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A Review on Antiparkinson Activity

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Abstract

Parkinson's disease (PD) is the second most common neurodegenerative ailment after Alzheimer's disease. Currently, existing drugs for PD works by boosting dopaminergic transmission in the brain, hence reducing symptoms of PD. Unfortunately, these medicament does not stop progression of sickness. There are several herbs in the globe which have been used to treat PD since centuries by different medicinal systems such as Traditional Chinese Medicinal (TCM) system, Indian Ayurvedic system of medicine, Siddha medicine system and Unani medicine system. In this review article, we have provided some information on medicinal herbs which have proven antiparkinson efficacy in different research studies

Keywords: Parkinson's disease, Neurodegenerative, Carbidopa-Levodopa, Ashwagandha, Antioxidant

Introduction

Parkinson's disease (PD) is a neurodegenerative condition that primarily affects the motor system by causing damage to brain nerve cells. The structure and function of the central or peripheral nerve systems gradually deteriorate as a result of neurodegenerative diseases. Parkinson's disease causes the loss of dopaminergic neurons in the substantia nigra and basal ganglia, two deep brain regions [1]. The midbrain's substantia nigra regulates the body's equilibrium and motions. Damage to the nerve cells in such areas prevents them from regenerating, which leads to a permanent loss of nerve cells. Dopamine is a neurotransmitter that is produced by the nerve cells in the substantia nigra. In the brain, dopamine is a crucial neurotransmitter that helps neurons communicate with one another. Dopamine production decreases as Parkinson's disease (PD) kills nerve cells in the substantia nigra. Dopamine deficiency in the brain disrupts neuronal transmission. Parkinson's disease pathogenesis is thought to be caused by protein misfolding and ubiquitin-proteasome pathway malfunction [1]. Tremors, bradykinesia, stiffness, balance issues, walking difficulties, erectile dysfunction, urinary dysfunction, and memory issues are all signs of Parkinson's disease [21]. One kind of postural abnormality that is uncommon in Parkinson's disease is camptocormia. The thoracolumbar spine is characterized by excessive bending, which might worsen when walking [2]. Sleep disturbance, anxiety, sadness, exhaustion, constipation, and anosmia are a few non-motor symptoms [7]. According to one study, tremors may appear up to two years prior to a PD diagnosis [21]. Finger movement difficulties, such as changes in writing or typing (e.g., difficulty using a keyboard), may be early signs

of Parkinson's disease [22]. About 1% of people in this age bracket have Parkinson's disease, which often first manifests in those 60 years of age or older. On average, 20 out of 100,000 Americans suffer with Parkinson's disease. When between 50% and 80% of the substantia nigra's nerve cells have been destroyed, motor symptoms often start [3]. The American Parkinson Disease Association estimates that between 10% and 20% of people with Parkinson's disease are younger than 50. Males are 1.5 times more likely than females to get Parkinson's disease [4]. The precise causation of Parkinson's disease is still unknown. Oxidative stress, reactive oxygen species generation, neuroinflammation, mitochondrial dysfunction, compromised dopamine metabolism, and other processes cause Parkinson's disease [36, 12]. PD may be brought on by an oxidative phosphorylation deficiency [2]. Researchers have discovered a few genetic abnormalities that could be the origin of Parkinson's disease. Certain genes and their variations, including UCH-L1, DJ-1, LRRK2, and PINK1, are probably involved in the pathophysiology of Parkinson's disease [35]. The study of genetics has been crucial in determining potential causes and treatments in recent years. Its symptoms might be lessened by a few restricted drugs and surgical procedures. Some benefits of using herbal remedies for Parkinson's disease include less side effects even after long-term use, strong neuroprotective action, affordability, and accessibility. Several plants that have demonstrated antiparkinson action in various studies have been mentioned in this review article. Numerous plants have been utilized for thousands of years to treat disorders of the nervous system in various traditional medical systems.

