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REVIEW ARTICLE

Exploring Phytomedicine's Potential in Managing Parkinson's Disease: Unveiling Neuroprotective Compounds from Medicinal Plants

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Abstract

Phytomedicine, derived from plants, offers potential in managing Parkinson's symptoms due to its neuroprotective compounds. The review explores neurodegenerative diseases, focusing on Parkinson's Disease (PD), emphasising its challenges, prevalence, and multifaceted aetiology. It delves into PD's neuropathology, highlighting mitochondrial dysfunction, oxidative stress, and genetic factors while examining the current therapeutic approaches and their limitations. The paper investigates the neuroprotective potential of medicinal plants, particularly *Bacopa monnieri, Curcuma longa, Camellia sinensis, Mucuna pruriens, Ginkgo biloba,* and *Withania somnifera* in PD management. It details their impact on PD pathology, neuroprotective mechanisms, and effectiveness in preclinical models, underscoring their potential as alternative or adjunctive therapies for PD treatment. The review establishes these botanical compounds as promising avenues for novel therapeutic strategies against PD.

Major Findings: Medicinal plants such as *B. monnieri, M. pruriens,* and *C. longa* demonstrate significant neuroprotective effects against Parkinson's disease, highlighting their potential as alternative therapies to supplement current treatments.

Keywords: Anti-inflammatory, Antioxidant, Neurodegenerative Disease, Parkinson's Disease, Phytochemicals

1. Introduction

Neurodegenerative Diseases (NDs) include various chronic and progressive disorders that impact the central nervous system, marked by the slow decline and loss of neurons. They represent a significant public health concern, increasingly influencing global death rates and health issues, especially in older populations. The growing elderly demographic has significantly contributed to the increase in NDs[1,2]. These diseases, which are linked to ageing, present considerable challenges because they are irreversible, lack effective therapies, and bring social and economic consequences[3].

Globally, approximately 1% of adults over 60 have Parkinson's Disease (PD), the second most prevalent neurodegenerative illness among NDs after Alzheimer's disease[4]. It is characterised by the formation of Lewy bodies and the degeneration of dopaminergic neurons in the nigrostriatal pathway. The quality of life for patients who are diagnosed is significantly impacted by the motor symptoms caused by the death of these neurons, which include bradykinesia, stiffness, and tremors. Although research continues, there is currently no cure for PD; available treatments primarily aim to manage symptoms and improve the overall quality of life for patients.

The distinctive neuropathological feature of PD is the gradual decline of dopamine-producing neurons, specifically in the Substantia Nigra pars compacta (SNpc) area of the brain, coupled with the development of Lewy bodies[5-8]. This neuronal degeneration is the root cause of both classical motor symptoms and various non-motor symptoms associated with PD[9,10].

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While the exact cause is not definitively understood, the onset of Parkinson's disease results from a combination of multiple and diverse risk factors, including factors such as age, ethnicity, gender, genetic elements, and environmental influences[11,12].

Emerging research highlights mitochondrial dysfunction and altered oxidative stress as critical contributors to PD pathogenesis[13-15]. Mitochondrial health and dynamics play a pivotal role in neuronal function, with any disruption potentially leading to cell death, as observed in patients with PD and animal models of the condition exhibit a reduction in mitochondrial function, particularly a decrease in the activity of mitochondrial complexes[16,17]. Mitochondria's involvement in maintaining synaptic activity and their role in mitophagy underscores their significance in neuronal health[18,19]. Consequently, mitochondria emerge as primary targets for understanding and addressing neuronal loss in neurodegenerative disorders. However, current knowledge about PD's aetiology remains somewhat limited despite significant research advancements in recent decades.

Current therapeutic approaches for PD primarily revolve around restoring dopamine levels and associated signalling pathways. Levodopa (L-DOPA) stands as a mainstay treatment, providing initial relief by slowing disease progression, often administered with carbidopa to mitigate its side effects[20]. Additionally, monoamine oxidase B (MAO-B) inhibitors are employed to manage PD symptoms by curbing oxidative stress and mitochondrial dysfunction associated with increased MAO-B activity during dopamine metabolism[21]. Strategies focusing on optimising Reactive Oxygen Species (ROS) levels and improving mitochondrial function are actively under consideration in the quest for effective therapies[22].

Amidst this landscape, various avenues of investigation, including pharmacological interventions utilising natural extracts from medicinal plants, show promise in PD management[22–31]. While the exact molecular mechanisms underlying their actions remain elusive, these plant-based compounds appear to target the optimisation of ROS production, presenting potential avenues for therapeutic benefit[32]. Recent research has identified several medicinal plants like *B. monnieri, W. somnifera, C. longa, M. pruriens, G. Biloba,* and *C. sinensis* that demonstrate neuroprotective properties against PD[32] (Figure 1). Consequently, this study aims to delve into the neuroprotective potential of these natural herbs and their roles in shaping novel therapeutic strategies against PD.



Figure 1. Medicinal plants against Parkinson's disease.

2. Overview of Parkinson's Disease

In PD, a progressive neurodegenerative disease, dopaminergic neurons in the substantia nigra pars compacta region of the midbrain are selectively lost, resulting in a decrease in striatal dopamine levels[32,33]. Its impact spans the Central Nervous System (CNS), causing motor, behavioural symptoms, and gut dysfunctions. Analysis of brains affected by PD revealed alterations in mitochondrial function, heightened oxidative stress, impaired lysosomal activity, protein aggregation, compromised degradation processes, accumulation of iron, inflammation, and activation of glial cells. (Figure 2). Diagnosis hinges on postmortem brain autopsies revealing α-synuclein protein (α-SYN) inclusion bodies, known as Lewy body pathology (LP)[34-44]. Interestingly, LP isn't confined to PD patients brain tissue but also extends to their Enteric Nervous System (ENS), suggesting involvement of ENS neurons[44,45].

This dual presence of symptoms and LP inside and outside the CNS raises queries about LP's formation, spread, and its effects on intra- and extra-CNS neurons. Braak *et al.*,[46] pivotal work in 2003 revealed a correlation between LP presence and disease severity in PD. LP, predominantly located in the lower brainstem in early stages, progresses deeper into the midbrain with advancing disease severity. They proposed PD progression stages based on LP presence in different brain regions. Notably, LP's early presence in the brainstem and ENS led to the hypothesis that it might originate in the gut and spread to the CNS via connected neurons[47]. This theory potentially explains the precedence of gut dysfunction in PD preceding CNS symptoms and the apparent protective effect of vagus nerve severance against PD development[34,37,48-54].

Subsequent research delved into understanding gut dysfunction in CNS-centric PD models. Experiments involving neurotoxic models showed alterations in gut function, along with changes in neurotransmitter synthesis enzymes, indicating significant ENS involvement independent of CNS disease[55,56]. Other studies demonstrated the transfer of gut-based pathology to the brain, potentially through the Gut-Brain Axis (GBA), leading to CNS pathology, neurodegeneration, and symptom onset, findings further supported by subsequent experiments[57-60]. These investigations showcased a bidirectional transmission of pathology between the gut and the brain, unveiling the prion-like phenomenon as a pivotal role in the transmission of PD pathology from the gut to the brain.

Previous studies indicated that fetal neurons, initially healthy, exhibit PD characteristics upon transplantation into PD patients[61,62]. Demonstrations by the Brundin group and others in laboratory settings revealed that misfolded α-SYN proteins infiltrate healthy cells, prompting the endogenous α-SYN in these cells also to misfold and aggregate, using the misfolded proteins as a model[63,64]. Kim *et al.*, established the significance of

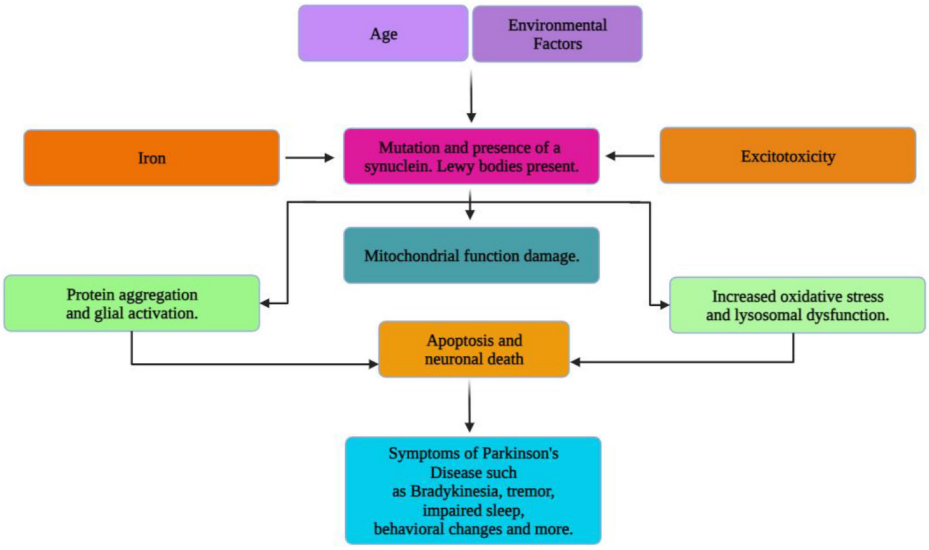


Figure 2. Pathology of Parkinson's disease.

this prion-like behaviour in transmitting PD pathology from the gut to the brain[60]. Notably, in experiments where mice underwent vagotomy after PFF injection, PD symptoms and Central Nervous System (CNS) neurodegeneration did not manifest. This implies that the pathology triggered by PFFs is transmitted through the vagus nerve to the CNS, resulting in the depletion of dopaminergic neurons and the emergence of motor and behavioural symptoms. As a result, we have confirmed Braak's theory, pointing to an origin of PD pathology beyond the CNS, and have pinpointed the vagus nerve as a critical conduit for introducing this pathology into the CNS. The specific processes related to the absorption of PFFs by the enteric nervous system (ENS) or the Glymphatic Brain Pathway (GBA), as well as the cellular locations where templated aggregation takes place, remain uncertain. These mechanisms might potentially involve LAG3 receptor-mediated endocytosis observed in CNS neurons[65].

Moreover, studies using gut inoculation models in mice illustrated persistent gut dysfunction in the absence of significant and enduring structural changes in the ENS, mirroring observations in postmortem intestinal tissues of PD patients[66,67]. This persistence of intestinal dysfunction despite a structurally normal ENS raises questions about the underlying mechanisms, potentially involving challenges in newborn neuron function amidst exacerbated tissue pathology[68].

Genome-Wide Association Studies (GWAS) have pinpointed numerous loci associated with PD, contributing significantly to the hereditary aspect of the condition. Nevertheless, mutations by themselves may not be adequate to initiate early-onset CNS symptoms, as evidenced in specific transgenic models[69,70]. The discrepancy in pathology development between congenital presence of mutations and induced gut inoculation suggests potential age-dependent clearance mechanisms in the CNS.

