effects of herbal treatments on hormonal systems relevant to Parkinson's disease. It examines the relationship between traditional knowledge and modern medicine by assessing the efficacy of plant-based remedies compared with known pharmaceutical therapies based on clinical evidence. This thorough synthesis provides a broader translational perspective that may aid the development of evidence-based phytotherapeutic approaches for Parkinson's disease.

2. Methodology

The present study was carried out as a structured narrative review aiming to systematically outline the available information on phytotherapeutic techniques for the treatment of PD, focusing on bioactive chemicals, neuroprotective mechanisms and clinical implications. This review is not a formal systematic review or meta-analysis, but a controlled and reproducible technique for searching the literature was used to provide transparency and minimise selection bias. Keywords such as Parkinson, compounds, disease, phytotherapy, Chinese traditional, herbal medicine, herb, phytochemicals, therapeutic, and pharmacological activities were used to obtain relevant information from online platforms, including Google Scholar, Web of Science, PubMed, Research4Life, Springer, and ScienceDirect.

The search strategy combined Medical Subject Headings (MeSH) where applicable and free-text keywords using Boolean operators. Studies were selected according to predefined inclusion and exclusion criteria. Inclusion criteria include original research articles published in peer-reviewed journals; *In vitro*, *in vivo*, and clinical studies investigating phytotherapeutic interventions for Parkinson's disease; Studies evaluating medicinal plants, plant extracts, isolated phytochemicals, or herbal formulations with demonstrated neuroprotective activity; Studies reporting molecular mechanisms, pharmacological effects, behavioural outcomes, or clinical efficacy relevant to Parkinson's disease; and Studies published in peer-reviewed journals in the English language were considered irrespective of the country of origin. Exclusion criteria include conference abstracts, editorials, commentaries, letters, book chapters, dissertations, and unpublished literature; Duplicate publications; Studies unrelated to Parkinson's disease or phytotherapeutic interventions; Studies lacking sufficient experimental or methodological information; and non-English publications (10).

All retrieved records were imported into a reference management software package, and duplicate records were removed. The authors independently evaluated potential eligible full-text articles. Disagreements were resolved through discussion and consensus. Reasons for exclusion

at the full-text stage included an irrelevant disease model, the absence of a phytotherapeutic intervention, insufficient experimental data, duplicate publication, or unavailable full text. The study selection process is presented using a PRISMA flow diagram (**Figure 1**). The relevant information from each eligible study was independently extracted by the reviewers using a standardized Microsoft Excel data extraction sheet. The extracted variables included: First author and publication year; Country of study; Study design (in vitro, in vivo, or clinical); Medicinal plant or herbal formulation; Bioactive compound(s); Experimental Parkinson's disease model; Intervention details and dosage;

Duration of treatment; Molecular targets and neuroprotective mechanisms; Major pharmacological findings; and Clinical relevance and limitations. The included studies were synthesised narratively and organised into thematic sections addressing (i) bioactive phytochemicals, (ii) neuroprotective mechanisms, (iii) preclinical evidence, and (iv) available clinical studies and future therapeutic perspectives. Following the literature search and screening process, 4589 records were identified across all databases. After duplicate removal and eligibility assessment, 74 studies fulfilled the predefined inclusion criteria and were included in the final qualitative synthesis.

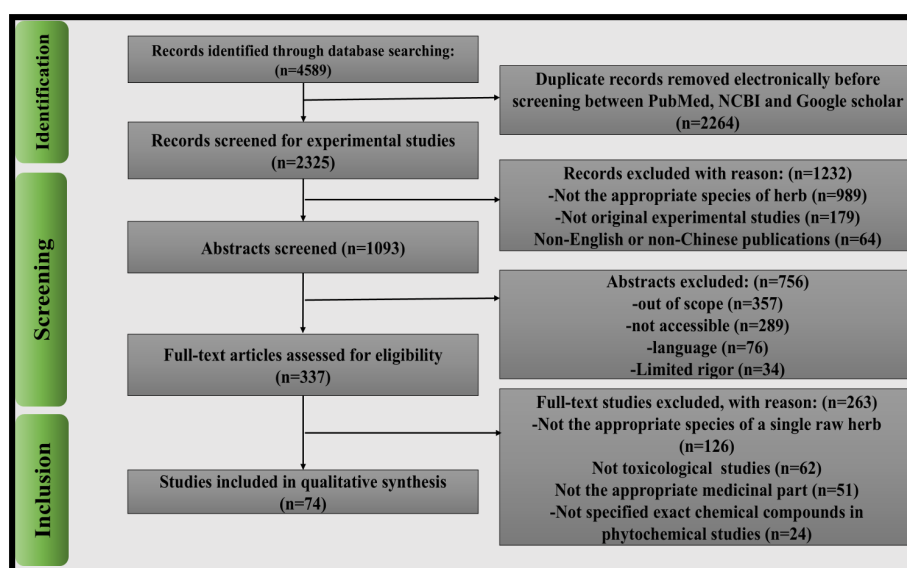


Figure 1: Picture showing PRISMA flow chart of the methodology.

2.1 Quality Assessment, Risk of Bias and Certainty of Evidence

As this evaluation was conducted as a structured narrative review, no formal study-level risk-of-bias assessment was carried out using techniques such as SYRCLE RoB, RoB 2 or the Newcastle–Ottawa Scale. However, methodological quality of included research was severely reviewed throughout data synthesis. Special attention was given to study design, phytochemical characterisation, botanical authenticity, experimental models, outcome measurements and reporting of statistical results. Several preclinical trials reported promising neuroprotective effects, but methodological flaws were often present, including poor extract standardisation, poor botanical authentication, small sample sizes, and a lack of reporting of randomisation and blinding. Moreover, the number of well-designed clinical studies is still low, hindering the translation of preclinical findings into clinical practice. These methodological issues have been raised throughout this study and underscore the need for more rigorous design of future investigations. As this is a structured narrative evaluation, a formal GRADE assessment was not undertaken. However, in evidence synthesis, the certainty and directness of evidence were taken into

consideration. Evidence from randomised clinical trials was seen as more direct and clinically relevant than evidence generated from animal or in vitro investigations. Evidence based purely on preclinical studies was considered with care due to the inherent constraints of converting experimental findings to human Parkinson's disease. These factors have been included throughout the debate and recommendations for further research (10).

3. Overview of Parkinson's disease

Parkinson's disease is the second most prevalent neurodegenerative disorder and the leading movement-related condition. It is marked by synucleinopathy, a pathological state involving damage to neurons in particular brain regions, leading to hallmark motor symptoms such as tremors, muscle stiffness, and postural instability. It has been noted that the nigrostriatal pathway's dopamine depletion is linked to the disease's progression. In order to control muscle function, dopamine links the corpus striatum with the substantia nigra. Motor abnormalities, including sluggish movement, resting tremor, and muscle rigidity, are characteristic of PD. In patients with Parkinson's disease, Lewy bodies,

which are abnormal intracytoplasmic protein inclusions primarily composed of aggregated α -synuclein, are a char-

acteristic pathological hallmark of the disease (14).

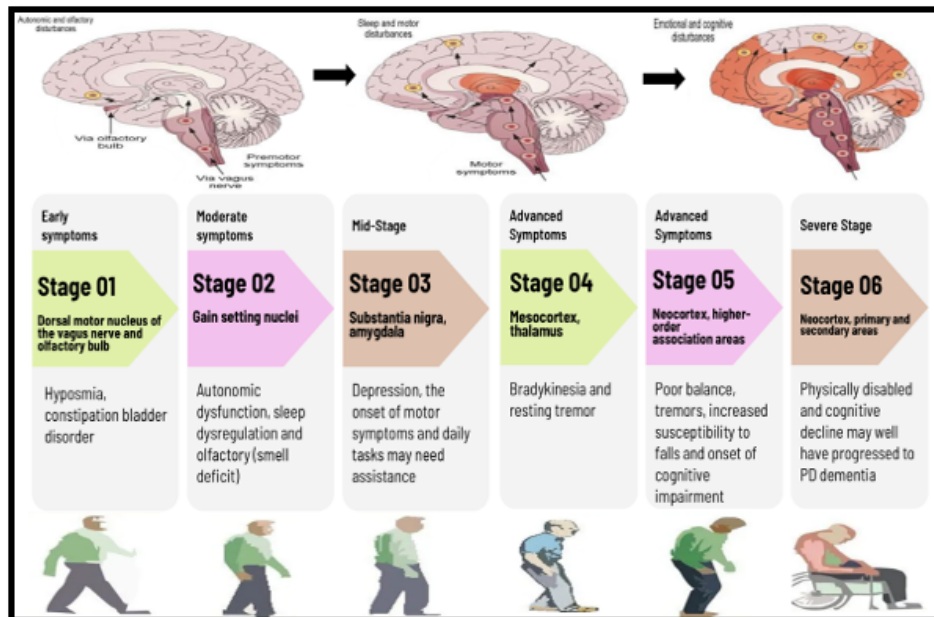


Figure 2: Flow chart of progression stages of PD. The progression of PD from its early or prodromal stage to its advanced phases, which are marked by severe motor and non-motor symptoms, is depicted in this Figure. Neuronal degeneration and increasing functional impairment are two important pathological and clinical characteristics associated with each stage, as highlighted in the flow chart. It offers a condensed synopsis of the disease's development to help comprehend PD's slow course and clinical symptoms (16).

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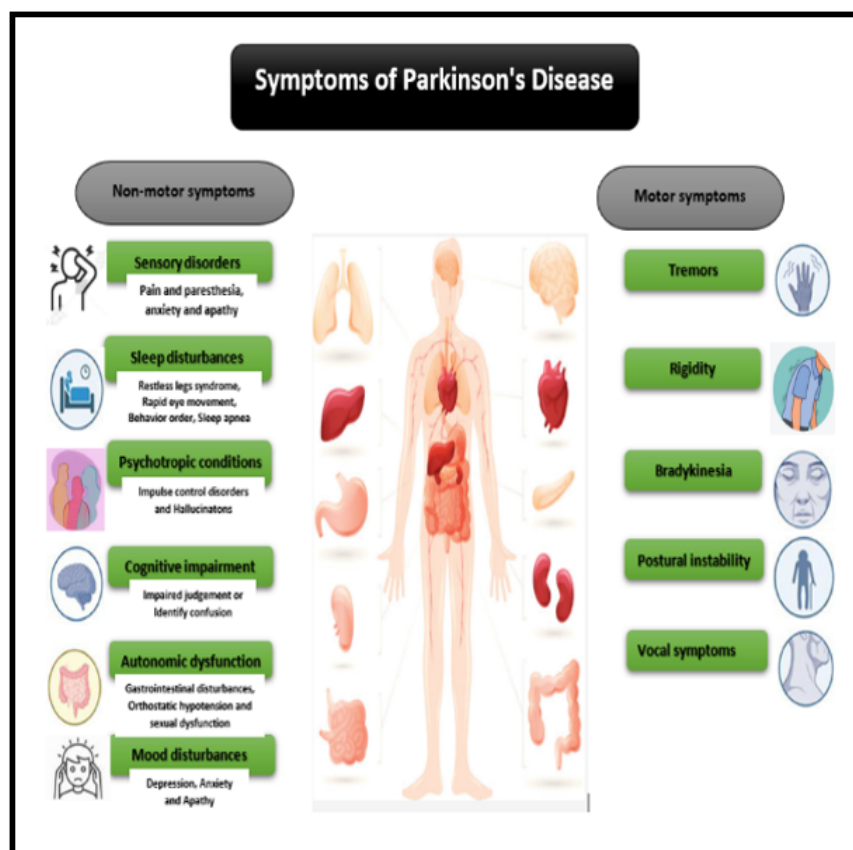


Figure 3: The variety of non-motor and motor symptoms that patients with Parkinson's disease experience (17,19).