Table No. 1: Some drugs which are commonly used in the treatment of Parkinson's disease

Class	Drugs
Dopamine precursor	Levodopa
Peripheral DOPA decarboxylase inhibitors	Carbidopa, Benserazide
Monoamine oxidase-B (MAO-B) inhibitors	Selegiline, Rasagiline
Catechol-O-methyltransferase (COMT) inhibitors	Tolcapone, Entacapone
Dopamine agonists	Bromocriptine, Pramipexole, Ropinirole [40]
N-Methyl-D-aspartate receptor (NMDA) Antagonist	Amantadine [41]
Anticholinergics drugs	Trihexyphenidyl [42], Biperiden, Procyclidine
Antihistamines	Orphenadrine

It is a traditional Chinese medicine used to lessen Parkinson's disease symptoms. This medication is frequently used as an adjuvant treatment for essential hypertension (EH) [13]. Eleven different herbs are combined to form TGY. Traditional Chinese Medicine (TCM) practitioners frequently prescribe it to treat Parkinson's disease (PD) symptoms like paralysis and tremors. One study examined the neuroprotective effects of Tian Ma Gou Teng Yin (TGY) on Drosophila PD models caused by rotenone. The study discovered that Drosophila PD models have improved locomotive function and a higher survival rate. Additionally, the study examined the neuroprotective effects of TGY on the rotenone-treated SH-SY5Y human neuroblastoma cell line. In SH-SY5Y cells, TYG reduces apoptotic cell death. Additionally, the study discovered that in hemiparkinsonian rats, TGY reduces the death of dopaminergic neurons [6]. It demonstrates that Parkinson's disease can be treated with TGY. But additional investigation into this medication is needed.

MEDICINAL PLANTS HAVING ANTIPARKINSON ACTIVITY

Withaniasomnira (Ashwagandha)

Family:Solanace

Ashwagandha, commonly known as Indian ginseng, is a well-known herb that has been used for over 4,000 years. In the Indian Ayurvedic medical system, it is one of the most significant herbs. It is a medication used as a nerve tonic. It has active chemical components

that can scavenge free radicals, such as alkaloids (isopelletierine) and steroidal lactones (withaferin A, withanone) [8][9]. Nervous and sexual issues can be effectively treated with dried ashwagandha roots. The actions of ashwagandha are adaptogenic. One study examined the neuroprotective benefits of Withania somnifera (Ws) in mice that had been exposed to oxidative stress and cognitive impairment caused by bisphenol A (BPA). Cognitive problems have been linked to BPA. To cause cognitive deficits, one group of mice was given 50 µg/Kg bw/day of BPA. Another group was given BPA orally along with 100 mg/kg bw/day of Withania somnifera root extract. The group of mice that got BPA + Withania somnifera extract took less time to reach hidden platforms in the Morris water maze test than the BPA-intoxicated group, according to the study. The study discovered that, in comparison to the BPA-intoxicated mice group, the Ws root extract treatment exhibits greater spontaneous alteration ($P < 0.05$) and entries in arms ($P < 0.001$) in the Y-maze test. According to the study's findings, BPA-induced cognitive and memory impairments in mice are mitigated by Withania somnifera root extract. NMDA receptors are significantly lost when BPA is administered to mice. NMDA receptors were much higher in the WS to BPA treatment group than in the BPA-intoxicated mice group [10].

Ginkgo biloba (Maidentree)

Family:Gink goaceae

Chinese medicine has been using ginkgo biloba for thousands of years. Ginkgo biloba leaves are extracted to make the majority of its products. Ginkgo biloba extract has demonstrated neuroprotective and antioxidant properties. Cognitive functioning can be enhanced by its extract [37]. It probably functions by inhibiting monoamine B, which reduces dopamine breakdown [11]. Ginkgo biloba contains ginkgolide B, a platelet activating factor (PAF). The neuroprotective properties of ginkgo leaf extract may be attributed to ginkgolides. In one instance, an elderly patient had Parkinson's disease that was getting worse. The patient was previously receiving treatment with carbidopa-levodopa, which provides some alleviation as the severity of the falls increases. Ginkgo biloba extract was administered to the patient three times a day. The substance was standardized to include 2% bilobalide, 6% terpene lactones, and 24% ginkgo flavon glycosides. During treatment, the patient is also given some multivitamins. The patient stops falling after six weeks of medication, and 80–90% of their Parkinson's disease symptoms have improved [11]. Ginkgo biloba seems to work by preserving dopamine levels in the brain and having antioxidant and free radical-scavenging qualities. In one study, the effects of EGb 761 ginkgo biloba extract were examined in rats. According to the study, taking EGb 716 orally for 14 days at a dose of 100 mg/kg-1 daily) raises rats' levels of noradrenaline and extracellular dopamine [37]. This demonstrates Ginkgo biloba's neuroprotective properties.

