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A REVIEW: PARKINSONISM AND ITS TREATMENT

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ABSTRACT

There are a number of neurodegenerative diseases that have been associated with Parkinsonism. There are a wide variety of symptoms associated with Parkinsonism, including a slew of symptoms that may eventually lead to programmed cell death as a result of selective and progressive degeneration of dopaminergic neurons. It is unknown what causes parkinsonism; however, recent studies suggest that oxidative stress produces apoptosis, leading to mitochondrial defects and neuro-inflammation. There were many agents used in models of PD, like Oxidopamine, MPTP, rotenone, and neurotoxin etc., It has become more popular to use traditional Chinese medicine or conventional pharmacological ideas to treat Parkinson's disease (PD) in China in recent years. All herbal medications and herbal formulations were tested in vitro as well as in vivo on PD models. As per respective genera or pharmacological activity, relevant chemicals including herbal blends with anti-Parkinsonian properties were included. The plant species used to make these herbal remedies were from 18 families and 24 genera, including *Acanthopanax, Alpinia* as well as *Astragalus.* Anti-Parkinsonian drugs can be developed by using these herbal remedies. Clinical studies should pay more attention to species in such genera and families, as they may hold the most promise for further research. Further investigation is needed to determine the active components of herbal extracts and compatibility laws of herbal formulas.

KEYWORDS: Parkinsonism Disease, Herbal drugs for parkinsonism, traditional medicine, oxidative stress.

INTRODUCTION

The term "parkinsonism" refers to a syndrome that is associated with Parkinson's disease (PD). In Parkinson's disease, the dopaminergic neurons of the substantia nigra pars compacta in the ventral midbrain gradually deteriorate. There is a loss of motor skills associated with Parkinsonism. The amount of dopamine released into the striatum decreases when neurons producing the neurotransmitter die. As a result, Parkinson's disease manifests symptoms such as rigidity, bradykinesia, resting tremors, and difficulty starting movements.[1] In developed countries, it is estimated that less than 0.3 percent of the general population has Parkinson's disease, whereas approximately 1 percent of people over the age of 60 have the condition.[2,3]

It is possible for people of any and all racial and cultural backgrounds to be afflicted, with men being marginally more likely to develop the disorder.[4,5]

"Shaking palsy" is the name given to PD in TCM. A person with shaking palsy suffers from tremors, numbness, limpness, and weak limbs. An insufficiency of liver-kidney yin and a shortage of qi-blood are the hallmarks of PD.[6,7]

Around the country, more than one lakh plant species has been found, more than twenty thousand of which are therapeutic herbs.[8]

The origin and pathophysiology of PD have not yet been fully understood. Despite the fact that no model has been able to recapitulate all pathological features of PD, preclinical models have greatly contributed to our understanding of the disease. There were three neurotoxins that had proved most successful so far in mimicking PD's *In vitro and In vivo:* Oxidopamine, rotenone and MPTP. A free radical was generated when oxidopamine was taken up by the dopamine transporter.

Herbal remedies have gained increasing attention in recent years as a way to manage or mitigate Parkinson's disease.

Recently, research has shown some active chemicals derived from herbal remedies, herbal extracts, and herbal formulations can impact Parkinson's disease models *in vitro* and *in vivo*.[9,10]

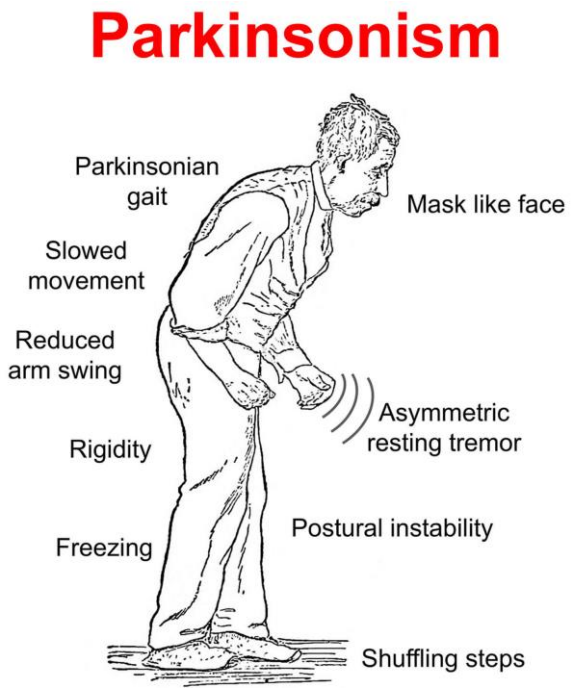

Fig:1 General characteristics of Parkinsonism Disorder.

