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HERBS AND PHYTOCHEMICALS WITH ANTIPARKINSONIAN ACTIVITY

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ABSTRACT

Parkinson's disease, a most common neurodegenerative disorder, is characterized by bradykinesia, muscular rigidity, tremors and impairment of postural balance. Pathophysiology of the disease is not clear so far. Conventional drugs (levodopa / carbidopa, catechol o-methyl transferase (COMT) inhibitors, monoamine oxidase-B (MAO-B) inhibitors, etc) fail to cure the disease and can cause motor fluctuations (on/off phenomenon) along with other serious side effects. Herbal plants and their phytochemicals might potentially offer a novel neuroprotective approach; and are reported to produce beneficial effects in this disease. The present review describes some plants and their extracts & phytochemicals exhibiting beneficial pharmacological properties relevant to Parkinson's disease treatment.

KEYWORDS: Parkinsonism, Medicinal plants, Levo dopa, Macuna pruriens, Genistein.

INTRODUCTION

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease, affecting 1% of the population over the age of 65 years and 4–5% of the population over the age of 85 years.[1,2] The pathophysiological hallmark of PD is the loss of the pigmented dopaminergic neurons in the substantia nigra pars compacta region of midbrain that culminates in the major clinical symptoms of PD.[3] Progressive loss of dopamine containing neurons is a feature of normal aging, however, most people do not lose the 70-80% of dopamine neurons required to cause symptomatic PD. Without treatment PD progresses over 5-10 years to a rigid, akinetic state. Death frequently results from complications of immobility. PD is characterized by bradykinesia, muscular rigidity, tremors, and impairment of postural balance leading to disturbances of gait.[3] Other non motor features include sleep disorders, depression, cognitive impairment, mood fluctuations,[4] psychosis and dementia,[5] Treatments of PD include levodopa, dopamine receptor agonists, catechol o-methyl transferase (COMT) inhibitors, monoamine oxidase-B (MAO-B) inhibitors, anticholinergics and amantadine.[6] Levodopa dramatically improves the motor symptoms of PD and remains the gold standard antiparkinsonian treatment.[7] However, its chronic use is frequently associated with dyskinesia or motor fluctuations (on/off phenomenon). Current treatments are mainly symptomatic and can temporarily slow down disease progression, but can not halt this. To date there is a lack of effective preventive strategies for PD. Therefore, safe and effective treatment strategies are urgently required for management of PD. Plant extracts have a wide range of medicinal properties and has been used to treat many types of diseases. *Lycium Chinensis* Miller, plant has been used as an anti aging therapy and a treatment of neurodegenerative diseases[8] and recent research has confirmed neuroprotective effect of the fruits of plant in a rat model.[9] Herbal plants and their phytochemicals might potentially offer a novel neuroprotective approach in a neurodegenerative diseases and might be developed for therapeutic use. This review describes some plants and their extracts & phytochemicals exhibiting beneficial pharmacological properties relevant to PD treatment.

METHODS

Data Collection: The data for present review was collected form internet, online journals and from various Ayurvedic texts like database on medicinal plants used in Ayurveda, central council for research in Ayurveda and Sidha, Department of ISH & H, Ministry of Health & Family Welfare, Govt. of India, New Delhi, Volumes 1-8, Reviews on medicinal plants, Volumes 1-9 (ICMR, New Delhi). Most of the papers reviewed herein pertinent to herbal medicine research were published in internationally recognized peer reviewed journals. Some of the medicinal plants / extracts and their isolated active phytochemicals reported to be useful for the prevention and treatment of neurodegenerative disorders particularly parkinson's disease are:

1. Bacopa monnieri L (Scrophulariaceae) Eng- Thyme leaved gratiola, Hindi- Brahmi. Small creeping, marshy with branched 10-25 cm long. Distributed throughout India, ascending to an altitude of 1320 m in marshy places, Bangladesh, Pakistan and Sri Lanka. Alcoholic extract of the plant increased learning performance in rats and activity attributed to saponin mixture containing bacosides A, B & others. Clinical reports showed antianxiety and adaptogenic effects. It is a brain tonic[10] and possess antiapoptotic,[11] antioxidant[12] and memory enhancing properties. *B. monnieri* has been shown to reduce level of oxidative stress in fruit flies and thereby inhibiting dopamine depletion with decreased mortality rate.[13] In a caenorhabditis elegans transgenic model of PD, positive results (decreased alpha synuclein protein, preventive dopaminergic neurodegeneration and restorating lipid contents) has been reported in *B. monnieri* treated 6-hydroxydopamine (6-OHDA) models of Parkinson's disease.[14] Therefore, *B. monnieri* has its proven potential as an antiparkinsonian agent.