Bacopamonniri (Brahmi)
Family:Scrophulariaceae

In Indian Ayurvedic medicine, Bacopa monnieri, often known as Brahmi, is a common herb used to treat neurological issues. It is frequently included in Ayurvedic treatments for cognitive impairment. Bacopa monnieri appears to have a feeding impact on neurons when administered moderately and over an extended period of time [14]. It seems that bacopa monnieri enhances cerebral circulation. Bacosides A and B found in Bacopa monnieri leaves may be the cause of the plant's neuro-beneficial properties [15]. The preventive effect of Bacopa monnieri against Rotenone-induced Parkinson's disease in PC 12 cell lines was examined in one study (R. Wudayagiri et al., 2017). It has been discovered that Bacopa monnieri protects against Parkinson's disease caused by rotenone. PC 12 cells, which have many traits with substantia nigra cells, are used in the study. According to the study, pre-treating PC 12 cells with Bacopa monnieri (BM) extract increases cell viability by 27% as compared to rotenone treatment. This demonstrates Bacopa monnieri's ability to prevent Parkinson's disease caused by rotenone [24].

Mucuna pruriens (velvetbean
Family:Fabaceae

The cowhage or velvet bean, Mucuna pruriens, also known as Atmagupta, is a tropical legume that is mostly found in tropical regions of Central and South America, Africa, and India [17]. Mucuna pruriens seed powder has been utilized to cure a variety of dysfunctions in the Unani and Ayurvedic medical systems. This herb has been used to treat Parkinson's disease in Ayurveda. L-DOPA ranges from 3.1 to 6.1% in mucuna pruriens seeds. The seed contains traces of nicotine and serotonin [30]. The effects of Mucuna pruriens (MP) in individuals with advanced Parkinson's disease were examined in one study (Roberto Cilia et al. 2017). Using 100/25 mg dispersible tablets at 3.5 mg/kg as a reference, the study examined the safety and effectiveness of a single dose consumption of Mucuna pruriens powder, which was made from its roasted seeds. According to the study, a high dose of Mucuna pruriens (17.5 mg/kg) exhibits greater motor improvement at 90 and 180 minutes, fewer dyskinesia and longer ON duration, and less adverse effects when compared to LD+DDCI and LD-DDCI, whereas a low dose of Mucuna pruriens (12.5 mg/kg) yields similar motor responses with fewer dyskinesia and adverse effects when compared with LD+DDCI [16]. L-DOPA, gallic acid, phytic acid, quercetin, and catechin are found in Mucuna pruriens. L-DOPA and other phytochemicals found in mucuna pruriens aqueous extract may prevent dopaminergic neurons in the substantia nigra from degenerating [18].

Lycium barbarum (wolfberry) Family-Solanaceae

Lycium barbarum, often known as Chinese wolfberry or Murali (India), is widely distributed in Tibet, Mongolia, Northern China, and many other nations. The Chinese medical system has been using this plant for 2000 years. This plant's berry is consumed raw. Its berry is used to make wine, tea, and juice, which are then consumed. Tablets, tinctures, and powders are made from the fruit [23]. Because Lycium barbarum L. contains Lycium barbarum polysaccharide (LBP), which has potent antioxidant properties, it acts as a neuroprotective agent by lowering oxidative stress in the brain [20]. One study examined the neuroprotective effects of LBP in rats treated with $CoCl_2$ in vivo and PC12 cells treated with H_2O_2 in vitro. According to the study, LBP prevents PC12 cells' Nrf2/HO-1 signaling from being reduced by H_2O_2. By upregulating Nrf2/HO-1 signaling, LBP exhibits neuroprotective efficacy against neurotoxicity [19].

