ISSN: 2633-4828 Vol. 6 No.1, January, 2024

International Journal of Applied Engineering & Technology

MEDICINAL PLANTS: A PROMISING APPROACH FOR THE TREATMENT OF PARKINSON'S DISEASE

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ABSTRACT

Parkinson's disease is a neurodegenerative disorder characterized by the progressive loss of dopaminergic neurons, leading to both motor and non-motor symptoms. This degeneration is driven by a complex interplay among genetic predisposition, environmental exposures, protein aggregation, oxidative stress, mitochondrial dysfunction, and inflammation, culminating in the deterioration of dopaminergic neurons in the substantia nigra of the brain. Existing therapeutic interventions are primarily geared toward symptom relief and address only a limited array of the disease's underlying pathophysiological mechanisms. Consequently, a multi-targeted treatment strategy is imperative for effective management of Parkinson's disease, necessitating the identification of efficacious therapeutic combinations. Medicinal plants, long utilized in traditional medicine and still prevalent in various cultures, have been investigated in animal models for their capacity to inhibit neurodegeneration and ameliorate cognitive impairments. Owing to their neuroprotective attributes and potential for symptom alleviation, these medicinal plants have garnered significant research interest. This review elucidates the research on a diverse range of medicinal plants that have been examined for their therapeutic potential in mitigating symptoms and arresting disease progression in animal models.

Keywords: Parkinsons disease, Natural medicine, Oxidative stress, Neuroinflammation, Neuronal loss

INTRODUCTION

Neurodegenerative diseases comprise a category of disorders characterized by degenerative alterations in specific brain tissues, resulting in sensory and motor deficits. Parkinson's disease (PD) ranks as the second most prevalent neurodegenerative disorder, following Alzheimer's disease (1). PD manifests progressively, featuring symptoms such as tremors, rigidity, bradykinesia, and postural instability (2). The disorder arises from the depletion of dopamine-producing cells in the substantia nigra (SN) of the brain (3). While the majority of PD cases are sporadic with unidentified etiology, a minor proportion exhibit a genetic basis. Mutations in genes like PARKIN, PINK1, and LRRK2 have been linked to familial forms of PD, particularly in early-onset cases (4,5). Additionally, evidence suggests that factors such as repeated head injuries and prolonged use of antipsychotic drugs may elevate the risk of developing PD (6,7). Environmental contributors, although not definitively understood, include exposure to toxins like pesticides and herbicides (8). Other potential risk factors under scrutiny encompass rural residency, well water consumption, and occupations involving industrial chemicals or heavy metals (9). Individuals with PD are also more susceptible to depression, anxiety, sleep disorders, and cognitive impairments (10).

The prevalence and incidence of PD escalate with age, being relatively uncommon in individuals below 50 but increasing significantly thereafter. Globally, the prevalence ranges from 0.3% to 3% among individuals aged 65 and above (11,12). Young-onset PD is defined as the manifestation of symptoms before the age of 50, although the specific age range may vary across studies (13). Conversely, late-onset PD constitutes the majority of cases, with symptoms typically appearing post-50 (14,15).

Gender-wise, PD affects both males and females, albeit with a slight male predominance. Various factors, including hormonal, genetic, and environmental influences, contribute to this gender disparity, although the precise mechanisms are not yet fully understood (16,17). Further research is warranted to comprehensively understand these gender-specific differences and their underlying mechanisms.

PATHOPHYSIOLOGY OF THE PARKINSON'S DISEASE

In 1912, Sir Lewy first identified the accumulation of abnormal proteinaceous material in dopamine-producing neurons in individuals afflicted with PD (18). Subsequent research has established that this accumulated material is primarily composed of α-synuclein, a lipid-binding protein typically localized to synapses. The Synuclein Alpha (SNCA) gene encodes α-synuclein, although mutations in this gene are relatively rare. While the function of α-synuclein remains incompletely understood, it is postulated to inhibit apoptosis and regulate glucose levels (19).