PD doesn't consistently start in the gut. While some patients experience a gut-to-brain progression following Braak's stages (known as prodromal PD), others might undergo a brain-to-gut progression. Recent studies indicate that intervening primarily in the CNS can trigger PD pathology initially, leading to substantial neurochemical and physiological alterations in the gut afterwards[71,72]. PD's progression might not uniformly start in the gut; in some cases follow a brain-to-gut route. Recent discoveries utilising imaging methods have associated the presence or absence of Rapid Eye Movement (REM) Sleep Behaviour Disorder (RBD) with distinct pathways, underscoring the significance of utilising markers to monitor the progression of the disorder[73].

Additionally, PD patients often experience hyperalgesia, indicating alterations in nociceptive spinal circuits. Studies in animal models demonstrated PD pathology in sympathetic system ganglia and spinal cord regions, hinting at alternative non-vagal routes for pathology spread and contributing to nonmotor symptoms in PD[74,75].

While neural connections predominantly drive PD pathology transmission, alternate pathways like glymphatic, immunologic, endothelial, or cerebrospinal circulation pathways also play a role. This hypothesis gains significance given the lack of pathology in neighbouring nuclei of LP-affected regions in advanced PD patients[76].

3. Role of Medicinal Plants in PD

The exploration of medicinal plants for managing various diseases, including PD, has been extensive. PD involves the loss of dopamine-producing neurons, resulting in motor symptoms like tremors and impaired movement[77]. While a definitive cure is yet to be found, medicinal plants present promising avenues for alleviating PD symptoms and potentially slowing its progression.

Many of these plants exhibit neuroprotective qualities, shielding neurons from damage caused by oxidative stress, inflammation, and protein misfolding, all associated with PD. For instance, *G. biloba*, *C. longa* (turmeric), and Ginseng contain compounds that might safeguard neurons and support their survival[78]. Oxidative stress is a significant contributor to neuronal damage in PD. Plants rich in antioxidants, such as green tea (*C. sinensis*), berries like blueberries and strawberries, and herbs like rosemary, have the potential to combat oxidative stress and reduce PD symptoms[79]. Chronic inflammation exacerbates PD, but medicinal plants like ginger, cinnamon, and garlic possess anti-inflammatory compounds that could alleviate inflammation in PD.

Certain plants may influence dopamine levels or its receptors[80]. *M. pruriens*, for instance, contains L-DOPA, a dopamine precursor, showing promise in managing PD symptoms. Additionally, plants like *B. monnieri* modulate cholinergic transmission, potentially aiding cognitive functions affected in PD[81].

Medicinal plants harbour antioxidants like polyphenols, flavonoids, and vitamins C and E. These compounds scavenge free radicals, reducing oxidative stress and safeguarding neurons. For example, curcumin, found in turmeric, inhibits inflammatory pathways, potentially slowing PD progression[82]. Furthermore, compounds like flavonoids and phytochemicals in these plants promote neuronal survival by enhancing cellular defence mechanisms against stressors and toxins. *M. pruriens*, containing L-DOPA, supplements decreased dopamine levels in PD by crossing the blood-brain barrier and converting into dopamine. Some plants impact neurotransmitter systems. *B. monnieri*, for instance, enhances acetylcholine levels, potentially improving cognitive functions affected in PD[83].

Numerous nutraceuticals have demonstrated neuroprotective characteristics in experimental models, presenting potential alternatives to synthetic drug compounds like L-DOPA, which frequently lead to undesirable side effects. These nutraceuticals operate through various mechanisms, including scavenging ROS/free radicals, chelating iron, preventing apoptosis, reducing inflammation, maintaining mitochondrial homeostasis, and modulating cell signalling pathways. Importantly, many of these nutraceuticals engage in multiple mechanistic pathways rather than relying on a singular mechanism[84].

3.1 *Bacopa monnieri* (Waterhyssop or Brahmi)

Bacopa monnieri, also known as Brahmi (Bm), is a perennial plant highly regarded for its medicinal properties. Studies have highlighted its diverse benefits, including antioxidative, anti-inflammatory, neuroprotective, anti-microbial, and memory-enhancing properties. Extracts from *B. monnieri* have shown promise in enhancing cognitive functions[85-90].

Furthermore, studies suggest that BME demonstrates anti-Parkinsonism effects in animal models, including both transgenic and toxin-induced models[25,91,92], indicating its potential effectiveness in addressing PD. BME has been shown to have protective abilities against toxins like Paraquat (PQ) by reducing oxidative stress in mice and Drosophila[93,94]. Similar positive outcomes were observed in models of PD induced by Rotenone in Drosophila and mice[95,96].

In specific PD models, BME supplementation has been shown to alleviate oxidative stress, decrease apoptosis, reduce α-synuclein aggregation, and slow down the degeneration of dopamine-producing neurons[25,96]. It also mitigates rotenone-induced cytotoxicity in dopamine-producing neurons by enhancing antioxidative enzyme activity and improving redox status[95,97].

Additionally, in dopamine-producing cell lines impacted by toxins, BME promotes improved mitochondrial function by boosting the activity of mitochondrial complex I, preserving mitochondrial membrane potential (Cm), and reviving the activity of Electron Transport Chain (ETC) complexes[94,98]. Additionally, it enhances the activity of Tyrosine Hydroxylase (TH). It stimulates the expression of neurogenic genes in specific brain regions, leading to improvements in locomotor activity and cognitive abilities in animal models of Parkinson's disease.

These findings collectively suggest that BME holds significant promise as an herbal treatment for anti-Parkinsonism. However, further comprehensive studies are warranted to fully comprehend its mechanisms of action for potential utilisation as a drug target against PD.

3.2 *Mucuna pruriens* (Velvet bean)

The medicinal worth of the tropical legume plant known as *M. pruriens* (Mp) has been acknowledged for a considerable period. Its seeds boast anti-inflammatory properties and have been historically used to combat ulcers, helminthiasis, and nephropathy[99]. Dating back to ancient times, *M. pruriens* has been an integral part of ayurvedic medicine, specifically in providing symptomatic relief for PD[100]. One of the key components found in *M. pruriens* seeds is levodopa[101], considered the gold standard in PD treatment. However, the significance of *M. pruriens* might extend beyond levodopa alone. Therefore, further investigation is needed to explore other constituents within *M. pruriens* seeds and their potential roles in PD.

Both animal model and human subject studies have demonstrated that supplementing with

M. pruriens seeds enhances locomotor behaviour[97,102-104]. Research indicates that *M. pruriens* improves the body's redox status by reducing oxidative stress through its antioxidant properties and ability to chelate metals[102,103,105]. Additionally, the extract from *M. pruriens* seeds boosts essential mitochondrial and synaptic functions vital for the survival of neurons. It also increases TH expression in models of PD using Drosophila and mice[102,103]. Significantly, research has demonstrated that the rapid onset of action, extended duration, and absence of heightened adverse effects of *M. pruriens* seed powder distinguish it from synthetic levodopa treatment. Consequently, it seems that *M. pruriens* seed extract is more proficient in handling Parkinson's disease compared to artificial levodopa[97]. This advantage likely stems from additional components present in *M. pruriens* seeds that aid in combating the disease. Thus, further exploration in this area is essential for a comprehensive understanding.

Moreover, comparative analysis between the effects of *M. pruriens* seed extract and another herbal drug, BME, in a mouse model of PD has indicated BME's superior effectiveness over *M. pruriens* seed extract[92]. However, future research is necessary to delve deeper into the comparative efficacy of herbal drugs for potential use in managing PD.

3.3 *W. somnifera* (Indian Ginseng or *Ashwagandha*)

Withania somnifera, commonly known as *Ashwagandha*, holds a significant place in Indian traditional medicine and has been utilised for its medicinal properties for centuries[106]. This botanical marvel presents extensive medicinal potential, recognised for its aphrodisiac qualities and its ability to act as a nerve tonic, enhancing cognitive functions like learning and memory[107]. The roots of *W. somnifera* demonstrate a wide array of benefits, including anxiolytic, antidepressant, antioxidant, anti-inflammatory, anti-carcinogenic, and memory-enhancing properties[108-111]. These attributes indicate its potential application in various disorders, including PD[112,113].

Research illustrates that *W. somnifera* root extract shows promise in normalising oxidative stress in a mouse model of PD induced by MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) by increasing levels of glutathione (GSH) and glutathione peroxidase (GPx)[113,114]. Additionally, it appears to elevate dopamine (DA) levels in the striatum, enhancing motor functions in PD mouse models treated with *W. somnifera*[113]. Studies on rat models induced with 6-Hydroxydopamine (6-OHDA) also indicate that *W. somnifera* extract mitigates oxidative stress, normalises antioxidant levels, and improves TH expression[112,115]. Moreover, in a mouse model of PD induced by Maneb-PQ, the ethanolic extract of *W. somnifera* reduces iNOS expression and enhances locomotor function[112,115]. These findings collectively highlight the potential of *W. somnifera* in combating PD in rodent models.

However, observations in the Drosophila model of PD present contradictory results. Some studies suggest that *W. somnifera* extract supplementation fails to rescue the PD phenotype[97,116], while others demonstrate its effectiveness in doing so[117,118]. Thus, further studies are needed to conclusively determine *W. somnifera's* potential in the Drosophila model of PD. Moreover, *W. somnifera* treatment improves mitochondrial function, further reinforcing its potential in PD treatment[117].

Parkinson's Disease (PD) is marked by the degeneration of neurons that produce dopamine, making the regulation of apoptosis vital. In the maneb-PQ mouse model of PD, administering *W. somnifera* enhances Bcl-2 expression and reduces Bax levels, effectively influencing apoptosis[119]. This highlights the promising role of *W. somnifera* in the development of treatments for PD. However, further research is needed to comprehensively assess its effectiveness in treating this condition.

3.4 *C. longa* (Turmeric)

Turmeric, scientifically named *C. longa*, has been employed since ancient times as a traditional solution for alleviating sprains and reducing swelling resulting from injuries[120]. Extensive research underscores its remarkable medicinal properties, including antioxidative, anti-inflammatory, antimicrobial, anticarcinogenic, and antidepressant characteristics[121-128]. Additionally, it demonstrates protective effects on the brain by combating ageing, preventing neuronal loss, alleviating behavioural impairments, and safeguarding the integrity of the blood-brain barrier (BBB)[129-131], while also showing potential in the treatment of neurodegenerative diseases such as Alzheimer's (AD) and Parkinson's disease (PD)[131-133].

Studies highlight curcumin, a key component of *C. longa*, for its antioxidant function and its ability to elevate striatal dopamine (DA) levels in rat models of PD. It demonstrates potential in protecting dopaminergic neuronal cells by mitigating GSH depletion, preserving mitochondrial complex I activity, and shielding against nitrosative stress and brain mitochondrial damage *in vitro*[134,135]. Furthermore, research on a 6-OHDA-induced rat model of PD reveals curcumin's role in protecting against abnormal changes in the neurons within the substantia nigra (SN) area of the brain. This intervention leads to increased levels of glutathione peroxidase (GPx), superoxide dismutase (SOD) and reduced malondialdehyde (MDA) levels, upregulated DA and acetylcholine (ACh) levels, and significant improvements in memory function[136].

