

The Potential Role of Plants in the Treatment of Parkinson's Disease: Traditional Review

Bitkilerin Parkinson Hastalığının Tedavisindeki Potansiyel Rolü: Geleneksel Derleme

 Serap CANLI^a,  Mehlika BENLİ^b

^aDepartment of Elderly Care, Ankara University Haymana Vocational School, Ankara, Türkiye

^bDepartment of Biology, Ankara University Faculty of Science, Ankara, Türkiye

ABSTRACT Parkinson is a slowly progressive brain disease of a neurodegenerative nature. It is manifested by a lack of dopamine in the brain. This neurological disease is usually seen over the age of 60. It has major symptoms such as resting tremor, bradykinesia, rigidity and posterior reflex disorder. In the studies conducted, the cause of neural degeneration is not fully explained, but it is agreed that hereditary predisposition, environmental toxins and aging play an important role and it is a multifactorial disease. Parkinson's treatment is lifelong and the dopamine hormone supplements used in treatment are aimed at reducing symptoms. A lots of herbal products contain active components which are known to possess antioxidant action. Hence, the potential role of herbal products in treating Parkinson's disease (PD) cannot be undermined. In our article, some plants used to reduce the symptoms of PD and their mechanisms of action are discussed. Among these plants are *Acanthopanax senticosus*, *Anemopaegma mirandum*, *Bacopa monniera*, *Scutellaria baicalensis Georgi* (Labiatae), Bushen Huoxue Granuls, *Carthamus tinctorius* L., *Cassiae semen*, *Centella asiatica*, *Chrysanthemum morifolium Ramat*, *Chunghyuldan*, *Curcuma longa*, *Erythrina velutina* Willd, *Gastrodia elata* Blume, *Ginkgo biloba*, *Hypericum perforatum*, *Juglandis semen* (Walnut), *Lycium barbarum* L. (Gojiberry fruit), *Mucuna pruriens* (Velvet bean), *Paeoniae Alba Radix* (White Peony Root), *Peganum harmala* L., *Plumbago scandens*, *Pueraria lobata*, Resveratrol, *Thuja orientalis* and *Vicia faba* (Fava Bean). With further studies, it is possible to prepare new drugs from these naturally sourced herbs.

Keywords: Aged; Parkinson's disease; medicinal plants; traditional medicine

ÖZET Parkinson, nörodegeneratif nitelikte yavaş ilerleyen bir beyin hastalığıdır. Beyinde dopamin eksikliği ile kendini gösterir. Bu nörolojik hastalık genellikle 60 yaş üzerinde görülür. İstirahat tremoru, bradikinezi, rijidite ve posterior refleks bozukluğu gibi majör semptomları vardır. Yapılan çalışmalarda, nöral dejenerasyonun nedeni tam olarak açıklanamamakla birlikte kalıtsal yatkınlık, çevresel toksinler ve yaşlanmanın önemli rol oynadığı ve multifaktöriyel bir hastalık olduğu kabul edilmektedir. Parkinson tedavisi ömür boyu sürer ve tedavide kullanılan dopamin hormon takviyeleri ile semptomların azaltılması amaçlanır. Birçok bitki antioksidan etkiye sahip olduğu bilinen aktif bileşenler içermektedir. Bu nedenle bitkilerin Parkinson hastalığının tedavisindeki potansiyel rolü göz ardı edilmemelidir. Yazımızda, Parkinson hastalığının semptomlarını azaltmak için kullanılan bazı bitkiler ve etki mekanizmaları ele alınmıştır. Bu bitkiler arasında *Acanthopanax senticosus*, *Anemopaegma mirandum*, *Bacopa monniera*, *Scutellaria baicalensis Georgi* (Labiatae), Bushen Huoxue Granuls, *Carthamus tinctorius* L., *Cassiae semen*, *Centella asiatica*, *Chrysanthemum morifolium Ramat*, *Chunghyuldan*, *Curcuma longa*, *Erythrina velutina* Willd, *Gastrodia elata* Blume, *Ginkgo biloba*, *Hypericum perforatum*, *Juglandis semen* (Ceviz), *Lycium barbarum* L. (Gojiberry meyvesi), *Mucuna pruriens* (Kadife fasülye), *Paeoniae Alba Radix* (Beyaz Şakayık Kökü), *Peganum harmala* L., *Plumbago scandens*, *Pueraria lobata*, Resveratrol, *Thuja orientalis* and *Vicia faba* (Bakla) bulunmaktadır. Daha ileri çalışmalar ile bu doğal kaynaklı bitkilerden yeni ilaçlar hazırlamak mümkün olabilir.

Anahtar Kelimeler: Yaşlı; Parkinson hastalığı; şifalı bitkiler; geleneksel tıp

Parkinson's disease (PD) is characterized by the degeneration of dopaminergic neurons, and it is a progressive neuro-degenerative disease based on age.¹ This disease which was first defined by James

Parkinson in 1817 progresses with multiple symptoms.² Clinical symptoms of the disease are; such motor symptoms as bradykinesia, rigidity, trembles at rest and postural instability; and non-motor symp-

Correspondence: Mehlika BENLİ

Department of Biology, Ankara University Faculty of Science, Ankara, Türkiye

E-mail: benli@science.ankara.edu.tr



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toms like sleeping disorders, neuropsychiatric indications, dysautonomia, sensory complaints and gastrointestinal side effects.^{3,4} Motor function disorders also affect daily life activities while causing problems in mobility. Problems related with balance and walking may also lead to injuries, falls and inability to perform daily activities.⁵ Although the exact cause of the disease is not known, it is reported that many factors such as oxidative stress, free radical formation, mitochondrial dysfunction, apoptosis and neuro-inflammation and genetic tendency also play a role in the disease.^{6,7}

PD starts on average at the age of 60's, but it may have an early start in between the ages of 20 and 40. It may develop in males nearly one and a half times faster than it does in females. Although the disease itself is not the main cause of fatality, Parkinson patients generally die of complications like infection.⁸