Curcuma longa (Turmeric)

Family: Zingiberaceae

For thousands of years, Ayurveda and Siddha have employed curcuma longa. This medication is used to treat a number of conditions, including wounds, GIT issues, skin conditions like acne, lung conditions, stomach conditions, and liver issues [26]. The rhizomes of Curcuma longa possess anti-inflammatory, antioxidant, antimicrobial, antifungal, antiviral, antibacterial, and chemoprotective qualities [27, 28, 29]. The primary active component of Curcuma longa, which is utilized as an active component in numerous traditional herbal preparations, is curcumin.
By preventing apoptosis, curcuma longa extract has been shown to have neuroprotective properties. Curcuma longa's dose-dependent effects on SH-SY5Y human neuroblastoma cells were examined in one study. The endogenous neurotoxine salsolinol was employed to induce neurotoxicity in SH-SY5Y cells. Dopaminergic neurons are harmed by salsolinol. According to the study, curcuma longa extract significantly lessens the inhibition of cell development. Different dosages of Curcuma longa extract (0.05 mg/ml and 0.1 mg/ml at 24 and 48 hours) showed significantly downregulated mRNA expression levels of p53, Bax, and caspase 3 ($P<0.05$), indicating that the extract has a neuroprotective effect via inhibiting apoptosis. This demonstrates a neuroprotective effect against neurotoxicity caused by salsolinol in human neuroblastoma cells SH-SY5Y [26].

Centella asiatica (GotuKola) Family: Apiaceae

The tropical medicinal plant Centella asiatica is primarily found in China, Indonesia, Malaysia, and India. Centella asiatica has been used to treat nervine issues and enhance memory in both Indian Ayurvedic medicine and Traditional

Chinese medicine. It is referred to as Mandookaparni in Ayurveda and is well known as Gotu kola worldwide [32]. By preventing the development of amyloid plaque in the brain and protecting against neurotoxicity in Parkinson's disease, this herb appears to have neuroprotective properties in Alzheimer's disease [33]. In one study, Sprague-Dawley rats are used to test the neuroprotective benefits of Centella asiatica extract. According to the study, centella asiatica extract (300 mg/kg for 21 days) reverses oxidative damage and reduces MPTP-induced peroxide generation in the hippocampus and striatum. They discovered that the levels of antioxidant enzymes and total antioxidants were higher in these areas. The study also found that serum lipid hydroperoxides and protein carbonyl concentration significantly decreased [34].

Ficus religiosa (Pippala tree) Family: Moraceae

Ficus religiosa, also called Pippala in Sanskrit and Pipal tree in English, has long been used as an antidiabetic, antiulcer, antibacterial, anticancer, anticonvulsant, and antiasthmatic medication.

Petroleum ether extract of Ficus religiosa, Ficus religiosa leaves (PEFRE) exhibits antiparkinson effects in rats with Parkinson's disease induced by 6-hydroxydopamine (6-OHDA), according to a study by J. Bhangale and S. Acharya. In comparison to rats administered with 6-OHDA, the study demonstrates that oral administration of PEFRE at doses of 200 and 400 mg/kg considerably ($P < 0.001$) increases locomotor activity (from day 20 to 55). The impact of PEFRE on 6-OHDA-induced Parkinson's disease in rats using a rotarod apparatus was also examined in this study. In comparison to animals with Parkinson's disease, the study discovered that long-term oral treatment of PEFRE at dosages of 200 and 400 mg/kg significantly ($P <0.001$) increases the decline of time from day 15 to 55 [39]. This demonstrates Ficus religiosa's antiparkinson properties.

Conclusion

Important details regarding the antiparkinson activity of many medicinal plants were included in this review article. Positive research indicates that natural herbs can slow the progression of Parkinson's disease through a variety of neuroprotective mechanisms, including antioxidants, enhanced dopamine levels and transmission, apoptosis inhibition, and other mechanisms that stop the brain's dopaminergic neurons from dying. In order to develop a widely used herbal medication that can either cure or slow the progression of Parkinson's disease, we need to do more thorough research at the molecular level of the complex variety of chemical constituents found in plant materials.