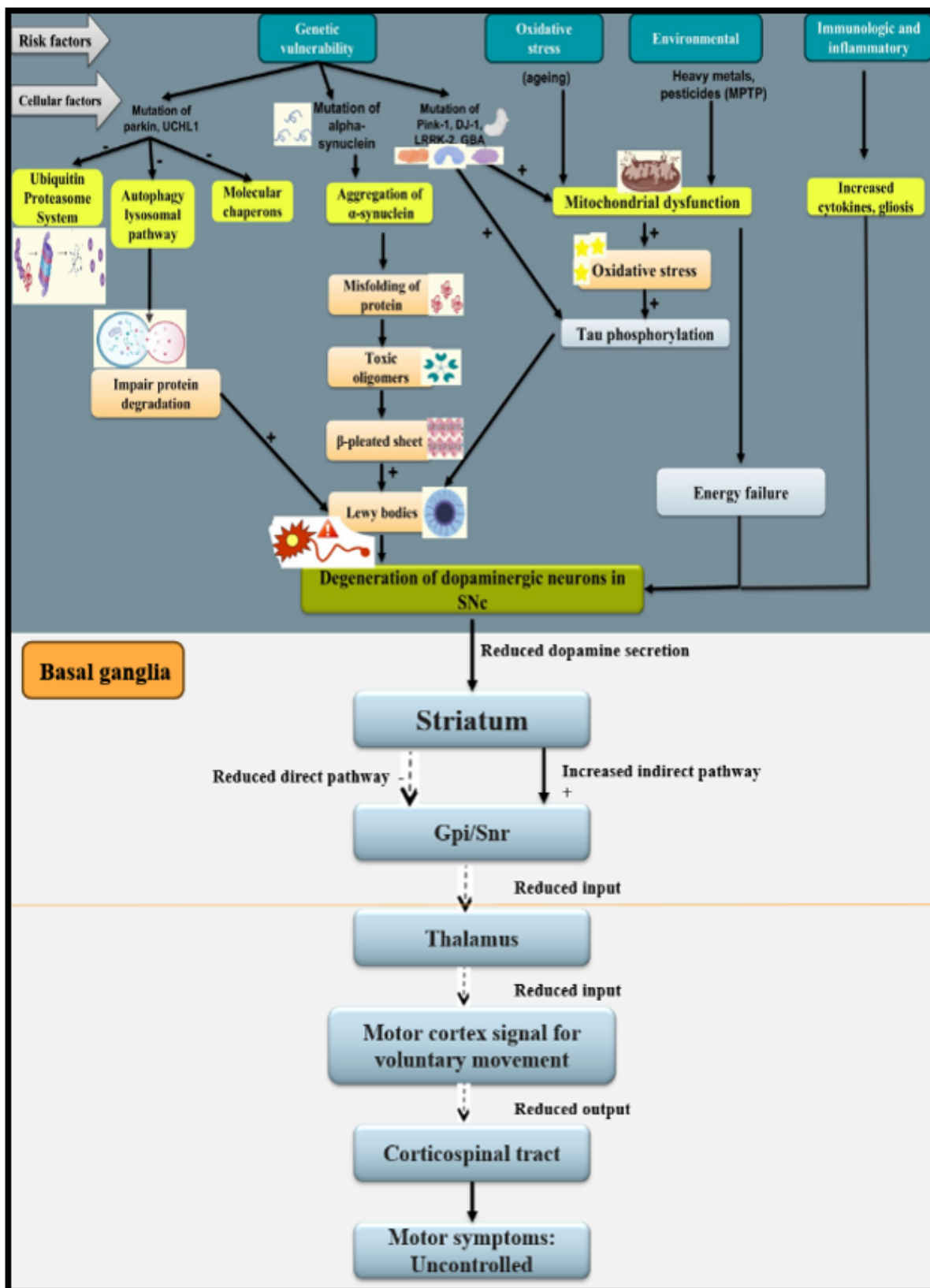


Figure 4: Mechanisms of neuroprotection by phytochemicals of medicinal plants in Parkinson's disease. The figure shows the modulation of oxidative stress, neuroinflammation, mitochondrial dysfunction, α -synuclein aggregation, apoptosis, and the survival of dopaminergic neurons by the major classes of phytochemicals (19).

3.1 Pathophysiology

Parkinson's disease is a progressive neurodegenerative disorder characterised by the selective degeneration of dopaminergic (A9) neurons within the substantia nigra pars compacta (SNpc), resulting in depletion of dopamine in the striatum. The disease is neuropathologically characterised by the presence of Lewy bodies, composed primarily of aggregated α -synuclein. Synuclein (syn) that has been truncated at the carboxy terminus congregates and accumulates in pathogenic inclusions. In addition to erythrocytes, neurons also exhibit haemoglobin (Hb) expression. PD-susceptible mesencephalic dopaminergic neurones possess a higher concentration of it than resistant neurones (15). Neuronal Hb is largely confined to cell bodies under normal conditions, including the cytoplasm, mitochondria, and nucleus. Nevertheless, when dopaminergic neurones were exposed to α -syn, the formation of the Hb α -syn complex was triggered in the cytoplasm and mitochondria. Reduced levels of free mitochondrial haemoglobin, haemoglobin aggregation within the nucleus, and impaired transport of haemoglobin from the cytoplasm to mitochondria have all been linked to the pathological development of Parkinson's disease and neuronal cell damage. Studies have demonstrated that overexpression of Hb increases cell susceptibility in an in vitro Parkinson's disease model and induces cytoplasmic and nucleolar aggregates in mice (16). **Figure 2** shows the schematic representation of the main pathogenic mechanisms involved in Parkinson's disease. Oxidative stress, mitochondrial dysfunction and neuroinflammation are involved in the progressive degeneration of dopaminergic neurons, leading to the onset and progression of motor and non-motor symptoms.

3.2 Symptoms of Parkinson's disease

Indicators of underlying nerve dysfunction in PD include a wide range of non-motor symptoms, including sleep disorders, autonomic irregularities, sensory abnormalities, neuropsychiatric problems, and cognitive deterioration. PD is a complicated disease that causes both motor and non-motor symptoms as it worsens, as seen in **Figure 3**. Based on the emergence of various symptoms, it can be divided into three stages: preclinical, prodromal, and clinical (17). Without any discernible clinical symptoms, a fixed neurodegeneration starts in the substantia nigra during the preclinical period. A prodromal phase follows, lasting over a decade and marked by persistent neuronal loss and specific non-motor symptoms.

The first stage of Parkinson's disease, which is followed by motor symptoms such as tremors, bradykinesia, and stiffness, occurs when 40–60% of dopaminergic cells stop functioning. Much research has demonstrated that some of the most important influencing elements for the preclinical stage are genetic, lifestyle and environmental factors. At stage 2, dopamine transporter scanning and synuclein lev-

els in peripheral tissue, blood, and cerebrospinal fluid are promising evidence for early PD diagnosis and detection (18). In the clinical stages, Lewy body formation and multiple system atrophy are ultimately identified as biomarkers. Multiple factors contribute to neurodegeneration in PD, as outlined in **Table 1** and **Figure 4**.

4. Therapeutic Plants and Bioactive Phytochemicals in PD

4.1 Therapeutic plants

For thousands of years, people have used herbal medicines made from natural plant materials or extracts to treat and prevent illnesses. For hundreds of years, traditional healing systems such as Ayurveda and Traditional Chinese Medicine (TCM) have used plant-based medicines to treat a wide range of illnesses, including neurodegenerative disorders (21). Before the pharmaceutical industry expanded in the 19th century, people mainly relied on herbal remedies for treatment. This makes them useful for finding new drugs today. Over time, many of these traditional medicines have been carefully refined, and in certain cases, they have even become part of modern medicine (22, 23).

The standard treatment for PD comprises levodopa, dopamine agonists, and surgical interventions such as deep brain stimulation. However, these traditional therapies can be expensive and carry several adverse effects. Furthermore, the majority approved medications for neurodegenerative diseases only treat clinical symptoms; they do not provide a cure. This emphasizes the need for new therapeutic approaches that aim to alter the pathways that contribute to neuronal dysfunction and death (23).

Herbal medicines and other complementary and alternative therapies have recently gained popularity as potential options for addressing multiple pathogenic pathways linked to neurodegeneration. It has been demonstrated that herbal remedies made from fruits, vegetables, and plants possess antioxidant, anti-inflammatory, and neuroprotective properties (6, 24). Advances in understanding the mechanisms underlying herbal remedies have made it increasingly feasible to pursue evidence-based treatment approaches for neurodegenerative diseases. High concentrations of other nutrients in medicinal plants confer health benefits and enhance nutritional value by modulating metabolic processes. Because of their various pharmacological properties, which may help reduce both non-motor and motor symptoms, these plants have attracted increasing attention as complementary therapies in PD management (25). **Table 2** presents the effectiveness of a few well-known medicinal plants that have been studied for their mechanisms of action in treating Parkinson's disease. These species were chosen for the wide range of functions they are credited with, which collectively have the potential to modulate pathophysiological processes linked to Parkinson's disease (**Figure 5**).

Table 1: The primary factors and their associated pathophysiological features in Parkinson's disease (6, 20).

S. No.	Main causes	Pathophysiological observations/ activity
1.	Protein misfolding	α -synuclein is a 140 amino acid presynaptic protein implicated in synaptic vesicle trafficking and neurotransmitter release. Genetic mutations and post-translational changes drive misfolding of α -synuclein into β -sheet-rich oligomers and fibrillar aggregates. There is growing evidence that these misfolded species may transmit from neuron to neuron in a prion-like manner and so contribute to the gradual neurodegeneration in Parkinson's disease.
2.	Mitochondrial dysfunction	Reduced mitochondrial Complex I activity, impaired mitophagy associated with PINK1 and Parkin mutations, mitochondrial dysfunction linked to DJ-1 deficiency, and altered mitochondrial dynamics (increased fission and oxidative stress) associated with LRRK2 mutations contribute to mitochondrial homeostasis disruption and the pathogenesis of Parkinson's disease.
3.	Lysosomal disorders	Impaired lysosomal function results in failure to degrade misfolded α -synuclein, which further promotes α -synuclein aggregation and contributes to PD pathogenesis.
a.	Autophagy-Lysosomal Pathway	This pathway is crucial for maintaining α -synuclein proteostasis. This disorder impairs α -synuclein clearance, causing toxic accumulation and propagation, which further disrupts lysosomal biogenesis in a vicious cycle. Parkinson's disease is marked by defects in macro, micro, and chaperone-mediated autophagy, with reduced LAMP2a and Hsc70 levels in the CNS.
b.	Glucocerebrosidase	GBA1 mutations reduce glucocerebrosidase (GCase) activity, causing lipid substrate buildup, disrupted autophagy, and α -synuclein accumulation, leading to Lewy bodies and neurodegeneration. Impaired GCase trafficking worsens lysosomal dysfunction, making the cycle of disease worse in Parkinson's disease.
c.	LRRK2	Mutant LRRK2 disrupts Rab protein-mediated vesicle trafficking, reduces Rab7 activity, and inhibits CMA by suppressing LAMP2a, impairing autophagy. As a result, α -synuclein builds up, dopaminergic neurons die, and oxidative stress occurs. Together, these changes contribute to the development of Parkinson's disease.
4.	Inflammation	Parkinson's disease is associated with chronic neuroinflammation characterised by activation of microglia and astrocytes, leading to the release of pro-inflammatory cytokines that contribute to dopaminergic neuronal damage.
a.	Microglia	Microglia exhibit dynamic activation states. Aggregated α -synuclein, PAMPs, DAMPs and LPS promote a predominantly pro-inflammatory (M1-like) phenotype in Parkinson's disease, resulting in persistent neuroinflammation and damage of dopaminergic neurons, whereas anti-inflammatory (M2-like) responses support tissue repair and neuronal survival.
b.	Astrocytes	Astrocytes exhibit reactive changes, including hypertrophy, increased GFAP expression, and a predominantly A1-like phenotype. These changes are associated with neuroinflammation, blood-brain barrier dysfunction, and dopaminergic neuronal injury in Parkinson's disease.
c.	TLRs	Misfolded α -synuclein is a DAMP and activates TLRs. TLR2 enhances microglial activation while TLR4 is involved in α -synuclein identification and clearance. Impaired TLR signalling leads to persistent neuroinflammation and dopaminergic neuronal loss.
d.	Pro-inflammatory Cytokines and Parkinson's Disease	Activated microglia emit pro-inflammatory cytokines such as TNF- α , IL-1 β , and IL-6 that enhance neuroinflammatory responses, which may lead to dopaminergic neuron damage. IL-1 β is a pro-inflammatory cytokine that enhances inflammatory signalling through IL-1 receptor activation and is associated with the development and progression of Parkinson's disease.
5.	Gut-Brain Axis Dysfunction	Disruptions in gut microbiota composition and heightened intestinal permeability ("leaky gut") may trigger neuroinflammation and alpha-synuclein propagation.
6.	Calcium Dysregulation	Dysregulated calcium signalling, often due to mutations in calcium-related proteins, contributes to neuronal vulnerability.
7.	Blood-Brain Barrier Dysfunction	Increased blood-brain barrier permeability allows harmful substances to reach the brain, fueling inflammation and damaging neurons.

PINK1- PTEN-induced kinase 1; PAMP- pathogen-associated molecular pattern; DAMP- damage-associated molecular pattern; LPS- lipopolysaccharide; GFAP- glial fibrillary acidic protein; TLRs- Toll-like receptors; TNF- α -tumor necrosis factor-alpha; CMA- chaperone-mediated autophagy; GBA1- glucocerebrosidase 1; Hsc70- heat shock cognate protein 70; LAMP-2A- lysosome-associated membrane protein type 2A; LRRK2- leucine-rich repeat kinase 2; DJ-1,- Parkinsonism associated deglycase (protein DJ-1); GCase- glucocerebrosidase; IL-1 β -Interleukin-1 β ; and IL-1- Interleukin-1.

Several experimental investigations have shown the therapeutic potential of medicinal plants in Parkinson's disease, although the repeatability and generalizability of these results vary. Several well-studied phytotherapeutic agents such as *Panax ginseng*, *Curcuma longa*, *Camellia sinensis*, and *Withania somnifera* have consistently shown neuroprotective effects in independent investigations using different toxin-induced PD models, including MPTP, 6-hydroxydopamine (6-OHDA), and rotenone models. However, many additional medicinal plants have been tested in only one laboratory or one experimental paradigm, and this makes us less confident about the robustness of the stated efficacy. Moreover, most preclinical research has been performed in male rodents, with female animals being strikingly underrepresented in the literature, despite increasing awareness of sex-specific distinctions in the pathogenesis and treatment responses in Parkinson's disease.

Evidence from genetic models of Parkinson's disease, such as α -synuclein- or LRRK2-based models, and validation in large-animal systems is likewise very limited. Therefore, although existing preclinical data provide robust evidence to support the neuroprotective potential of several medicinal plants, future studies should focus on independent replication, inclusion of both sexes, and validation across multiple species and complementary models of Parkinson's disease to enhance the translational reliability of these findings.