Recent findings suggest that pre-treatment with curcumin followed by exposure to PINK1 siRNA cells enhances mitochondrial respiration, ATP production, restores mitochondrial membrane potential, and decreases apoptosis[29]. Consequently, curcumin demonstrates potential as a therapeutic option for PD. Additionally, a derivative known as curcumin-glucoside exhibits the ability to bind to the oligomeric form of alpha-synuclein, preventing further fibrillization, a crucial discovery for potential disease-modifying agents in PD[137]. Importantly, curcumin displays no toxicity, further supporting its suitability for PD treatment[138]. Given these compelling findings, *C. longa* presents itself as a promising candidate for clinical studies in the context of PD therapy.

3.5 *Gingko biloba* (Maidenhair Tree)

Ginkgo biloba (Gb) seeds, noted in ancient Chinese herbals, hold medicinal value[139]. *G. biloba* (Gb) exhibits antioxidative, anti-inflammatory, anti-ageing, and neuroprotective properties[140-144]. Specifically, studies highlight EGb 761, an extract from *G. biloba* (Gb), as a potential neuroprotective agent in PD animal models[112,145-148].

Research demonstrates that EGb 761 can reduce behavioural deficits in a rat model induced by 6-OHDA, enhancing locomotor activity, muscle coordination, and reducing oxidative stress by upregulating GSH levels and activity of GSH-dependent enzymes[112,146]. Moreover, *G. biloba* (Gb) supplementation in this model improves dopamine levels and its metabolites, hinting at its potential in PD therapeutics. Similar studies also indicate Gb's ability to diminish oxidative stress[147,149].

In various rat models induced by MPTP or reserpine, EGb 761 supplementation displays promising effects by enhancing dopamine levels, reducing oxidative stress and apoptosis, stabilising redox status, improving mitochondrial functioning, ATP production, and mitigating the toxic effects of levodopa used in PD treatment[145,148,149].

Notably, EGb 761, with its low molecular weight and capability to traverse the BBB[150], suggests the potential of *G. biloba* (Gb) in PD therapeutics. However, validating its efficacy necessitates initial clinical trials.

3.6 *C. sinensis* (Tea plant)

The *C. sinensis* plant is renowned for its diverse range of tea types, such as green tea, black tea, oolong tea, and white tea. Among these, black tea stands out as the most prominent, constituting over 70% of the overall tea production. Tea possesses medicinal properties attributed to its various flavonoids and antioxidants[151]. This review delves into the significance of black and green tea concerning PD therapy.

3.6.1 Green tea

Green tea, derived from the steamed and dried leaves of Cs, has gained popularity due to its numerous health benefits. Cs is rich in polyphenols known for their array of properties such as antioxidative, antimicrobial, anti-inflammatory, anti-carcinogenic, anti-arthritic, and neuroprotective features[153-161]. Studies indicate that Cs supplementation can reduce the risks associated with PD[162].

The primary component of green tea, catechins, especially epigallocatechin-3-gallate (EGCG) found in green tea extract, has shown neuroprotective effects in PD mouse models induced by MPTP. This effect is attributed to its antioxidative nature and ability to chelate iron[163]. Moreover, supplementing Cs polyphenols in rat models induced by 6-OHDA tends to enhance the redox status, inhibiting the ROS-NO pathway and thereby safeguarding DA-ergic neurons in the midbrain and striatum[24].

Research has shown that polyphenols from Cs can protect dopaminergic neurons in mice from MPP+ toxicity by inhibiting the dopamine transporter (DAT),

which prevents MPP+ from being taken up via DAT[164]. Furthermore, EGCG, a compound sourced from Cs, has been demonstrated to inhibit inducible nitric oxide synthase (iNOS) in mouse models affected by MPTP, specifically in PD[165]. Recent findings also support that EGCG safeguards dopaminergic neurons from MPTP toxicity in models of Parkinson's disease by reducing iron levels in the nigral region of the brain and mitigating oxidative stress[166].

These findings collectively suggest the neuroprotective potential of Cs, particularly in the context of PD. Consequently, future investigations focusing on understanding its mechanisms of action could pave the way for leveraging Cs as a promising therapeutic strategy against PD.

3.6.2 Black Tea

The extensively consumed and oxidised variety of tea, known as black tea, is produced through a fermentation process[151]. It contains theaflavin, a compound with medicinal properties, and its antioxidant effects are akin to catechins present in green tea[167]. Black tea has demonstrated both antioxidative and neuroprotective properties[168]. In a rat model of PD induced by 6-OHDA, black tea exhibited protective effects on dopaminergic neurons, as evidenced by improved tyrosine hydroxylase (TH) expression in the substantia nigra (SN) region of the brain[169]. Notably, pre-treatment with black tea before 6-OHDA administration enhanced its neuroprotective efficacy[169]. Although the specific neuroprotective mechanism remains unclear, it is attributed to the presence of theaflavin, a polyphenolic compound found in black tea and recognised as one of the most potent catechins in Cs[167].

Additionally, theaflavin has been noted for its ability to enhance the expression of TH and DAT in the nigral region of C57BL/6 mouse brains subjected to MPTP exposure. In parallel, theaflavin demonstrated antiapoptotic properties in a Parkinson's disease model induced by MPTP, as indicated by a reduction in Caspase levels[3,8,9]. Furthermore, recent research revealed that adding black tea to a transgenic Drosophila model of Parkinson's disease, which expresses human alpha-synuclein, led to increased dopamine levels and decreased oxidative stress[170]. Consequently, black tea appears to possess significant neuroprotective effects, similar to those of green tea.

A study conducted by the Singapore Chinese Health Study team suggested that drinking black tea, as opposed to green tea, is linked to a lower risk of PD[171]. This highlights the need for comparative studies to shed light on the molecular mechanisms behind the effects of both types of tea. Importantly, chlorogenic acid found in black tea has been shown to increase total plasma homocysteine (Hcy) levels in humans[172]. This is particularly significant since elevated Hcy levels are connected to PD[173,174] and may affect mitochondrial pathways involved in neuronal cell death[175]. Therefore, future research should carefully evaluate the implications of black tea supplementation given these findings. The effects of medicinal plants and their active compounds on the treatment of PD are outlined in Table 1.

Table 1. Medicinal plants effective for Parkinson's disease

Plant	Used model	Concentration	Key active compounds	Effects
Tinospora cordifolia	Rat induced by 6-OHDA	200, 400 mg/kg	Berberine, Tinosporin	Ramped up the dopamine. Reduced (Fe) asymmetry ratio. Decreased MDA levels. Activation of mitochondrial complex I. Improved locomotor activity.
Sesame seed oil (SO)	Mice induced by 6-OHDA	Mixed diet	Lignans (*e.g.*, sesamin)	Increased levels of glutathione reductase (GR), glutathione-S-transferase (GST), glutathione peroxidase (GPx), catalase (CAT), glutathione (GSH), and TBA reactive substance (TBARS). halt Nox2 and Cox2 activating phosphorylation. expression of MnSOD was restored.

Table 1. Continued...

Plant	Used model	Concentration	Key active compounds	Effects
Carthamus tinctorius L.	(MPTP)-lesioned rat	70, 35 mg/kg	Carthamin, Hydroxysafflor yellow A	Improve your actions and performance—inhibition of the overexpression or aggregation of α-synuclein. Reactive astrocytes are inhibited by reperfusion.
Chaenomeles speciosa	*In vitro* and *in vivo* assays, Chinese hamster ovary (CHO) cells, 6-OHDA (MPTP)-lesioned rats	250, 500, 1000 mg/kg	Triterpenoids, Polyphenols	Tyrosine hydroxylase-immunoreactive neurons were considerably more prevalent in the substantia nigra. D8 cell viability has increased. Apomorphine-induced rotational turning resulted in a time-dependent reduction in abnormal turns.
Portulaca oleracea Paeonia suffruticosa	Rat induced by 6-OHDA. (MPTP)-lesioned mice	200, 400 mg/kg 25, 50 mg/kg	Omega-3 fatty acids, Flavonoids	Improved raising and cross-over in an open field test. In the open field exam, the greater the distance travelled. Increased total striatal dopamine. Prevented dopaminergic neurons from dying. Akt and the mitochondrial OXPHOS complexes are reversed.
Mucuna pruriens	Rat induced by 6-OHDA	40, 80, 120 mg/kg	L-DOPA, Nicotine, Serotonin	Lowered risk of drug-related dyskinesias. Rise in nigrostriatal catecholamines. Catecholamine content.
Hyoscyamus niger seeds	Unilateral intrastriatal injection of rotenone in rats	125, 250, 500 mg/kg	Tropane alkaloids	No significant motor deficits. Enhancement of GSH contents and activities of GPX, SOD and CAT.
Hibiscus asper leaves	Rat induced by 6-OHDA	50, 100 mg/kg	Flavonoids, Anthocyanins	Elevation of SOD, GPX and CAT activities and the level of total GSH. Reduced MDA level.
Gynostemma pentaphyllum	Rat induced by 6-OHDA	10, 30 mg/kg	Gypenosides	Dopamine, 3,4-dihydroxyphenylacetic acid, homovanillic acid, and norepinephrine levels in the striatum were restored. Reduced the loss of substantia nigra TH-immunopositive neurons.
Ginkgo biloba	Rat induced by 6-OHDA	50, 100, 150 mg/kg	Ginkgolides, Bilobalide	Improved coordination of muscles and locomotor activities. Increased levels of GSH. Lower production of TBARS. Increased activity of CAT and SOD. Increase in the number of striatal dopaminergic D2 receptors.
Fructus alpiniaoxyphylla	Zebrafish and PC12 cell models	20% solution	Nootkatone, Tannins	Degeneration of dopaminergic (DA) neurons was reversed. Reduced deficiencies in movement. PC12 cells treated with 6-OHDA showed increased vitality. Apoptosis in cells is reduced.
Delphinium denudatum	Rat induced by 6-OHDA	200, 400, 600 mg/kg	Alkaloids (*e.g.*, Methyllycaconitine)	Decreased levels of MDA. Increased GSH levels. Increased CAT and SOD activity. Higher levels of dopamine.

4. Conclusion

Our research, which aims to compile the latest experimental findings on the anti-Parkinsonian effects of medicinal plants and their active components, underscores the ongoing need for further research. We highlight the diverse anti-Parkinsonian properties exhibited by different natural compounds and herbal extracts, suggesting that various neurotoxic models of PD serve as valuable platforms for discovering potential anti-Parkinsonian treatments. This could potentially pave the way for novel drugs derived from herbal sources. However, the effectiveness of plant extracts and their active components in PD models requires further scrutiny in upcoming empirical studies. Additionally, a more comprehensive understanding of the active components and mechanisms of action within herbal extracts remains a priority for future research.