In the pathophysiology of PD, α-synuclein aggregates become increasingly neurotoxic. These aggregates can propagate from one neuron to another, initiating in the medulla's neurons and ascending through the brain stem, eventually extending into the limbic structures and the neocortex.

Mitochondrial dysfunction has also been observed alongside α-synuclein accumulation. However, the role of mitochondrial dysfunction—whether as an initiator, propagator, or bystander—in PD remains ambiguous (20). The synergistic action of PINK1 and PARKIN facilitates the clearance of dysfunctional mitochondria through mitophagy, a process compromised by defects in either PINK1 or PARKIN. Notably, levels of mitochondrial complex I, a component of the oxidative phosphorylation cascade, are found to be reduced in the brains of patients with sporadic PD (21) (Fig. 1). The gut microbiome plays a pivotal role in various physiological processes, including homeostasis maintenance, immunomodulation, and the regulation of both the central nervous system (CNS) and the enteric nervous system (ENS) (22). Accumulating evidence supports the existence of a bidirectional communication system between the CNS, gut microflora, and the ENS, commonly referred to as the microbiota-gut-brain axis (MGBA). This axis is implicated in the development of sporadic PD (23).

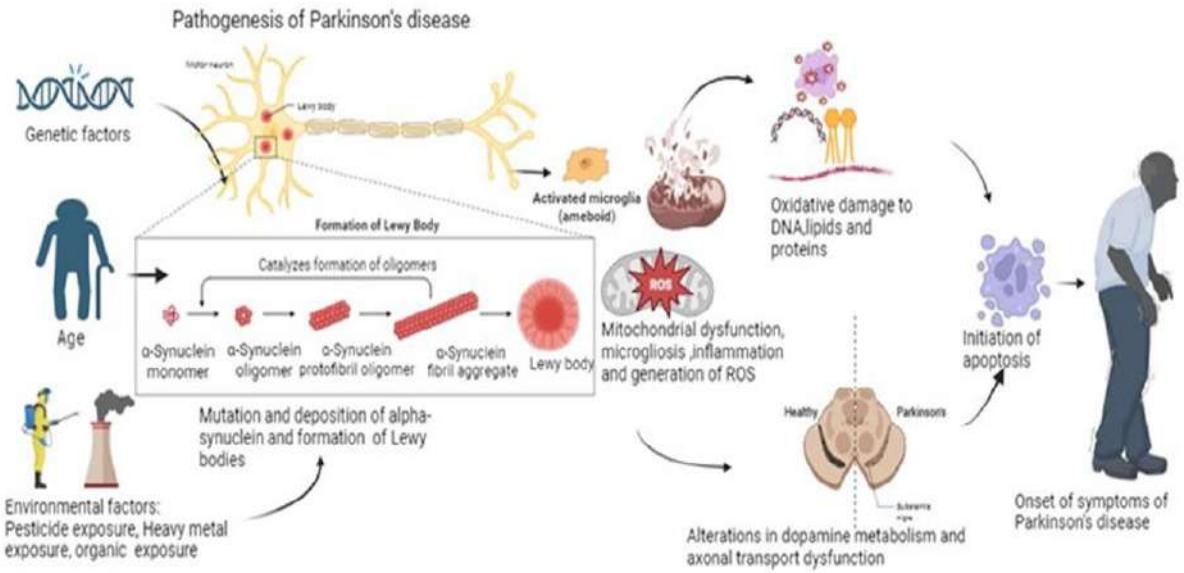

Fig 1: Pathophysiology of Parkinsons disease exhibit various processes, including substantia neurons undergoing programmed cell death, mitochondrial function changes, increased oxidative stress, lysosomal dysfunction, protein aggregation, inflammation, and glial activation.

PROSPECTS FOR HERBAL MEDICINAL PLANTS IN TREATMENT OF PARKINSON'S DISEASE

Herbal medicines, comprising natural botanical compounds or extracts, have been employed for millennia to treat and prevent diseases. Traditional medical systems such as Traditional Chinese Medicine (TCM) and Ayurveda have long utilized plant-derived remedies for a broad spectrum of ailments, including neurodegenerative diseases (24). These herbal products serve as valuable sources for novel drug discovery, especially considering their historical use in medical treatment prior to the rapid expansion of the pharmaceutical industry in the 19th century, over time, these herbal medicines have been refined and integrated into contemporary healthcare practices (25).