2. Camellia sinensis Linn (Theaceae) Eng- Tea plant, Hindi- Chai. A variable evergreen shrub or a small tree found in Assam and hilly regions to the East and South of it. It is mainly cultivated in the hilly districts of North Bengal & South India. The natural product (-)-Epigallocatechin-3-gallate (EGCG) is the major polyphenolic bioactive component of *C. sinensis* and has been recognized as potent neuroprotective agent against oxidative stress, neuroinflammation, protein aggregation, autophagy and neuronal cell death in vitro as well as in vivo.[15] Anti-inflammatory and antioxidant activity of *C. sinensis* has been reported by many authors.[16] EGCG administered in mice (25 mg/kg, po) prevented loss of dopaminergic neurons in the substantia nigra and preserved striatal levels of dopamine.[17] EGCG prevented the accumulation of iron and alpha-synuclein in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-treated mice. These effects have been attributed to the antioxidant activity and iron-chelating properties of EGCG, respectively.[18] Pinto et al 2015[19] have demonstrated neuroprotective effect of *C. sinensis* on the striatal 6-OHDA model of PD in rats by decreased rotational behavior, increased locomotor activity, antidepressive effects, and improvement of cognitive dysfunction, as compared to the untreated 6-OHDA-lesioned group. Further, they showed that *C. sinensis* reversed, at least partly, the behavioral changes observed in the untreated 6-OHDA lesioned animals, at very low doses and reversed the decreased locomotor activity observed in the untreated lesioned group; and similar results had been reported with the forced swimming test and water maze test, indicative of antidepressant and spatial learning effects, respectively. EGCG was found to have a potential therapeutic effect against lipopolysaccharide induced neurotoxicity in male Sprague Dawley rats via reducing TNFα and NO inflammatory mediators and preserving dopamine (DA) level in midbrain.[20]

3. Centella asiatica **Linn (Apiaceae) Eng-** Indian Penny Wort, Hindi- Mandookaparni. A perennial herb commonly found in moist areas and in crop fields and other waste places throughout India upto an altitude of 600m. Results of a double blind trial of Mandookaparni on mentally retarded children showed a very significant increase in general ability and behavioural pattern when drug was given for a short period of 12 weeks.[21] Traditionally *C. asiatica* has been used as a brain tonic in Ayurveda & Chinese medicine. *C. asiatica* has been shown to possess antioxidative effect and reduce mitochondrial dysfunction induced by fungal neurotoxin (3-nitro propionic acid) in mice by affective malondialdehyde (MDA) and radical oxygen species.[22] In experimentally induced PD in rats, *C. asiatica* extract protected the mitochondrial damage. Chloroform methanol extract of *C. asiatica* showed free radical scavenging effect in monosodium glutamate (MSG) stressed rats.[23] Neuroprotective effect of *C. asiatica* extract has also been reported in old aged rat brain via decreasing protein carbonyl content and lipid peroxidation. Aqueous extract of *C. asiatica* has been shown to reverse the neurotoxic effect in MPTP-induced Parkinsonism in aged Sprague- Dawley rats.[24]

4. Erigeron breviscapus. Lopez & Calvo 2011[25] demonstrated neuroprotective effects of the *Erigeron breviscapus* and *C. sinensis* against hydrogen peroxide induced toxicity in PC-12-cells.