5. Author Contribution

Sangeetha Saravanan: conceptualised the review, conducted the literature survey, and drafted the manuscript. Navinkumar Malligarjunan: Assisted in data curation, analysis, and manuscript editing. Gomathy Subramanian: provided critical revisions, supervised the work, and approved the final version for submission. All authors have read and agreed to the published version of the manuscript.

6. References

1. Heemels MT. Neurodegenerative diseases. Nature. 2016; 539(7628):179-180. https://doi.org/10.1038/539179a PMid:27830810
2. Feigin VL, Abajobir AA, Abate KH, Abd-Allah F, Abdulle AM, Abera SF, *et al*. Global, regional, and national burden of neurological disorders during 1990-2015: A systematic analysis for the Global Burden of Disease Study 2015. Lancet Neurol. 2017; 16(11):877-897.
3. Hung CW, Chen YC, Hsieh WL, Chiou SH, Kao CL. Ageing and neurodegenerative diseases. Ageing Res Rev. 2010; 9:S36-S46. https://doi.org/10.1016/j.arr.2010.08.006 PMid:20732460
4. De Lau LM, Breteler MM. Epidemiology of Parkinson's disease. Lancet Neurol. 2006; 5(6):525-535. https://doi.org/10.1016/S1474-4422(06)70471-9 PMid:16713924
5. Spillantini MG, Schmidt ML, Lee VM, Trojanowski JQ, Jakes R, Goedert M. α-Synuclein in Lewy bodies. Nature. 1997; 388(6645):839-840. https://doi.org/10.1038/42166 PMid:9278044
6. Jellinger KA. Pathology of Parkinson's disease: Changes other than the nigrostriatal pathway. Mol Chem Neuropathol. 1991; 14:153-197. https://doi.org/10.1007/BF03159935 PMid:1958262
7. Savitt JM, Dawson VL, Dawson TM. Diagnosis and treatment of Parkinson's disease: Molecules to medicine. J Clin Invest. 2006; 116(7):1744-1754. https://doi.org/10.1172/JCI29178 PMid:16823471 PMCid:PMC1483178
8. Van Den Eeden SK, Tanner CM, Bernstein AL, Fross RD, Leimpeter A, Bloch DA, *et al*. Incidence of Parkinson's disease: Variation by age, gender, and race/ethnicity. Am J Epidemiol. 2003; 157(11):1015-1022. https://doi.org/10.1093/aje/kwg068 PMid:12777365
9. Forno LS. The neuropathology of Parkinson'S Disease: The Lewy body as a clue to the nerve cell degeneration. Progress in Parkinson research; 1988. p. 11-21. https://doi.org/10.1007/978-1-4613-0759-4_2
10. Franco R, Li S, Rodriguez-Rocha H, Burns M, Panayiotidis MI. Molecular mechanisms of pesticide-induced neurotoxicity: Relevance to Parkinson's disease. Chem Biol Interact. 2010; 188(2):289-300. https://doi.org/10.1016/j.cbi.2010.06.003 PMid:20542017 PMCid:PMC2942983
11. Khoo TK, Yarnall AJ, Duncan GW, Coleman S, O'Brien JT, Brooks DJ, *et al*. The spectrum of nonmotor symptoms in early Parkinson disease. Neurology. 2013; 80(3):276-281. https://doi.org/10.1212/WNL.0b013e31827deb74 PMid:23319473 PMCid:PMC3589180
12. Simon-Sanchez J, Scholz S, Fung HC, Matarin M, Hernandez D, Gibbs JR, *et al*. Genome-wide SNP assay reveals structural genomic variation, extended homozygosity, and cell-line induced alterations in normal individuals. Hum Mol Genet. 2007; 16(1):1-4. https://doi.org/10.1093/hmg/ddl436 PMid:17116639
13. Bose A, Beal MF. Mitochondrial dysfunction in Parkinson's disease. J Neurochem. 2016; 139:216-231. https://doi.org/10.1111/jnc.13731 PMid:27546335
14. Hauser DN, Hastings TG. Mitochondrial dysfunction and oxidative stress in Parkinson's disease and monogenic parkinsonism. Neurobiol Dis. 2013; 51:35-42. https://doi.org/10.1016/j.nbd.2012.10.011 PMid:23064436 PMCid:PMC3565564
15. Jiang T, Sun Q, Chen S. Oxidative stress: A major pathogenesis and potential therapeutic target of antioxidative agents in Parkinson's disease and Alzheimer's disease. Prog Neurobiol. 2016; 147:1-9. https://doi.org/10.1016/j.pneurobio.2016.07.005 PMid:27769868
16. Michel PP, Hirsch EC, Hunot S. Understanding dopaminergic cell death pathways in Parkinson disease. Neuron. 2016; 90(4):675-691. https://doi.org/10.1016/j.neuron.2016.03.038 PMid:27196972

17. Schapira AH, Cooper JM, Dexter D, Clark JB, Jenner P, Marsden CD. Mitochondrial complex I deficiency in Parkinson's disease. J Neurochem. 1990; 54(3):823-827. https://doi.org/10.1111/j.1471-4159.1990.tb02325.x PMid:2154550
18. Ono T, Isobe K, Nakada K, Hayashi JI. Human cells are protected from mitochondrial dysfunction by complementation of DNA products in fused mitochondria. Nat Genet. 2001; 28(3):272-275. https://doi.org/10.1038/90116 PMid:11431699
19. Verstreken P, Ly CV, Venken KJ, Koh TW, Zhou Y, Bellen HJ. Synaptic mitochondria are critical for mobilization of reserve pool vesicles at Drosophila neuromuscular junctions. Neuron. 2005; 47(3):365-378. https://doi.org/10.1016/j.neuron.2005.06.018 PMid:16055061
20. Yuan H, Zhang ZW, Liang LW, Shen Q, Wang XD, Ren SM, *et al*. Treatment strategies for Parkinson's disease. Neurosci Bull. 2010; 26(1):66. https://doi.org/10.1007/s12264-010-0302-z PMid:20101274 PMCid:PMC5552548
21. LeWitt PA, Fahn S. Levodopa therapy for Parkinson disease: A look backward and forward. Neurology. 2016; 86(14 Supplement 1): S3-S12. https://doi.org/10.1212/WNL.0000000000002509 PMid:27044648
22. Sarrafchi A, Bahmani M, Shirzad H, Rafieian-Kopaei M. Oxidative stress, and Parkinson's disease: New hopes in treatment with herbal antioxidants. Curr Pharm Des. 2016; 22(2):238-246. https://doi.org/10.2174/1381612822666151112151653 PMid:26561062
23. Connolly BS, Lang AE. Pharmacological treatment of Parkinson disease: A review. JAMA. 2014; 311(16):1670-1683. https://doi.org/10.1001/jama.2014.3654 PMid:24756517
24. Guo S, Yan J, Yang T, Yang X, Bezard E, Zhao B. Protective effects of green tea polyphenols in the 6-OHDA rat model of Parkinson's disease through inhibition of ROS-NO pathway. Biol Psychiatry. 2007; 62(12):1353-1362. https://doi.org/10.1016/j.biopsych.2007.04.020 PMid:17624318
25. Jadiya P, Khan A, Sammi SR, Kaur S, Mir SS, Nazir A. Anti-Parkinsonian effects of Bacopa monnieri: insights from transgenic and pharmacological Caenorhabditis elegans models of Parkinson's disease. Biochem Biophys Res Commun. 2011; 413(4):605-610. https://doi.org/10.1016/j.bbrc.2011.09.010 PMid:21925152
26. Kasture S, Pontis S, Pinna A, Schintu N, Spina L, Longoni R, *et al*. Assessment of symptomatic and neuroprotective efficacy of *Mucuna pruriens* seed extract in rodent model of Parkinson's disease. Neurotox Res. 2009; 15:111-122. https://doi.org/10.1007/s12640-009-9011-7 PMid:19384573
27. Khuwaja G, Khan MM, Ishrat T, Ahmad A, Raza SS, Ashafaq M, *et al*. Neuroprotective effects of curcumin on 6-hydroxydopamine-induced Parkinsonism in rats: Behavioural, neurochemical and immunohistochemical studies. Brain Res. 2011; 1368:254-263. https://doi.org/10.1016/j.brainres.2010.10.023 PMid:20951685
28. Nagashayana N, Sankarankutty P, Nampoothiri MR, Mohan PK, Mohanakumar KP. Association of L-DOPA with recovery following Ayurveda medication in Parkinson's disease. J Neurol Sci. 2000; 176(2):124-127. https://doi.org/10.1016/S0022-510X(00)00329-4 PMid:10930594
29. Van der Merwe C, Van Dyk HC, Engelbrecht L, van der Westhuizen FH, Kinnear C, Loos B, *et al*. Curcumin rescues a PINK1 knock down SH-SY5Y cellular model of Parkinson's disease from mitochondrial dysfunction and cell death. Mol Neurobiol. 2017; 54:2752-2762. https://doi.org/10.1007/s12035-016-9843-0 PMid:27003823
30. Yadav SK, Rai SN, Singh SP. *Mucuna pruriens* reduces inducible nitric oxide synthase expression in Parkinsonian mice model. J Chem Neuroanat. 2017; 80:1-10. https://doi.org/10.1016/j.jchemneu.2016.11.009 PMid:27919828
31. Zbarsky V, Datla KP, Parkar S, Rai DK, Aruoma OI, Dexter DT. Neuroprotective properties of the natural phenolic antioxidants curcumin and naringenin but not quercetin and fisetin in a 6-OHDA model of Parkinson's disease. Free Radic Res. 2005; 39(10):1119-1125. https://doi.org/10.1080/10715760500233113 PMid:16298737
32. Surmeier DJ, Guzmán JN, Sánchez-Padilla J, Goldberg JA. What causes the death of dopaminergic neurons in Parkinson's disease? Prog Brain Res. 2010; 183:59-77. https://doi.org/10.1016/S0079-6123(10)83004-3 PMid:20696315
33. Dauer W, Przedborski S. Parkinson's disease: Mechanisms and models. Neuron. 2003; 39(6):889-909. https://doi.org/10.1016/S0896-6273(03)00568-3 PMid:12971891
34. Przedborski S. The two-century journey of Parkinson disease research. Nat Rev Neurosci. 2017; 18(4):251-259. https://doi.org/10.1038/nrn.2017.25 PMid:28303016
35. Reich SG. Diagnosing Parkinson's disease. Therapy of Movement Disorders: A Case-Based Approach; 2019. p. 3-6. https://doi.org/10.1007/978-3-319-97897-0_1
36. Palaniyappan R, Arthanari S, Subramanian M, Periyasamy P, Pethappachetty P, Ganesan R, Prakash M, Govindaraj A. Nanotechnology-driven approaches in overcoming drug delivery challenges for neurodegenerative diseases. Indian Journal of Pharmaceutical Education and Research. 2024 Nov 19;58(4s):s1185-200.
37. Braak H, Del Tredici K, Rüb U, De Vos RA, Steur EN, Braak E. Staging of brain pathology related to sporadic Parkinson's disease. Neurobiol Aging. 2003; 24(2):197-211. https://doi.org/10.1016/S0197-4580(02)00065-9 PMid:12498954
38. Li S, Le W. Milestones of Parkinson's disease research: 200 years of history and beyond. Neurosci Bull. 2017; 33:598-602. https://doi.org/10.1007/s12264-017-0178-2 PMid:28895075 PMCid:PMC5636740
39. Goedert M, Spillantini MG, Del Tredici K, Braak H. 100 years of Lewy pathology. Nat Rev Neurol. 2013; 9(1):13-24. https://doi.org/10.1038/nrneurol.2012.242 PMid:23183883
40. Stefanis L. α-synuclein in Parkinson's disease. Cold Spring Harb Perspect Med. 2012; 2(2):a009399. https://