Conventional treatments for PD encompass levodopa, dopamine agonists, and surgical interventions like deep brain stimulation. However, these standard therapies often come with a range of side effects and can be financially burdensome. Moreover, most approved drugs primarily address clinical symptoms without offering curative solutions for neurodegenerative conditions. This underscores the need for innovative treatment strategies aimed at modulating the pathways leading to neuronal death and dysfunction (26).

In recent years, there has been a growing interest in alternative and complementary therapies, including herbal medications, as potential strategies for targeting various pathological pathways implicated in neurodegeneration. Herbal therapies derived from plants, fruits, and vegetables have been shown to exert antioxidant, anti-inflammatory, and neuroprotective effects (27,28). Advances in understanding the mechanisms of action of herbal medicines have paved the way for evidence-based approaches in treating neurodegenerative diseases.

This review focuses on the following medicinal plants: *Curcuma longa, Asparagus racemosus, Ginkgo biloba, Ginseng, Cannabis, Centella asiatica, Withania somnifera,* and *Bacopa monnieri* (Fig. 2). These species were selected based on their prevalence in the study area and their diverse range of attributed actions, which collectively hold promise for ameliorating the pathophysiological processes associated with PD.

Fig 2: This review focuses on exploring herbal medicinal plants that have been studied for their potential therapeutic effects in the treatment of Parkinson's disease: Curcuma Longa, Asparagus racemosus, Withania somnifera, Gingko biloba, Ginseng, Cannabis, Centella asiatica, Bacopa monnieri.

CURCUMA LONGA

"*Curcuma longa (C. longa),* commonly known as turmeric, is a perennial flowering plant belonging to the Zingiberaceae (ginger) family. Indigenous to the Indian subcontinent and Southeast Asia, it has been cultivated for millennia for culinary, medicinal, and cultural applications (29). The plant is renowned for its vibrant yellow-orange rhizomes, which serve as its primary component and have diverse uses. Various significant cultivars of *C. longa* are grown globally (30).

The plant contains an array of bioactive compounds, including curcuminoids (curcumin, demethoxycurcumin, bisdemethoxycurcumin), turmerones, and essential oils (alpha-turmerone, beta-turmerone, zingiberene). Among these, *curcumin* is the most extensively studied compound, responsible for the plant's characteristic color and numerous health benefits. It exhibits anti-inflammatory and antioxidant properties and has been rigorously investigated for its potential medicinal applications. Traditional medicine systems like Ayurveda and Traditional Chinese Medicine frequently employ curcumin for its anti-inflammatory, antibacterial, and digestive properties (31, 32).

Oral administration of *C. longa* has been shown to significantly mitigate anxiety, depression-like behaviors, learning-related memory impairments, and motor activity decline. These beneficial effects were correlated with reduced brain levels of lipid peroxidation (LPO), tumor necrosis factor (TNF), and α-synuclein, as well as elevated levels of cognition-related proteins like Synaptosomal-Associated Protein-25 (SNAP-25) and Brain-Derived Neurotrophic Factor (BDNF). These findings suggest that *C. longa* ameliorates PD-like symptoms by attenuating oxidative and pro-inflammatory stress in 6-hydroxydopamine-infused PD model rats (33).

Sharma, N., and Nehru, B. investigated the effects of *curcumin* on a PD model induced by lipopolysaccharide (LPS). Their study revealed that curcumin supplementation inhibited LPS-induced upregulation of intrinsic apoptotic pathway proteins (Bax, Bcl-2, Caspase 3, and Caspase 9) and proinflammatory cytokines (TNF-α, IL-1β, and IL-1). Additionally, curcumin enhanced the glutathione system and reduced iron accumulation in dopaminergic neurons, as evidenced by atomic absorption spectroscopy (AAS) and Prussian blue staining. The study concluded that *curcumin* could serve as a potential therapeutic option for molecularly targeted therapy in PD (34).