PD is a disease affecting roughly 10 million people around the world. PD has generally taken the second place in neurological disorders during the years with disability according to the study on Global Disease Burden and Risk Factors. Global fatalities related to PD increased by 42.4% and reached to 117.4% from 2005 to 2015 and thousands of people lost their lives due to PD as a result of aging population.⁹

With increasing incidence, the prevalence of the PD, which seriously damages the physical and mental health of the patients and causes a big economical burden on both the families and the general society is expected to double by 2040 depending on the demographic changes and life expectancy.⁹

Drugs including levodopa, dopamine receptor agonists, monoamine oxidase (MAO) inhibitors, catechol-o methyltransferase inhibitors and dopamine replacement therapies have been used in the treatment of PD.¹⁰ However, existing treatments cannot prevent the process of the disease and may lead to some side effects.¹¹

This gradually increases the need and demand for safer, more secure and more efficient alternative and complementary medical treatment approaches. According to the definition made by National Center of Complementary and Alternative Medicine, Com-

plementary and Alternative Medicine which has its own health and medicine services (not regarded as medicine) are the systems, products and applications which are an indispensable part of traditional medicine.¹² Manipulative therapies like massage or chiropractic, body and mind therapies like yoga or relaxation, energy therapies like Reiki can be given as an example for such approaches.¹³ Another approach is the use of bioactive materials like vitamins or herbal supplements for the treatment or prevention of the PD. This study has been carried out to assess the effects of the plants which are used or can be used for the treatment of the PD.

PD AND HERBAL TREATMENT

The use of herbal medicine in the treatment of PD has been found in the old classical books in Chinese medicine, and additionally it has been observed that especially in recent years it has become more and more common in Asian countries and its popularity is continuing to rise in those countries.^{14,15} Due to the fact that some earlier studies have found that there is no evidence which shows that herbal medicine is practised for PD it has been confirmed in some other studies that plants have an important role in the treatment of PD.¹⁶ Moreover, it has also been stated in those studies that some plants used for the treatment of the PD is more efficient and safer than the synthetic drugs.¹⁷

The variety of the type of the supplements used for herbal treatment, one of the most frequent applied alternative methods for the PD, has been numerous, but they have generally not been taken under doctor's guidance.^{18,19}

Some plants which have been reported to have an important effect on the treatment of PD and their effects are as follows:

***Acanthopanax senticosus*:** It has been shown in the study carried out in 2005 by Fujikawa et al. that the hot water extracts of the cover of the root of *A. senticosus* has enabled an important increase in the levels of ethanol and dopamine, and it has a prophylactic effect on the dysfunctional attitudes of Parkinsonism such as depression, catalepsy and bradycardia.²⁰

***Anemopaegma mirandum*:** Valverde et al. studied the effect of *Anemopaegma* extracts in-vitro parkinsonian models on the neuroprotective activity of neuroblastoma human cells.²¹ It has been reported that it increases the survival of the cell by protecting the cytoplasmic membrane and mitochondrial membranes in human neuroblastoma cells.²¹

***Bacopa monniera*:** In a study carried out on rats by Jyoti and Sharma it has been found that *B. monniera* whole plant ethanolic extract has a therapeutic effect on the treatment of Parkinsonism resulting from neurotoxicity related to aluminium.²² In another study carried out with *B. monnieri* extract, it has been observed that it supports free radicals wiping mechanisms and that it also protects the cells in the prefrontal cortex, hippocampus against striatum cytotoxicity and deoxyribonucleic acid damage.²³

***Scutellaria baicalensis* Georgi (Labiatae):** Over 40 compounds have been isolated so far from *S. baicalensis*, the plant belonging to important traditional Chinese medicine, including flavonoid, terpenoids, volatile fats and polysaccharides. These compounds show various pharmacological activities on the nerve system and the immune system, and the protection of the liver, including anti-tumor, antibacterial, antiviral, antioxidant influences.²⁴ Baicalein, is an active compound derived from a dried root of *S. baicalensis*. It has been found that ethanolic extraction of baicalein decreases the level of nitric oxide inhibits apoptosis, the consumption of adenosine triphosphate, and the destruction of the membrane, encourages mitochondrial active respiration, and it has also been found that the plant has a protective effect on the mitochondria.^{25,26} Effects like the decrease in muscular trembles and the improvement in damaged motor activity have been observed in the studies carried out on rats and mice.²⁷

Bushen Huoxue Granuls: Bushen Huoxue (BSHXR), is a classical herbal prescription to feed the kidney and to stimulate the blood circulation. It consists of 6 plants: *Astragali radix*, *Angelicae sinensis radix*, *Ligustici Chuanxiong Rhizoma*, *Cuscutae semen*, *Taxilli Herba*, and *Dipsaci Radix* and the main active components of BSHXR are ferulic acid, kalikosin-7-glukopiranosid, hyperoside, quercitrin

and asperosaponin.²⁸ BSHXR Granuls is a traditional Chinese medical product which is claimed to have less neurological side effect symptoms compared to synthetic medicines. This plant has shown a high success rate in the improvement of life quality of the Parkinson's patients in the repair of motor functional disorders by decreasing muscle tension and in the treatment of depression and abnormal attitudes related with the PD by increasing norepinephrine and serotonin levels.^{29,30}

***Carthamus tinctorius* L.:** More commonly known name as safflower, *C. tinctorius* L. is a commonly used plant in the treatment of cerebrovascular diseases in classical Chinese medicine.¹⁷ According to an animal study, safflower has been shown to increase the body weight of the Parkinson's rats and to improve their behaviour.³¹

***Cassiae semen*:** Ju et al. have reported that the daily oral use of ethanolic extraction of Cassiae semen (*Cassia obtusifolia* root) for a period of 15 days significantly inhibits mobility disorders and the loss of cells in the PD models.³²