doi.org/10.1101/cshperspect.a009399 PMid:22355802 PMCid:PMC3281589

41. Vargas JY, Grudina C, Zurzolo C. The prion-like spreading of α-synuclein: From *in vitro* to *in vivo* models of Parkinson's disease. Ageing Res Rev. 2019; 50:89-101. https://doi.org/10.1016/j.arr.2019.01.012 PMid:30690184
42. Shahmoradian SH, Lewis AJ, Genoud C, Hench J, Moors TE, Navarro PP, *et al*. Lewy pathology in Parkinson's disease consists of crowded organelles and lipid membranes. Nat Neurosci. 2019; 22(7):1099-1109. https://doi.org/10.1038/s41593-019-0423-2 PMid:31235907
43. Kalia LV, Kalia SK. α-synuclein and Lewy pathology in Parkinson's disease. Curr Opin Neurol. 2015; 28(4):375-381. https://doi.org/10.1097/WCO.0000000000000215 PMid:26110807
44. Wakabayashi K, Takahashi H, Takeda S, Ohama E, Ikuta F. Parkinson's disease: The presence of Lewy bodies in Auerbach's and Meissner's plexuses. Acta Neuropathol. 1988; 76:217-21. https://doi.org/10.1007/BF00687767 PMid:2850698
45. Wj K. Parkinson's disease and megacolon: Concentric hyaline inclusions (Lewy bodies) in enteric ganglion cells. Neurology. 1987; 37:1253-1255. https://doi.org/10.1212/WNL.37.7.1253 PMid:3037441
46. Braak H, Del Tredici K. Neuropathological staging of brain pathology in sporadic Parkinson's disease: separating the wheat from the chaff. Journal of Parkinson's disease. 2017 Mar 6;7(s1):S71-85.
47. Braak H, de Vos RA, Bohl J, Del Tredici K. Gastric α-synuclein immunoreactive inclusions in Meissner's and Auerbach's plexuses in cases staged for Parkinson's disease-related brain pathology. Neurosci Lett. 2006; 396(1):67-72. https://doi.org/10.1016/j.neulet.2005.11.012 PMid:16330147
48. Stirpe P, Hoffman M, Badiali D, Colosimo C. Constipation: An emerging risk factor for Parkinson's disease? Eur J Neurol. 2016; 23(11):1606-1613. https://doi.org/10.1111/ene.13082 PMid:27444575
49. Abbott RD, Petrovitch H, White LR, Masaki KH, Tanner CM, Curb JD, *et al*. Frequency of bowel movements and the future risk of Parkinson's disease. Neurology. 2001; 57(3):456-462. https://doi.org/10.1212/WNL.57.3.456 PMid:11502913
50. Savica R, Carlin JM, Grossardt BR, Bower JH, Ahlskog JE, Maraganore DM, Bharucha AE, Rocca WA. Medical records documentation of constipation preceding Parkinson disease: A case-control study. Neurology. 2009; 73(21):1752-1758. https://doi.org/10.1212/WNL.0b013e3181c34af5 PMid:19933976 PMCid:PMC2788809
51. Adams-Carr KL, Bestwick JP, Shribman S, Lees A, Schrag A, Noyce AJ. Constipation preceding Parkinson's disease: A systematic review and meta-analysis. J Neurol Neurosur Psychiat. 2016; 87(7):710-716. https://doi.org/10.1136/jnnp-2015-311680 PMid:26345189
52. Fu P, Gao M, Yung KK. Association of intestinal disorders with Parkinson's disease and Alzheimer's disease: A systematic review and meta-analysis. ACS Chem Neurosci. 2019; 11(3):395-405. https://doi.org/10.1021/acschemneuro.9b00607 PMid:31876406
53. Svensson E, Horváth-Puhó E, Thomsen RW, Djurhuus JC, Pedersen L, Borghammer P, *et al*. Vagotomy and subsequent risk of Parkinson's disease. Ann Neurol. 2015; 78(4):522-529. https://doi.org/10.1002/ana.24448 PMid:26031848
54. Liu B, Fang F, Pedersen NL, Tillander A, Ludvigsson JF, Ekbom A, *et al*. Vagotomy and Parkinson disease: A Swedish register-based matched-cohort study. Neurology. 2017; 88(21):1996-2002. https://doi.org/10.1212/WNL.0000000000003961 PMid:28446653 PMCid:PMC5440238
55. Zhang X, Li Y, Liu C, Fan R, Wang P, Zheng L, *et al*. Alteration of enteric monoamines with monoamine receptors and colonic dysmotility in 6-hydroxydopamine-induced Parkinson's disease rats. Transl Res. 2015; 166(2):152-162. https://doi.org/10.1016/j.trsl.2015.02.003 PMid:25766133
56. Zhu HC, Zhao J, Luo CY, Li QQ. Gastrointestinal dysfunction in a Parkinson's disease rat model and the changes of dopaminergic, nitric oxidergic, and cholinergic neurotransmitters in myenteric plexus. J Mol Neurosci. 2012; 47:15-25. https://doi.org/10.1007/s12031-011-9560-0 PMid:21647710 PMCid:PMC3338324
57. Anselmi L, Bove C, Coleman FH, Le K, Subramanian MP, Venkiteswaran K, *et al*. Ingestion of subthreshold doses of environmental toxins induces ascending Parkinsonism in the rat. NPJ Parkinsons Dis. 2018; 4(1):30. https://doi.org/10.1038/s41531-018-0066-0 PMid:30302391 PMCid:PMC6160447
58. Holmqvist S, Chutna O, Bousset L, Aldrin-Kirk P, Li W, Björklund T, *et al*. Direct evidence of Parkinson pathology spread from the gastrointestinal tract to the brain in rats. Acta Neuropathol. 2014; 128:805-820. https://doi.org/10.1007/s00401-014-1343-6 PMid:25296989
59. Manfredsson FP, Luk KC, Benskey MJ, Gezer A, Garcia J, Kuhn NC, *et al*. Induction of alpha-synuclein pathology in the enteric nervous system of the rat and non-human primate results in gastrointestinal dysmotility and transient CNS pathology. Neurobiol Dis. 2018; 112:106-118. https://doi.org/10.1016/j.nbd.2018.01.008 PMid:29341898 PMCid:PMC5890443
60. Kim S, Kwon SH, Kam TI, Panicker N, Karuppagounder SS, Lee S, *et al*. Transneuronal propagation of pathologic α-synuclein from the gut to the brain models Parkinson's disease. Neuron. 2019; 103(4):627-641. https://doi.org/10.1016/j.neuron.2019.05.035 PMid:31255487 PMCid:PMC6706297

61. Li JY, Englund E, Holton JL, Soulet D, Hagell P, Lees AJ, *et al*. Lewy bodies in grafted neurons in subjects with Parkinson's disease suggest host-to-graft disease propagation. Nat Med. 2008; 14(5):501-503. https://doi.org/10.1038/nm1746 PMid:18391963
62. Kordower JH, Chu Y, Hauser RA, Freeman TB, Olanow CW. Lewy body-like pathology in long-term embryonic nigral transplants in Parkinson's disease. Nat Med. 2008; 14(5):504-506. https://doi.org/10.1038/nm1747 PMid:18391962
63. Angot E, Brundin P. Dissecting the potential molecular mechanisms underlying α-synuclein cell-to-cell transfer in Parkinson's disease. Parkinsonism and related disorders. 2009; 15:S143-S147.https://doi.org/10.1016/S1353-8020(09)70802-8 PMid:20082977
64. Angot E, Steiner JA, Hansen C, Li JY, Brundin P. Are synucleinopathies prion-like disorders?. Lancet Neurol. 2010 Nov 1;9(11):1128-38. https://doi.org/10.1016/S1474-4422(10)70213-1 PMid:20846907
65. Mao X, Ou MT, Karuppagounder SS, Kam TI, Yin X, Xiong Y, Ge P, Umanah GE, Brahmachari S, Shin JH, Kang HC. Pathological α-synuclein transmission initiated by binding lymphocyte-activation gene 3. Science. 2016; 353(6307):aah3374. https://doi.org/10.1126/science.aah3374 PMid:27708076 PMCid:PMC5510615
66. Challis C, Hori A, Sampson TR, Yoo BB, Challis RC, Hamilton AM, *et al*. Gut-seeded α-synuclein fibrils promote gut dysfunction and brain pathology specifically in aged mice. Nat Neurosci. 2020; 23(3):327-336. https://doi.org/10.1038/s41593-020-0589-7 PMid:32066981 PMCid:PMC7065967
67. Annerino DM, Arshad S, Taylor GM, Adler CH, Beach TG, Greene JG. Parkinson's disease is not associated with gastrointestinal myenteric ganglion neuron loss. Acta Neuropathol. 2012; 124:665-680. https://doi.org/10.1007/s00401-012-1040-2 PMid:22941241 PMCid:PMC3473167
68. Baumuratov AS, Antony PM, Ostaszewski M, He F, Salamanca L, Antunes L, *et al*. Enteric neurons from Parkinson's disease patients display *ex vivo* aberrations in mitochondrial structure. Sci Rep. 2016;6(1):33117. https://doi.org/10.1038/srep33117 PMid:27624977 PMCid:PMC5021970
69. Bandres-Ciga S, Diez-Fairen M, Kim JJ, Singleton AB. Genetics of Parkinson's disease: An introspection of its journey towards precision medicine. Neurobiol Dis. 2020; 137:104782. https://doi.org/10.1016/j.nbd.2020.104782 PMid:31991247 PMCid:PMC7064061
70. Kuo YM, Li Z, Jiao Y, Gaborit N, Pani AK, Orrison BM, *et al*. Extensive enteric nervous system abnormalities in mice transgenic for artificial chromosomes containing Parkinson disease-associated α-synuclein gene mutations precede central nervous system changes. Hum Mol Genet. 2010; 19(9):1633-1650. https://doi.org/10.1093/hmg/ddq038 PMid:20106867 PMCid:PMC2850613
71. Colucci M, Cervio M, Faniglione M, De Angelis S, Pajoro M, Levandis G, *et al*. Intestinal dysmotility and enteric neurochemical changes in a Parkinson's disease rat model. Auton Neurosci. 2012; 169(2):77-86. https://doi.org/10.1016/j.autneu.2012.04.005 PMid:22608184
72. O'Donovan SM, Crowley EK, Brown JR, O'Sullivan O, O'Leary OF, Timmons S, *et al*. Nigral overexpression of α-synuclein in a rat Parkinson's disease model indicates alterations in the enteric nervous system and the gut microbiome. Neurogastroenterol Motil. 2020; 32(1):e13726. https://doi.org/10.1111/nmo.13726 PMid:31576631
73. Horsager J, Andersen KB, Knudsen K, Skjærbæk C, Fedorova TD, Okkels N, *et al*. Brain-first versus body-first Parkinson's disease: A multimodal imaging case-control study. Brain. 2020; 143(10):3077-3088. https://doi.org/10.1093/brain/awaa238 PMid:32830221
74. Buhmann C, Kassubek J, Jost WH. Management of pain in Parkinson's disease. J Parkinsons Dis. 2020; 10(s1):S37-S48. https://doi.org/10.3233/JPD-202069 PMid:32568113 PMCid:PMC7592654
75. Van Den Berge N, Ferreira N, Gram H, Mikkelsen TW, Alstrup AK, Casadei N, *et al*. Evidence for bidirectional and trans-synaptic parasympathetic and sympathetic propagation of alpha-synuclein in rats. Acta Neuropathol. 2019; 138(4):535-550. https://doi.org/10.1007/s00401-019-02040-w PMid:31254094 PMCid:PMC6778265
76. Surmeier DJ, Obeso JA, Halliday GM. Selective neuronal vulnerability in Parkinson disease. Nat Rev Neurosci. 2017; 18(2):101-113. https://doi.org/10.1038/nrn.2016.178 PMid:28104909 PMCid:PMC5564322
77. Khazdair MR, Kianmehr M, Anaeigoudari A. Effects of medicinal plants and flavonoids on Parkinson's disease: A review on basic and clinical evidences. Adv Pharm Bull. 2021; 11(2):224. https://doi.org/10.34172/apb.2021.026 PMid:33880344 PMCid:PMC8046395
78. Iriti M, Vitalini S, Fico G, Faoro F. Neuroprotective herbs and foods from different traditional medicines and diets. Molecules. 2010; 15(5):3517-3555. https://doi.org/10.3390/molecules15053517 PMid:20657497 PMCid:PMC6263339
79. Marino A, Battaglini M, Moles N, Ciofani G. Natural antioxidant compounds as potential pharmaceutical tools against neurodegenerative diseases. ACS Omega. 2022; 7(30):25974-25990. https://doi.org/10.1021/acsomega.2c03291 PMid:35936442 PMCid:PMC9352343
80. Dhanalakshmi C, Thenmozhi AJ, Manivasagam T, Essa MM, Khan MA. Spices and Parkinson's disease. Food and Parkinson's Disease; Nova Science Publishing, Inc.: New York, NY, USA. 2016.
81. Nataraj J, Manivasagam T, Thenmozhi AJ, Essa MM, Khan MA. Antiparkinsonic effect of black tea and its components. Food and Parkinson's Disease; 2016.
82. Nebrisi EE. Neuroprotective activities of curcumin in Parkinson's disease: A review of the literature. Int J Mol Sci.