Importantly, reporting of experimental factors, including animal sex, strain, age and laboratory-to-laboratory repeatability, is varied across the published literature. Standardised study designs and multicenter preclinical validation would increase the reliability and comparability of future investigations.



Figure 5: Various plants are used to treat Parkinson's disease. (Source: Google)

Table 2: The effects of different plants in treating Parkinson's disease.

S. No.	Plant name	Family	Study Design and Model	Doses used	Principal findings	Limitation	Reference
1.	<i>Allium sativum</i> L. (Garlic)	Amaryllidaceae	Animal study (MPTP-induced mice)	100–500 mg/kg	↑ Dopamine synthesis, ↑ locomotor function, ↓ lipid peroxidation and superoxide formation, and ↑ SOD activity.	Only preclinical evidence reported.	14
2.	<i>Alpinia oxyphylla</i> L. (Sharp-leaf galangal)	Zingiberaceae	Preclinical (animal + cell-based) (6-OHDA or MPTP-induced neurotoxic rodent models; 6-OHDA-treated PC12 cells)	100–400 mg/kg/day	Decreased cellular apoptosis, repaired dopaminergic (DA) neurone degeneration, improved the lifespan of PC12 cells treated with 6-OHDA, and reduced the locomotor deficits.	Mixed animal and cell-based evidence; no clinical validation reported.	26
3.	<i>Angelica sinensis</i> (Oliv.) Diels (Female ginseng)	Apiaceae	Experimental study (6-OHDA-induced <i>C. elegans</i> models)	50 µM	Induction of Autophagy.	Evidence limited to an invertebrate experimental model.	27
4.	<i>Asparagus racemosus</i> Willd. (Shatavari)	Asparagaceae	Preclinical study <i>C. elegans</i> and Mice model	200 mg/kg	Upregulated pdr-1, ubc-12, and pink-1, reduced α-synuclein aggregation and lipid accumulation, decreased lipid peroxidation and protein carbonyl content, increased GPx and GSH levels, and modulated ubiquitin-proteasome system	Preclinical evidence only; no human studies reported.	26
5.	<i>Bacopa monnieri</i> (L.) Wettst. (Brahmi)	Plantaginaceae	Animal study (MPTP- and Rotenone-induced mice)	40–80 mg/kg	Reduced oxidative stress and apoptosis, enhanced Bcl-2 expression, increased dopamine levels, improved motor performance, reduced α-synuclein accumulation in the striatum, substantia nigra, and hippocampus.	Findings derived from toxin-induced animal models; translational relevance remains uncertain.	21
6.	<i>Buddleja cordata</i> Kunth (Butterfly Bush)	Scrophulariaceae	Animal study (MPP-induced rats)	1.5 mg/kg	Inhibition of MAO-A and MAO-B, suggesting reduced dopamine metabolism	Evidence limited to pre-clinical animal study; no clinical validation reported.	28
7.	<i>Cajanus cajan</i> (L.) Huth (Pigeon pea)	Fabaceae	Cell-based and zebrafish study (6-OHDA-induced SH-SY5Y cells and zebrafish model)	Up to 200 µM	Nrf2/ARE/HO-1 signalling cascade activation, indicating antioxidant and cryoprotective effects	Findings derived from cell-based and zebrafish models only.	26
8.	<i>Camellia Sinensis</i> (L.) Kuntze (Tea plant)	Theaceae	Preclinical in vivo and in vitro PD models	20 mg/kg	Prevents lipid peroxidation and shows antioxidant qualities.	Dose range and experimental conditions require verification from the primary study	24, 28
9.	<i>Cannabis sativa</i> L. (Marijuana)	Cannabaceae	Animal model (Male Sprague–Dawley rats and transgenic mouse model)	20 mg/kg/day	Increased expression of ubiquitin-like proteasomes and SOD-3, reduced dopaminergic neuron degeneration and apoptosis, preserved cell viability, improved motor function and protected substantia nigra.	Multiple experimental models used; individual study characteristics should be verified from the original publication.	21
10.	<i>Cassia obtusifolia</i> L. (Sickle pod)	Fabaceae	Cell-based and animal study (6-OHDA-induced PC12 cells; MPTP-induced PD mouse model)	100–400 mg/kg	ROS generation is decreased, and mitochondrial membrane depolarisation and MPP-associated mitochondrial dysfunction are attenuated.	Combined in vitro and in vivo findings; detailed methodological information should be extracted from the primary study.	27
11.	<i>Centella asiatica</i> (L.) Urb. (Indian Pennywort)	Apiaceae	Cell-based and animal study (LPS-induced BV2 microglial cells, MPP-induced SH-SY5Y cells and MPTP-induced PD mouse model)	10–100 nM	Protects dopaminergic neurons, reduces neuroinflammation, increases neurotrophic signalling (PI3K/Akt/mTOR) and reduces MAPK-mediated neuronal damage.	Only preclinical evidence.	14
12.	<i>Cinnamomum osmophloeum</i> Kaneh. (Indigenous cinnamon)	Lauraceae	In vitro models	25 µM	Prevents oxidative stress and improves antioxidant defence	Parkinson-specific animal validation limited in original accessible literature.	24
13.	<i>Citrus sinensis</i> (L.) Osbeck (Orange)	Rutaceae	Animal study (6- OHD-induced Parkinsonian rodent model)	100–400 mg/kg	Reduces LPS/IFN-induced TNF-α generation in glial cells and suppresses iNOS expression, p38, MAPK and STAT-1 activation.	Only preclinical study.	24
14.	<i>Coffea arabica</i> L. (Arabian coffee)	Rubiaceae	Cell-based and animal study (GLUTag cell line and rotenone-induced PD mice).	1, 5, 10, 20, 40, and 100 g/mL; 50 mg/kg	Serves as the secretagogue for GLP-1, reduced dopaminergic neuronal degeneration and improved motor performance through adenosine A2A receptor antagonism.	Most evidence concerns caffeine rather than whole plant extract.	20
15.	<i>Crocus sativa</i> L. (Saffron)	Iridaceae	Animal study (6- OHD-induced rat model)	30-50 mg/kg	Protection of dopaminergic cells, increase TH levels and inhibition of cell death of neurons	Only preclinical study.	14
16.	<i>Curcuma longa</i> L. (Turmeric)	Zingiberaceae	Cell-based and Animal study (SH-SY5Y cells, MPTP-, rotenone- and 6-OHDA-induced rodent model)	0.001-0.4 mg/ml and 50-200 mg/kg	Inhibition of the brain's MAO-A enzyme, reduces mitochondrial ROS formation, attenuates salsolinol-induced toxicity, down-regulates caspase-3 activity, increases dopamine and serotonin levels, amelioration of mitochondrial dysfunction and cognitive impairments, reduction of neurological impairments and an increase in the ischaemia-reperfusion NeuN-labeled neurones.	Evidence derived from multiple experimental models; standardisation of curcumin formulations and doses remains limited.	29
17.	<i>Delphinium denudatum</i> Wall. (Jadwar)	Ranunculaceae	Animal study (6-OHDA, rotenone or MPTP-induced PD models in rodents)	50–200 mg/kg	Decreased levels of malondialdehyde (MDA), elevated GSH, CAT and SOD activity, elevated dopamine levels and improved motor impairment by attenuating oxidative stress.	No clinical validation; findings limited to experimental animal studies.	28

S. No.	Plant name	Family	Study Design and Model	Doses used	Principal findings	Limitation	Reference
18.	<i>Eleutherococcus senticosus</i> (Rupr. & Maxim.) Maxim. (Devil's Bush)	Araliaceae	Animal study (MPTP+-induced mouse model)	4.5 g/kg	Improved locomotor performance and protected nigrostriatal dopaminergic neurons through multitarget neuroprotective mechanisms.	Evidence based on a limited number of preclinical investigations.	26
19.	<i>Geranium robertianum</i> L. (Herb-Robert)	Geraniaceae	Cell culture study (MPP+-induced SH-SY5Y cell)	0–200 µg/mL	Reduced intracellular ROS, inhibited apoptosis and improved neuronal viability, demonstrating antioxidant and cryoprotective properties.	Findings restricted to an in vitro neuronal model.	28
20.	<i>Ginkgo biloba</i> L. (Maidenhair tree)	Ginkgoaceae	In vitro study (KCl-induced SH-SY5Y cells)	10, 40, and 80 µM	Promoted autophagic clearance of α -synuclein aggregates, thereby reducing neuronal toxicity and improving cell survival.	Mechanistic evidence available; further in vivo and clinical validation is required.	30
21.	<i>Glycine max</i> (L.) Merr. (Soybean)	Fabaceae	Animal study (Wistar rat model of PD)	10–100 mg/kg	Reduced cell death and genotoxicity by modulation of the RAGE/LRP-1 pathway, resulting in improved neuroprotection and behavioural recovery.	Evidence limited to experimental studies.	28
22.	<i>Juglans regia</i> L. (Walnut)	Juglandaceae	In vitro and in vivo study (6-OHDA- and MPTP-induced rodent models; rat C6 astrocyte cells)	100–500 mg/kg; 50–200 µg/ml	Prevented the degeneration of neurons caused by 6-OHDA, inhibited the activity of MAO-B, reduced oxidative stress and improved neuronal survival.	Considerable methodological heterogeneity among experimental studies.	24
23.	<i>Morus alba</i> L. (White mulberry)	Moraceae	In vitro and in vivo study (6-OHDA-mediated neurotoxic cell models and rodent PD models)	200–400 mg/kg	Reduces bradykinesia and dopaminergic neuronal damage in the substantia nigra, stabilises mitochondrial membrane potential, and regulates the expression of apoptosis-related proteins such as Bcl-2, Bax, and caspase-3.	No human clinical studies available to validate neuroprotective efficacy.	28
24.	<i>Mucuna pruriens</i> (L.) DC. (Velvet bean)	Fabaceae	Animal and clinical studies (6-OHDA-induced mice, MPTP-induced rats).	400 mg/kg; 2.5; 5 g/kg/day; 15–30 g	Replenishment of endogenous neurotransmitters in the substantia nigra, including serotonin, dopamine, and norepinephrine, showed rapid onset of action and produced antiparkinsonian effects comparable or superior to conventional levodopa therapy.	Clinical evidence remains limited by relatively small sample sizes and short treatment periods.	31
25.	<i>Myrica esculenta</i> Buch. Ham. ex D. Don (Hairy Bayberry)	Myricaceae	Animal study (Haloperidol-induced rats)	50, 100, and 200 mg/kg	Increased endogenous antioxidant defence, reduced oxidative stress and improved behavioural abnormalities associated with parkinsonism.	Evidence restricted to single experimental model; clinical validation is lacking.	28
26.	<i>Nigella sativa</i> L. (Black cumin)	Ranunculaceae	Animal and clinical studies (Perphenazine-induced mice, haloperidol-induced rats and patients with PD)	100–500 mg/kg	Reduction of catalepsy, increase in GSH content, reduction in lipid peroxidation and nitrite levels, enhancement of the muscular rigidity, enhancement of cognition, attention and memory, reduction in mood stabilisation, anxiety, and cognitive modulation.	Clinical evidence is limited and heterogeneous with respect to study design and treatment duration.	14
27.	<i>Panax ginseng</i> C.A. Mey. (Asian ginseng)	Araliaceae	Animal study (MPTP-induced rat model)	100–400 mg/kg	Decreased T-cell infiltration and increased expression of glutathione cysteine ligase regulatory and modulatory subunits lowered ROS production, activated the Wnt/ β -catenin signalling pathway, and provided neuroprotection against MPTP-induced toxicity.	Evidence largely restricted to experimental animal studies; additional clinical validation is required.	26
28.	<i>Polygonum cuspidatum</i> Siebold & Zucc. (Japanese Knotweed)	Polygonaceae	Animal study (6-OHDA-induced mice and male Wistar rats)	10–100 mg/kg	Alleviated DA depletion, upregulated antioxidant enzyme status, reduced oxidative stress and improved behavioural deficits, primarily attributed to resveratrol-rich constituents.	Neuroprotective effects are mainly attributed to resveratrol; contribution of whole-plant extract requires further investigation.	32
29.	<i>Polyscias fruticose</i> (L.) Harms (Ming tree)	Araliaceae	In vivo study <i>Drosophila melanogaster</i> (dUCH knock-down model)	1–16 mg/mL	Reduced the degradation of dopaminergic neurons, improved locomotor activity and demonstrated neuroprotective effects through modulation of oxidative stress pathways.	Findings are based primarily on a <i>Drosophila</i> model and require validation in mammalian systems.	27
30.	<i>Psidium guajava</i> L. (Guava)	Myrtaceae	Animal study (MPTP-induced PD mouse models)	5–50 mol/L	Reduced dopamine depletion and attenuated behavioural abnormalities, protected dopaminergic neurons and improved motor coordination through antioxidant mechanisms.	Limited number of experimental studies and absence of clinical evidence.	28
31.	<i>Rosmarinus officinalis</i> L. (Rosemary)	Lamiaceae	In vitro and in vivo study (6-OHDA-lesioned rat model, MPTP Model)	50–150 mg/kg, 100–200 mg/kg	Boost DA levels, control the Bcl-2/Bax ratio, protect matrix metalloproteases by reducing intracellular ROS production, and increase cell survival.	Evidence is derived primarily from preclinical studies; clinical efficacy remains unverified	33
32.	<i>Salvia miltiorrhiza</i> Burge (Red Sage)	Lamiaceae	In vitro and in vivo study (MPP+ or 6-OHDA-induced neuronal models)	20 or 40 µg/mL	Maintaining ROS levels, releasing changes in the nuclear morphology of cells, reducing the Bax/Bcl-2 ratio and caspase-3 activation.	Most available evidence is limited to experimental cellular and animal models.	27