Further research has demonstrated that *curcumin* protects against 6-hydroxydopamine (6-OHDA)-induced deficits in the substantia nigra's neurological function. These protective effects were associated with improved cognitive abilities, elevated antioxidant enzyme levels, reduced oxidative stress indicators, and increased dopamine and acetylcholine levels (35).

A recent study using a 6-OHDA rat model of PD found that *curcumin* also provided neuroprotection against dopaminergic neuron loss in the substantia nigra and caudoputamen, while significantly reducing aberrant motor behavior (36).

In summary, *curcumin* has exhibited promise in animal models of PD by reducing oxidative stress, preserving dopamine-producing cells, exerting anti-inflammatory effects, inhibiting α-synuclein aggregation, enhancing mitochondrial function, and ameliorating motor deficits. However, limited studies have explored the molecular pathways underlying the efficacy of *C. longa* as a treatment for PD. Further research is warranted to ascertain the optimal dosage and molecular mechanisms which are of *C. longa*, thereby validating its potential as a treatment option for PD.

ASPARAGUS RACEMOSUS

Asparagus racemosus (*A. racemosus*) is a climbing perennial plant native to India, Sri Lanka, and the Himalayas, and belongs to the Asparagaceae family. Commonly known as Shatavari or Wild Asparagus, the plant features feathery leaves, small white flowers, and scarlet berries. Predominantly, its root is utilized in Ayurvedic medicine and is esteemed as a revitalizing herb, often referred to as the 'Queen of Herbs'. The plant contains an array of bioactive compounds, including steroids (diosgenin, smilagenin), saponins (such as shatavarins), shatavarin IV (SIV), asparagamine A, polysaccharides, and flavonoids (quercetin, rutin) (37). While *A. racemosus* is generally classified as a single species, natural variations in plant characteristics can occur due to factors such as geographical location, climatic conditions, and cultivation practices. However, these variations are not typically recognized as distinct varieties within the species (38).

Research on the neuroprotective properties of *A. racemosus* has yielded promising results, particularly in studies using Caenorhabditis elegans (C. elegans). SIV, a bioactive compound isolated from *A. racemosus*, has been shown to reduce oxidative stress and extend lifespan in PD-induced C. elegans. SIV enhances the expression of stress response and antioxidant genes while reducing intracellular reactive oxygen species (ROS) and oxidative damage. Furthermore, SIV has demonstrated the ability to decrease lipid accumulation and α-synuclein aggregation, thereby ameliorating PD symptoms in C. elegans. These effects may be attributed to the upregulation of PD-related genes such as pdr-1, ubc-12, and pink-1, as well as alterations in the ubiquitin-mediated proteasomal system (39). Another study indicated that mice supplemented with *A. racemosus* extract exhibited increased glutathione peroxidase (GPx) activity and glutathione (GSH) content, along with reduced membranal lipid peroxidation and protein carbonyl levels. These changes could potentially confer protection against kainic acid (KA)-induced hippocampal and striatal neuronal damage (40).

The animal model studies suggest that *A. racemosus* and its herbal combinations may offer therapeutic benefits in PD. Further research is needed to elucidate the broader cellular effects of *A. racemosus* as a potential treatment option for PD.

GINGKO BILOBA

Ginkgo biloba (GBE), also known as ginkgo or maidenhair tree, belongs to the Ginkgoaceae family and stands as the sole extant species within this family, with all other members being extinct (41). The tree is characterized by its fan-shaped leaves that transition to a golden-yellow hue in the autumn. Notably, the tree is dioecious, meaning male and female trees exist separately, with only the latter producing seeds. Leaves and seeds of the ginkgo tree have been employed for millennia in traditional Chinese medicine to enhance cognitive function, improve circulation, and promote general well-being (42).

The phytochemical profile of GBE includes flavonoids (quercetin, kaempferol, and isorhamnetin), terpenoids (ginkgolides and bilobalide), ginkgolic acids, proanthocyanidins, and organic acids (caffeic acid and ferulic acid). These compounds are recognized for their antibacterial, antifungal, anticancer, antioxidant, anti-inflammatory, and neuroprotective properties (43).