5. Ginkgo biloba **L (Ginkgoaceae) Eng-**Maiden hair tree, Hindi- Balkuwari. Tree with pyramidal form, reaching a height of 30 m; leaves petiolar, lamina fan-shaped, bilobed; dioecious; mature seeds orange-coloured and are about the size of an apricot. *Ginkgo biloba* has been shown to possess neuroprotective, antioxidative and iron chelating properties in 6-hydroxy dopamine (6-OHDA) induced parkinsonian in rats.[26] EGb761 is a standardized extract of the leaves of the *G. biloba* tree and is characterized by its main fractions, the flavonols (mainly isorhamnetin, kaempferol and quercetin: 22–27%) and the terpene lactone (5–7%), These two fractions are thought to be, at least partly, responsible for potential neuroprotective properties of EGb761.[27] Other active constituents comprises ginkgolides ABC & M, sesquiterpenic trilactone and bilobalide. Bilobalide reduce damage caused by global brain ischemia & glutamate-induced excitotoxic neuronal death.[28] Bilobalide has also been reported significantly to restore the behavioral changes induced by 6-OHDA and to inhibit loss of tyrosine hydroxylase-positive neurons, decreased the activation of NF-kappaB, and protected dopaminergic neurons from apoptosis in 6-OHDA induced rat model of PD significantly.[29] EGb761also inhibited oxidative stress induced by MPTP model of parkinsonoim in mice[30] and significantly decreased drug induced rotation and produced significant restoration of striatal DA and its metabolites in rats,[31] the beneficial effects of EGb761 in parkinsonism may be due to its potent MAO inhibitory activity which prevents degradation of DA and increase its availability. When given concurrently, EGb761 reduced neurotoxic effects of levodopa.[32] Presently standardized extracts are widely prescribed in Europe & US for symptomatic treatment of Alzheimer's disease, cerebral insufficiency & improvement of memory. A clinical trial concluded that the *G. biloba* extract EGb 761, specifically in a dose of 240 mg daily, was both safe and effective in the treatment of patients with dementia associated with neuropsychiatric features.[33]

6. Ganoderma lucidum is a fungus that grows from the tops of stumps or submerged logs and is found in most parts of the world. Extract of *Gonoderma lucidum* inhibited Staurosporine induced apoptosis by 30-50% in a dose dependent manner. The oil from *ganoderma lucidum* spores showed neuroprotective effect on pathological changes in the substantia nigra and behaviors of MPTP induced model of PD in mice. Treatment with ganoderma spores oil increased survival of dopamine neurons in the substantia nigra and levels of dopamine in the striatum, attenuated involuntary motor sympotoms.[34] *Ganoderma lucidum* extract has been shown to protect dopaminergic neurons through inhibiting the production of inflammatory mediators by activated microglia.[35] Neuroprotective effect of extract may be due to free radical scavenging properties of this plant.[36]

***7. Glycyrrhiza glabra* Linn (Fabaceae) Eng-** Liquorice, Hindi- Mulhatti. It is a hardy herb attaining height upto 2m. It is distributed in the subtropical and warm temperate regions of the world. In India it is reported to be cultivated in Baramulla, Srinagar, Jammu, Dehradun, Delhi & South India. Pharmacological studies demonstrated antioxidant, anti-inflammatory & neuroprotective properties of this plant.[37]

***8. Lycium chinense* Mill (solanaceae):** Common name Wolfberry, It is a deciduous perennial shrub to 5' tall. *L. chinensis* Miller, a traditional herbal medicine used in China, Korea and Japan has been shown to have hypotensive, hypoglycemic and antipyretic effects in animal studies. Aqueous methanol extract of *L. chinense*, exhibited inhibitory effect on MAO-B in rat brain homogenates and therefore has been proposed as a good candidate for use in delaying the progressive degeneration caused by neurological diseases.[38] This plant has also been used as an antiaging therapy and a treatment of neurodegenerative diseases,[8] Recently neuroprotective effect from the fruit of this plant in a rat model of trimethyltin induced learning and memory impairment has been confirmed.[9] *Lycium chinense* Miller extracts have been shown to produce beneficial effects in Parkinson's disease by attenuating rotenone induced toxicity in PC12 cells.[39]

***9. Macuna pruriens* Linn (Fabaceae) Eng-** Common cowitch, Hindi- Kaunch Herbaceous twining annuals, pods 5-10 cm long curved, distributed all over India upto 100m in Himalyas & in Andaman, Nicobar islands. It has been used for treating parkinsonism in Ayurvedic system of medicine.[40] Studies showed that seeds of *M. pruriens* contain levodopa as one of the active constituents. Pharmacological studies demonstrated that L-dopa free fraction of seed exhibited potent antiparkinsonian effect in mice (200mg/Kg, ip). In a clinical trial in 62 patients with parkinson's disease (46 males & 16 females, mean age 59±9 years) treated for 12 weeks with HP200 powder (7.6g orally). Statistically significant reductions in Hoehn & Yahr stage and Unified Parkinson's Disease Rating Scale (UPDRS) scores were seen from base line to the end of the 12 weak treatment.[41] *M. pruriens* has been shown to antagonize motor symptoms of parkinson's disease in 6-OHDA induced rat model of PD.[42] *M. pruriens* reported to reduce dyskinesia in MPTP monkey model[43] and hemi parkinsonian rat model.[44] It has shown to be as effective as pure levodopa /carbidopa in the treatment of Parkinson's disease.[45] In 1978, Vaidya et al.[46] reported the beneficial effects of *M. pruriens* in patients with PD in an open clinical trial, however no further information is available.