S. No.	Plant name	Family	Study Design and Model	Doses used	Principal findings	Limitation	Reference
33.	<i>Schisandra chinensis</i> (Turcz.) Baill. (Chinese Magnolia wine)	Schisandraceae	Cell-based and animal study (6-OHDA-induced SH-SY5Y cells and mice)	100 µM	Prevents miR-34a from negatively modifying the Nrf2 pathway, resulting in reduced oxidative stress and enhanced neuronal survival.	Mechanistic evidence is promising but requires validation in clinical studies.	27
34.	<i>Scutellaria baicalensis</i> Georgi (Baikal skullcap)	Lamiaceae	In vitro and in vivo study (Multiple MPP+ and MPTP-induced Parkinson's disease)	Up to 500 mg/kg	Activated Nrf2/MEF2D signalling, inhibited Bax and cleaved caspase-3 expression, increased Bcl-2 levels, enhanced striatal dopamine concentration and promoted neurotrophic factor production.	Considerable heterogeneity exists among experimental models and treatment regimens.	27
35.	<i>Sida cordifolia</i> Forsk. (Bala)	Malvaceae	Animal study Rotenone-induced Parkinsonian rat model	500 mg/kg	Reduces ROS levels, inhibits pro-inflammatory cytokines such as TNF-α and IL-6, protects nigral dopaminergic neurons, and improves behavioural deficits.	Neuroprotective efficacy has not yet been confirmed in human clinical trials.	28
36.	<i>Sphaerocoryne affinis</i> (Teijsm. & Binn.) Ridl. (Romdoul)	Annonaceae	In vitro and in vivo study (DPPH antioxidant assay and fly model of PD)	3, 6, 12, and 18 mg/mL	Demonstrated potent antioxidant activity, reduced locomotor deficits and protected dopaminergic neurons against degeneration in the fly model.	Evidence is limited to antioxidant assays and a <i>Drosophila</i> model; mammalian validation is lacking.	28
37.	<i>Uncaria rhynchophylla</i> (Miq.) Miq. (Cat's claw)	Rubiaceae	In vitro and in vivo study (SH-SY5Y cell line, MPP+ or 6-OHDA-induced Mouse models)	50–200 mg/kg	Preserved neuronal viability, restored GSH levels, attenuated dopaminergic neuronal loss and reduced apomorphine-induced rotational behaviour through antioxidant and anti-apoptotic mechanisms.	Most available evidence is preclinical; clinical studies are unavailable.	27
38.	<i>Withania somnifera</i> (L.) Dunal	Solanaceae	Animal study (Parkinsonian mouse model)	300 mg/kg/day	Upregulated TH expression in the SN region, reduced oxidative stress, preserved dopaminergic neurons, and improved motor performance.	Neuroprotective efficacy in large, well-designed clinical trials.	34, 35
39.	<i>Zingiber officinale</i> Roscoe (Ginger)	Zingiberaceae	Animal study (Rat model of Parkinsonism)	500, 1,000, and 1,500 mg/day	Attenuated dopamine depletion, normalised dopamine metabolites (homovanillic acid and DOPAC), enhanced endogenous antioxidative defences, and reduced oxidative damage.	Evidence is primarily derived from experimental animal studies with heterogeneous treatment protocols.	36

6-OHDA- 6-hydroxydopamine; MPTP- 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; MPP- 1-methyl-4-phenylpyridinium; LPS- lipopolysaccharide; SH-SY5Y- human neuroblastoma cell line; BV2- murine microglial cell line; PC12- rat pheochromocytoma cell line; ROS- reactive oxygen species; MAO-A- monoamine oxidase A; MAO-B- monoamine oxidase B; Nrf2- nuclear factor erythroid 2-related factor 2; ARE- antioxidant response element; HO-1- heme oxygenase-1; SOD- superoxide dismutase; CAT- catalase; GSH- reduced glutathione; GPx- glutathione peroxidase; TH- tyrosine hydroxylase; TNF-α- tumour necrosis factor-α; IL- interleukin; COX-2- cyclooxygenase-2; NOS- nitric oxide synthase; iNOS- inducible nitric oxide synthase; DOPAC- 3,4-dihydroxyphenylacetic acid; HVA- homovanillic acid; DA- dopamine; PDR-1- Parkinson's disease-related protein 1; UBC-12- ubiquitin-conjugating enzyme 12; PINK1- PTEN-induced kinase 1; BCL-2- B-cell lymphoma 2; PI3K/Akt/mTOR- phosphoinositide 3-kinase/protein kinase B/mechanistic target of rapamycin; MAPK- mitogen-activated protein kinase; MDA- malondialdehyde; RAGE/LRP1- receptor for advanced glycation end products/low-density lipoprotein receptor-related protein 1; miR-34a- microRNA-34a; and MEF2D- myocyte enhancer factor 2D.

4.2 Bioactive Compounds for the Parkinson's Disease Treatment

Polyphenolic compounds

Daily use of polyphenols has demonstrated beneficial effects, providing defence against several illnesses. Polyphenols have strong antioxidant properties and improve endothelial function (27). An essential component in protecting against diseases including Parkinson's, diabetes, cancer, Alzheimer's, and cardiovascular disorders is the consumption of polyphenols through food. These chemicals also have properties that protect the liver, kill bacteria, and reduce inflammation, underscoring their benefits for human health (20). Moreover, studies have shown that a diet rich in polyphenols restores synapsin 1-dependent synaptic plasticity and brain-derived neurotrophic factor (BDNF) levels. These results support the role of polyphenols in enhancing neurogenesis in the hippocampus, as well as memory and learning abilities. Consequently, polyphenols contribute to the preservation of brain health by directly influencing the CNS and enhancing supportive systems. Recent studies have rigorously investigated several polyphenols for their potential neuroprotective effects in Parkinson's disease, highlighting promising avenues for further research and

therapeutic development (37).

The polyphenolic compound curcumin, known as diferuloylmethane, is derived from the rhizome of the plant *Curcuma longa*. It has several biological functions. Among its notable attributes are its antioxidant, anti-inflammatory, and metal-chelating properties, which may mitigate inflammation and oxidative stress in the brain (29). Extensive preclinical research on animal models of Parkinson's disease shows that curcumin can protect dopaminergic neurons from degeneration and help with movement problems. Resveratrol, a polyphenolic component, has attracted interest for its possible neuroprotective effects in many neurodegenerative illnesses, including Parkinson's disease. Resveratrol, a bioactive compound present in grapes, berries, and several other plant sources, has attracted considerable attention for its neuroprotective properties. Studies have shown that it can reduce oxidative stress, enhance dopamine levels, and protect dopaminergic neurons from degeneration in experimental models of Parkinson's disease (32). Zingerone, found in ginger rhizomes, has shown promise in protecting nerve cells in laboratory studies. It can suppress pro-inflammatory markers, including interleukin-1β (IL-1β) and glial fibrillary acidic protein. This

helps prevent astrocyte activation and protects hippocampal nerve cells from damage under LPS-induced stress. Pre-treatment with zingerone has also been linked to higher dopamine levels in the nigrostriatal pathway, which may help protect against nerve cell loss and ease Parkinson's symptoms (36). In addition to resveratrol, the compounds listed in **Table 3** exhibit protective effects against neuronal damage, inflammation, and oxidative stress. These results suggest they could be useful as therapeutic agents for managing Parkinson's disease.

Alkaloids

Alkaloids are a class of natural compounds with diverse medicinal applications. In recent years, there has been growing interest in using plant-derived alkaloids to treat this disease (38). Researchers are investigating these molecules as potential novel therapeutics because they exert a wide range of effects on living organisms (39). Some of these alkaloids, such as acetylcorynoline, have shown significant biological effects. Acetylcorynoline, a compound from *Corydalis bungeana*, protects neurons in experimental models of Parkinson's disease. It protects dopaminergic neurons, decreases the build-up of α -synuclein and restores dopamine levels. These effects are believed to be mediated at least in part by up-regulation of rpn-5, a proteasome regulatory subunit implicated in protein degradation, thus enhancing proteostasis and lowering neurodegenerative disease (40).

Terpenes

Terpenes are a diverse group of chemicals found in many plants and essential oils. Recent research suggests that some terpenes may help protect nerve cells, making them an important area of study for Parkinson's disease. Their potential to protect neurons has drawn attention because it could lead to new treatments for Parkinson's disease (37). Researchers are interested in studying the properties of these substances to find new ways of controlling diseases (41). Among the terpenes investigated, the most significant are carnosic acid and ginkgolide B. Carnosic acid, a compound mostly found in rosemary, has shown promising antioxidant capabilities in cellular models of neurodegeneration. It affects the enzymes superoxide dismutase, gamma-glutamylcysteine synthetase, and glutathione reductase, improving the body's defences. It triggers the Nrf2 signalling pathway and increases BDNF release, which protects and supports brain cells (33). It regulates intracellular calcium levels, suppressing caspase-3 and apoptosis. Ginkgolide B is another active diterpene of *Ginkgo biloba* that has several protective effects on nerve cells. It helps control calcium levels inside cells, thereby inhibiting caspase-3 activation and cell death. *Ginkgo* mRNA expresses the D28K-binding protein, which helps nerve fibres grow in dopamine-producing neurons, potentially slowing disease progression. Lab investigations suggest that ginkgolide B restores calbindin D28K mRNA levels, supporting its protective properties. Terpenes modulate astrocyte activity, reduce oxidative damage, and prevent myelin loss. This makes them promising

treatments for the disease (30).

4.3 Herbal Remedies with Neuroprotective Properties Against Parkinson's Disease

Over the past few decades, numerous Chinese herbal formulations have been investigated in human trials and animal studies for the treatment of Parkinson's disease.

Banxia-Houpo-Tang (BHT): The traditional Chinese herbal remedy has been shown to improve the swallowing reflex in patients with Parkinson's disease and reduce the risk of pneumonia in patients with dementia (43). BHT reduced oxidative stress, as indicated by changes in malondialdehyde levels, although its effects on SOD levels were inconsistent. BHT also affects the blood lipid profile, particularly low-density lipoprotein cholesterol, inflammation, and other aspects of the immune system. Additionally, it influences hippocampal volume, which in turn affects neuroprotection, synaptic plasticity, neurogenesis, and BDNF expression (44).

Kami-Shoyo-San (KSS): It is made up of several medicinal herbs that are well-known in TCM and also helps individuals with Parkinson's disease who have tremors brought on by psychosis. KSS helps protect nerve cells by altering neuronal survival and increasing neurotrophic signalling. For instance, it can activate the BDNF pathway, which prevents neurons from dying or becoming toxic. Kami-Shoyo-San may improve neurological function and reduce motor problems in Parkinson's disease, suggesting it could be a useful additional treatment (45).

Bushen-Yanggan-Xifeng Decoction (BYX): Zhou et al. (46) found that Bushen-Yanggan-Xifeng Decoction can improve neuronal function in experimental models of Parkinson's disease by raising dopamine and serotonin levels in the striatum. This traditional recipe also helps protect dopaminergic neurons in the substantia nigra and has been shown to improve motor coordination and balance in animal tests.

Neuroinflammation is reduced, and neuron loss is stopped. These seem to be the main mechanisms. The decoction blocks key signalling pathways, such as NF- κ B and JNK. This lowers pro-inflammatory cytokines like TNF- α and IL-1. It also supports dopaminergic function by preserving tyrosine hydroxylase-positive neurons and regulating dopamine breakdown. These findings suggest that Bushen-Yanggan-Xifeng Decoction may help treat Parkinson's disease by acting on the brain to protect neurons, reduce inflammation, and alter neuronal function, thereby preventing neuronal death and improving movement.

Chuanxiong-Chatiao-Pulvis (CXCT): In rat models of MPTP-induced Parkinson's disease, Chuanxiong-Chatiao-Pulvis (CXCT) has been shown to improve motor symptoms and prevent the loss of dopaminergic neurons (47). Researchers have found that this mixture protects neurons from MPTP, a substance often used to induce Parkinson's disease in experimental models.

Table 3: Phytoconstituents and their effects on PD.