Studies involving rotenone-induced PD rat models have shown that oral administration of rotenone led to increased lipid peroxidation, reduced antioxidant levels, dopamine depletion, elevated acetylcholinesterase activity, and heightened proinflammatory cytokines. Conversely, treatment with GBE extract significantly ameliorated these adverse effects, reducing oxidative stress and inflammation, restoring antioxidant levels, and enhancing dopamine expression (44). Further research indicated that GBE therapy improved locomotor activity and reduced methane dicarboxylic aldehyde expression in A53T-synuclein transgenic mice. It also elevated the expression of tyrosine hydroxylase and dopamine transporter, thereby mitigating the onset of PD. These outcomes were attributed to GBE's antioxidative properties and its ability to maintain dopamine homeostasis (45).

Moreover, Ginkgolide B (GB) and Ginkgolide K (GK), active constituents of GBE, have been examined in SH-SY5Y cell lines overexpressing the A53T mutant α-synuclein protein. GK treatment enhanced cell viability while reducing cell death. Intriguingly, GK, but not GB, facilitated the autophagic clearance of A53T α-synuclein and modulated signaling pathways governing both cell death and α-synuclein removal (46).

These findings collectively point to the potential therapeutic utility of GBE in the management of PD.

GINSENG

Ginseng, particularly Panax ginseng, commonly referred to as Korean or Asian ginseng, has a long-standing history in traditional herbal medicine, notably in Traditional Chinese Medicine (TCM). This medicinal plant predominantly grows in the northern temperate zone's mountain forests, with cultivation or harvesting occurring in countries such as Korea, China, Japan, America, and Russia. Belonging to the Araliaceae family, ginseng is characterized by its fleshy root, which serves as the primary component for medicinal applications (47).

The phytochemical composition of *ginseng* is intricate, comprising a diverse array of bioactive compounds like ginsenosides, ginseng polysaccharides, volatile oils (terpenoids, alcohols, fatty acids), peptides, and amino acids. Ginsenosides, the principal active constituents, are credited with the plant's wide-ranging therapeutic and pharmacological effects, including immunomodulation, anticancer properties, antifatigue, antiaging, antidepressant effects, antidiabetic, anti-inflammatory, and cognitive enhancement (48).

Ginsenoside Rg3, a specific bioactive molecule derived from Panax ginseng, has garnered interest for its potential neuroprotective properties. Han et al. explored the neuroprotective capabilities of Ginsenoside Rg3 in a rotenone-induced animal model of PD. Rotenone, a pesticide, induces oxidative stress and dopaminergic neurodegeneration, thereby serving as an effective model for Parkinson's disease research. The study found that Ginsenoside Rg3 mitigated the production of reactive oxygen species and enhanced the expression of glutathione cysteine ligase regulatory and modulatory subunits in the substantia nigra, suggesting that its neuroprotective effects are partially attributed to its antioxidative properties (49).

In a comprehensive in vivo and in vitro study by Zhou et al., dopaminergic cell loss induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) was ameliorated following intraperitoneal injections of Rg1 for 15 days in PD rat models. In vitro experiments revealed that Rg1 pretreatment increased cell viability and reduced 1-methyl-4-phenylpyridinium (MPP+)-induced cell death. The study concluded that Rg1 conferred neuroprotection against MPTP toxicity in the substantia nigra, reduced T-cell infiltration, and offered an immunological avenue for PD treatment, acting through the Wnt/β-catenin signaling pathway (50).

Collectively, these findings underscore the potential of *ginsenosides* and their derivatives as prospective therapeutic agents for the prevention and treatment of neurodegenerative diseases. Further research is warranted to elucidate the molecular signaling pathways involved and to determine optimal dosing regimens.