10. Panax ginseng C.A. Mayer (Araliaceae) *P. ginseng* root is the most popular traditional medicine in China, Korea and Japan. *P. ginseng* has been reported to possess neuroprotective, antioxidant, antiapoptotic and immunostimulatory properties and extracts have been reported to protect against neurotoxicity in vitro and in vivo models of PD. *P. ginseng* extract G115 blocked the loss of tyrosine hydroxylase (TH) (+) cells in substantia nigra and reduced locomotor dysfunction in MPTP induced PD model C57BL/6 mice and rats.[47] In an in vitro study, ginseng saponins have shown positive effects of enhancing neurite growth of dopaminergic SK-N-SH neuroblastoma cells. Ginsenosides (Rb1 and Rg1) have been demonstrated to increase neuritic growth in 1-methyl-4-phenylpyridinium (MPP+) or glutamate stressed primary cultured mesencephalic dopaminergic cells in vitro.[48] Ginseng has been suggested to inhibit both N-methyl-D-aspartate (NMDA) and non-NMDA glutamate receptors resulting in reduction of Ca^{2+} over-influx into neurons and thus protecting the cells from neurodegeneration mediated via Ca^{2+} overload.[49] Ginseng has also been reported to attenuate dopamine-induced apoptotic cell death through suppression of intracellular oxidative stress and therefore, rescue neurons against apoptosis induced by exogenous dopamine in PC12 cells.[50] Ginseng exerted neuroprotective effect in experimental PD model in vitro in which SH-SY5Y cells were injured by MPP+ and in MPTP induced in vivo model of mouse.[51]

***11. Peltophorum africanum* (Fabaceae) (Weeping wattle).**It is a tree with a dense rounded to spreading crown, greyish stem, fern-like stipules and clustered fruits and is widespread in south Africa and most tropical areas. Bizimanyera et. al.[52] reported neuroprotective and antioxidant properties from the bark and root extracts of *P. africanum*.

12. Polygonum cuspidatum (Polygonaceae) inhibited staurosporin induced apoptosis in dose dependent manner.[36]

***13. Schizandra chinensis* (Magnoliaceae).** Extracts of *S. chinensis* inhibited staurosporin induced apoptosis by 30-50% in a dose dependent manner. The extract showed neuroprotective, antioxidant & free radical scavenging activities.[36] Schisantherin A, a dibenzocyclooctadiene lignan from the fruit of *S. chinensis* protects 6-OHDA-induced dopaminergic neuron damage in zebrafish and cytotoxicity in human neuroblastoma SH-SY5Y cells through the ROS/NO and AKT/GSK3β pathways.[53]

14. Smilacis chinae rhizome exhibited a neuroprotective effect in an in vitro model of N-methyl D aspartate (NMDA) induced neurotoxicity. It showed a similar effect in an in vivo model of focal cerebral ischemia.[54]

15. Scutellaria baicalensis Geogri (Lamiaceae). *Scutellaria baicalensis* Geogri (SBG) is native of China and the dried roots are rich in flavones such as baicalin, baicalein and wogonin. Baicalin and baicalein flavones from *S. baicalensis* have been shown to possess antioxidant, anti-inflammatory and cognitive enhancing properties.[55] Marked reduction in tremors, mitigation of astroglial response and increased tyrosine hydroxylase positive neurons in substantia nigra have been reported in 6-OHDA lesioned rat models in vivo and in vitro.[56] Mu et al 2011[57] demonstrated similar results in MPTP mice models of PD along with inhibition of dopamine turnover. Further, baicalein has also been reported to increase dopamine and 5HT levels in the striatum in MPTP mice models of PD.[58] Baicalein has been shown to prevent 6-OHDA–induced oxidative damage in PC12 cells by activating Keap1/Nrf2/HO-1 channels, as well as PKCα and PI3K/AKT signal channels.[59]