***Centella asiatica*:** *C. asiatica*, is a traditional medicine existing in Indian medicine and it is used in Ayurveda. Ayurveda expresses an approach which defines beneficial or harmful foods, medicines or attitudes for life and consciousness and which eradicates spiritual and physical sufferings.³³ Haleagrahara and Ponnusamy have studied the effect of this traditional plant used in Indian medicine.³⁴ In another study, they have found that the watery extraction of *C. asiatica* is effective against Parkinsonism, and it has led to an antioxidant activity in the hippocampus and corpus striatum area of the brain. The enzyme inhibition of *C. asiatica* (gotu kola) has been reported to have different effect mechanisms like preventing the formation of amyloid plaque in Alzheimer disease, and decreasing dopamine neurotoxicity and oxidative stress in PD and has been shown to have an important neuroprotection.³⁵ Also in another study *C. asiatica* and its main components have been found to be effective in neurological diseases, endocrine diseases, skin diseases, cardiovascular diseases, gastrointestinal diseases, immunity diseases and gynecologic diseases. In conclusion, *C. asiatica* and

triterpenoids have been shown to have useful effects on neurological disorders and skin diseases in clinical studies (anti-inflammatory, anti-oxidative stress, anti-apoptotic effects and mitochondrial function improvement).³⁶

***Chrysanthemum morifolium* Ramat:** Kim et al. who used chrysanthemum water extract in in-vitro parkinsonism model in the determination of life in cell culture, and have assessed the measurement of reactive oxygen types within the cell and the activity of the cleaning of free radicals.³⁷ They have established that various *C. morifolium* water extraction concentrations like 1, 10, 100 g/mL weakens the death of the cells, and shows a strong antioxidant cleaning activity for superoxide, hydroxyl and alchile radicals.

Chunghyuldan: Chunghyuldan (CHD), is an herbal complex consisting ethanol extraction and it is made up of *Scutellariae Radix*, *Coptidis Rhizoma*, *Phellodendri Cortex*, *Gardeniae Fructus*, and *Rhei Rhizoma*. It has shown recurrent ischemic stroke antihypertensive, antiatherosclerotic and inhibitor effects in experimental and clinical studies. Moreover, it has displayed neuroprotective effects in cerebrovascular and parkinson's models. It has been thought that these effects can be effective in the prevention of the recurrence of ischemic strokes. Therefore, CHD can be an effective and promising medicine in the treatment of cerebrovascular and cardiovascular diseases.³⁸ It has been reported to have anti-ischemic, anti-hyperlipidemic, and antioxidative effects.³⁹ In addition to this, its effects on the PD has also been investigated. Evidences which show that it inhibits the mitochondrial dysfunction, a responsible mechanism for the PD and decreases the behavioral symptoms like bradycardia have been provided.

***Curcuma longa*:** *C. longa*, a member of the ginger family (Zingiberaceae) has rhizomas under the soil. *C. longa*, has been used for the treatment of contagious diseases, inflammation, and various diseases like stomach, liver and blood diseases in traditional Indian medicine for thousands of years. Curcumin, is a big polyphenol isolated from the *C. Longa* rhizome. It has a wide pharmacological effect like anti-oxidant, anti-inflammatory, antimicrobial, antitumor and hep-

atoprotective activities.⁴⁰ Moreover, it has been reported in an article prepared by Labban that curcumin is effective in various neurological disorders like major depression, and in neurological diseases like late-onset dyskinesia and diabetic neuropathy.^{41,42}

***Erythrina velutina* Willd.:** It is a tree used in the treatment of central nervous system diseases in traditional medicine in Brazil. It has been claimed that the extraction obtained from this tree may have a potential effect in the treatment of the PD because it is protective for the neurons and decreases neurotoxicity.⁴³

***Gastrodia elata* Blume:** *G. elata* is used for neurological disorders as an anticonvulsant, analgesic and a sedative drug. Various neurodegenerative models are characterized by oxidative stress in the brain and inflammation, which leads to the death of cells via outer multiple cell and inner cell signal ways. The blockage of certain signal cascades may symbolize a compensation therapy for the damaged brain tissue. Anti-oxidative and anti-inflammatory compounds isolated from natural resources and various synthetic chemicals have been investigated. It has been shown that *G. elata* rhizom extraction and its compounds specifically protect neuronal cells in various pre-clinic brain damage models and regains the brain function by inhibiting oxidative stress and inflammatory.⁴⁴ Gastrodin, which is a phenolic glucoside, is the main bioactive component of Rhizoma *Gastrodiae*. Gastrodin has a wide range of useful effects on the central nervous system diseases and among its effective mechanisms are the modulation of the neurotransmitters, the repression of antioxidative, anti-inflammatory, microglial activation, the regulation of mitochondrial levels, and up-regulation of neurotrophins.⁴⁵ It is a traditional plant used to alleviate the symptoms of diseases like vertigo and epilepsy especially in the Eastern countries. It has been reported as a result of the finding that this plant protects cells against apoptosis and that this plant may have a supporting effect in the treatment of the PD.^{17,46}

***Ginkgo biloba*:** *G. biloba*, is a plant which is claimed to treat potential antioxidant neuroprotective and cerebrovascular diseases.⁴⁷ Therefore, it is com-

monly observed to be used in the Far East. Various animal studies performed with the extraction of *G. biloba* are important because they suggest that *G. biloba* has a neuroprotective effect and it may assist in the inhibition of oxidative stress in the PD due to its antioxidant effects.⁴⁸

***Hypericum perforatum*:** *Hypericum* species have been used in the treatment of various diseases since the ancient times. *H. perforatum* has been reported to be a useful drug in the treatment of neurological disorders such as koksidiinia, menopausal neurosis, headache, hydrophobia, hypersensitivity, mental ailments, neuralgia, paralysis, spastic paralysis, spinal convulsion, spinal irritation, and stiff neck.⁴⁹ Mohanasundari et al. have shown that the ethanolic extraction of *H. perforatum* allows a significant amount of healing in the dopamine level and prevents biochemical changes like the decrease in the lipid peroxidation.⁵⁰ On the other hand, Sánchez-Reus et al. found in their study carried out 45 days to treat rats with *H. perforatum* that *H. perforatum* extraction had an antioxidant effect and neuroprotective activity in the cell.⁵¹ *H. perforatum* and some main compounds have a protective effect in neurotoxicity, and thus it is potentially a useful activity in the treatment of neurodegenerative diseases like Alzheimer and PD.⁵²

***Juglandis semen* (Walnut):** Choi et al. have studied the neuroprotective effects of walnuts in the PD models.⁵³ As a result of the study they have found that water extraction of the walnut has protected the dopaminergic neurons as a MAO inhibitor with an antioxidant activity against neurotoxicity and has treated the symptoms in the rat models with Parkinson's. Considering all these results, walnut can be said to be a potential plant in the prevention and treatment of PD.