2021; 22(20):11248. https://doi.org/10.3390/ijms222011248 PMid:34681908 PMCid:PMC8537234
83. Deokar G, Kakulte H, Kshirsagar S. Phytochemistry and pharmacological activity of Mucuna pruriens: A review. Pharm Biol Eval. 2016; 3(1):50-59.
84. Hang L, Basil AH, Lim KL. Nutraceuticals in Parkinson's disease. Neuromol Med. 2016; 18:306-321. https://doi.org/10.1007/s12017-016-8398-6 PMid:27147525 PMCid:PMC4983279
85. Kumar S, Mondal AC. Neuroprotective, neurotrophic and antioxidative role of Bacopa monnieri on CUS induced model of depression in rat. Neurochem Res. 2016; 41:3083-3094. https://doi.org/10.1007/s11064-016-2029-3 PMid:27506204
86. Mathur A, Verma SK, Purohit R, Singh SK, Mathur D, Prasad GB, *et al*. Pharmacological investigation of *Bacopa monnieri* on the basis of antioxidant, antimicrobial and anti-inflammatory properties. J Chem Pharm Res. 2010; 2(6):191-198.
87. Uabundit N, Wattanathorn J, Mucimapura S, Ingkaninan K. Cognitive enhancement and neuroprotective effects of *Bacopa monnieri* in Alzheimer's disease model. J Ethnopharmacol. 2010; 127(1):26-31. https://doi.org/10.1016/j.jep.2009.09.056 PMid:19808086
88. Morgan A, Stevens J. Does *Bacopa monnieri* improve memory performance in older persons? Results of a randomized, placebo-controlled, double-blind trial. J Altern Complement Med. 2010; 16(7):753-759. https://doi.org/10.1089/acm.2009.0342 PMid:20590480
89. Hazra S, Kumar S, Saha GK, Mondal AC. Reversion of BDNF, Akt and CREB in hippocampus of chronic unpredictable stress induced rats: Effects of phytochemical, *Bacopa Monnieri*. Psychiatry Investig. 2017; 14(1):74. https://doi.org/10.4306/pi.2017.14.1.74 PMid:28096878 PMCid:PMC5240459
90. Kumar N, Abichandani LG, Thawani V, Gharpure KJ, Naidu MU, Ramana GV. Efficacy of standardized extract of *Bacopa monnieri* (Bacognize®) on cognitive functions of medical students: a six-week, randomized placebo-controlled trial. Evid Based Complement Alternat Med. 2016; 2016. https://doi.org/10.1155/2016/4103423 PMid:27803728 PMCid:PMC5075615
91. Hosamani R. Neuroprotective efficacy of *Bacopa monnieri* against rotenone induced oxidative stress and neurotoxicity in *Drosophila melanogaster*. Neurotoxicology. 2009; 30(6):977-985. https://doi.org/10.1016/j.neuro.2009.08.012 PMid:19744517
92. Singh B, Pandey S, Verma R, Ansari JA, Mahdi AA. Comparative evaluation of extract of *Bacopa monnieri* and *Mucuna pruriens* as neuroprotectant in MPTP model of Parkinson's disease.
93. Hosamani R, Krishna G, Muralidhara. Standardized *Bacopa monnieri* extract ameliorates acute paraquat-induced oxidative stress, and neurotoxicity in prepubertal mice brain. Nut Neurosci. 2016; 19(10):434-446. https://doi.org/10.1179/1476830514Y.0000000149 PMid:25153704
94. Hosamani R. Prophylactic treatment with *Bacopa monnieri* leaf powder mitigates paraquat-induced oxidative perturbations and lethality in *Drosophila melanogaster*. Indian J Biochem Biophys. 2010; 47(2):75-82.
95. Shinomol GK, Mythri RB, Bharath MMS, Muralidhara. *Bacopa monnieri* extract offsets rotenone-induced cytotoxicity in dopaminergic cells and oxidative impairments in mice brain. Cell Mol Neurobiol. 2012; 32:455-465. https://doi.org/10.1007/s10571-011-9776-0 PMid:22160863 PMCid:PMC11881801
96. Siddique YH, Mujtaba SF, Faisal M, Jyoti S, Naz F. The effect of *Bacopa monnieri* leaf extract on dietary supplementation in transgenic Drosophila model of Parkinson's disease. Eur J Integr Med. 2014; 6(5):571-580. https://doi.org/10.1016/j.eujim.2014.05.007
97. Jansen RL, Brogan B, Whitworth AJ, Okello EJ. Effects of five Ayurvedic herbs on locomotor behaviour in a *Drosophila melanogaster* Parkinson's disease model. Phytother Res. 2014; 28(12):1789-1795. https://doi.org/10.1002/ptr.5199 PMid:25091506 PMCid:PMC4310928
98. Singh M, Murthy V, Ramassamy C. Standardized extracts of *Bacopa monniera* protect against MPP+-and paraquat-induced toxicity by modulating mitochondrial activities, proteasomal functions, and redox pathways. Toxicol Sci. 2012; 125(1):219-232. https://doi.org/10.1093/toxsci/kfr255 PMid:21972102
99. Verma DM, Balakrishnan NP, Dixit RD. Flora of Madhya Pradesh: Pteridophytes and Angiosperms (Ranunculaceae to Plumbaginaceae). Botanical Survey of India; 1993.
100. Ovallath S, Deepa P. The history of parkinsonism: descriptions in ancient Indian medical literature. Mov Disord. 2013; 28(5):566-568. https://doi.org/10.1002/mds.25420 PMid:23483637
101. Damodaran M, Ramaswamy R. Isolation of l-3: 4-dihydroxyphenylalanine from the seeds of Mucuna pruriens. Biochem J. 1937; 31(12):2149. https://doi.org/10.1042/bj0312149 PMid:16746556 PMCid:PMC1267191
102. Poddighe S, De Rose F, Marotta R, Ruffilli R, Fanti M, Secci PP, *et al*. *Mucuna pruriens* (Velvet bean) rescues motor, olfactory, mitochondrial and synaptic impairment in PINK1B9 Drosophila melanogaster genetic model of Parkinson's disease. PLoS One. 2014; 9(10):e110802. https://doi.org/10.1371/journal.pone.0110802 PMid:25340511 PMCid:PMC4207759
103. Yadav SK, Prakash J, Chouhan S, Singh SP. *Mucuna pruriens* seed extract reduces oxidative stress in nigrostriatal tissue and improves neurobehavioral activity in paraquat-induced Parkinsonian mouse model. Neurochem Int. 2013; 62(8):1039-1047. https://doi.org/10.1016/j.neuint.2013.03.015 PMid:23562769