***16. Withania somnifera* (L)** Dunal Eng- Winter cherry, Indian ginseng, Hindi- Ashwagandha. Erect tomentose shrub, 30-150 cm high. It is found throughout the drier parts of India in waste places and on bunds in areas of upper Gangetic plain, West Bengal, Bihar, Orissa, Gujarat, Konkan, Karnataka & Coimbatore. *W. somnifera* fruit extract has been shown to possess antiaging, antioxidant, free radical scavenging, adaptogenic and immunomodulatory properties.[60] Antiparkinsonian effect of *W. somnifera* extract was evaluated in 6-OHDA induced parkinsonism in rats. Treatment with *W. somnifera* extract reversed some symptoms of PD such as decreased striatal dopamine level, increased lipid peroxidation, increased dopaminergic D_2 receptors, reduced nigral glutathione level, reduced activity of SOD, Catalase and lessened tyrosine hydroxylase expression.[61] Neuroprotective effects of *W. somnifera* has also been reported in maneb paraquat induced parkinsonism in mice.[62] Administration of *W. somnifera* root extract in MPTP mice model of PD caused increase in the level of dopamine, 3, 4- dihydroxy phenylacetic acid (DOPAC), homovanillic acid (HVA), glutathione, glutamine peroxidase and normalized levels of lipid peroxidation marker i.e. thiobarbituric acid reactive substance (TBARS).[63]

Neuroprotective phytochemicals

1. Curcumin (diferuloylmethane), the well-known component of yellow curry spice derived from the rhizome of *Curcuma longa* L (Zingiberaceae) Eng-Turmeric Hindi- Haldi, has been used as a food preservative and herbal medicine in India for hundreds of years. Rhizome of *Curcuma longa* L contains curcuminoids (curcumin, demethoxy curcumin & bis demethoxy curcumin) as its active phytochemical. Curcuminoids possess anti-inflammatory, antioxidant, proapoptotic, antiproliferative, wound healing and antiparkinsonian effects. Several studies in cellular and animal models indicated that curcumin is a neuroprotective agent in neurodegenerative disorders such as PD.[64 ,65] Curcumin has been reported to protect substantia nigra (SN) neurons, improves striatal dopamine levels and chelates Fe2+, in 6-OHDA administered rats.[66] Curcumin produces increase in the density of dopaminergic neurons in the SN.[67] Mythri et al. 2011[68] has observed that chronic dietary consumption of turmeric caused an increase in the tyrosine hydroxylase (TH) positive neurons in the SN, in consistent with earlier reports of Kim et al. 2008,[69] and Xu et al. 2007[70] who reported that curcumin contributes to neurogenesis. Apart from MPTP model, curcumin has been found to be neuroprotective in 6-OHDA-induced hemiparkinsonian mice model where 6-OHDA-induced loss of striatal TH fibers and nigral TH-immunoreactive neurons had decreased.[71]

2. Gastrodin, the predominant constituent of the rhizome of *Gastrodia elata* Blume (Orchidaceae), a Chinese herbal medicine, has long been used for treating vertigo, general paralysis, epilepsy, tetanus, stroke, dementia and Parkinson's disease. Methanol extract of *Gastrodiae Rhizoma* or the pure compound vanillyl alcohol reduced oxidative stress and cell apoptosis in both SH-SY5Y and MN9D dopaminergic cell lines in response to the damage induced by MPP+.[72-73] Gastrodin was shown to reduce the loss of TH-positive cells in a rotenone-induced model of PD by protecting dopaminergic neurons, down-regulateding nigral IL-1β expression resulting in a restraining of neuroinflammation during the damage and improved muscle rigidity and endurance in PD rats.[74] It has been reported to mobilizes neuro-protective capacities used and is used often for the treatment of headache, convulsions, hypertension and neurodegenerative diseases.[75] Gastrodin has been reported to protect dopaminergic neurons in SH-SY5Y cells stressed with MPP+ through regulating free radicals, Bax/Bcl- 2 mRNA, caspase-3, and cleaved poly(ADP-ribose) polymerase. It also showed neuroprotective effects in MPTP induced mouse PD model by ameliorating bradykinesia and motor impairment in the pole and rotarod tests, respectively.[76] Gastrodin prevented motor deficits and oxidative stress in the MPTP mouse model of PD via interrupting extracellular signal regulated protein kinases (ERK) 1/2-nuclear factor erythroid 2-related factor 2 (Nrf2) signaling pathway.[77]