***Lycium barbarum* L. (Gojiberry fruit):** Gojiberry fruit is rich in nutritious elements like a natural derivative of ascorbic acid 2-O-β-D-glikopiranosil-L-ascorbic acid (vitamin C) and is medically important.⁵⁴ It has been established that the main active component of *L. barbarum* L. fruit has a strong antioxidant activity, and for this reason the potential neuroprotective effect of *L. barbarum* L. has been studied. In one

of these studies, it has been found that there is an increase in cellular activity and a decrease in mouse brain tissue apoptosis.^{55,56}

***Mucuna pruriens* (Velvet bean):** *M. pruriens* is a tropical legume that has been used in Ayurvedic medicine for centuries to treat PD and contains high levels of L-dopa. In the ancient Indian medical system, *M. pruriens* was traditionally used in the treatment of PD.⁵⁷ Various studies have been carried out on *M. pruriens*. Katzenschlager et al. have proved that *M. pruriens* can be used in the potential treatment of dyskinesia related with L-dopa.⁵⁷ *M. pruriens*, is the best-known natural source of L-dopa, which is a golden standard in the treatment of Parkinsonism.⁵⁸ Moreover, it has also been reported that in animal models *M. pruriens* extractions have neuroprotective effects like the regain of endogenous dopamine production and the decrease of oxidative stress.⁵⁹ *M. pruriens* was traditionally used in ancient Indian medicine for the treatment of the PD. It has been demonstrated in an article published by Lampariello et al. that *M. pruriens* has anti-Parkinson's and neuroprotective effects which may be associated with anti-oxidant activity.⁶⁰ In addition, the antioxidant activity of *M. pruriens* has shown the ability to wipe out hydroxyl radicals and the reactive oxygen types in a laboratory environment.⁵⁹ *M. pruriens*, is a legume used for thousands of years in the treatment of the PD. *M. pruriens*, contains the 2 components of levodopa and mitochondrial electron transport chain; coenzyme Q10 and nicotinic adenine dinucleotide. The result of the studies carried out on 60 patients for a period of 12 weeks has shown that *M. pruriens* alleviates the symptoms of the PD.⁶⁰ In another study, it has been found that the same plant extraction improved the biochemical and behavioral anomalies of the rats with Parkinson's.⁶¹

***Paeoniae Alba Radix* (White Peony Root):** It is a Chinese herbal medicine used for many different health problems like injuries, nose bleedings and paeniflorin, which is regarded as the main bioactive component of *Paeoniae Alba Radix*, is claimed to decrease neurological disorders in rats.^{62,63}

***Peganum harmala* L.:** *Peganum harmala* L. which is a hairless plant is thought to decrease the ox-

TABLE 1: Examples of studies containing potential benefits of herbs for Parkinson's disease.

Study	Active ingredient	Location in the plant	Duration and amount	The environment in which study data are evaluated	Effect
Fujikawa et al., 2005	Acanthopanax senticosus Harms (ASH)	Trunk bark	Extract distilled water from stem bark of ASH (250 mg/kg) once a day for 2 weeks	In vivo	Prophylactic effect on bradykinesia and depressive behaviors
Valverde et al., 2008	Extract of Anemopaegma mianandum (Catuaba)	Dry trunk bark	Three different concentrations of Catuaba extract 0.312, 0.625 and 1,250 mg/mL	In vitro	Increase in cell viability, cytoplasmic membrane and mitochondrial membrane preservation
Jyoti and Sharma, 2006	Ethanol extract of Bacopa	Whole of plant	40 mg/kg/day for 5 weeks	In vivo	Increase in antioxidant activity, decrease in oxidative stress
Jeong et al., 2011	Scutellaria baicalensis Georgia ethanol extract and main components	Whole of plant	50 and 100 mg/kg	In vivo	Reduction in oxidative damage and neuroinflammation, preventing memory impairment
Abiat et al., 2016	Standardized flavonoid extract from safflower	-	35 or 70 mg/kg/day	In vivo	Developing grip strength
Silva et al., 2016	Erythrina velutina ethanol extract	Trunk bark	-	In vitro	Neuroprotective activity
Almad et al., 2005	Ginkgo biloba extract	Whole standard raw ginkgo biloba plant	Three different concentrations of Ginkgo biloba 50, 100 and 150 mg/kg for 3 weeks	In vivo	Protection against Parkinsonism
Sánchez-Reus et al., 2007	Hypericum perforatum extract	-	Intraperitoneally 0.5 mL/kg for 45 days	In vivo	Reducing oxidative stress
Choi et al., 2016	Juglandis semen extract	Whole polyphenol-rich juicy walnut	100 mg/kg/day for 6 days	In vitro and in vivo	Protective effect on dopaminergic damage, positive effect on poor motor coordination, postural balance and bradykinesia
Cao et al., 2017	Active ingredient of Lycium barbarum L.	-	0, 50, 100, 200 or 400 µM H2O2 and/or 125, 250, 500, 800 or 1,000 µg/mL for 24 hours	In vitro and in vivo	Protective effect against nephrotoxicity
Liu et al., 2007	Paeoniflorin extracted from Paeoniae radix	Root part of the plant	2.5, 5 and 10 mg/kg twice daily for 11 days	In vivo	Behavioral improvement
Xiao et al., 2017	Pueraria lobata Isoflavonoids	Root part of the plant	80 or 160 mg/kg single dose	In vivo	Neuroprotective effect

oxidative stress and protect the dopaminergic neurons.⁶⁴ It has also been determined in one study that *P. harmala* has increased the muscle stiffness, decreased the lipid and oxidation levels of the brain and prevented the degeneration of the dopaminergic neurons in the treated group.⁶⁵