CAUSES

Although numerous pathogenetic factors, including peroxidation, free radical production, mitochondrial malfunction, apoptosis, and neuroinflammation, are yet unknown as the specific etiology of disease.[11,12]

DIAGNOSIS

There are a number of clinical manifestations, such as normal aging, essential tremor, drug-induced parkinsonism, Parkinson-plus syndromes, and normal pressure hydrocephalus, but primarily it is diagnosed through a clinical examination.[13] Dystopia responsive to dopa and Huntington's disease with juvenile onset are uncommon conditions associated with parkinsonism.[14] MRI, EEG, PET, CT and SPECT are necessary in atypical cases.[15-17] Laboratory tests can include CBCs, chemistry panels, urine analyses, and blood glucose tests. Heart evaluation may also include an EKG.

TREATMENT

A synthetic drug treatment consists of the following.

1. Levodopa

Levodopa is decarboxylated by the presynaptic terminals of stratum dopaminergic neurons, which is the primary treatment for parkinsonism. Levodopa's therapeutic effectiveness in Parkinson's disease is attributed to its half-life of one to three hours. 0.5 to 2 hours after oral administration, the drug reaches its peak plasma levels.[18] A combination of entacapone (an inhibitor of COMBT) and peripheral dopa decarboxylase inhibitors, such as carbidopa or benserazide, can also inhibit its degradation. Nearly 80% of patients with Parkinson's disease benefit from levodopa initially in terms of stiffness, hypokinesia, tremor, and bradykinesia, while about 20% experience a significant improvement in motion.

2. Selegiline

Selegiline, a specific MAO-B antagonist that shields dopamine from intraneuronal degradation and reduces dopamine metabolism while also being discovered to raise dopamine in the brain, was first used as a supplement to levodopa.

3. D_2 AGONIST

Several newer non-ergot medications including ropinirole, pramipexole, rotigotine and apomorphine as well as the ergot derivatives bromocriptine.

4. ACETYLCHOLINE AGONIST

The inhibition of dopaminergic nerve terminals by benztropine, Trihexyphenidyl, procyclidine and biperiden interferes with the compensatory suppression of dopamine by muscarinic acetylcholine receptors.

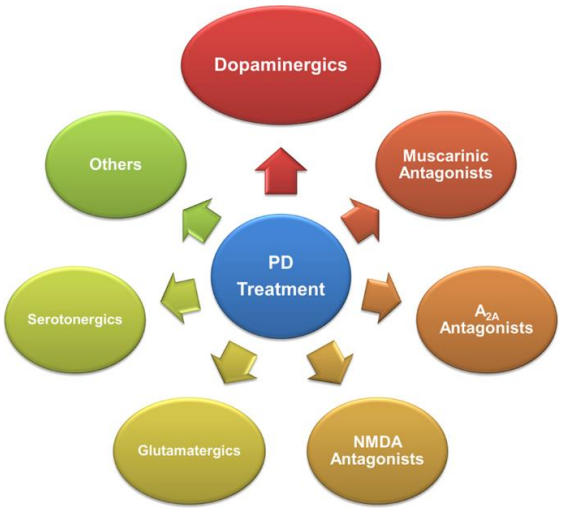

Fig 2: Synthetic drugs used for PD.

TREATMENT BY HERBS

In treating parkinsonism, the following herbs have shown significant effects.

