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TRADITIONAL APPROACH TO THE TREATMENT OF PARKINSON'S DISEASE

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ABSTRACT

Parkinson's disease is defined as a neurodegenerative disorder which is characterized by progressively occurring dopaminergic neuronal cell loss in the substantia nigra par compacta of the midbrain. The motor symptoms of Parkinson's disease include tremors, bradykinesia, rigidity and postural instability apart from the non motor symptoms such as micrographia, depression, fatigue, anxiety and pain. The motor symptoms occur as a result of brain nigrostriatal system degeneration. As a consequence of side effects of the synthetic drugs, it has compelled researchers to obtain therapeutic methods to obtain them from nature so as to provide effective treatment with the principles of herbal therapy as an alternative management; as nature undeniably has been the most excellent remedy for all the illnesses to the mankind. In India, the practice of using plant materials as medicine had begun in Vedic times (1500 – 1000 B.C) and thus providing valuable information on the medicinal properties of the plants. Several studies have been conducted that had reported many plants possessing properties that may alleviate the parkinsonism condition and the symptoms related to it.

KEYWORDS: Parkinson's Disease, Traditional Approach, Levodopa, Herbal Plants, Mucuna Puriens.

INTRODUCTION

Parkinson's disease (PD) is defined as a neurodegenerative disorder characterized by gradually occurring dopaminergic neuronal cell death in the substantia nigra par compacta of the midbrain. The four cardinal symptoms are tremors, bradykinesia, rigidity and postural

instability.[1] The name Parkinson's disease is acquired after James Parkinson, who reported many of the clinical features of the disease in his works entitled "*Essay on the shaking palsy"* in 1817.[2] The major symptoms occur due to brain nigrostriatal system degeneration. Apart from the loss of dopaminergic neurons in the susbstantia nigra pars compacta in the brain, it is also followed by decrease in levels of striatal dopamine (DA) and its metabolites, including 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA).[3]

Pathology

➢ **Neuron Loss**

Loss of dopaminergic neurons in the substantia nigra pars compacta is the characteristic feature of PD. This selective depletion of DA in the central nervous system affects the motor co-ordination in the PD patients, in spite of the fact that there are several groups of DA neurons in the central nervous system.[4] A reduction of ~ 80% DA of striatum results in motor symptoms.[5]

➢ **Lewy Bodies**

An additional finding is the Lewy Body (LB). It is a protein rich inclusion present inside the cytoplasm of the cell. It is spherical in shape and eosinophilic. A-synuclein protein is a major constituent of LB[6] along with ubiquitin, proteases.[7] Since the DA cells consists of pigment melanin, its progressive loss causes depigmentation of that area that is markedly visible.[6]

Pathophysiology

The pathogenesis and etiology are completely understood but several factors have been outlined of DA cell death.

➢ **Oxidative Stress**

The imbalance between the levels of Reactive Oxygen Species (ROS) produced and the human body's capability to detoxify them thereby kindling a vulnerable state of cellular damage. ROS such as superoxide anion radical, hydroxyl radical and hydrogen peroxide generally requires activation of molecular oxygen. 20% of the total oxygen supply of the body is consumed by the brain and of which a major proportion s converted to ROS. Neurons, glia and electron transport chain in the mitochondria are the major sites.[8] Oxidative Stress is supposed to play a major role in the pathophysiology of PD.[9]

- **Mitochondrial Dysfunction**

The neural activity in the brain utilizes the power generated by the oxidative phosphorylation, which is the main mechanism of the mitochondria. During this process, intermediates such as superoxide and hydrogen peroxide are also produced that leads to contribution of ROS to PD.[10]

Several other mechanisms have known to be involved such as protein aggregation and misfolding, inflammation, excitotoxicity, apoptosis, loss of trophic factors and other cell death pathways.[11]

Role of Medicinal Plants

Nature by far has the best remedy for all the diseases to man. As a result of side effects of the synthetic drugs, it has driven researchers to obtain healing methods back to nature so as to provide efficient treatment with the principles of herbal therapy as an alternative treatment.[12] Many plants contain specific medicinal role without being used for their nutrition value in human diet and therefore, such plants may well be used in the treatment of specific problems. Plant extracts may possess enormous potential as lead neuroprotective compounds in the treatment of Parkinson disease.[13]

Pd Treatment in India

The ancient Indian medical system of Ayurveda had first described PD under the name Kampavata (kampa meaning tremors). Herbal preparations were used that consisted of anticholinergics, L-dopa and monoamine oxidase inhibitors not only in in India but also in China and the Amazon basin. In India the practice of using plant tissues as medicine had began in Vedic times (1500 – 1000B.C). The powder of *Mucuna puriens* seeds was used to treat PD although the prevalence was low in India. In Ayurveda, nearly 18 preparations consisted of *M. puriens* from among several formulations described.[14] Upon research it was found that the seeds of *M. puriens* contain Levodopa, which helps in the enhancement of the PD symptoms.[13]

Table. (1): List of plants showing anti-parkinson's activity.