CANNABIS

Cannabis, known by various names such as marijuana, hemp, ganja, and Mary Jane, belongs to the Cannabaceae family. The Cannabis genus comprises multiple species, including Cannabis sativa, Cannabis indica, and Cannabis ruderalis. Originating in Central Asia, *Cannabis* has disseminated globally through trade and exploration. Historically utilized in cultural and religious practices, its medicinal attributes have been chronicled in ancient texts. *Cannabis* contains an array of over 500 bioactive compounds, including cannabinoids like 9-psychoactive tetrahydrocannabinol (9-THC) and nonpsychoactive cannabidiol (CBD), terpenes, flavonoids, and other compounds such as fatty acids, amino acids, and vitamins (51).

Cannabinoids exert their pharmacological actions primarily through interactions with cannabinoid receptors, among other receptors. Specifically, CBD interacts with CB1 and CB2 receptors, functioning as a negative allosteric modulator and inverse agonist, and as an agonist of TRPV1. These interactions contribute to reduced neuroinflammation and oxidative stress. The endocannabinoid signaling system modulates various brain functions, including nociception, motor activity, and memory, and plays a role in cell survival and death decisions in both the central and peripheral nervous systems (52).

A study employing a Parkinson's disease (PD) experimental model induced by O-6 hydroxy dopamine (O-6HDA) neurotoxicity in Male Sprague–Dawley rats revealed that cannabinoids did not induce overactivity of the endocannabinoid signaling system within two weeks post-lesion. The study also reported decreased mRNA levels for VR1 receptors, which aligns with the receptor's presence in nigrostriatal neurons affected by 6-hydroxydopamine (51).

In an in vitro PD model, CBD demonstrated neuroprotective effects. Specifically, CBD reduced apoptosis and maintained cell viability in brain cells exposed to the neurotoxin MPP+. These neuroprotective effects were mediated through the activation of ERK and AKT/mTOR pathways, potentially modulating autophagy, a critical factor in PD (53).

Zhao et al. explored the impact of CBD on PD using a transgenic mouse model. The study found that CBD exposure improved motor deficits and conferred protection to the substantia nigra region. CBD's neuroprotective effects were attributed to metabolic interactions between the gut and brain (54).

Another investigation assessed the neuroprotective efficacy of CBD in transgenic C. elegans PD models. The study found that CBD reduced dopaminergic neuron degeneration, ameliorated food-sensing behavioral impairments, and mitigated α-Syn aggregative toxicity. Additionally, CBD enhanced the expression of ubiquitin-like proteasomes and superoxide dismutase 3 (SOD-3), while reducing reactive oxygen species in 6-OHDA intoxicated worms (55).

To fully comprehend the therapeutic potential of CBD in PD, additional research, encompassing animal studies and clinical trials, is imperative. Key considerations for future studies include determining the precise concentrations of CBD and the duration of treatment.

CENTELLA ASIATICA

Centella asiatica (C.asiatica) is an herb used in traditional medicine in Southeast Asian nations as well as several other regions of the world, including northern Australia and the Western Pacific to treat a wide range of illness. C. asiatica is also known as Indian pennywort in English, Gotu kola in Sri Lanka, Brahmi in Hindi, Mandukaparni in Ayurveda, Buak bok in Thailand, Kaki kuda in Indonesia, Yuhong-yuhong in the Philippines and Pegaga in Malaysia. C. asiatica belongs to the Apiaceae family (56).

C. asiatica contains amino acids, alkaloids, carbohydrates, vitamins, minerals, terpenes and phenolic compounds. Terpenes are the predominant group of chemical elements of CA, with triterpenes being the major and most important component of CA. The triterpenes found in CA are mostly pentacyclic triterpenic acids, such as the asiatic acid madecassic acid, asiaticoside and madecassoside (57).

C. asiatica has been used for a wide range of medical applications, including treatment of gastrointestinal disorders, skin diseases, fever, and cognitive and memory problems. Studies of the plant extract and its bioactive compounds have showed a comprehensive range of pharmacological and therapeutic effects, including anti-ulcer anti-microbial, cytoprotective, anti-inflammatory, and antioxidant properties. The bioactive components of *C. asiatica* readily cross the blood brain barrier and exert beneficial neuroactive effects in neurodegenerative disease including PD (58).