104. Singhal B, Lalkaka J, Sankhla C. Epidemiology and treatment of Parkinson's disease in India. Parkinsonism Relat Disord. 2003; 9:105-109. https://doi.org/10.1016/S1353-8020(03)00024-5 PMid:12915075
105. Dhanasekaran M, Tharakan B, Manyam BV. Antiparkinson drug-*Mucuna pruriens* shows antioxidant and metal chelating activity. Phytother Res. 2008; 22(1):6-11. https://doi.org/10.1002/ptr.2109 PMid:18064727
106. Mirjalili MH, Moyano E, Bonfill M, Cusido RM, Palazón J. Steroidal lactones from *Withania somnifera*, an ancient plant for novel medicine. Molecules. 2009; 14(7):2373-2393. https://doi.org/10.3390/molecules14072373 PMid:19633611 PMCid:PMC6255378
107. Williamson EM. Major herbs of Ayurveda; 2002.
108. Bhattacharya SK, Bhattacharya A, Sairam K, Ghosal S. Anxiolytic-antidepressant activity of *Withania somnifera* glycowithanolides: An experimental study. Phytomedicine. 2000; 7(6):463-469. https://doi.org/10.1016/S0944-7113(00)80030-6 PMid:11194174
109. Sun GY, Li R, Cui J, Hannink M, Gu Z, Fritsche KL, *et al*. *Withania somnifera* and its with anolides attenuate oxidative and inflammatory responses and upregulate antioxidant responses in BV-2 microglial cells. Neuromolecular Med. 2016; 18:241-252. https://doi.org/10.1007/s12017-016-8411-0 PMid:27209361
110. Rai M, Jogee PS, Agarkar G, Santos CA. Anticancer activities of *Withania somnifera*: Current research, formulations, and future perspectives. Pharm Biol. 2016; 54(2):189-197. https://doi.org/10.3109/13880209.2015.1027778 PMid:25845640
111. Shivamurthy S, Manchukonda RS, Ramadas D. Evaluation of learning and memory enhancing activities of protein extract of *Withania somnifera* (Ashwagandha) in Wistar albino rats. Int J Basic Clin Pharmacol. 2016; 5(2):453-457. https://doi.org/10.18203/2319-2003.ijbcp20160761
112. Ahmad M, Saleem S, Ahmad AS, Ansari MA, Yousuf S, Hoda MN, *et al*. Neuroprotective effects of *Withania somnifera* on 6-hydroxydopamine induced Parkinsonism in rats. Hum Exp Toxicol. 2005; 24(3):137-147. https://doi.org/10.1191/0960327105ht509oa PMid:15901053
113. RajaSankar S, Manivasagam T, Sankar V, Prakash S, Muthusamy R, Krishnamurti A, *et al*. *Withania somnifera* root extract improves catecholamines and physiological abnormalities seen in a Parkinson's disease model mouse. J Ethnopharmacol. 2009; 125(3):369-373. https://doi.org/10.1016/j.jep.2009.08.003 PMid:19666100
114. Sankar SR, Manivasagam T, Krishnamurti A, Ramanathan M. The neuroprotective effect of *Withania somnifera* root extract in MPTP-intoxicated mice: An analysis of behavioral and biochemical varibles. Cell Mol Biol Lett. 2007; 12:473-481. https://doi.org/10.2478/s11658-007-0015-0 PMid:17415533 PMCid:PMC6275882
115. Prakash J, Yadav SK, Chouhan S, Singh SP. Neuroprotective role of *Withania somnifera* root extract in Maneb-Paraquat induced mouse model of parkinsonism. Neurochem Res. 2013; 38:972-980. https://doi.org/10.1007/s11064-013-1005-4 PMid:23430469
116. Siddique YH, Mujtaba SF, Faisal M, Naz F. Effect of *Withania somnifera* leaf extract on the dietary supplementation in transgenic Drosophila model of Parkinson's disease. All Results J Biol. 2015; 6(2):16-23.
117. De Rose F, Marotta R, Poddighe S, Talani G, Catelani T, Setzu MD, *et al*. Functional and morphological correlates in the Drosophila LRRK2 loss-of-function model of Parkinson's disease: Drug effects of *Withania somnifera* (Dunal) administration. PLoS One. 2016; 11(1):e0146140. https://doi.org/10.1371/journal.pone.0146140 PMid:26727265 PMCid:PMC4699764
118. Manjunath MJ, Muralidhara. Standardized extract of *Withania somnifera* (Ashwagandha) markedly offsets rotenone-induced locomotor deficits, oxidative impairments and neurotoxicity in Drosophila melanogaster. J Food Sci Technol. 2015; 52:1971-1981. https://doi.org/10.1007/s13197-013-1219-0 PMid:25829577 PMCid:PMC4375188
119. Prakash J, Chouhan S, Yadav SK, Westfall S, Rai SN, Singh SP. *Withania somnifera* alleviates parkinsonian phenotypes by inhibiting apoptotic pathways in dopaminergic neurons. Neurochem Res. 2014; 39:2527-2536. https://doi.org/10.1007/s11064-014-1443-7 PMid:25403619
120. Ammon HP, Wahl MA. Pharmacology of *Curcuma longa*. Planta Med. 1991; 57(01):1-7. https://doi.org/10.1055/s-2006-960004 PMid:2062949
121. Motterlini R, Foresti R, Bassi R, Green CJ. Curcumin, an antioxidant and anti-inflammatory agent, induces heme oxygenase-1 and protects endothelial cells against oxidative stress. Free Radic Biol Med. 2000; 28(8):1303-1312. https://doi.org/10.1016/S0891-5849(00)00294-X PMid:10889462
122. Srivastava S, Saksena AK, Khattri S, Kumar S, Dagur RS. *Curcuma longa* extract reduces inflammatory and oxidative stress biomarkers in osteoarthritis of knee: A four-month, double-blind, randomized, placebo-controlled trial. Inflammopharmacology. 2016; 24:377-388. https://doi.org/10.1007/s10787-016-0289-9 PMid:27761693
123. Bundy R, Walker AF, Middleton RW, Booth J. Turmeric extract may improve irritable bowel syndrome symptomology in otherwise healthy adults: A pilot study. J Altern Complement Med. 2004; 10(6):1015-1018. https://doi.org/10.1089/acm.2004.10.1015 PMid:15673996
124. Surh YJ, Chun KS, Cha HH, Han SS, Keum YS, Park KK, *et al*. Molecular mechanisms underlying chemopreventive activities of anti-inflammatory phytochemicals: Down-regulation of COX-2 and iNOS through suppression of NF-κB activation. Mutat Res-Fund Mol M. 2001; 480:243-268. https://doi.org/10.1016/S0027-5107(01)00183-X PMid:11506818
125. Gunes H, Gulen D, Mutlu R, Gumus A, Tas T, Topkaya AE. Antibacterial effects of curcumin: An *in vitro* minimum

inhibitory concentration study. Toxicol Ind Health. 2016; 32(2):246-250. https://doi.org/10.1177/0748233713498458 PMid:24097361

126. Allegra A, Innao V, Russo S, Gerace D, Alonci A, Musolino C. Anticancer activity of curcumin and its analogues: preclinical and clinical studies. Cancer Investig. 2017; 35(1):1-22. https://doi.org/10.1080/07357907.2016.1247166 PMid:27996308
127. Chaurasia S, Chaubey P, Patel RR, Kumar N, Mishra B. Curcumin-polymeric nanoparticles against colon-26 tumor-bearing mice: cytotoxicity, pharmacokinetic and anticancer efficacy studies. Drug Dev Ind Pharm. 2016; 42(5):694-700. https://doi.org/10.3109/03639045.2015.1064941 PMid:26165247
128. Chang XR, Wang L, Li J, Wu DS. Analysis of anti-depressant potential of curcumin against depression induced male albino wistar rats. Brain Res. 2016; 1642:219-225. https://doi.org/10.1016/j.brainres.2016.03.010 PMid:26972530
129. Bala K, Tripathy BC, Sharma D. Neuroprotective and anti-ageing effects of curcumin in aged rat brain regions. Biogerontology. 2006; 7:81-89. https://doi.org/10.1007/s10522-006-6495-x PMid:16802111
130. Wang Q, Sun AY, Simonyi A, Jensen MD, Shelat PB, Rottinghaus GE, *et al*. Neuroprotective mechanisms of curcumin against cerebral ischemia-induced neuronal apoptosis and behavioral deficits. J Neurosci Res. 2005; 82(1):138-148. https://doi.org/10.1002/jnr.20610 PMid:16075466
131. Jiang J, Wang W, Sun YJ, Hu M, Li F, Zhu DY. Neuroprotective effect of curcumin on focal cerebral ischemic rats by preventing blood-brain barrier damage. Eur J Pharmacol. 2007; 561(1-3):54-62. https://doi.org/10.1016/j.ejphar.2006.12.028 PMid:17303117
132. Garcia-Alloza M, Borrelli LA, Rozkalne A, Hyman BT, Bacskai BJ. Curcumin labels amyloid pathology *in vivo*, disrupts existing plaques, and partially restores distorted neurites in an Alzheimer mouse model. J Neurochem. 2007; 102(4):1095-1104. https://doi.org/10.1111/j.1471-4159.2007.04613.x PMid:17472706
133. Mythri RB, Bharath MMS. Curcumin: A potential neuroprotective agent in Parkinson's disease. Curr Pharm Des. 2012; 18(1):91-99. https://doi.org/10.2174/138161212798918995 PMid:22211691
134. Jagatha B, Mythri RB, Vali S, Bharath MS. Curcumin treatment alleviates the effects of glutathione depletion *in vitro* and *in vivo*: Therapeutic implications for Parkinson's disease explained via *in silico* studies. Free Radic Biol Med. 2008; 44(5):907-917. https://doi.org/10.1016/j.freeradbiomed.2007.11.011 PMid:18166164
135. Mythri RB, Harish G, Dubey SK, Misra K, Bharath MMS. Glutamoyl diester of the dietary polyphenol curcumin offers improved protection against peroxynitrite-mediated nitrosative stress and damage of brain mitochondria *in vitro*: Implications for Parkinson's disease. Mol Cell Biochem. 2011; 347:135-143. https://doi.org/10.1007/s11010-010-0621-4 PMid:20972609
136. Song S, Nie Q, Li Z, Du G. Curcumin improves neurofunctions of 6-OHDA-induced parkinsonian rats. Pathol Res Pract. 2016; 212(4):247-251. https://doi.org/10.1016/j.prp.2015.11.012 PMid:26922613
137. Gadad BS, Subramanya PK, Pullabhatla S, Shantharam IS, Rao KS. Curcumin-glucoside, a novel synthetic derivative of curcumin, inhibits α-synuclein oligomer formation: Relevance to Parkinson's disease. Curr Pharm Des. 2012; 18(1):76-84. https://doi.org/10.2174/138161212798919093 PMid:22211690
138. Storka A, Vcelar B, Klickovic U, Gouya G, Weisshaar S, Aschauer S, *et al*. Safety, tolerability and pharmacokinetics of liposomal curcumin (Lipocurc™) in healthy humans. Int J Clin Pharmacol Ther. 2015; 53(1):54-65. https://doi.org/10.5414/CP202076 PMid:25500488
139. Chan EW, Lim YY, Chew YL. Antioxidant activity of *Camellia sinensis* leaves and tea from a lowland plantation in Malaysia. Food Chem. 2007; 102(4):1214-1222. https://doi.org/10.1016/j.foodchem.2006.07.009
140. Tulsulkar J, Shah ZA. *Ginkgo biloba* prevents transient global ischemia-induced delayed hippocampal neuronal death through antioxidant and anti-inflammatory mechanism. Neurochem Int. 2013; 62(2):189-197. https://doi.org/10.1016/j.neuint.2012.11.017 PMid:23228346 PMCid:PMC3568207
141. Hsieh SK, Chung TY, Li YC, Lo YH, Lin NH, Kuo PC, *et al*. *Ginkgoghrelins*, unique acylated flavonoid diglycosides in *Folium Ginkgo*, stimulate growth hormone secretion via activation of the ghrelin receptor. J Ethnopharmacol. 2016; 193:237-247. https://doi.org/10.1016/j.jep.2016.08.015 PMid:27523747
142. Kuchta K, Qiao HX, Huang HB, Fang L, Chen Y, Wang RW. The neuroprotective activity of a proanthocyanidin enriched *Ginkgo biloba* L. leaves extract *in vitro* and *in vivo*. Planta Med. 2016; 82(S 01):P1067. https://doi.org/10.1055/s-0036-1597042
143. Rojas C, Rojas-Castaneda J, Rojas P. Antioxidant properties of a *Ginkgo biloba* leaf extract (EGb 761) in animal models of Alzheimer's and Parkinson's diseases. Curr Top Nutraceutical Res. 2016; 14(1):1.
144. Zhou X, Qi Y, Chen T. Long-term pre-treatment of antioxidant *Ginkgo biloba* extract EGb-761 attenuates cerebral-ischemia-induced neuronal damage in aged mice. Biomed Pharmacother. 2017; 85:256-263. https://doi.org/10.1016/j.biopha.2016.11.013 PMid:27863840
145. El-Ghazaly MA, Sadik NA, Rashed ER, Abd-El-Fattah AA. Neuroprotective effect of EGb761® and low-dose whole-body γ-irradiation in a rat model of Parkinson's disease.