S. No	Botanical Name (Family)	Vernacular Name	Part of the plant used	Active Constituents
1.	*Albizia adianthifolia* (Fabaceae)	Flat crown	Leaves	Flavanoids, phenols[15]
2.	*Allium sativum* (Amaryllidaceae)	Garlic	Peeled Cloves	Flavanoids, polyphenols organopsulphur compounds[16]
3.	*Aloe vera* (Lilliaceae)	Barbados aloe	Leaf gel	Anthraquinones, tannic acid, flavanoids, minerals[17]
4.	*Anacardium occidentale* (Anacardiaceae)	Cashew	Cashew peduncle	Phenolic compounds[18]
5.	*Ananas cosmosus* (Bromeliaceae)	Pineapple	Fruits	Ananasate, beta-sitosterol, Chlorogenic acid, rutin, naringenin, bromelin,glysocides, Flavonoids and neurotransmitters[19]
6.	*Artemisia nilagirica (*Asteraceae*)*	Indian wormwood	Leaves with flowering tops	Flavonoids, alkaloids, tannins, glycosides, phenol, terpenoids, amino acids, quinines, saponins and polysaccharides, essential oils[20]
7.	*Banisteropsis caapi* (Malpighiaceae)	*Ayahuasca* Vine	Plant extract	Banisterine, harmala alkaloids[21]
8.	*Biophytum sensitivum* (Oxalidaceae)	Little tree plant	Alcoholic extract	L-dopa,polyphenols, Flavonoids[22]
9.	*Brassica nigra* (Brassicaceae)	Black Mustard	Seeds	Flavonoids, carbohydrates, glycosides, proteins and alkaloids[23]
10.	*Brassica oleracea* (Brassicaceae)	Cabbage	Whole plant	Flavanoids[24]
11.	*Camellia sinensis* (Theaceae)	Green Tea	Leaves	Epicatechin and Epigallocatechin, Gallate[25]
12.	*Canscora decussata* (Gentianaceae)	Shankapushpi	Whole plant	Mangiferin[26]
13.	*Cassia auriculata* (Caesalpiniaceae)	Senna	Leaves	Alkaloids,polyphenols, saponins, flavonoids and tannins[27]
14.	*Centella asiatica* (Apiaceae)	Indian penny wort	Leaves	Asiaticoside[28]
15.	*Cistanche deserticola* (Orobanchaceae)	Desert broomrape	Stem	Acteoside[13]
16.	*Cistanche tubulosa* (Orobanchaceae)	Desert hyacinth	Stem	Echinacoside[13]
17.	*Cuminum cyminum* (Apiaceae)	Cumin	Fruit	Cuminol, cymine, cuminaldehyde, limonene, eugenol, α & β-pinenes, terpenes and glucosides[29]
18.	*Curcuma longa* (Zingiberaceae)	Turmeric	Root	Curcumin[30]
19.	*Cynodon dactylon* (Graminiae)	Bermuda grass	Plant	Crude proteins, carbohydrates, mineral constituents, oxides of

				magnesium, phosphorous, calcium, sodium and potassium, vitamin C, carotene, hydroquinone, levoglucosenone, furfural, hexadecanoic acid, ethyl ester, linolenic acid, ethyl ester and d-Mannose[31]
20.	*Elaeocarpus ganitrus* (Elaeocarpaceae)	Rudraksha	Ethanol extract	Flavaoids and Alkaloids[32]
21.	*Ficus religiosa* (Moraceae)	Peepal	Leaves	Alkaloids[33]
22.	*Ganoderma lucidum* (Ganodermataceae)	Reishi mushroom	Mushroom	Polysaccharides, triterpenes, and peptidoglycans[34]
23.	*Garcinia indica* (Clusiaceae)	Kokam	Fruit	Garcinol, hydroxyl citric acid, citric acid, malic acid, polyphenols, carbohydrates, anthocyanin pigments, and ascorbic acid[35]
24.	*Gastrodia elata* (Orchidaceae)	Japanese orchid	Plant extract	Gastrodin[13]
25.	*Gingko biloba* (Ginkgoaceae)	Maidenhair tree	Leaves	Flavanoids, Terpenoids (Ginkgolides and bilobalides)[36]
26.	*Gymnostemma pentaphyllum* (Cucurbitaceae)	Jiaogulan	Leaves	Gypenosides[37]
27.	*Hylocereus undatus* (Cactaceae)	White Pitaya	Fruit	Carbohydrate, Proteins and amino acids, Alkaloids, Terpenoids and Steroids, Glycoside and Flavanoids, Tannins and phenolic compounds, Saponins[38]
28.	*Hyocyamus niger* (Solanaceae)	Nightshade	Seeds[39]	Glycosides, Flavanoids, saponins, steroids, phenols, alkaloids[40]
29.	*Juglandis semen* (Juglandaceae)	Walnut	Seed	Polyphenol, Caffeic acid and its phenethyl ester derivative[3]
30.	*Juniperus communis* (Cupressacceae)	Common juniper	Methanolic extract	Camphene, d-alpha pinene, formic acid, acetic acid, wax, gum, cyclohexinl, terpene, ascorbic acid, cardinene, juniper camphor and monoterpeneydrocarbons[41]
31.	*Leucas aspera* (Lamiaceae)	Thumba	Ethanol extract of whole plant	Leucasin[42]
32.	*Mucuna macrocarpa* (Leguminosae)	-	Seed	L- Dopa[43]
33.	*Nardostachys jatamansi* (Valirenaceae)	Jatamamshi	Hydro alcoholic extract of Root	Steroids, Sterols, Glycosides. Carbohydrates, Akaloids, Tannins, Terpenes, Gums, Mucilage[44]
34.	*Nelumbonucifera* (Nymphaeaceae)	Sacred lotus	Methanolic Seed extract	Alkaloid, Glycoside, Flavonoids, Tannins, Phenolics, Carbohydrates, Proteins and Amino Acids[45]
35.	*Nigella sativa* (Ranunculaceae)	Black cumin	Hydro alcoholic	Antioxidants (Thyoquinone)[46]