According to Teerapattarakan, N. et al., a methanolic extract of *C. asiatica* containing asiaticoside could enhance movement in a rotenone-induced zebrafish PD model by stabilising dopamine neurotransmitter and reducing -synuclein aggregation, which prevent the degeneration of dopaminergic neuronal cells from progressing (59). The studies also found that supplementing with *C. asiatica* decreased lipid hydroperoxide levels and protein carbonyl content and markedly raised levels of total antioxidants and antioxidant enzymes in the corpus striatum and hippocampus in MPTP-induced parkinsonism in elderly Sprague-Dawley rats (60). Madecassoside's neuroprotective effects included reversing dopamine depletion, lowering MDA levels while significantly increasing GSH levels, the Bcl-2/Bax ratio, and BDNF protein expression, which were all affected by the parkinsonism-inducing compound 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) (61). Another study found that substantia nigra neurons' dendritic branching points and dendritic intersections increased when *C. asiatica* leaf extract was taken orally (62). Due to its capacity to reduce Parkinson's symptoms including a-synuclein aggregation and expression, increase motility, and enhance dopamine levels, *C. asiatica* has the potential to be developed as an anti-Parkinson's disease treatment (63).

C. asiatica leaf extract works well to reduce oxidative stress in the brains of PD model fly brains and postpones the loss of climbing ability and activity pattern. In MPTP-induced Parkinson's disease, *C. asiatica* can reduce dopamine levels, tyrosine hydroxylase activity, and cognition (64). Jansen et al, using a Drosophila melanogaster PD model based on the loss of function of phosphatase and tensin-induced putative kinase 1 (PINK1), examined five Ayurvedic herbs to determine their impact on climbing capacity. Unexpectedly, *C. asiatica* treated group showed a striking decline in the capacity of the WT flies to ascend. The fact that *C. asiatica* had a negative impact on WT flies' ability to climb and no favourable impact on PINK1 flies may have been owing to CA's toxicity to Drosophila or the incorrect dosage used in the experiment (65).

These results indicate that C. *asiatica* is a more advantageous and efficient treatment option for PD, but additional research is needed to determine whether the chemical components of the *C. asiatica* are more advantageous for PD patients. As a result, additional clinical trials are needed to isolate the compounds and find the compounds that are best suited to treat PD.

WITHANIA SOMNIFERA

Withania somnifera (L.) is used as one of the main medications in Indian ayurvedic medicine. It belongs to a family of Solanaceae family in plant kingdom. It is also called as "Indian Ginseng" or "Indian Winter Cherry" in English. In Urdu, it is known as "Asgand," and in Sanskrit, it is known as "Ashwagandha" (66).

The biologically active chemical constituents of *W. somnifera* include alkaloids (isopelletierine, anaferine, cuseohygrine, anahygrine, etc.) and steroidal lactones (withanolides, withaferins). W. somnifera has been reported to exhibit numerous properties, including antioxidant, memory enhancing, antiparkinsonian, anti-inflammatory, anti-tumor, immunomodulatory, and anti-neuropsychiatric disease effects (67).

In a PD animal model, the neuroprotective ability of the *W. somnifera* root extract was assessed against MB-PQ-induced dopaminergic neurodegeneration it has the ability to increase the numbers of TH positive cells in the SN area of the MB-PQ-induced PD animal brain while simultaneously decreasing the oxidative stress that is present in nigrostriatal tissues. Therefore, it seems that the up-regulation of TH expression in the SN region of the brain is the main cause of the improvement in walking pattern observed in the *W.somnifera* -treated PD mice. It is clear from this study W.somnifera has considerable antioxidant capability and that through preventing neurodegeneration, its ROS scavenging property plays a significant role in the prevention of PD (68).

W. somnifera root extract demonstrated neuroprotective effects showing a capacity to increase the viability of SH-SY5Y cells, a Parkinson's Disease model, to increase glutathione peroxidase and thiol transferase enzyme activities, to modulate the expression of oxidative stress response proteins; peroxiredoxin I, VGF and vimentin, to increase intracellular ATP levels and to modulate redox regulation by decreasing glutathionylated protein levels. These results suggest that KSM-66 is a promising lead drug target for modulating cell damage and cell death due to oxidative stress (69).