Plumbago scandens: The effects of *P. scandens* at various dosages have been investigated at animal models. Ethanol extraction of *P. scandens* and total acetate fraction have suppressed the trembles for 60 minutes at the doses of 1,000 and 2,000 mg/kg depending on the dosage. Moreover, locomotor activity, the presence of catalepsy and palpebral ptozsis have decreased, and therefore it has been claimed to have a therapeutic effect against Parkinsonism.⁶⁶

Pueraria lobata: It is present in traditional Chinese medicine *P. lobata* willd. It is commonly used in the treatment of cardiovascular and cerebrovascular diseases, diabetes, Alzheimer, PD, endometriosis and cancer. Puerarin, obtained from the plant root, has been reported to have some pharmacologic effects like vasodilation, antioxidant, anti-inflammatory, alleviating pain, improving bone development, inhibiting alcohol consumption and decreasing insulin resistance.⁶⁷ Isoflavonoids, are the so-called active component of *P. lobata* and they have shown a significant neuro-protective effect against cerebrovascular disorders, hypertension and the PD.⁶⁸

It has been acknowledged that apoptosis of the dopaminergic neurons is a key mechanism in the patho-

genesis of the PD. Puerarin, which is obtained from the root of *P. lobata*, has been used in the treatment of ischemic heart diseases and cerebrovascular diseases as an oxygen free radical cleaner. With a study, puerarinin has been shown to alleviate oxidative stress and apoptosis and to protect dopaminergic neurons against retonon toxicity.⁶⁹

Resveratrol: Resveratrol, is a natural polyphenol found in plants like grapes and strawberries.⁷⁰ There have been various studies on the effects of resveratrol. It has been suggested in those studies that resveratrol has cardioprotective effects by decreasing free radicals and hydroperoxide enzymes, and that it can protect the cell against apoptosis and may play a role in animal models in the treatment of test motor disorders, oxidative stress and loss of neurons.^{71,72}

Thuja orientalis: *Thuja orientalis* is a commonly seen tree in India and a well-known tree in traditional Eastern medicine. Neuroinflammation, increasing microglial activation and oxidative stress are the new methods in the management of the PD. It is significant to note that *T. orientalis* has a neuroprotective effect against toxicity.⁷³

Vicia faba (Fava Bean): It is a plant containing high concentrations of levodopa.⁷⁴ Although there are a limited number of studies carried out on this plant, there are signs and findings that it has strong dopaminergic effects including dysnesia.⁷⁵

Some examples of studies carried out with the plants listed above are given in [Table 1](#).

LIMITATIONS OF THE STUDY

The fact that there are no certain terms or key words to obtain the information existing in the literature and also that there is no special database may be the limitations of the study.

CONCLUSION

PD is today regarded as an important illness which affects mainly the elder population, their care givers and the care systems. It has been reported that the existing medication used for the treatment of this dis-

ease whose underlying mechanism has not been completely understood yet has a limited effect on the disease. It is for this reason thought that various methods like herbal treatment may have a useful potential therapeutic effect by treating the symptoms of the PD since traditional, complementary and alternative medical applications have commonly been used in the prevention and treatment of various diseases in the world. A number of herbal plant, or plant based medicine have been reported to be efficient in the treatment and prevention of the PD. It has been focused in many of the studies in the literature that these plants have neuroprotective, antioxidant, anti-inflammatory, and antiapoptosis effects. Herbal compounds whose efficiency have been established and whose details have been analyzed in depth can be used alternatively for those who suffer from serious side effects especially after a long medicine treatment. However, there is still need for clinical studies about herbal treatment which can be used alternatively to treat the PD, and there is also a need for studying the potential advantages of plant preparations more and especially a need for clinical comparisons with the standard medications.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Serap Canli, Mehlika Benli; **Design:** Serap Canli, Mehlika Benli; **Control/Supervision:** Serap Canli, Mehlika Benli; **Data Collection and/or Processing:** Serap Canli, Mehlika Benli; **Analysis and/or Interpretation:** Serap Canli, Mehlika Benli; **Literature Review:** Serap Canli, Mehlika Benli; **Writing the Article:** Serap Canli, Mehlika Benli; **Critical Review:** Mehlika Benli; **References and Fundings:** Serap Canli, Mehlika Benli.