S. No.	Phytochemical class	Phytoconstituents	Botanical source	Potential Effects on Parkinson's disease	References
1	Polyphenols (Flavonoids)	Acacetin	<i>Chrysanthemum morifolium</i> Ramat.	Increased DA levels, dopamine-producing neuron cells, iNOS (inducible NO synthase), and increased (cyclooxygenase-2) glial activation.	28
2	Polyphenols (Flavonoids)	Baicalein	<i>Scutellaria baicalensis</i> Georgi	Reduces muscular tremor, enhances tyrosine hydroxylase (TH)-positive neurones, enhances neurite outgrowth of PC12 cells, and improves SH-SY5Y cell death.	26
3	Polyphenols (Flavonoids)	Epigallocatechin-3-gallate (EGCG)	<i>Camellia sinensis</i> (L.) Kuntze	An upregulation of reactivators such as SIRT1 protein expression, peroxisome proliferator-activated receptors (PPARs), and their coactivator PGC-1 α has been observed.	24
4	Polyphenols (Flavonoids)	Fustin	<i>Rhus verniciflua</i> Stokes	Reduces p38 phosphorylation, activation of Caspase3, ROS production, and the ratio of Bax/Bcl-2 to further aid in suppressing cell apoptosis.	5
5	Polyphenols (Flavonoids)	Genistein	<i>Glycine max</i> (L.) Merr.	Neuroprotection, anti-cancer, cardio protection, obesity prevention, antioxidant activity and anti-inflammatory effects.	28
6	Polyphenols (Flavonoids)	Kaempferol	<i>Ginkgo biloba</i> L.	Enhances cerebral blood flow and cognitive performance.	30
7	Polyphenols (Flavonoids)	Puerarin	<i>Pueraria montana</i> var. <i>lobata</i> (Willd.) Maesen & S.M.Almeida ex Sanjappa & Predeep	Neuroprotective effects and improves motor function	27
8	Polyphenols (Flavonoids)	Quercetin	Many fruits and vegetables	Increased dopamine and decreased protein carbonyl content	37
9	Polyphenols (Flavonoids)	Silymarin	<i>Silybum marianum</i> (L.) Gaertn. (Milk Thistle)	Demonstrates anti-inflammatory and antioxidant qualities.	42
10	Polyphenols (Flavonoids)	Theaflavin	<i>Camellia sinensis</i> (L.) Kuntze (Black tea)	Preventing the neurotoxicity caused by beta-amyloid and alpha-synuclein because of its possible antioxidant qualities.	26
11	Polyphenols (non-flavonoids)	6-Shogaol (6S)	<i>Zingiber officinalis</i> Roscoe	Avoids striatal dopamine depletion, MPTP-induced motor dysfunction, and destruction of dopaminergic neurones.	26, 36
12	Polyphenols (non-flavonoids)	Caffeic acid	<i>Coffea arabica</i> L. (Coffee, fruits, vegetables)	Prevent caspase-3 activation, limit the release of cytochrome c caused by Ca ²⁺ , and halt cell death.	24
13	Polyphenols (non-flavonoids)	Curcumin	<i>Curcuma longa</i> L.	Malondialdehyde decreased and catalase, glutathione, SOD, glutathione reductase, tyrosine hydroxylase, and other enzymes increased in brain tissue.	29
14	Polyphenols (non-flavonoids)	Ellagic acid	Various dicotyledonous plants	Reduced contralateral rotations, longer strides, and lower levels of IL-1 β and TNF- α in brain tissue	24
15	Polyphenols (non-flavonoids)	Gallic acid	<i>Vitis vinifera</i> L.	Lower malondialdehyde levels in brain tissue, raised GPx, raised total thiol in brain tissue, and improved passive avoidance memory.	24
16	Polyphenols (non-flavonoids)	para-Coumaric acid	<i>Solanum lycopersicum</i> L.	Inhibits apoptosis and the production of ROS, reduces axon degeneration in sciatic nerves.	24
17	Polyphenols (non-flavonoids)	Resveratrol	<i>Polygonum cuspidatum</i> Siebold & Zucc.	Decrease in 2, cytosolic SIRT1, phospho-JNK-1, and ROS production within the cell.	32
18	Polyphenols (non-flavonoids)	Rosmarinic acid	<i>Salvia miltiorrhiza</i> Burge	Boost DA levels, regulate the Bcl-2/Bax ratio, protect matrix metalloproteases by preventing intracellular ROS production, and increase cell survival.	27
19	Polyphenols (non-flavonoids)	Sesamol	<i>Sesamum indicum</i> L.	Encourage antioxidative defence mechanisms that limit transcription and eliminate free radicals.	28
20	Polyphenols (non-flavonoids)	Syringic acid	Edible plants and fruits (<i>Vitis vinifera</i> L.)	Decrease lipid peroxidation, improve GSH levels, and overcome pro-inflammatory cytokine expression, such as TNF-alpha, COX-2 enzyme, and interleukin (IL)-1.	24
21	Polyphenols (non-flavonoids)	Zingerone	<i>Zingiber officinalis</i> Roscoe	Depletion of dopamine and its byproducts, homovanillic acid and DOPAC, increases the antioxidative defenses, including hydroxyl action and superoxide scavenging.	36
22	Alkaloids	Acetylcholine	<i>Corydalis bungeana</i> Turcz.	Enhanced expression of the proteasome-governing component rpn-5 and enhanced proteasome-mediated protein degradation	40
23	Alkaloids	Isopelletierine	<i>Withania somnifera</i> (L.) Dunal	Exhibits antioxidant and anti-inflammatory properties	34, 35
24	Terpenes	Astaxanthine	<i>Adonis aestivalis</i> L.	Antioxidant, neuroprotective, anti-inflammatory	28
25	Terpenes	Astragaloside IV	<i>Astragalus membranaceus</i> Fisch.ex. Bunge	Besides facilitating neurite expansion and inhibiting dopaminergic neuron degeneration, it also elevated the levels of NOS and TH immune reactivities in dopaminergic neurones.	27
26	Terpenes	Beta-sitosterol	<i>Saraca indica</i> L.	Antioxidant properties	28
27	Terpenes	Betulinic acid	<i>Bacopa monnieri</i> (L.) Wettst.	Protects against neurodegeneration and demonstrates antioxidant qualities.	14

S. No.	Phytochemical class	Phytoconstituents	Botanical source	Potential Effects on Parkinson's disease	References
28	Terpenes	Carnosic acid	<i>Rosmarinus officinalis</i> L.	C-glutamate-cysteine ligase catalytic subunit protein expression was elevated; lipid peroxidation, GSH, apomorphine-induced rotation, locomotor activity, caspase 3 cleavage, poly (ADP ribose) polymerase (PARP) cleavage, and the Bcl-2/Bax ratio were all decreased.	33
29	Terpenes	Celastrrol	<i>Tripterygium wilfordii</i> Hook. f.	Dopaminergic neuron loss reduces the exhaustion of DA and DOPAC levels.	26
30	Terpenes	Ginkgolide B	<i>Ginkgo biloba</i> L.	Restoring the calbindin D28K mRNA protein.	30
31	Terpenes	Ginsenoside Rg1	<i>Panax ginseng</i> C.A. Mey.	Enhanced survival, cell viability was restored, Bax up-regulation was restored, Bcl-2 mRNA and protein expression was down-regulated, and 6-OHDA-induced apoptosis was attenuated.	27
32	Terpenes	Honokiol	<i>Magnolia officinalis</i> L.	Protecting against neurodegeneration and improving motor function	27
33	Terpenes	Salvinorin A	<i>Salvia divinorum</i>	Interfere with dopamine transporter function by interacting with the kappa opioid receptor.	5

DA- dopamine; TH- tyrosine hydroxylase; ROS- reactive oxygen species; SIRT1- sirtuin 1; PPARs- peroxisome proliferator-activated receptors; PGC-1 α - peroxisome proliferator-activated receptor gamma coactivator-1 alpha; Bax- Bcl-2-associated X protein; Bcl-2- B-cell lymphoma 2; PC12- rat pheochromocytoma cell line; SH-SY5Y- human neuroblastoma cell line; MPTP- 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; MPP- 1-methyl-4-phenylpyridinium; DPPH- 2,2-diphenyl-1-picrylhydrazyl; IL-1 β - interleukin-1 beta; TNF- α - tumour necrosis factor-alpha; GPx- glutathione peroxidase; GSH- reduced glutathione; SOD- superoxide dismutase; COX-2- cyclooxygenase-2; PARP- poly(ADP-ribose) polymerase; JNK- c-Jun N-terminal kinase; DOPAC- 3,4-dihydroxyphenylacetic acid; and NOS- nitric oxide synthase.

The main ways CXCT protects are through its strong anti-inflammatory and antioxidant effects. It helps keep neurons healthy in the substantia nigra, the part of the brain most affected by Parkinson's disease, by lowering oxidative stress and inflammation.

Chuanxiong-Chatiao-Pulvis (CXCT): In rat models of MPTP-induced Parkinson's disease, Chuanxiong-Chatiao-Pulvis (CXCT) has been shown to improve motor symptoms and prevent the loss of dopaminergic neurons (47). Researchers have found that this mixture protects neurons from MPTP, a substance often used to induce Parkinson's disease in experimental models. The main ways CXCT protects are through its strong anti-inflammatory and antioxidant effects. It helps keep neurons healthy in the substantia nigra, the part of the brain most affected by Parkinson's disease, by lowering oxidative stress and inflammation.

Huanglian-Jiedu Decoction (HJ): In a 2008 study, Jin et al. (48) demonstrated that the treatment protected PC12 cells against MPP-induced neurotoxicity, increasing cell survival, and suggesting a possible neuroprotective role. Research shows that Huanglian-Jiedu Decoction (HLJDD) protects nerve cells from damage caused by 1-methyl-4-phenylpyridinium (MPP), a toxin commonly used to mimic Parkinson's disease. This formula mainly reduces oxidative stress and protects dopaminergic neurons from damage through its anti-inflammatory and antioxidant effects. HLJDD also affects key cell-signalling pathways essential for neuronal survival. It helps regulate mitochondrial function and lowers inflammatory mediators.

The Liuwei-Dihuang Pill (LD): Additional studies have demonstrated that Liuwei-Dihuang-Pill provides protection to dopaminergic neurons against MPTP-induced toxicity in experimental models of Parkinson's disease. Its neuroprotective effects are largely attributed to its antioxidant and anti-apoptotic properties, which help reduce oxidative stress and maintain mitochondrial function in neuronal cells. Liuwei-Dihuang-Pill has shown effectiveness in alle-

viating motor impairments in Parkinsonian animal models and in sustaining dopamine levels in the striatum (49).

San-Huang-Xie-Xin-Tang (SHXXT): It has demonstrated a significant increase in the quantity of tyrosine hydroxylase-positive neurons in the substantia nigra pars compacta (SNpc) and enhancement of motor function in both in vitro and in vivo MPTP-induced Parkinson's disease models. Studies demonstrate that SHXXT helps maintain dopaminergic neurons in the substantia nigra, which are crucial for dopamine production. The formulation exhibits antioxidant and anti-inflammatory properties that mitigate oxidative damage and neuroinflammation, both of which are associated with neuronal death in Parkinson's disease (50).

Tianma-Gouteng-Yin (TGY): Multiple independent investigations on PD rats have shown that this formulation protects dopaminergic neurons from oxidative stress-induced death. The formula alters the functionality of inflammatory signalling pathways and enhances mitochondrial performance, thereby promoting neuronal survival (51).

Zhen-Wu-Tang (ZWT): It is a traditional remedy that has shown potential in MPTP-induced models of Parkinson's disease. It helps maintain dopamine levels and facilitates the expression of dopamine transporter mRNA. It improves motor symptoms by preserving dopaminergic neurons and stabilising dopamine metabolism. Its antioxidant and anti-inflammatory qualities can also lessen neuronal damage (52).

Zhichan-Soup (ZS): Zhichan-Soup has been shown to be advantageous for neuronal cell differentiation models of Parkinson's disease. Also seems to help repair injured brain nerve cells. This drug can enhance motor and cognitive skills by promoting neuronal survival and proliferation in the substantia nigra (53).

Jia-Jian-Di-Huang-Yin-Zi Decoction (JJDHYZ): It is a modified herbal preparation that has shown promising neuroprotective effects in animal models of PD. It helps restore

dopamine levels, reduce the loss of dopaminergic neurons, and increase the synthesis of glial cell line-derived neurotrophic factor (GDNF), thereby improving neuronal survival in MPTP-induced rats (54).

Bu-Shen-Jie-Du-Fang (BSJDF): It has long been utilized for motor issues. Recent research suggests that it may promote autophagic activity in MPP⁺-induced Parkinson's disease cell models (55). Promoting autophagy and reducing oxidative stress are favourable for neuronal survival and protect dopaminergic neurons from injury.

Hua-Feng-Dan (HFD): It's a complex traditional Chinese medicine formulation that involves minerals such as cinnabar (HgS) and realgar (As₄S₄), as well as plant-based substances. Experiments have shown that it can protect neurons, reduce dopaminergic neuronal death, and decrease neurotoxin-induced behavioural problems, including those induced by rotenone and lipopolysaccharide (LPS) (56). Its antioxidant and anti-inflammatory properties help to fight oxidative stress and neuroinflammation. However, Hua-Feng-Dan contains the mineral constituents of HgS and As₄S₄, which may lead to mercury and arsenic exposure. Hence, despite the claimed neuroprotective effects, the possible heavy metal toxicity has to be taken into consideration, and only standardised formulations with quality control and well-established safety profiles should be administered. Accordingly, the use of Hua-Feng-Dan requires careful risk-benefit assessment, particularly in vulnerable populations and during long-term administration. Long-term safety still has to be shown in further clinical research.

Some herbs, e.g., *Sida cordifolia* (Bala), combined with sesame oil, have long been used to treat nervous issues. An initial study suggests that its use, notably in massage with a therapeutic oil, may help patients with Parkinson's disease improve their motor function and overall quality of life. However, there is not much evidence at this time, and more well-designed clinical studies are needed to confirm that it is safe and effective. Overall, the traditional formulations appear to have neuroprotective, anti-inflammatory and neuromodulatory benefits, although robust clinical data is lacking. They must undergo complete, controlled clinical trials to determine whether they are safe and effective for treating Parkinson's disease. Additional study is needed to clarify their significance as adjunctive therapy alongside current treatments (Table 4) (57).