References

1. Dauer W, Przedborski S. Parkinson's disease: mechanisms and models. Neuron 2003 Sep 11;39(6):889-909.DOI: 10.1016/s0896-6273(03)00568-3. PMID: 12971891
2. J Jankovic. Parkinson’s disease: clinical features and diagnosis. Journal of Neurology, Neurosurgery & Psychiatry 2008;79:368–376. doi:10.1136/jnnp.2007.131045
3. DeMaagd G, Philip A. Parkinson's Disease and Its Management: Part 1: Disease Entity, Risk Factors, Pathophysiology, Clinical Presentation, and Diagnosis. P T. 2015;40(8):504–532.
4. Moisan F, Kab S, Mohamed F, et al. Journal of Neurol Neurosurg Psychiatry. 2016;87:952–957. doi:10.1136/jnnp-2015-312283. Parkinson disease male-to-female ratios increase with age: French nationwide study and meta-analysis. 2016;87:952–957. doi:10.1136/jnnp-2015-312283
5. Hinz M, Stein A, Cole T. Parkinson's disease: carbidopa, nausea, and dyskinesia. Clin Pharmacol. 2014;6:189–194. Published 2014 Nov 14. doi:10.2147/CPAA.S72234
6. Liu LF, Song JX, Lu JH, Huang YY, Zeng Y, Chen LL, Durairajan SS, Han QB, Li M. Tianma Gouteng Yin, a Traditional Chinese Medicine decoction, exerts neuroprotective effects in animal and cellular models of Parkinson's disease. Sci Rep. 2015 Nov 18;5:16862. doi: 10.1038/srep16862. PMID: 26578166; PMCID: PMC4649620.
7. DeMaagd G, Philip A. Parkinson's Disease and Its Management: Part 1: Disease Entity, Risk Factors, Pathophysiology, Clinical Presentation, and Diagnosis. P T. 2015

Aug;40(8):504-32. PMID: 26236139; PM Singh N, Rai SN, Singh D, Singh SP (2015) Withania somnifera shows ability to counter Parkinson's Disease: An Update. SOJ Neurol 2(2), 1-4. DOI: http://dx.doi.org/10.15226/2374-6858/2/2/00120

8. Singh N, Bhalla M, de Jager P, Gilca M. An overview on ashwagandha: a Rasayana (rejuvenator) of Ayurveda. Afr J Tradit Complement Altern Med. 2011;8(5 Suppl):208-13. doi: 10.4314/ajtcam.v8i5S.9. Epub 2011 Jul 3. PMID: 22754076; PMCID: PMC3252722.
9. Birla H, Keswani C, Rai S.N. et al. Neuroprotective effects of Withania somnifera in BPA induced-cognitive dysfunction and oxidative stress in mice. Behav Brain Funct 15, 9 (2019). https://doi.org/10.1186/s12993-019-0160-4
10. Conrad GD. Is Ginkgo biloba and/or a Multivitamin-multimineral Supplement a Therapeutic Option for Parkinson's Disease? A Case Report. Glob Adv Health Med. 2014 Jul;3(4):43-4. doi: 10.7453/gahmj.2013.096. PMID: 25105077; PMCID: PMC4104556.
11. Tanaka K, Galduróz RF, Gobbi LT, Galduróz JC. Ginkgo biloba extract in an animal model of Parkinson's disease: a systematic review. Curr Neuropharmacol. 2013 Jul;11(4):430-5. doi: 10.2174/1570159X11311040006. PMID: 24381532; PMCID: PMC3744905.