REFERENCES

- de Lau LM, Breteler MM. Epidemiology of Parkinson's disease. *Lancet Neurol.* 2006;5(6):525-35. [Crossref] [PubMed]
- Parkinson J. An essay on the shaking palsy. 1817. *J Neuropsychiatry Clin Neurosci.* 2002;14(2):223-36; discussion 222. [Crossref] [PubMed]
- Lill CM. Genetics of Parkinson's disease. *Mol Cell Probes.* 2016;30(6):386-96. Erratum in: *Mol Cell Probes.* 2020;52:101537. [Crossref] [PubMed]
- Tysnes OB, Storstein A. Epidemiology of Parkinson's disease. *J Neural Transm (Vienna).* 2017;124(8):901-5. [Crossref] [PubMed]
- Tinelli M, Kanavos P, Grimaccia F. The Value of Early Diagnosis and Treatment in Parkinson's Disease (A Literature Review of the Potential Clinical and Socioeconomic Impact of Targeting Unmet Needs in Parkinson's Disease). 1st ed. England: LSE Consulting; 2016.
- Mosley RL, Benner EJ, Kadiu I, Thomas M, Boska MD, Hasan K, et al. Neuroinflammation, oxidative stress and the pathogenesis of Parkinson's disease. *Clin Neurosci Res.* 2006;6(5):261-81. [Crossref] [PubMed] [PMC]
- Fearnley JM, Lees AJ. Ageing and Parkinson's disease: substantia nigra regional selectivity. *Brain.* 1991;114 (Pt 5):2283-301. [Crossref] [PubMed]
- Van Den Eeden SK, Tanner CM, Bernstein AL, Fross RD, Leimpeper A, Bloch DA, et al. Incidence of Parkinson's disease: variation by age, gender, and race/ethnicity. *Am J Epidemiol.* 2003;157(11):1015-22. [Crossref] [PubMed]
- GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet.* 2018;392(10159):1789-858. Erratum in: *Lancet.* 2019;393(10190):e44. [PubMed] [PMC]
- Rogers G, Davies D, Pink J, Cooper P. Parkinson's disease: summary of updated NICE guidance. *BMJ.* 2017;358:j1951. Erratum in: *BMJ.* 2019;364:i961. [Crossref] [PubMed]
- Jenner P. Treatment of the later stages of Parkinson's disease - pharmacological approaches now and in the future. *Transl Neurodegener.* 2015;4:3. [Crossref] [PubMed] [PMC]
- National Center for Complementary and Integrative Health [Internet]. Complementary, alternative, or integrative health: What's in a name? 2021. (Cited: January 28, 2022). Available from: [Link]
- Finseth TA, Hedeman JL, Brown RP 2nd, Johnson KI, Binder MS, Kluger BM. Self-reported efficacy of cannabis and other complementary medicine modalities by Parkinson's disease patients in Colorado. *Evid Based Complement Alternat Med.* 2015;2015:874849. [Crossref] [PubMed] [PMC]
- Zheng GQ. Therapeutic history of Parkinson's disease in Chinese medical treatises. *J Altern Complement Med.* 2009;15(11):1223-30. [Crossref] [PubMed]
- Yin R, Xue J, Tan Y, Fang C, Hu C, Yang Q, et al. The positive role and mechanism of herbal medicine in Parkinson's disease. *Oxid Med Cell Longev.* 2021;2021:9923331. [Crossref] [PubMed] [PMC]
- Zhang G, Xiong N, Zhang Z, Liu L, Huang J, Yang J, et al. Effectiveness of traditional Chinese medicine as an adjunct therapy for Parkinson's disease: a systematic review and meta-analysis. *PLoS One.* 2015;10(3):e0118498. [Crossref] [PubMed] [PMC]
- Amro MS, Teoh SL, Norzana AG, Srijit D. The potential role of herbal products in the treatment of Parkinson's disease. *Clin Ter.* 2018;169(1):e23-e33. [PubMed]
- Rajendran PR, Thompson RE, Reich SG. The use of alternative therapies by patients with Parkinson's disease. *Neurology.* 2001;57(5):790-4. [Crossref] [PubMed]
- Ovallath S, Deepa P. The history of parkinsonism: descriptions in ancient Indian medical literature. *Mov Disord.* 2013;28(5):566-8. [Crossref] [PubMed]
- Fujikawa T, Miguchi S, Kanada N, Nakai N, Ogata M, Suzuki I, et al. *Acanthopanax senticosus* Harms as a prophylactic for MPTP-induced Parkinson's disease in rats. *J Ethnopharmacol.* 2005;97(2):375-81. [Crossref] [PubMed]
- Valverde G De Andrade D, Madureira de Oliveria D, Barreto G, Bertolino LA, Saraceno E, et al. Effects of the extract of *Anemopaegma mirandum* (Catauba) on Rotenone-induced apoptosis in human neuroblastomas SH-SY5Y cells. *Brain Res.* 2008;1198:188-96. [Crossref] [PubMed]
- Jyoti A, Sharma D. Neuroprotective role of *Bacopa monniera* extract against aluminium-induced oxidative stress in the hippocampus of rat brain. *Neurotoxicology.* 2006;27(4):451-7. [Crossref] [PubMed]
- Chaudhari KS, Tiwari NR, Tiwari RR, Sharma RS. Neurocognitive effect of nootropic drug *Brahmi* (*Bacopa monnieri*) in Alzheimer's disease. *Ann Neurosci.* 2017;24(2):111-22. [Crossref] [PubMed] [PMC]
- Zhao T, Tang H, Xie L, Zheng Y, Ma Z, Sun Q, et al. *Scutellaria baicalensis* Georgi. (Lamiaceae): a review of its traditional uses, botany, phytochemistry, pharmacology and toxicology. *J Pharm Pharmacol.* 2019;71(9):1353-69. [Crossref] [PubMed]
- Jeong K, Shin YC, Park S, Park JS, Kim N, Um JY. Ethanol extract of *Scutellaria baicalensis* Georgi prevents oxidative damage and neuroinflammation and memorial impairments in artificial senescence mice. *J Biomed Sci.* 2011;18:14. [Crossref] [PubMed] [PMC]
- Li XX, He GR, Mu X, Xu B, Tian S, Yu X, et al. Protective effects of baicalin against rotenone-induced neurotoxicity in PC12 cells and isolated rat brain mitochondria. *Eur J Pharmacol.* 2012;674(2-3):227-33. [Crossref] [PubMed]
- Mu X, He GR, Yuan X, Li XX, Du GH. Baicalin protects the brain against neuron impairments induced by MPTP in C57BL/6 mice. *Pharmacol Biochem Behav.* 2011;98(2):286-91. [Crossref] [PubMed]
- Ding J, Tan X, Song K, Ma W, Xiao J, Song Y, et al. *Bushen huoxue* recipe alleviates implantation loss in mice by enhancing estrogen-progesterone signals and promoting decidual angiogenesis through FGF2 during early pregnancy. *Front Pharmacol.* 2018;9:437. [Crossref] [PubMed] [PMC]
- Yang MH, Li M, Dou YQ, Liu Y, Luo XD, Chen JZ, et al. [Effects of *Bushen Huoxue* Granule on motor function in patients with Parkinson's disease: a multicenter, randomized, double-blind and placebo-controlled trial]. *Zhong Xi Yi Jie He Xue Bao.* 2010;8(3):231-7. Chinese. [Crossref] [PubMed]
- Li M, Yang MH, Liu Y. [Effects of Chinese herbal medicine *Bushen Huoxue* Granule on quality of life of patients with Parkinson disease: a randomized, double-blinded and placebo-controlled trial]. *Zhong Xi Yi Jie He Xue Bao.* 2012;10(3):310-7. Chinese. [Crossref] [PubMed]
- Ablat N, Lv D, Ren R, Xiaokaiti Y, Ma X, Zhao X, et al. Neuroprotective effects of a standardized flavonoid extract from safflower against a rotenone-induced rat model of Parkinson's disease. *Molecules.* 2016;21(9):1107. [Crossref] [PubMed] [PMC]
- Ju MS, Kim HG, Choi JG, Ryu JH, Hur J, Kim YJ, et al. *Cassiae semen*, a seed of *Cassia obtusifolia*, has neuroprotective effects in Parkinson's disease models. *Food Chem Toxicol.* 2010;48(8-9):2037-44. [Crossref] [PubMed]
- Frawley D, Ranade S. *Ayurveda, Nature's Medicine*. 2nd ed. Wisconsin: Lotus Press; 2012.
- Haleagrahara N, Ponnusamy K. Neuroprotective effect of *Centella asiatica* extract (CAE) on experimentally induced parkinsonism in aged Sprague-Dawley rats. *J Toxicol Sci.* 2010;35(1):41-7. [Crossref] [PubMed]
- Orhan IE. *Centella asiatica* (L.) urban: from traditional medicine to modern medicine with neuroprotective potential. *Evid Based Complement Alternat Med.* 2012;2012:946259. [Crossref] [PubMed] [PMC]
- Sun B, Wu L, Wu Y, Zhang C, Qin L, Hayashi M, et al. Therapeutic potential of *Centella asiatica* and its triterpenes: a review. *Front Pharmacol.* 2020;11:568032. [Crossref] [PubMed] [PMC]