4.4 Herbal Interventions for Modulating Hormonal Systems in PD

Parkinson's disease is a complex disorder in which various hormonal systems become dysfunctional and dopamine-producing neurons are lost. Sex hormones (such as estrogen and testosterone) and neurohormones (such as dopamine, serotonin, cortisol and melatonin) are important for the proper functioning of the central and peripheral nervous systems. If these hormones are out of balance, people with PD may have problems with movement, mood,

and sleep. Alterations in various hormonal pathways have been described in Parkinson's disease; nevertheless, their precise contribution to disease development and their treatment potential remain under investigation. For thousands of years, herbal medicine has been used to treat many illnesses. Due to the bioactive constituents, plant-derived treatments are promising for the management of Parkinson's disease. Several phytochemicals have demonstrated antioxidant, anti-inflammatory and neuroprotective properties in experimental models, although evidence for direct hormonal modulation in Parkinson's disease remains limited. These compounds may help ease symptoms of Parkinson's disease, such as impaired neuronal function, altered hormonal responses to stress, and a slower rate of neurodegeneration (42).

4.5 Adaptogenic Herbs and Stress Hormones

Altered cortisol regulation has been reported in some patients with Parkinson's disease and may contribute to stress-related symptoms. There is great interest in the stress response and cortisol-regulation capacities of adaptogenic herbs which could enhance resistance to stress, thereby decreasing the mental and physical burden of neurodegenerative diseases. *Withania somnifera* (Ashwagandha) is a well-known adaptogen in Ayurvedic medicine believed to reduce cortisol levels and improve stress resilience (34). The plant's major active ingredients, especially withanolides, have anti-inflammatory properties that may help protect the central nervous system. Studies have shown that Ashwagandha improves motor function and reduces dopaminergic neuronal loss in rats with Parkinson's disease. Limited clinical evidence suggests improvement in selected non-motor symptoms; however, robust PD-specific evidence remains insufficient (35). Another adaptogenic herb, *Rhodiola rosea*, has been researched for its effects on the hypothalamic-pituitary-adrenal (HPA) axis and cortisol lowering. In animal models of Parkinson's disease, it may protect neurons by enhancing mitochondrial activity and lowering oxidative stress. This data suggests that *Rhodiola rosea* may lessen symptoms of Parkinson's disease. However, the evidence is currently limited to preclinical studies and its clinical relevance in PD remains to be established (10).

4.6 Sex Hormones and Parkinson's Disease

Sex hormones such as estrogen, testosterone, and others are all associated with the development and progression of Parkinson's disease. This is especially the case for women after menopause. So, scientists are looking at plant-based chemicals that might influence hormone levels and give some protection for the brain. Soybeans and soy products are sources of phytoestrogens called isoflavones, which can mimic some of estrogen's effects. These substances might protect nerve cells by regulating neurotransmitter systems and lowering oxidative stress.

Table 4: Traditional Chinese medicine compounds for the treatment of PD.

Name	Composition of TCM	Target	Efficacy	References
Banxia-Houpo-Tang	3 grams of <i>Poria cocos</i> , 6 grams of <i>Pinellia ternata</i> , 3 grams of <i>Magnolia obovata</i> , 2 grams of <i>Perilla frutescens</i> , and 1 gram of <i>Zingiber officinale</i>	Brain regions (cortex, hippocampus, striatum), microglial signalling, swallowing reflex pathways	Improves swallowing reflex in PD patients and reduces dysphagia risk; modulates neuronal signalling and may show antidepressant and neuroprotective effects	43
Kami-Shoyo-San	3 g <i>Paeonia lactiflora</i> , 1.5 g <i>Glycyrrhiza uralensis</i> , 3 g <i>Poria cocos</i> , 3 g <i>Angelica acutiloba</i> , 3 g <i>Bupleurum falcatum</i> , 2 g <i>Gardenia jasminoides</i> , 3 g <i>Atractylodes lancea</i> , 1 g <i>Zingiber officinale</i> , 2 g <i>Paeonia suffruticosa</i> , and 1 g <i>Menthae arvensis</i>	Neurotransmitter systems related to tremor and mood regulation	Reduces tremor and neuropsychiatric symptoms in Parkinsonian conditions	45
Bushen-Yanggan-Xifeng Decoction	15 g of <i>Rehmannia glutinosa</i> , 15 g of <i>Paeonia lactiflora</i> , 15 g of <i>Uncaria</i> spp., and 9 g of <i>Polygonum multiflorum</i>	Dopamine (DA) receptors, neurotransmitters (DA, 5-HT) in striatum	Enhances neurotransmitter levels and improves neuronal function in PD models	46
Chuanxiong-Chatiao-Pulvis	6 g of <i>Angelicae Dahuricae</i> Radix, 6 g of <i>Glycyrrhizae</i> Radix et Rhizoma, 12 g of <i>Schizonepeta tenuifolia</i> , 12 g of <i>Ligusticum chuanxiong</i> , 3 g of <i>Asari</i> Radix et Rhizoma, 12 g of <i>Mentha haplocalyx</i> , 4.5 g of <i>Saposhnikovia divaricata</i> , 6 g of <i>Notopterygii</i> Rhizoma et Radix, and 4.5 g of green tea	Cerebral blood circulation, neuroinflammation pathways	Improves cerebral circulation, reduces neuroinflammation, and alleviates headache, dizziness, and tremor-like neurological symptoms	47
Huanglian-Jiedu Decoction	<i>Radix scutellariae</i> , <i>Rhizoma coptidis</i> , <i>Fructus gardeniae</i> , and <i>Cortex phellodendri</i> with a weight ratio of 2: 3: 3: 2	Cellular apoptosis pathways; PC12 neuronal cells	Protects neuronal cells from MPP-induced injury and oxidative stress (OS)	48
Liuwei-Dihuang-Pill	9 g <i>Paeonia suffruticosa</i> , 12 g Corni Fructus Praeparata, 12 g <i>Dioscorea opposita</i> , 24 g <i>Rehmanniae</i> Radix Praeparata, 9 g <i>Alisma orientalis</i> and 9 g <i>Poria cocos</i>	Dopaminergic neuron survival, oxidative stress signalling	Reduces neuronal damage, suppresses oxidative stress-induced apoptosis, and improves motor activity in Parkinson's disease models	49
San-Huang-Xie-Xin-Tang	5 g <i>Scutellaria baicalensis</i> , 5 g <i>Coptis chinensis</i> and 10 g <i>Rheum officinale</i>	Tyrosine hydroxylase-positive neurons in substantia nigra (SNpc)	Increases TH-positive neurons and improves motor activity in PD mice	50
Tianma-Gouteng-Yin	12 g <i>Uncariae Ramulus cum Uncis</i> , 9 g <i>Fuling</i> she, 9 g <i>Gastrodia elata</i> Bl., 18 g <i>Haliotidis Concha</i> , 9 g <i>Eucommia ulmoides</i> Oliv., 9 g <i>Leonurus japonicus</i> Houtt, 12 g <i>Cyathula officinalis</i> Kuan, 9 g <i>Taxillus chinensis</i> (DC.), 9 g <i>Gardenia jasminoides</i> Ellis, and 9 g <i>Polygoni Multiflori</i> Caulis	Dopaminergic neuron apoptosis, Bcl-2/Bax signalling pathway	Prevents apoptosis of dopaminergic neurons, reduces OS, and improves motor function in Parkinson's disease models	51
Zhen-Wu-Tang	10 g <i>Zingiber officinale</i> , 10 g <i>Poria cocos</i> , 10 g <i>Atractylodes macrocephala</i> , 30 g <i>Paeonia lactiflora</i> , 10 g <i>Typhonium giganteum</i>	Mitochondrial function, neuronal energy metabolism	Maintains dopamine levels and DAT mRNA in PD animal models.	52
Zhichan-Soup	12 g <i>Salvia miltiorrhiza</i> , 10 g <i>Anemarrhena asphodeloides</i> , 18 g <i>Uncaria rhynchophylla</i> , 15 g <i>Astragalus mongholicus</i> , 15 g <i>Paeonia lactiflora</i> , 10 g <i>Gastrodia elata</i> , 9 g <i>Cimicifugae</i> Rhizoma	Neural stem cells (NSC) differentiation pathway	Promotes differentiation of neural stem cells and improves neuronal repair in PD models.	53
Jia-Jian-Di-Huang-Yin-Zi Decoction	<i>Cornus Officinalis</i> , <i>Rehmannia glutinosa</i> , <i>Cistanche deserticola</i> , <i>Paeonia lactiflora</i> , <i>Morinda officinalis</i> , <i>Asparagus cochinchinensis</i> , <i>Angelica sinensis</i> , with a weight ratio of 0.6: 1: 1: 1: 1: 1: 1	Dopamine metabolism, neurotrophic factors (GDNF)	Decreases apoptosis of dopaminergic neurons, restores dopamine levels, and increases GDNF, improving motor deficits	54
Bu-ShenJie-Du-Fang	<i>Cistanche deserticola</i> , <i>Rehmannia glutinosa</i> , <i>Puerariae</i> Radix, Antelope Horn Powder, <i>Glycyrrhiza uralensis</i> , <i>Paeonia lactiflora</i> Pall, <i>Scutellariae</i> Radix, <i>Angelica sinensis</i> , <i>Coptidis</i> Rhizoma, and with a weight ratio of 5: 5: 5: 1: 2: 4: 4: 4 contents	Autophagy signalling pathways	Enhances neuronal cell survival via activation of autophagy in PD cell models	55
Hua-Feng-Dan	Tianma (<i>Gastrodia elata</i>), Cangshu (<i>Atractylodes japonica</i>), Jingjie (<i>Nepeta cataria</i>), Tiannanxing (<i>Arisaema erubescens</i>), Jiangchan (<i>Bombyx batryticatus</i>), Baifuzi (<i>Aconitum coreanum</i>) and Quanxie (<i>Buthus martensii</i>)	Dopaminergic neuron survival; neuroinflammation	Improves tremor and motor dysfunction by modulating dopamine transmission and protecting neurons	56

OS- oxidative stress; DA- dopamine, GDNF- glial cell line-derived neurotrophic factor; and PD- Parkinson's disease

Experimental investigations reveal that phytoestrogens can affect dopaminergic signalling and oxidative stress pathways. Studies have also found they may help to lessen feelings of hopelessness and worry. *Tribulus terrestris* has been explored mostly for its effects on testosterone metabolism and androgen control, not as a direct therapeutic interven-

tion for Parkinson's disease. Although changes in sex hormones have been proposed to affect dopaminergic neurodegeneration, there is currently no evidence of a therapeutic effect of *T. terrestris* on Parkinson's disease symptoms or hormone-mediated neuroprotection in humans. Therefore, the possible involvement of *T. terrestris* in the

treatment of Parkinson's disease is yet hypothetical and should be validated by carefully designed pre-clinical research and appropriate randomised clinical trials (58).

4.7 Melatonin and Sleep Disorders in PD

Insomnia, restless legs, and frequent awakening are common sleep issues among people with Parkinson's disease. Melatonin, a hormone that regulates sleep cycles, may be associated with these problems. Some herbal therapies have shown the ability to improve sleep quality by influencing melatonin-related pathways and other neurotransmitter systems involved in sleep regulation. However, the exact effects of these interventions on melatonin secretion remain to be fully explored. Herbal sleep aids, such as valerian root (*Valeriana officinalis*), are quite common. It may improve sleep quality by modulating GABAergic and melatonin-related pathways. Many are turning to herbal remedies as safer alternatives to traditional sleep medications, since they tend to have fewer side effects. Studies on St. John's Wort (*Hypericum perforatum*) have suggested it may help with sleep. Its main targets are melatonin circuits and neurotransmitters like serotonin. It may also help reduce anxiety and despair, and help Parkinson's patients get to sleep. However, the existing clinical evidence is still limited, and these findings should be regarded with caution. Importantly, St. John's wort is a powerful inducer of cytochrome P450 enzymes (especially CYP3A4) and the drug transporter P-glycoprotein, which can change the pharmacokinetics and therapeutic efficacy of co-administered drugs. In addition, due to its serotonergic activity, simultaneous usage with antidepressants or other serotonergic drugs may raise the risk of serotonin syndrome. Thus, caution should be exercised in the use of St. John's wort in patients who are on conventional pharmacotherapy, and possible herb-drug interactions should be cautiously assessed before clinical use (59).

4.8 Insulin Regulation and Metabolic Health

Problems with insulin signalling may raise the risk of neuronal death. The new evidence links PD to insulin resistance. Insulin resistance and impaired glucose metabolism aggravate brain damage and highlight the need for metabolic management. Much research has examined the influence of several medicinal herbs on insulin sensitivity and glycemic management. *Cinnamomum verum* (cinnamon) has been studied for its effect on blood glucose lowering, insulin action, blood glucose level stabilisation, and oxidative stress. Cinnamon's metabolic and antioxidant actions suggest it may help address nerve damage and metabolic issues associated with Parkinson's disease. However, these observations are derived primarily from experimental studies, and clinical evidence in Parkinson's disease remains limited. The second herb is fenugreek, or *Trigonella foenum-graecum*, which helps manage insulin levels. The active ingredient responsible for the anti-inflammatory

and insulin-enhancing effects is 4-Hydroxyisoleucine. Experimental investigations have shown that fenugreek has insulin-sensitising and anti-inflammatory characteristics, but its therapeutic use in Parkinson's disease is yet exploratory and requires clinical validation (60).