Toxicol Ind Health. 2015; 31(12):1128-1143. https://doi.org/10.1177/0748233713487251 PMid:23696346

146. Kim MS, Lee JI, Lee WY, Kim SE. Neuroprotective effect of *Ginkgo biloba* L. extract in a rat model of Parkinson's disease. Phytother Res. 2004; 18(8):663-666. https://doi.org/10.1002/ptr.1486 PMid:15472919
147. Rojas P, Serrano-García N, Mares-Sámano JJ, Medina-Campos ON, Pedraza-Chaverri J, Ögren SO. EGb761 protects against nigrostriatal dopaminergic neurotoxicity in 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine-induced Parkinsonism in mice: role of oxidative stress. European J Neurosci. 2008; 28(1):41-50. https://doi.org/10.1111/j.1460-9568.2008.06314.x PMid:18662333
148. Fei C, Sheng-Gang S, Tong E. Experimental study on the neuronal toxical effect of levodopa and the inhibition of *Ginkgo biloba* extract on Parkinson disease in rats. Neurolog Disord. 2013;1(3):1-3. https://doi.org/10.4172/2329-6895.1000126
149. Yang SF, Wu Q, Sun AS, Huang XN, Shi JS. Protective effect and mechanism of *Ginkgo biloba* leaf extracts for Parkinson disease induced by 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine. Acta Pharmacol Sin. 2001; 22(12):1089-1093.
150. DeFeudis FV. *Ginkgo biloba* extract (EGb 761): From chemistry to the clinic. Wiesbaden: Ullstein Medical; 1998.
151. Sharangi AB. Medicinal and therapeutic potentialities of tea (*Camellia sinensis* L.) - A review. Food Res Int. 2009; 42(5-6):529-535. https://doi.org/10.1016/j.foodres.2009.01.007
152. Cabrera C, Artacho R, Giménez R. Beneficial effects of green tea-a review. J Am Coll Nutr. 2006; 25(2):79-99. https://doi.org/10.1080/07315724.2006.10719518 PMid:16582024
153. Khan N, Mukhtar H. Tea polyphenols for health promotion. Life Sci. 2007; 81(7):519-533. https://doi.org/10.1016/j.lfs.2007.06.011 PMid:17655876 PMCid:PMC3220617
154. Chen H, Zhang M, Qu Z, Xie B. Antioxidant activities of different fractions of polysaccharide conjugates from green tea (*Camellia Sinensis*). Food Chem. 2008; 106(2):559-563. https://doi.org/10.1016/j.foodchem.2007.06.040
155. Chan EW, Soh EY, Tie PP, Law YP. Antioxidant and antibacterial properties of green, black, and herbal teas of *Camellia sinensis*. Pharmacogn Res. 2011; 3(4):266. https://doi.org/10.4103/0974-8490.89748 PMid:22224051 PMCid:PMC3249787
156. Thakur P, Chawla R, Goel R, Narula A, Arora R, Sharma RK. Antibacterial activity of aquo-alcoholic extract of *Camellia sinensis* against isolates of carbapenem resistant Escherichia coli and food borne pathogens. Int J Biol Pharm Res. 2015; 6:606-616.
157. Chen BT, Li WX, He RR, Li YF, Tsoi B, Zhai YJ, *et al*. Anti-inflammatory effects of a polyphenols-rich extract from tea (*Camellia sinensis*) flowers in acute and chronic mice models. Oxid Med Cell Longev. 2012. https://doi.org/10.1155/2012/537923 PMid:22900128 PMCid:PMC3413976
158. Boehm K, Borrelli F, Ernst E, Habacher G, Hung SK, Milazzo S, *et al*. Green tea (*Camellia sinensis*) for the prevention of cancer. Cochrane Database Syst Rev. 2009(3), CD005004. https://doi.org/10.1002/14651858.CD005004.pub2 PMid:19588362 PMCid:PMC6457677
159. Ravindranath MH, Saravanan TS, Monteclaro CC, Presser N, Ye X, Selvan SR, *et al*. Epicatechins purified from green tea (*Camellia sinensis*) differentially suppress growth of gender-dependent human cancer cell lines. Evid Based Complement Alternat Med. 2006; 3:237-247. https://doi.org/10.1093/ecam/nel003 PMid:16786054 PMCid:PMC1475929
160. Kim HR, Rajaiah R, Wu QL, Satpute SR, Tan MT, Simon JE, *et al*. Green tea protects rats against autoimmune arthritis by modulating disease-related immune events. J Nutr. 2008; 138(11):2111-2116. https://doi.org/10.3945/jn.108.089912 PMid:18936206 PMCid:PMC2693422
161. Boadas-Vaello P, Verdú E. Epigallocatechin-3-gallate treatment to promote neuroprotection and functional recovery after nervous system injury. Neural Regen. Res. 2015; 10(9):1390-1392. https://doi.org/10.4103/1673-5374.165502 PMid:26604890 PMCid:PMC4625495
162. Tanaka K, Miyake Y, Fukushima W, Sasaki S, Kiyohara C, Tsuboi Y, *et al*. Intake of Japanese and Chinese teas reduces risk of Parkinson's disease. Parkinsonism Relat Disord. 2011; 17(6):446-450. https://doi.org/10.1016/j.parkreldis.2011.02.016 PMid:21458354
163. Levites Y, Weinreb O, Maor G, Youdim MB, Mandel S. Green tea polyphenol (-)-epigallocatechin-3-gallate prevents N-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine-induced dopaminergic neurodegeneration. J Neurochem. 2001; 78(5):1073-1082. https://doi.org/10.1046/j.1471-4159.2001.00490.x PMid:11553681
164. Pan T, Fei J, Zhou X, Jankovic J, Le W. Effects of green tea polyphenols on dopamine uptake and on MPP+-induced dopamine neuron injury. Life Sci. 2003; 72(9):1073-1083. https://doi.org/10.1016/S0024-3205(02)02347-0 PMid:12495785
165. Kim JS, Kim JM, Jeong-Ja O, Jeon BS. Inhibition of inducible nitric oxide synthase expression and cell death by (−)-epigallocatechin-3-gallate, a green tea catechin, in the 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine mouse model of Parkinson's disease. J Clin Neurosci. 2010; 17(9):1165-1168. https://doi.org/10.1016/j.jocn.2010.01.042 PMid:20541420
166. Xu Q, Langley M, Kanthasamy A, Reddy M. Neurorescue effect of EGCG in an animal model of Parkinson's disease. FASEB J. 2016; 30:1174.11. https://doi.org/10.1096/fasebj.30.1_supplement.1174.11
167. Leung LK, Su Y, Chen R, Zhang Z, Huang Y, Chen ZY. Theaflavins in black tea and catechins in green tea are equally

effective antioxidants. J Nutr. 2001; 131(9):2248-2251. https://doi.org/10.1093/jn/131.9.2248 PMid:11533262

168. Joghataie MT, Roghani M, Negahdar F, Hashemi L. Protective effect of caffeine against neurodegeneration in a model of Parkinson's disease in rat: Behavioral and histochemical evidence. Parkinsonism Relat Disord. 2004; 10(8):465-468. https://doi.org/10.1016/j.parkreldis.2004.06.004 PMid:15542005
169. Chaturvedi RK, Shukla S, Seth K, Chauhan S, Sinha C, Shukla Y, *et al*. Neuroprotective and neurorescue effect of black tea extract in 6-hydroxydopamine-lesioned rat model of Parkinson's disease. Neurobiol Dis. 2006; 22(2):421-434. https://doi.org/10.1016/j.nbd.2005.12.008 PMid:16480889
170. Anandhan A, Tamilselvam K, Radhiga T, Rao S, Essa MM, Manivasagam T. Theaflavin, a black tea polyphenol, protects nigral dopaminergic neurons against chronic MPTP/probenecid induced Parkinson's disease. Brain Res. 2012; 1433:104-113. https://doi.org/10.1016/j.brainres.2011.11.021 PMid:22138428
171. Tan LC, Koh WP, Yuan JM, Wang R, Au WL, Tan JH, *et al*. Differential effects of black versus green tea on risk of Parkinson's disease in the Singapore Chinese Health Study. Am J Epidemiol. 2008; 167(5):553-560. https://doi.org/10.1093/aje/kwm338 PMid:18156141 PMCid:PMC2737529
172. Olthof MR, Hollman PC, Zock PL, Katan MB. Consumption of high doses of chlorogenic acid, present in coffee, or of black tea increases plasma total homocysteine concentrations in humans. Am J Clin Nutr. 2001; 73(3):532-538. https://doi.org/10.1093/ajcn/73.3.532 PMid:11237928
173. Blandini F, Fancellu R, Martignoni E, Mangiagalli A, Pacchetti C, Samuele A, *et al*. Plasma homocysteine and l-dopa metabolism in patients with Parkinson disease. Clinical Chem. 2001; 47(6):1102-1104. https://doi.org/10.1093/clinchem/47.6.1102 PMid:11375298
174. Dos Santos EF, Busanello EN, Miglioranza A, Zanatta Â, Barchak AG, Vargas CR, *et al*. Evidence that folic acid deficiency is a major determinant of hyperhomocysteinemia in Parkinson' s disease. Metab Brain Dis. 2009; 24:257-269. https://doi.org/10.1007/s11011-009-9139-4 PMid:19294496
175. Mattson MP, Shea TB. Folate and homocysteine metabolism in neural plasticity and neurodegenerative disorders. Trends Neurosci. 2003; 26(3):137-146. https://doi.org/10.1016/S0166-2236(03)00032-8 PMid:12591216