37. Kim IS, Koppula S, Park PJ, Kim EH, Kim CG, Choi WS, et al. Chrysanthe-mum morifolium Ramat (CM) extract protects human neuroblastoma SH-SY5Y cells against MPP⁺-induced cytotoxicity. *J Ethnopharmacol*. 2009;126(3):447-54. [[Crossref](#)] [[PubMed](#)]
38. Jung WS, Kwon S, Cho SY, Park SU, Moon SK, Park JM, et al. The effects of chunghyul-dan (A Korean medicine herbal complex) on cardiovascular and cerebrovascular diseases: a narrative review. *Evid Based Complement Alternat Med*. 2016;2016:2601740. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
39. Ko CN, Park IS, Park SU, Jung WS, Moon SK, Park JM, et al. Neuroprotective effect of Chunghyuldan (Qing Xue Dan) on hypoxia-reoxygenation induced damage of neuroblastoma 2a cell lines. *Chin J Integr Med*. 2013;19(12):940-4. [[Crossref](#)] [[PubMed](#)]
40. Tung BT, Nham DT, Hai NT, Thu DK. Curcuma longa, the polyphenolic Curcumin compound and pharmacological effects on liver. In: Watson R, Preedy VR, eds. *Dietary Interventions in Liver Disease Foods, Nutrients, and Dietary Supplements*. 1st ed. London, United Kingdom: Academic Press; 2019. p.125-34. [[Crossref](#)]
41. Labban L. Medicinal and pharmacological properties of Turmeric (Curcuma longa): A review. *J Pharm Biomed Sci*. 2014;5(1):17-23. [[Link](#)]
42. Gupta SC, Patchva S, Koh W, Aggarwal BB. Discovery of curcumin, a component of golden spice, and its miraculous biological activities. *Clin Exp Pharmacol Physiol*. 2012;39(3):283-99. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
43. Silva AH, Fonseca FN, Pimenta AT, Lima MS, Silveira ER, Viana GS, et al. Pharmacognostical analysis and protective effect of standardized extract and rizonic acid from erythrina velutina against 6-hydroxydopamine-induced neurotoxicity in SH-SY5Y cells. *Pharmacogn Mag*. 2016;12(48):307-12. [[PubMed](#)] [[PMC](#)]
44. Jang JH, Son Y, Kang SS, Bae CS, Kim JC, Kim SH, et al. Neuropharmacological potential of gastrodia elata blume and its components. *Evid Based Complement Alternat Med*. 2015;2015:309261. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
45. Liu Y, Gao J, Peng M, Meng H, Ma H, Cai P, et al. A review on central nervous system effects of gastrodin. *Front Pharmacol*. 2018;9:24. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
46. Kim IS, Choi DK, Jung HJ. Neuroprotective effects of vanillyl alcohol in Gastrodia elata Blume through suppression of oxidative stress and anti-apoptotic activity in toxin-induced dopaminergic MN9D cells. *Molecules*. 2011;16(7):5349-61. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
47. Zhang J, Sun HM, Bai LM, Xu H, Wu HX, Cui L. [Effect of Ginkgo biloba Pingchan Recipe on neuronal nitric oxide synthase mRNA expression in the brain of mouse models of Parkinson disease]. *Nan Fang Yi Ke Da Xue Xue Bao*. 2009;29(8):1735-40. [[PubMed](#)]
48. Ahmad M, Saleem S, Ahmad AS, Yousuf S, Ansari MA, Khan MB, et al. Ginkgo biloba affords dose-dependent protection against 6-hydroxydopamine-induced parkinsonism in rats: neurobehavioural, neurochemical and immunohistochemical evidences. *J Neurochem*. 2005;93(1):94-104. [[Crossref](#)] [[PubMed](#)]
49. Oztürk Y, Aydın S, Beis R, Başer KH, Berberoglu H. Effects of Hypericum perforatum L. and Hypericum calycinum L. extracts on the central nervous system in mice. *Phytomedicine*. 1996;3(2):139-46. [[Crossref](#)] [[PubMed](#)]
50. Mohanasundari M, Srinivasan MS, Sethupathy S, Sabesan M. Enhanced neuroprotective effect by combination of bromocriptine and Hypericum perforatum extract against MPTP-induced neurotoxicity in mice. *J Neurol Sci*. 2006;249(2):140-4. [[Crossref](#)] [[PubMed](#)]
51. Sánchez-Reus MI, Gómez del Río MA, Iglesias I, Elorza M, Slowing K, Benedí J. Standardized Hypericum perforatum reduces oxidative stress and increases gene expression of antioxidant enzymes on rotenone-exposed rats. *Neuropharmacology*. 2007;52(2):606-16. [[Crossref](#)] [[PubMed](#)]
52. Oliveira AI, Pinho C, Sarmento B, Dias AC. Neuroprotective activity of hypericum perforatum and its major components. *Front Plant Sci*. 2016;7:1004. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
53. Choi JG, Park G, Kim HG, Oh DS, Kim H, Oh MS. In vitro and in vivo neuroprotective effects of walnut (juglandis semen) in models of Parkinson's disease. *Int J Mol Sci*. 2016;17(1):108. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
54. Zhang Z, Liu X, Wu T, Liu J, Zhang X, Yang X, et al. Selective suppression of cervical cancer Hela cells by 2-O-β-D-glucopyranosyl-L-ascorbic acid isolated from the fruit of Lycium barbarum L. *Cell Biol Toxicol*. 2011;27(2):107-21. [[Crossref](#)] [[PubMed](#)]