1. *Withania somnifera*

According to a study, *W. somnifera* root extract has beneficial effects on parkinsonism Animals receive root extract treatments during seven days, followed by four days of MPTP treatment following 28 days of root extract treatments. At a dose of 100mg/kg, the extract significantly improved motor neuron function,

catecholamine levels, antioxidant levels, and prevented lipid peroxidation.[19]

2. *Acanthopanax senticosus*

It is a member of the *Alariaceae* family. In a study, it was discovered that *A. senticosus* stem bark extract in Ethanol (100 & 50%) and Warm water at a dose of 250 mg/kg p.o. significantly increases the levels of Dopamine in the striatum or action in the midbrain in order to prevent Parkinson's behavioral dysfunctions, such as bradykinesia, catalepsy, and depression. Oral administration of the extract for two weeks after I.P administration of MPTP exhibits cytoprotective effects in the SN and VTA.[20]

3. Jatamansi

The plant herb *Nardostachys jatamansi* belongs to the family Valirenaceae. Nardostachys jatamansi ethanolic extract has neuroprotective effects in 6-OHDA models of Parkinson's disease. A combination of the extract and a dopamine depletion test can be used to evaluate the extent of dopamine depletion in the nigrostriatal area. By pretreatment with Jatamansi, the striatum population of D2, activities of SOD, CAT and GSH were significantly increased by GSH-enhancing or antioxidant effects, while TH-IR fibre density was increased by pretreatment, indicating a dose-dependent increase in the number of neurons surviving and confirming the protective effects of *N. Jatamansi* ethanol extract.[21]

4. *Chrysanthemum* species

Chrysanthemum morifolium belongs to the family Asteraceae. *C. morifolium* extract used in an in vitro assay to induce 1-methyl-4-phenylpyridinium production. In addition, this method demonstrated the ability to determine viability, isolate RNA and analyze immune function, detect programmed cell death, measure ROS, and also scavenge free radicals.[22]

5. *Cassiae semen*

It belongs to the family, *Leguminosae*. Various doses of 0.1-50microgram per ml of ethanolic extract of this plant species were administered for 15 days and significantly decreased movement impairment and DA neuron loss. Neurotoxicity induced by 6-OHDAs and 1-methyl-4-phenylpyridinium in primary mesencephalic cultures mediated by antioxidative and antimitochondrial mechanisms.[23]

6. Mucuna pruriens

The family of the species belongs to be Leguminosae. It can be also known as Velvet bean. A study design showed that extract at a dose of 16 to 48 mg per kg which also contains small amount of levodopa has prominently mimic the latency step. It also showed a substantial antagonistic effect on both motor and sensory-motor impairments.[24]

7. Ginkgo

It was also called as *Pterophyllus salisburiensis.* A beneficial effect of this species on a study, showed that it was a powerful MAO inhibitor that prevents the breakdown of DA and increases its availability. After three weeks of pre-treatment with extract, striatal DA and its metabolites are significantly restored and rotation is significantly reduced. Free radicals are scavenged, MAO-B is suppressed, and antioxidant activity is increased.[25]

8. Bacopa or Brahmi

Bacopa monniera belongs to the family, *Scrophulariaceae.* An ethanolic extract of the whole plant is used to treat Parkinson's disease caused by aluminum neurotoxicity. As a result, it reduces SOD activity, prevents TBARS build-up, lipofuscin accumulation, and ultrastructural changes in the cells.[26]

9. Astragalus Radix

Pretreatment with astragaloside IV significantly and dose-dependently reduces the loss of dopaminergic neurons in oxidopamine-treated nigral cell cultures and increases TH and iNOS immunoreactivity.[27] In the process of self-oxidation, bendopa can produce free radicals that can contribute to Parkinson's disease. Astragalus polysaccharides reduce bendopa's neurotoxic effects, and the effects are time-dependent.[28]

10. *Psoralea species*

It is a dried ripened seed of *Psoralea corylifolia* belongs to the family, *Leguminosae*. A study on aqueous extract of *Psoralea* which shows that negative effects on the DA and NA transporters. Bakuchiol from this species has showed *invitro* dopaminergic neuroprotective and *invivo* anti-parkinsonism effects as well as regulating Mono amino functions.[29]