5. Preclinical and Clinical Evidence for Phytotherapeutic Interventions

Preclinical research of plant-derived compounds with prospective therapeutic effects against Parkinson's disease has revealed very encouraging findings. We need human clinical trials to determine whether they are safe and effective for real people to use. These trials are needed to see if these phytochemicals can help patients. Clinical data can guide researchers and health care professionals in making informed decisions about potential applications of plant-based medications in the treatment of Parkinson's disease. These treatments can be better understood in terms of their efficacy through painstaking, extensive inquiry. In the long term, this may help to enhance treatment regimens for Parkinson's disease and patients' quality of life (61). Current data reveal that few phytotherapeutic drugs have been translated to human clinical evaluation, but several of them have shown potential neuroprotective effects in preclinical studies. The main clinical interventions studied to date are *Mucuna pruriens*, *Curcuma longa*, *Coffea arabica* (caffeine), *Cannabis sativa* (cannabidiol), *Vicia faba*, *Bacopa monnieri*, *Eleutherococcus senticosus* and *Apium graveolens* (DL-3-n-butylphthalide). **Table 1** summarises the available preclinical research and **Table 5** the available human clinical evidence.

5.1 Evidence from Human Clinical Trials

Because neither patients nor researchers in a placebo-controlled experiment know which group they are in, this kind of clinical trial is considered the most trustworthy. Participants are randomly allocated to receive either the real medicine or a placebo (61). With this method, we can learn more about the treatment's efficacy and safety while also reducing prejudice. Researchers have used placebo-controlled methods in several clinical trials to study plant-based therapies for Parkinson's disease. The results have been varied, with some randomised controlled trials reporting small improvements in selected motor or non-motor outcomes. Still, other investigations have revealed no statistically significant benefits compared with placebo. Overall, data remain weak, as several studies had small sample numbers or exploratory approaches (62). Differences in research methods, sample sizes, or plant components could cause discrepancies. There is a lack of sufficient research on the efficacy of plant-based treatments for Parkinson's disease. Studies compare phytotherapeutic therapies with placebo to evaluate efficacy and safety, but the current evidence is not sufficient for conclusive clinical recommendations.

Even when results differ, understanding the science and selecting treatments based on evidence is aided (63).

Of the known clinical studies, *Mucuna pruriens* showed the most consistent improvements in motor symptoms and ON time compared with typical levodopa formulations. *Mucuna pruriens* seeds are a natural source of levodopa (L-DOPA), the metabolic precursor of dopamine and the major active ingredient responsible for its clinical effects in Parkinson's disease (31). In contrast, randomised placebo-controlled trials of curcumin, caffeine and cannabidiol generally indicated minimal or no significant improvement in motor outcomes, while selected non-motor symptoms or quality of life were improved in some studies (64, 65). DL-3-n-butylphthalide (*Apium graveolens*) and *Bacopa monnieri* exhibited promising preliminary results; nevertheless, these results need to be confirmed in larger multicenter controlled trials (21). The quality of the available clinical evidence varies greatly between studies. Some of the interventions that we reviewed had prospective registration, including the caffeine trial (ClinicalTrials.gov identifier: NCT01738178), the *Apium graveolens* DL-3-n-butylphthalide trial *Apium graveolens* (Chinese Clinical Trial Registry: ChiCTR1800018892), and the curcumin trial (Iranian Registry of Clinical Trials: IRCT20171123037600N1). Previous investigations of *Mucuna pruriens* and *Vicia faba* and the exploratory trial of cannabidiol did not record trial registration. This reflects variations in reporting criteria at the time these studies were done. Thus, the methodological quality and transparency of the available clinical evidence should be taken with caution (21).

Although several phytotherapeutic interventions have been investigated in clinical studies, the general certainty of evidence is low to moderate, mainly due to small sample sizes, heterogeneous study designs, limited trial registration, varying attrition rates and relatively short follow-up periods. Before these interventions can be routinely recommended for the management of PD, future multicentre randomised controlled trials using standardised formulations and clinically meaningful outcomes, like MDS-UPDRS, OFF time, dyskinesia, quality of life and long-term safety, are needed (10).

6. Comparison with Conventional Pharmacotherapy

In addition to placebo-controlled studies, many researchers have compared plant-based remedies with conventional medications used in clinical settings. *M. pruriens* may provide symptomatic improvement in motor function in selected patients comparable to conventional levodopa formulations according to randomised clinical studies. However, the available evidence is based on relatively small clinical studies and needs confirmation in larger multicentre trials. *M. pruriens* extract may contain more bioactive components, which could explain why its effects last longer

(31). However, the levodopa content in different preparations of *M. pruriens* varies significantly depending on the plant species, geographical origin, growth circumstances, processing methods and extraction procedures. Therefore, equivalent quantities of different preparations can yield significantly different levodopa dosages, indicating the need for standardised preparations with measured levodopa content to ensure consistent dosing, efficacy, and safety in future clinical research. Many preparations of *M. pruriens* do not contain the standardised peripheral decarboxylase inhibitors (carbidopa or benserazide) present in traditional levodopa preparations. Therefore, the peripheral conversion of levodopa to dopamine may vary between preparations and may influence levodopa bioavailability, therapeutic response and incidence of side effects. Thus, future therapeutic trials should examine standardised *M. pruriens* preparations in combination with suitable peripheral decarboxylase inhibitors or clearly state their levodopa content and formulation properties.

Further studies are required to validate these results and thoroughly evaluate the safety and possible adverse effects of *M. pruriens* treatment. This highlights the importance of cannabinoids, especially cannabidiol (CBD), as an adjunctive therapy to traditional Parkinson's treatment. Some of the earlier research looked promising, but more recent studies found no significant differences in motor function or total symptoms between the treatment and control groups. By exploring plant-based alternatives and weighing them against conventional treatments, we can better understand their benefits and drawbacks. This research may be interpreted carefully to aid healthcare providers in deciding whether to include these drugs in clinical practice. These studies can help inform future work to produce better, more evidence-based treatments for Parkinson's disease and identify topics for additional research (66). Of the clinical interventions available, *M. pruriens* is the only phytotherapeutic agent that has shown superiority over conventional levodopa in some clinical outcomes such as faster onset of action and prolonged ON time.

In contrast, plant-derived interventions have shown comparable safety but limited clinical efficacy. Significantly, none of the phytotherapeutic approaches currently available has shown convincing disease-modifying effects in adequately powered long-term human clinical trials. Presently, available information primarily endorses their possible role as supplementary symptomatic treatments, awaiting validation in bigger randomised controlled trials (31).

7. Combination Therapy and Synergistic Effects

Phytotherapeutic agents along with conventional antiparkinsonian medications has attracted considerable research interest because plant-derived compounds may target multiple pathogenic mechanisms simultaneously (67).

Table 5: Human clinical evidence for medicinal plants in Parkinson's disease.

Plants	Study design	Sample size	Diagnostic criteria	Intervention standardization	Dose	Comparator	Duration	Primary outcomes	Effect estimate	Reference
<i>Apium graveolens</i>	Prospective, single-centre, parallel-group, randomised controlled trial	103 PD patients	Idiopathic PD diagnosed according to the UK Parkinson's Disease Society Brain Bank Criteria	DL-3-n-butylphthalide (DL-NBP) capsules	200 mg three times daily (600 mg/day) + standard anti-parkinsonian therapy	Standard anti-parkinsonian therapy alone (control group)	24 weeks of treatment with follow-up to 48 weeks	UPDRS Part III (overall, tremor and non-tremor scores), PDQ-39, Pittsburgh Sleep Quality Index (PSQI), adverse events	DL-NBP produced significantly greater improvement in non-tremor UPDRS-III scores, sleep quality (PSQI) and quality of life (PDQ-39) compared with the control group. Tremor scores were not significantly different between groups.	21
<i>Bacopa monnieri</i> (Brahmi)	Pilot, interventional, randomised, double-blind, placebo-controlled, parallel-group trial	20 PD patients	Patients with clinically diagnosed PD	Commercialised standardised plant extract	225 mg/day or 450 mg/day (oral)	Matching placebo	90 days	Parkinson's Disease Quality of Life (PDQL), motor function, emotional function, social function	No significant improvement in overall motor symptoms or total PDQL scores versus placebo. However, the 450 mg/day group showed time-dependent improvement in emotional function, and quality-of-life measures correlated positively with motor outcomes. Authors concluded that <i>B. monnieri</i> may improve emotional function, but larger trials are required to confirm efficacy.	21
<i>Cannabis sativa</i> (cannabidiol)	Randomised, double-blind, placebo-controlled, exploratory trial	21 (placebo-7; CBD 75 mg/day-7; CBD 300 mg/day-7)	Idiopathic PD without dementia or major psychiatric illness	Highly purified cannabidiol (CBD)	75 mg/day or 300 mg/day (oral)	Matching placebo	6 weeks	UPDRS (motor and total score), PDQ-39 (quality of life), adverse events	No significant improvement in motor symptoms (UPDRS). The 300 mg/day CBD group showed a significant improvement in quality of life (PDQ-39 total score) compared with placebo, while 75 mg/day showed no significant benefit.	21
<i>Coffea arabica</i> (Caffeine)	Multicentre, randomised, double-blind, placebo-controlled, parallel-group trial	121 (60 caffeine; 61 placebo)	Idiopathic PD, disease duration 1-8 years, Hoehn and Yahr stage I-III, receiving stable anti-parkinsonian therapy	Pharmaceutical grade caffeine capsules	200 mg twice daily (400 mg/day)	Matching placebo	6-18 months (primary endpoint at 6 months)	MDS-UPDRS Part III (primary outcome); MDS-UPDRS Parts I & II; dyskinesia; sleep; cognition (MoCA); quality of life; safety	No clinically significant improvement in motor symptoms (MDS-UPDRS III difference 0.48 points; 95% CI 3.21 to 2.25). No significant improvement in quality of life or motor function. Mild transient improvement in day-time somnolence; slight increase in dyskinesia scores and a small decline in MoCA score with caffeine.	65
<i>Curcuma longa</i> (Curcumin nanomicelle)	Pilot randomised, triple-blind, placebo-controlled add-on trial	60 randomised (30 curcumin, 30 placebo); 42 completed (23 vs 19)	Idiopathic PD patients aged 30 years with clinically stable symptoms receiving standard anti-parkinsonian therapy	Naomicelle curcumin (enhanced bioavailability formulation)	80 mg/day orally	Matching placebo + routine anti-parkinsonian treatment	9 months	MDS-UPDRS (all parts), MDS-UPDRS Part III (motor examination), PDQ-39 (quality of life), adverse events	No significant improvement in total MDS-UPDRS or PDQ-39 compared with placebo. A significant difference was observed only in the overall trend of MDS-UPDRS Part III ($P = 0.04$), but post-hoc analyses did not confirm significant differences at individual follow-up visits.	64
<i>Eleutherococcus senticosus</i>	Clinical study	28 cases of early-stage primary Parkinson's disease	Early-stage primary Parkinson's disease	Water extract of <i>Eleutherococcus senticosus</i>	0.03 g/kg/day + levodopa 0.01 mg/kg	Levodopa (Methadopa)	12 weeks	Improvement in Motor Dysfunction Rating Scale for Parkinson's Disease (MDRSPD) score	Significant reduction in MDRSPD score, indicating improved motor function compared with baseline/standard therapy	10

Plants	Study design	Sample size	Diagnostic criteria	Intervention standardization	Dose	Comparator	Duration	Primary outcomes	Effect estimate	Reference
<i>Mucuna pruriens</i> (Velvet bean)	Randomised, double-blind, controlled crossover trial	8	Idiopathic PD with short duration levodopa response and motor fluctuations	Standardised seed powder containing natural L-DOPA	15 g and 30 g seed powder	Standard levodopa/carbidopa (200/50 mg)	Single-dose crossover with weekly washout intervals	UPDRS motor score, tapping speed, onset of action, ON time, dyskinesia (modified AIMS and Goetz scales), levodopa pharmacokinetics	30 g M. pruriens produced a significantly faster onset of action (34.6 vs 68.5 min; $p=0.021$), 21.9% longer ON time (~37 min; $p=0.021$), 110% higher peak plasma levodopa concentration, and 165.3% greater AUC than levodopa/carbidopa, without increasing dyskinesia.	31
<i>Vicia faba</i> (Broad bean/ Fava bean)	Prospective, uncontrolled clinical intervention study	6 patients with PD (plus 5 healthy volunteers for pharmacokinetic assessment)	Clinically diagnosed PD receiving levodopa therapy	Cooked beans (natural source of L-DOPA)	250 g cooked broad beans after 12-hour withdrawal from anti-parkinsonian medication	No placebo or active comparator	Single-dose study; 4 hr follow-up	Plasma levodopa concentration, motor improvement, dyskinesia	Plasma levodopa concentrations increased markedly after bean consumption, accompanied by substantial clinical improvement in motor symptoms. Three of six patients developed severe dyskinesias, consistent with the marked rise in plasma levodopa levels.	21

AE- adverse event; AIMS- Abnormal Involuntary Movement Scale; AUC- area under the plasma concentration–time curve; CBD- cannabidiol; ChiCTR- Chinese Clinical Trial Registry; CI- confidence interval; DL-NBP- DL-3-n-butylphthalide; GI- gastrointestinal; IRCT- Iranian Registry of Clinical Trials; MDS-UPDRS- Movement Disorder Society–Unified Parkinson's Disease Rating Scale; MoCA- Montreal Cognitive Assessment; ON time- duration of improved motor function following dopaminergic therapy; PD- Parkinson's disease; PDQ-39- Parkinson's Disease Questionnaire-39; PSQI- Pittsburgh Sleep Quality Index; QoL- quality of life; RCT- randomized controlled trial; UPDRS- Unified Parkinson's Disease Rating Scale.