55. Pearson JN, Patel M. The role of oxidative stress in organophosphate and nerve agent toxicity. *Ann N Y Acad Sci*. 2016;1378(1):17-24. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
56. Cao S, Du J, Hei Q. Lycium barbarum polysaccharide protects against neurotoxicity via the Nrf2-HO-1 pathway. *Exp Ther Med*. 2017;14(5):4919-27. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
57. Katzenschlager R, Evans A, Manson A, Patsalos PN, Ratnaraj N, Watt H, et al. Mucuna pruriens in Parkinson's disease: a double blind clinical and pharmacological study. *J Neurol Neurosurg Psychiatry*. 2004;75(12):1672-7. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
58. Pulikkalpara H, Kurup R, Mathew PJ, Baby S. Levodopa in Mucuna pruriens and its degradation. *Sci Rep*. 2015;5:11078. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
59. Manyam BV, Dhanasekaran M, Hare TA. Neuroprotective effects of the antiparkinson drug Mucuna pruriens. *Phytother Res*. 2004;18(9):706-12. [[Crossref](#)] [[PubMed](#)]
60. Lampariello LR, Cortelazzo A, Guerranti R, Sticozzi C, Valacchi G. The magic velvet bean of mucuna pruriens. *J Tradit Complement Med*. 2012;2(4):331-9. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
61. Rakeł D. Parkinson's disease. *Integrative Medicine*. 4th ed. Philadelphia: Elsevier; 2018. p.143-51.
62. Liu DZ, Xie KQ, Ji XQ, Ye Y, Jiang CL, Zhu XZ. Neuroprotective effect of paeoniflorin on cerebral ischemic rat by activating adenosine A1 receptor in a manner different from its classical agonists. *Br J Pharmacol*. 2005;146(4):604-11. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
63. Liu DZ, Zhu J, Jin DZ, Zhang LM, Ji XQ, Ye Y, et al. Behavioral recovery following sub-chronic paeoniflorin administration in the striatal 6-OHDA lesion rodent model of Parkinson's disease. *J Ethnopharmacol*. 2007;112(2):327-32. [[Crossref](#)] [[PubMed](#)]
64. Lopez-Real A, Rey P, Soto-Otero R, Mendez-Alvarez E, Labandeira-Garcia JL. Angiotensin-converting enzyme inhibition reduces oxidative stress and protects dopaminergic neurons in a 6-hydroxydopamine rat model of Parkinsonism. *J Neurosci Res*. 2005;81(6):865-73. [[Crossref](#)] [[PubMed](#)]
65. Rezaei M, Nasri S, Roughani M, Niknami Z, Ziai SA. Peganum Harmala L. Extract Reduces Oxidative Stress and Improves Symptoms in 6-Hydroxydopamine-Induced Parkinson's Disease in Rats. *Iran J Pharm Res*. 2016;15(1):275-81. [[PubMed](#)] [[PMC](#)]
66. Morais LC, Quintans-Júnior LJ, Franco CI, Almeida JR, Almeida RN. Antiparkinsonian-like effects of Plumbago scandens on tremorine-induced tremors methodology. *Pharmacol Biochem Behav*. 2004;79(4):745-9. [[Crossref](#)] [[PubMed](#)]
67. Zhou YX, Zhang H, Peng C. Puerarin: a review of pharmacological effects. *Phytother Res*. 2014;28(7):961-75. [[Crossref](#)] [[PubMed](#)]
68. Xiao B, Sun Z, Cao F, Wang L, Liao Y, Liu X, et al. Brain pharmacokinetics and the pharmacological effects on striatal neurotransmitter levels of Pueraria lobata isoflavonoids in rat. *Front Pharmacol*. 2017;8:599. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
69. Zhang X, Xiong J, Liu S, Wang L, Huang J, Liu L, et al. Puerarin protects dopaminergic neurons in Parkinson's disease models. *Neuroscience*. 2014;280:88-98. [[Crossref](#)] [[PubMed](#)]
70. Frémont L. Biological effects of resveratrol. *Life Sci*. 2000;66(8):663-73. [[Crossref](#)] [[PubMed](#)]
71. Bhat KPL, Kosmeder JW 2nd, Pezzuto JM. Biological effects of resveratrol. *Antioxid Redox Signal*. 2001;3(6):1041-64. [[Crossref](#)] [[PubMed](#)]

72. Lu KT, Ko MC, Chen BY, Huang JC, Hsieh CW, Lee MC, et al. Neuroprotective effects of resveratrol on MPTP-induced neuron loss mediated by free radical scavenging. *J Agric Food Chem*. 2008;56(16):6910-3. [[Crossref](#)] [[PubMed](#)]
73. Ju MS, Lee P, Kim HG, Lee KY, Hur J, Cho SH, et al. Protective effects of standardized Thuja orientalis leaves against 6-hydroxydopamine-induced neurotoxicity in SH-SY5Y cells. *Toxicol In Vitro*. 2010;24(3):759-65. [[Crossref](#)] [[PubMed](#)]
74. Kempster PA, Bogetic Z, Secombei JW, Martin HD, Balazs ND, Wahlqvist ML. Motor effects of broad beans (*Vicia faba*) in Parkinson's disease: single dose studies. *Asia Pac J Clin Nutr*. 1993;2(2):85-9. [[PubMed](#)]
75. Rijnthjes M. Knowing your beans in Parkinson's disease: a critical assessment of current knowledge about different beans and their compounds in the treatment of Parkinson's disease and in animal models. *Parkinsons Dis*. 2019;2019:1349509. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]