3. Paeoniflorin (Paeoniaceae) a major active component of Chinese herb *Paeoniae alba* Radix has shown neuroprotective effect in MPTP mouse model of PD (73). Subchronic treatment with Paeoniflorin had shown an alleviating effect on 6-OHDA induced neurological impairment in rats.[78]

4. Resveratrol, a polyphenolic compound naturally present in red wine, grapes, peanuts, berries & Pine has been shown to possess anti-inflammatory, antiapoptotic, antioxidant and neuroprotective properties.[79] Resveratol has shown neuroprotective effect in Balb/c mice by alleviating HPTP induced motor incoordination, oxidative stress and TH positive neuronal cell loss.[80] Reduced oxidative stress, microglial activation, neuro inflammation besides increasing number of TH positive cells and dopamine content have been reported in Pakquat and Maneb models of PD.[81] Nuroprotective effects of resveratol has also been reported in rotenone and 6-OHDA induced dopaminergic cell death.[82,83] Therfore, resveratol protects dopaminergic neurons by reducing inflammation, oxidative stress, diminishing dopamine apoptosis and by altering the expression of CYP2d22 as well as paraquat accumulation.[81]

5. Tenuigenin, Root of *Polygala tenuifolia* (polygalaceae) a traditional Korean medicine rich in tenuigenin, which is used for treating various cognitive problems associated with ageing and PD.[84] Neuroprotective effect of tenuigenin has been demonstrated against 6-OHDA induced cytotoxicity in SHSY54 cells by protecting mitochondrial damage by increasing glutathione, SOD levels and thereby increasing cell viability.[85] Tenuigenin protects against lipopolysaccharide induced neuroinflammatory damage in rats by improving TH immunoreactive neurons and dopamine levels in the striatum. Furthermore, lipopolysaccharide induced upgradation of TNFα and IL-1β was also overturned by tenuigenin.[86]

Miscellaneous agents

Chrysanthemum morifolium inhibited MPTP-induced cytotoxicity and maintained cell viability of SH-SY5Y cell line by preventing ROS formation, decreasing Bax/Bcl2 ratio and caspase-3 activation.[87]

Echinoside, an active compound of *Cistanche salsa* in a dose of 20mg/kg maintained striatal dopamine levels, reduced cell death, significantly increased the tyrosine hydroxylase enzyme expression, and reduced the activation of caspase-3 and caspase-8 expression in MPTP mouse model of PD.[88]

Silymarin preserved dopamine levels, diminished the number of apoptotic cells and preserved dopaminergic neurons in SN of MPTP- and 6-OHDA-intoxicated mice.[89]

Anemopaegma mirandum, a Brazilian tree, the extract of *Anemopaegma mirandum* produced protective effect on Rotenone-induced apoptosis in human neuroblastomas SHSY5Y cells.[90]

Valeriana officinalis increased the viability of SH-SY5Y cells in rotenone induced in vitro experimental model of PD.[91]

Tripterygium regelii reduced oxidative stress-induced cell death through the inhibition of apoptotic cascades, preserved mitochondrial function, and promoted tyrosine hydroxylase expression and brain-derived neurotrophic factor (BDNF) production in H2O2 treated SH-SY5Y cells.[92]

Uncaria rhynchophylla decreased cell death and ROS production; increased GSH levels in cultured PC12 cells, while 6-OHDA-induced caspase-3 activation was attenuated preventing cell death. Rotational behavior was significantly reduced in the 6-OHDA PD model.[93]

Isoflavones daidzin, daidzein and genistein contained in ***Pueraria thomsonii*** protected PC12 cells stimulated with 6-OHDA through the inhibition of the caspase- 3 activation.[94] Genistein also protected neurons from substantia nigra pars compact and attenuated the rotational behavior in a hemiparkinsonian 6-OHDA model.[95]

Psoralea corylifolia protected SK-N-SH cells from MPP+ intoxication and prevented the dopaminergic neurons loss in MPTP intoxicated mice by inhibition of the monoamine transporter.[96]

Rosmarinus officinalis protected dopaminergic neurons in different degenerative disease models.[97]

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