Most of the plant-derived compounds are being studied as adjuncts to existing antiparkinsonian drugs rather than as alternatives to established treatment (**Figure 5**). Although preclinical and limited clinical data suggest that some phytotherapeutic approaches may improve symptoms or treatment tolerance, the available evidence is insufficient to recommend replacing standard medication. Therefore, the use of herbal medications should only be in the presence of proper medical supervision and with evidence-based therapeutic care.

8. Challenges and Translational Considerations for Phytotherapeutics in PD

Parkinson's disease holds a lot of potential for plant-based therapeutics, but there are many obstacles to overcome. Phytochemicals are many and have neuroprotective and symptom-relieving benefits, but development is impeded by lack of standardisation, uncertain mechanisms of action, limited customisation, and lack of large-scale clinical trials. To understand these pathways and develop personalised PD treatments, in vitro assays, animal models and current imaging methods are required (67).

8.1 Phytotherapy Safety, Tolerability and Contraindications

Benefits and hazards must be balanced to find the best plant-based treatments for Parkinson's disease. Most plant compounds are safe when taken in small doses, but interactions with drugs or highly concentrated extracts can be dangerous (68). Interactions may increase the likelihood of side effects or decrease in effectiveness. Clinical studies require constant monitoring as people respond differently. For example, inappropriate dosage of *Mucuna pruriens*, a natural source of L-DOPA, has resulted in significant changes in motor performance (67).

Many herbal compounds have unknown long-term safety, especially in older adults. Special consideration should be given to potential adverse effects and drug interactions with phytotherapeutic therapies employed in Parkinson's disease. Natural levodopa preparations (e.g. *Mucuna pruriens*) may cause side effects similar to those of conventional levodopa therapy (e.g. dyskinesia, nausea and orthostatic hypotension), particularly when administered in inappropriate doses or in combination with other dopaminergic drugs. Furthermore, the simultaneous administration of phytotherapeutic drugs with levodopa, dopamine agonists, monoamine oxidase-B inhibitors or catechol-O-methyltransferase inhibitors may change the therapeutic response or raise the risk of adverse effects.

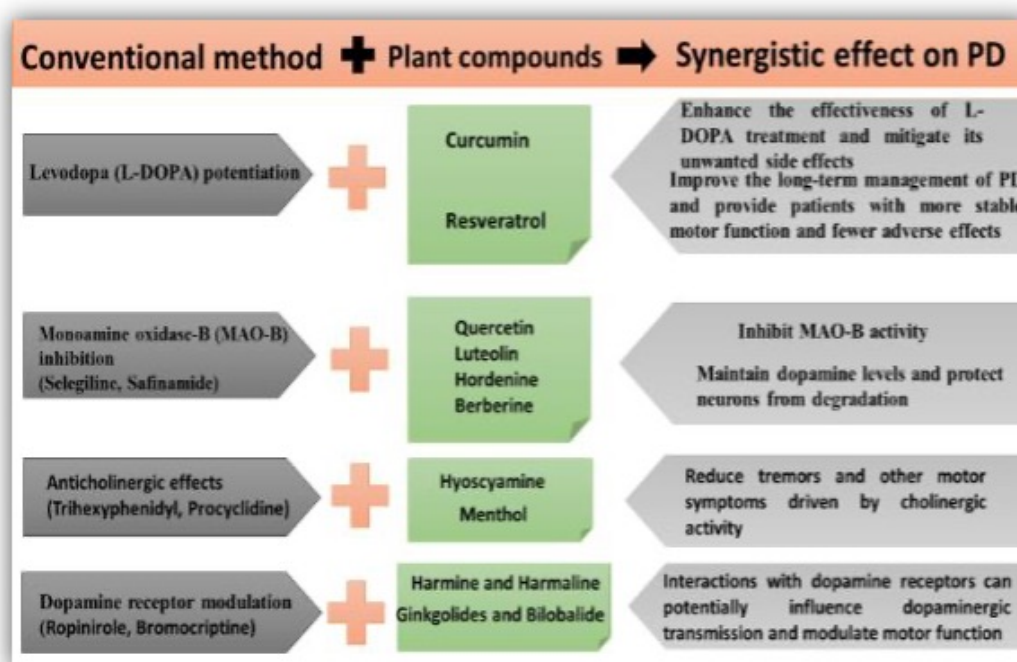


Figure 6: Plant products and their synergistic effects on PD (67).

Therefore, careful dose adjustment, clinical monitoring and study of potential herb-drug interactions are needed before phytotherapeutic approaches are included in normal clinical therapy of Parkinson's disease (21).

Properly controlled clinical studies are needed to determine the best dosages, standardise formulations, and assess the safety of treatments. To find a plant-based treatment for Parkinson's disease that is both safe and effective, doctors need to consider the pros and cons (69). In general, phytotherapeutic interventions were well tolerated, and no treatment-related significant side effects were regularly documented in human clinical studies. The adverse events most commonly observed during curcumin treatment were mild gastrointestinal complaints such as nausea, vomiting and gastroesophageal reflux, whereas DL-3-n-butylphthalide was occasionally associated with mild gastrointestinal discomfort, transient skin rash and reversible elevation of liver enzymes. Cannabidiol had a favourable safety profile with no major medication-related side effects. Caffeine administration was usually well tolerated, but minor sleeplessness and dyskinesia were recorded in a small proportion of patients (64). Conversely, excessive intake of *Vicia faba*, a natural source of L-DOPA, led to dyskinesia in certain patients due to increased plasma levodopa levels. In conclusion, these findings suggest that although phytotherapeutic interventions seem generally safe, well-designed clinical trials with long-term follow-up are needed to confirm their long-term safety, appropriate dosage and risk-benefit profile in patients with PD (70).

8.2 Pharmacokinetics and Bioavailability

Many plant-derived compounds have therapeutic potential. But the mechanisms underlying their actions remain unknown despite promising preclinical and clinical results. Complex interactions between phytochemicals and biological systems are challenging to study. Identifying molecular and cellular targets to improve treatment efficacy is necessary. Although many phytochemicals have been shown to exert neuroprotective effects in cellular and animal models of Parkinson's disease, the clinical translation of such compounds is limited by a lack of robust pharmacokinetic and bioavailability data (71). Plant-derived compounds often exhibit poor oral bioavailability, extensive first-pass metabolism, variable blood-brain barrier penetration and rapid systemic elimination, casting doubt on whether the effective concentrations observed in vitro can be achieved in human brain tissue. Herb-drug interactions can alter pharmacokinetics or impair the effectiveness of medicines used for Parkinson's. These combination drugs have to be shown to be safe and effective in rigorous preclinical and clinical trials (72). Thus, positive preclinical findings should be viewed with caution and should not be assumed to translate directly into clinical efficacy. Future studies should incorporate comprehensive pharmacokinetic evaluation, standardised formulations and dose-optimisation strategies to improve the clinical applicability of phytotherapeutic interventions.

8.3 Phytotherapy standardisation and regulatory considerations

A fundamental impediment to the clinical translation of phytotherapeutic interventions is the lack of formulation standardisation. The major problem is the diversity of active substances in phytotherapeutic treatments. Depending on plant species, geographical origin, cultivation practice, harvesting conditions, extraction methods and formulation procedures, the concentration of bioactive elements may vary. This means that different research studies often explore preparations with diverse phytochemical compositions, which prevents direct comparison of clinical results. Moreover, contamination, adulteration, species substitution, pesticide residues and microbiological contamination may impact the quality of herbal goods (58). This may compromise the safety and therapeutic efficacy of herbal products. Reproducibility of clinical outcomes is hampered by batch-to-batch variability in phytochemical composition. Therefore, for the safe clinical use of phytotherapeutic products, strict quality control, botanical authentication and regulated production techniques are needed. Another key obstacle for phytotherapeutic interventions is regulatory approval. Many herbal medications are promoted as dietary supplements and so are not subjected to the same severe regulatory process as conventional drugs in many countries. Product quality, purity and potency may vary and may affect efficacy and safety. However, before phytotherapeutic drugs may be used in ordinary clinical practice for Parkinson's disease, there is a need for appropriately powered multicentre randomised controlled trials, standardised formulations, long-term pharmacovigilance and conformity with international regulatory requirements (21). Future clinical trials should use standardised extracts with well-characterised phytochemical profiles, with proven quality-control techniques and manufacturing complying with Good Manufacturing Practice (GMP) for repeatability and batch-to-batch consistency (65).

8.4 Limitations of Current Preclinical Models and Translational Challenges

A further problem in the interpretation of the therapeutic potential of medicinal plants for PD is the differentiation between avoidance of experimental neurotoxin-induced harm and treatment of existing neurodegeneration. Most preclinical investigations are preventive or co-treatment designs in which plant extracts or phytochemicals are given before or concurrently with neurotoxic exposure. Thus, the claimed advantages are more likely to represent prevention against dopaminergic neuronal injury rather than reversal of established neuronal loss. In contrast, only a few studies test plant-derived substances after the PD-like pathology has been developed, which is closer to the clinical situation in patients who are treated only after symptom onset. Therefore, future studies should increasingly involve therapeutic intervention designs to see if phytochemicals might delay

disease development or restore neuronal function in existing PD (65). A further crucial point is the intrinsic limitation of the experimental PD models usually used. Toxin-induced models such as MPTP, 6-hydroxydopamine (6-OHDA) and rotenone have been frequently employed as they accurately recreate loss of dopaminergic neurons and motor impairments. However, these models depict acute or subacute toxin-mediated damage and do not fully mimic the gradual, complex and heterogeneous nature of idiopathic PD. They poorly recapitulate essential clinical features, including progressive α -synuclein aggregation, Lewy body development, a broad spectrum of nonmotor symptoms and the intricate interplay of ageing, genetic predisposition and environmental variables. Therefore, confirmation of putative medicinal plants in complementary chronic and genetic PD models with consistent experimental methods would increase the translational relevance and applicability of preclinical findings (68).

8.5 Future Perspectives and Research Priorities

Individual differences in genetic vulnerability, disease severity, and overall health influence the success or failure of treatment. Individualised medicine can be used to customise plant-based medicines to individual patient profiles. New technologies in biomarker discovery, pharmacogenomics, and metabolomics can assist clinicians in identifying which patients will benefit the most from plant-derived medicines (73). The integration of plant-based medications for Parkinson's disease requires substantial clinical data for its successful implementation. Thorough trials with standardised outcome measures, blinding, adequate patient selection, and long follow-up periods are necessary to prove safety and efficacy. If these obstacles can be removed, the therapeutic potential of plant-derived compounds for Parkinson's disease can be better understood, and their use in clinical practice can be expanded. Future research should also include developing standardised and chemically characterised phytotherapeutic products, conducting comprehensive pharmacokinetic and bioavailability studies, systematically assessing herb-drug interactions with conventional antiparkinsonian drugs, and conducting dose-optimisation studies to establish safe and effective therapeutic regimens. There is also a need for appropriately powered, multicentre, prospectively recorded randomised controlled trials with standardised outcome measures and long-term follow-up to demonstrate the therapeutic efficacy and safety of promising plant-derived therapies for Parkinson's disease (74). Moreover, advances in molecular pharmacology, biomarker-guided patient stratification and personalised medicine may allow for rational development of phytotherapeutic interventions. Together, these efforts will determine whether promising preclinical observations can be translated into safe, efficacious, and evidence-based therapeutic options for patients with Parkinson's disease.

9. Conclusion

Parkinson's disease is a chronic neurodegenerative condition with motor and cognitive impairments and remains a substantial therapeutic challenge. These treatments help patients manage symptoms but do not effectively stop disease progression. As a result, medicinal plants and their active phytochemicals have gained significant study interest due to their antioxidant, anti-inflammatory, mitochondrial protective, and neuromodulatory characteristics. Nonetheless, preclinical data is the best available evidence and should be viewed as hypothesis-generating rather than clinical certainty. These studies offer important mechanistic insights and identify promising therapeutic candidates, but their results require validation through rigorous human clinical investigations. Plant-derived compounds cannot yet be considered established therapies for Parkinson's disease, but may represent potential complementary interventions pending further evidence. Future research should focus on developing standardised phytotherapeutic formulations, conducting detailed pharmacokinetic and herb-drug interaction studies, optimising dosing, stratifying patients based on biomarkers, and conducting adequately powered, multicenter randomised controlled trials with long-term follow-up. Addressing these obstacles will be crucial to move promising preclinical data into safe, evidence-based clinical use. Plant-derived medicines may prove to be beneficial supplements to traditional Parkinson's disease treatment as phytochemistry, systems biology, and precision medicine continue to improve. However, their effectiveness, safety, and long-term clinical advantages must be proven by thorough human research.

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Conflict of Interest

None

Author Contributions

AA contributed to the research concept and design. PB, SKS, and AA were responsible for data collection and assembly, as well as interpretation and data analysis. PB, SKS, AS and AA also drafted the manuscript, while AA provided critical revisions. PB, SKS, AS and AA gave final approval for the article.

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