12. Wang J, Feng B, Yang X, Liu W, Liu Y, Zhang Y, Yu G, Li S, Zhang Y, Xiong X. Tianma gouteng yin as adjunctive treatment for essential hypertension: a systematic review of randomized controlled trials. Evid Based Complement Alternat Med. 2013;2013:706125. doi: 10.1155/2013/706125. Epub 2013 Apr 24. PMID: 23710230; PMCID: PMC3655574.
13. Aguiar S, Borowski T. Neuropharmacological review of the nootropic herb Bacopa monnieri. Rejuvenation Res. 2013 Aug;16(4):313-26. doi: 10.1089/rej.2013.1431. PMID: 23772955; PMCID: PMC3746283.
14. Jayshree Nellor, Cynthia Pauline, Kanchana Amarnath. Bacopa monnieri Phytochemicals Mediated Synthesis of Platinum Nanoparticles and Its Neurorescue Effect on 1-Methyl 4-Phenyl 1,2,3,6 Tetrahydropyridine-Induced Experimental Parkinsonism in Zebrafish. Volume 2013. Article ID 972391. doi: 10.1155/2013/972391
15. Cilia R, Laguna J, Cassani E, Cereda E, Pozzi NG, Isaias IU, Contin M, Barichella M, Pezzoli G. Mucuna pruriens in Parkinson disease: A double-blind, randomized, controlled, crossover study. Neurology. 2017 Aug 1;89(5):432-438. doi: 10.1212/WNL.0000000000004175. Epub 2017 Jul 5. PMID: 28679598; PMCID: PMC5539737.
16. Katzenschlager R, Evans A, Manson A, et al. Mucuna pruriens in Parkinson's disease: a double blind clinical and pharmacological study. J Neurol Neurosurg Psychiatry. 2004;75(12):1672–1677. doi:10.1136/jnnp.2003.028761
17. Rai SN, Birla H, Singh SS, et al. Mucuna pruriens Protects against MPTP Intoxicated Neuroinflammation in Parkinson's Disease through NF-κB/pAKT Signaling Pathways. Front Aging Neurosci. 2017;9:421. Published 2017 Dec 19. doi:10.3389/fnagi.2017.00421
18. Cao S, Du J, Hei Q. Lycium barbarum polysaccharide protects against neurotoxicity via the Nrf2-HO-1 pathway. Exp Ther Med. 2017 Nov;14(5):4919-4927. doi: 10.3892/etm.2017.5127. Epub 2017 Sep 19. PMID: 29201196; PMCID: PMC5704330.
19. Kai Gao, Meiyou Liu , Jinyi Cao, Minna Yao , Yunyang Lu, Jiankang Li, Xiaohe Zhu, Zhifu Yang ,and Aidong Wen. Protective Effects of Lycium barbarum Polysaccharide on 6-OHDA-Induced Apoptosis in PC12 Cells through the ROS-NO Pathway. Molecules 2015, 20, 293-308; doi:10.3390/molecules20010293.
20. Schrag A, Horsfall L, Walters K, Noyce A, Petersen I. Prediagnostic presentations of Parkinson's disease in primary care: a case-control study. Lancet Neurol. 2015;14(1):57–64. doi:10.1016/S1474-4422(14)70287-X
21. Adams WR. High-accuracy detection of early Parkinson's Disease using multiple characteristics of finger movement while typing. PLOS One. 2017 Nov 30;12(11):e0188226. doi:

10.1371/journal.pone.0188226. PMID: 29190695; PMCID: PMC5708704.
22. Gao Y, Wei Y, Wang Y, Gao F, Chen Z. Lycium Barbarum: A Traditional Chinese Herb and A Promising Anti-Aging Agent. Aging Dis. 2017;8(6):778–791. Published 2017 Dec 1. doi:10.14336/AD.2017.0725
23. Gunduluru Swathi, Ramaiah Chintha & Rajendra Wudayagiri. Protective role of Bacopa monnieri against Rotenone- induced Parkinson's disease in PC 12 cell lines. International Journal of Phytomedicine. Volume 9, NO. 2, 2017 doi: 10.5138/09750185.2008. Dorszewska J, Prendecki M, Lianeri M, Kozubski W. Molecular Effects of L-dopa Therapy in Parkinson's Disease. Curr Genomics. 2014 Feb;15(1):11-7. doi: 10.2174/1389202914666131210213042. PMID: 24653659; PMCID: PMC3958954.
24. Ma XW, Guo RY. Dose-dependent effect of Curcuma longa for the treatment of Parkinson's disease. Exp Ther Med. 2017 May;13(5):1799-1805. doi: 10.3892/etm.2017.4225. Epub 2017 Mar 10. PMID: 28565770; PMCID: PMC5443238.
25. Hatcher H, Planalp R, Cho J, Torti FM, Torti SV. Curcumin: from ancient medicine to current clinical trials. Cell Mol Life Sci. 2008 Jun;65(11):1631-52. doi: 10.1007/s00018-008-7452-4. PMID: 18324353; PMCID: PMC4686230.
26. Gupta A, Mahajan S, Sharma R. Evaluation of antimicrobial activity of Curcuma longa rhizome extract against Staphylococcus aureus. Biotechnol Rep (Amst). 2015 Feb 18;6:51-55. doi: 10.1016/j.btre.2015.02.001. PMID: 28626697; PMCID: PMC5466256.
27. Hewlings SJ, Kalman DS. Curcumin: A Review of Its' Effects on Human Health. Foods. 2017;6(10):92.Published 2017 Oct 22. doi:10.3390/foods6100092
28. K. Thyaga Raju et al. The Traditional uses and Pharmacological Activities of Mucuna Pruriens (L) Dc: A Comprehensive Review. Indo American Journal of Pharmaceutical Research.2017:7(01).
29. Zhu Huabin et al. "Carbidopa, a drug in use for management of Parkinson disease inhibits T cell activation and autoimmunity." PloS one vol. 12,9 e0183484. 12 Sep. 2017, doi:10.1371/journal.pone.0183484
30. Jamil SS, Nizami Q, Salam M. Centella asiatica (Linn.) Urban: a review. Natural Product Radiance. 2007;6(2):158–170.
31. V. Prakash, N. Jaiswal, and M. Srivastava. "A REVIEW ON MEDICINAL PROPERTIES OF CENTELLA ASIATICA". Asian Journal of Pharmaceutical and Clinical Research, Vol. 10, no. 10, Sept. 2017,pp. 69-74, doi:10.22159/ajpcr.2017.v10i10.20760
32. Haleagrahara Nagaraja & Ponnusamy Kumar. (2010). Neuroprotective effect of Centella asiatica extract (CAE) on experimentally induced Parkinsonism in aged Sprague–Dawley rats. The Journal of toxicological sciences. 35. 41-7. 10.2131/jts.35.41.
33. Thi Thanh, Nguyen, My Dung Vuu, Man Anh Huynh, Masamitsu Yamaguchi, Linh Thuoc Tran,Thi Phuong Thao Dang. Curcumin Effectively Rescued Parkinson's Disease-Like Phenotypes in a Novel Drosophila melanogaster Model with dUCH Knockdown. Oxidative Medicine and Cellular Longevity. Hindawi. Volume 2018. Article ID 2038267. doi: 10.1155/2018/2038267
34. Lehtonen Š, Sonninen TM, Wojciechowski S, Goldsteins G, Koistinaho J. Dysfunction of Cellular Proteostasis in Parkinson's Disease. Front Neurosci. 2019;13:457. Published 2019 May 10. doi:10.3389/fnins.2019.00457
35. Yoshitake T, Yoshitake S, Kehr J. The Ginkgo biloba extract EGb 761(R) and its main constituent flavonoids and ginkgolides increase extracellular dopamine levels in the rat prefrontal cortex. Br J Pharmacol. 2010 Feb 1;159(3):659-68. doi: 10.1111/j.1476-5381.2009.00580.x. Epub 2010 Jan 25. PMID: 20105177; PMCID: PMC2828029.
36. Chandrasekar SB, Bhanumathy M, Pawar AT, Somasundaram T. Phytopharmacology of Ficus religiosa. Pharmacogn Rev. 2010 Jul;4(8):195-9. doi: 10.4103/0973-7847.70918. PMID: 22228961; PMCID: PMC3249921.
37. Jitendra O. Bhangale. Sanjeev R. Acharya, Anti-Parkinson Activity of Petroleum Ether Extract of Ficus religiosa

(L.) Leaves. Hindawi Publishing Corporation. Advance in Pharmacological Science. Volume 2016. Article ID 9436106. 9 pages. doi: 10.1155/2016/9436106

38. Korczyn AD. Drug treatment of Parkinson's disease. Dialogues Clin Neurosci. 2004;6(3):315–322.
39. Vanle B, Olcott W, Jimenez J, Bashmi L, Danovitch I, IsHak WW. NMDA antagonists for treating the non-motor symptoms in Parkinson's disease. Transl Psychiatry. 2018;8(1):117. Published 2018 Jun 15. doi:10.1038/s41398-018-0162-2
40. Jilani TN, Sharma S. Trihexyphenidyl. [Updated 2019 Oct 21]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519488/
41. DeMaagd G, Philip A. Part 2: Introduction to the Pharmacotherapy of Parkinson's Disease, With a Focus on the Use of Dopaminergic Agents. P T. 2015 Sep;40(9):590-600. PMID: 26417179; PMCID: PMC4571848.