			extract of seeds	
36.	*Ocimum sanctum* (Lamiaceae)	Tulsi	Aqueous extract of the plant	Linalool, essential oils rich in phenolic compounds, flavonoids and anthocyanins[47]
37.	*Paeonia lactiflora* (Paeoniaceae)	Common garden peony	Herbal Extract	Albiflorin, Paeoniflorin, paeonol[48]
38.	*Panax ginseng* (Araliaceae)	Ninjin	Roots	Ginsenoside Rg1[49]
39.	*Parkinsonia aculeata* (Fabaceae)	Parkinsonia	Seeds	Flavonoids, phenolics[19]
40.	*Passiflora incarnata* (Passifloraceae)	Passion flower	Flowers	Flavonoids, Harmine and harmaline alkaloids[50]
41.	*Peganum harmala* (Zygophyllacea)	Harmal	Seeds[51]	Alkaloids[52]
42.	*Phaseolus vulgaris* (Fabaceae)	Red Kidney Bean	Seeds	L-dopa[53]
43.	*Plumbago zeylanica* (Plumbaginaceae)	Hydro alcoholic extract	Roots	Natural Dopamine[54]
44.	*Polygala tenuifolia* (Polygalaceae)	Chinese senega root	Roots	Anti-oxidant, anti-apoptic activity[55]
45.	*Portulaca oleracea* (Portulacaceae)	Red root	Aqueous and ethanolic extract	Catecholamines[56]
46.	*Prosopis chilensis* (leguminosea)	Algarrobo	Seeds	Protein, saponins[57]
47.	*Pueraria lobata* (Fabaceae)	Kudzu	Root	Puerarin[58]
48.	*Quercus infectoria* (Fabaceae)	Manjakani	Galls[9]	Tannins, Gallic acid, Ellagic acid, Syringic acid, beta-sitosterol, amentoflavonehexamethyl ether, methyl betulate, methyl olenate, hexagalloyl glucose AA K, VO E[59]
49.	*Rhodiola rosea* (Crassulaceae)	Golden root	-	Nitrigenmic phenolic compounds, Bioflavanoids polyphenols and triterpenes[60]
50.	*Scutellaria baicalensis* (Labiatae)	Baikal skullcap	Root	Baicalein[13]
51.	*Sida cordifolia* (Malvaceae)	Bala	Aqueous extract	Anti oxidants[61]
52.	*Solanum melongena* (Solanaceae)	Egg plant	Fruit	Phenolics (gallicacid,caffeoylputrescine, and 5-caffeoylquinic acid) and flavonoids (kaempferol, quercetin, naringenin)[62]
53.	*Tinospora cordifolia* (Menispermaceae)	Guduchi	Ethanol Extract	Berberine[63]
54.	*Trigonellafoenum-graecum* (Fabaceae)	Fenugreek	Seeds	Trigonelline[64]
55.	*Uncaria rhynchophylla*	Cat's Claw	Aqueous	Catechin[65]

	*(*Rubiaceae*)*		extract of whole plant	
56.	*Withania somnifera* (Solanaceae)	Ashwagandha	Root	Withanolides[66]

CONCLUSION

The side effects of the synthetic drugs used in the treatment of Parkinson's disease are evoking interest in the researchers to find out a therapy with effective and beneficial therapy to the patient. They are looking out at nature to provide with the active principles that may alleviate the symptoms and simultaneously provide efficacious remedy. Ayurveda provides valuable documentation of the medicinal plants with their properties. These plants can be used to look out for treatment purposes after their thorough study.

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