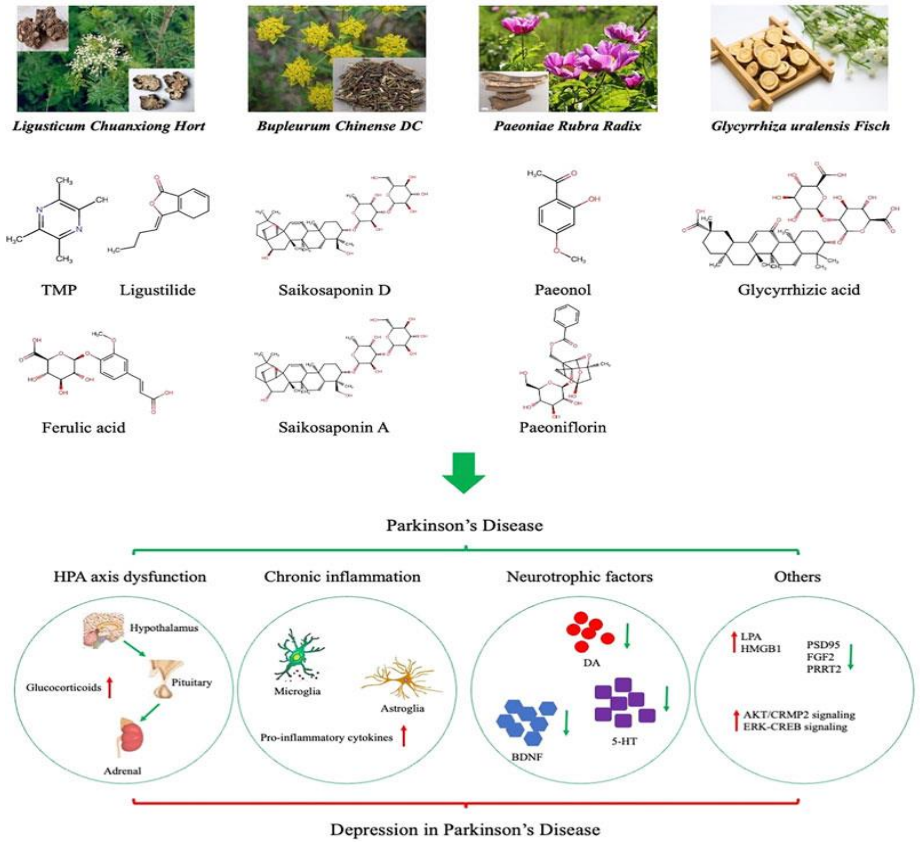

Fig 3: Some active ingredients of single herbal medicines used in treating depression in Parkinson's disease (DPD).

DISCUSSION

There have been numerous reports of herbal medication, or herbal formulations, acting effectively to treat and prevent parkinsonism. The majority of literature has concentrated on herbs like *T. orientalis, M. pruriens, G.biloba, P.scandens,* as well as several other ayurvedic, Chinese plants that have anti-oxidant, neuro-protective, as well as property against inflammation and programmed cell death. Dopamine, flavonoids, phenols and alkaloids present in herbs which has used to treat PDs. To produce a formulation, one should pay special attention to the pharmacological and phytochemical components of these herbs.

CONCLUSION

Plant-derived drugs are currently being used in a very small number of clinical settings. Biologically and pharmacologically, herbal medicines have diverse effects because they contain complex chemical combinations that combine to produce diverse biological and pharmacological effects. There have been numerous herbal extracts and constituents examined in this review that have therapeutic effects on animal models of Parkinson's disease. As a result of the current review, new pharmacotherapies from medicinal plants may be created to treat these disorders. The components of herbal medicines that have been well studied from a pharmacological viewpoint and from a behavioral standpoint may offer several potential candidates for further study that could eventually result in clinical applications. As conventional pharmacotherapeutic agents for treating parkinsonism are limited, as well as the high refractory and relapse rates, and the wide range of adverse side effects associated with long-term treatment, herbal remedies may be a valuable alternative for those with persistent conditions and those whose adverse side effects are intolerable.

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