Additional research has demonstrated that W. somnifera has neuroprotective benefits in rats with 6-OHDA-induced Parkinsonism by increasing the level of DA and its metabolites in the striatum and their antioxidant activity (70).

The evidence from the aforementioned trials suggests that ashwagandha has anti-Parkinson's properties, thus more research is required to determine its molecular pathways and recommended dosage.

BACOPA MONNIERI

Bacopa monnieri, (*B.monnieri*) commonly known as Brahmi or water hyssop, is a creeping perennial native to India and Australia. It thrives in warm wetlands and is characterized by its short, rectangular leaves and purple flowers. The plant belongs to the Scrophulariaceae family and is widely distributed across subtropical regions, including China, Taiwan, Vietnam, Sri Lanka, and India (71).

The plant is rich in bioactive compounds, primarily bacosides, which are dammarane-type triterpenoid saponins. Other significant constituents include alkaloids such as brahmine, nicotine, and herpestine, as well as D-mannitol, apigenin, hersaponin, monnierasides I–III, cucurbitacins, and plantainoside B (72).

B. monnieri holds a prominent place in Ayurvedic medicine, attributed to its diverse pharmacological properties, including anticholinesterase, antidepressant, anti-inflammatory, and anticancer activities. It is commonly employed for treating conditions like memory loss, anxiety, poor cognition, and concentration deficits (73).

The plant extract has demonstrated potent antioxidant capabilities, including the scavenging of superoxide anion and hydroxyl radicals. It also mitigates H2O2-induced cytotoxicity and DNA damage in human fibroblast cells. These antioxidant activities in various brain regions suggest its potential utility in neuroprotection and brain health (74).

Research has shown that the ethanolic extract of *B. monnieri* offers neuroprotection against MPTP-induced neurotoxicity in mice. The extract's potent antioxidant properties help mitigate oxidative stress in PD models. Treatment with *B. monnieri* improved motor behavior by reducing oxidative stress and apoptosis while elevating dopamine levels and Bcl-2 protein expression (75).

Further studies have indicated that pre-treatment with *B. monnieri* during rotenone-induced neurotoxicity in rats led to a significant reduction in pro-inflammatory cytokine levels. This was accompanied by decreased levels of α-synuclein and oxidative stress in various brain regions, including the hippocampus, substantia nigra, striatum, cortex, and brain stem (76).

Data from both in vivo studies and computational simulations suggest that phytochemicals from *B. monnieri* can either enhance dopamine synthesis or inhibit its breakdown, thereby maintaining dopamine concentrations in the brain (77).

Given the emerging evidence, ongoing research is focused on elucidating the molecular mechanisms and confirming the appropriate dosages for employing *B. monnieri* as a potential treatment for PD.

While these preliminary findings are promising, they underscore the necessity for a synergistic approach that marries traditional herbal wisdom with rigorous scientific inquiry. Such interdisciplinary collaborations are imperative for decoding the complex pharmacological landscapes of these natural compounds and for translating their therapeutic potential into clinically viable treatments for Parkinson’s disease.

CONCLUSION

It is clear from the current review that both in vitro and in vivo studies demonstrated the therapeutic benefits of herbal medicinal plants as a treatment for Parkinson's disease. It is able to do this through enhancing motor activity and exhibiting neuroprotective properties, which include anti-oxidative, anti-inflammatory, neurotransmitter conservation. In animal models of Parkinson's disease, recent investigations into the pharmacological potential of numerous herbal medicinal plants essential to traditional medicinal systems across diverse geographies have produced positive results. The creation of alternative medications for the treatment of Parkinson's disease has significant promise, as evidenced by the accumulation of data on herbal medicinal plants. Research needs to focus more on the active ingredients included in crude extracts in order to advance precision medicine and identify compounds with different complementary targets and effects. *Withania somnifera*, the plant that has been the focus of the majority of research on its beneficial effects in animal models of Parkinson's disease, may have the best possibility of yielding novel, useful compounds among the plants discussed in this review.

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