



REVIEW ON HERBAL DRUG IN TREATMENT OF PARKINSON'S DISEASE

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Abstract

Parkinson's disease (PD) is the world's most widespread chronic neuron degenerative motion condition affecting more than 10 million people. The characteristic hallmark of PD involves a progressive loss of dopaminergic neurons in the brain's Substantia Nigra. Considerable Beware of this paid recently to the Bio-friendly Usage plant-based products for neuron prevention, cure, and treatment Disease and is degenerative. The herbal drugs, therefore, are safer than other drugs. Herbal medicine has its roots in ancient civilizations. It includes the usage of medicinal plants to cure disease and enhance general well-being.

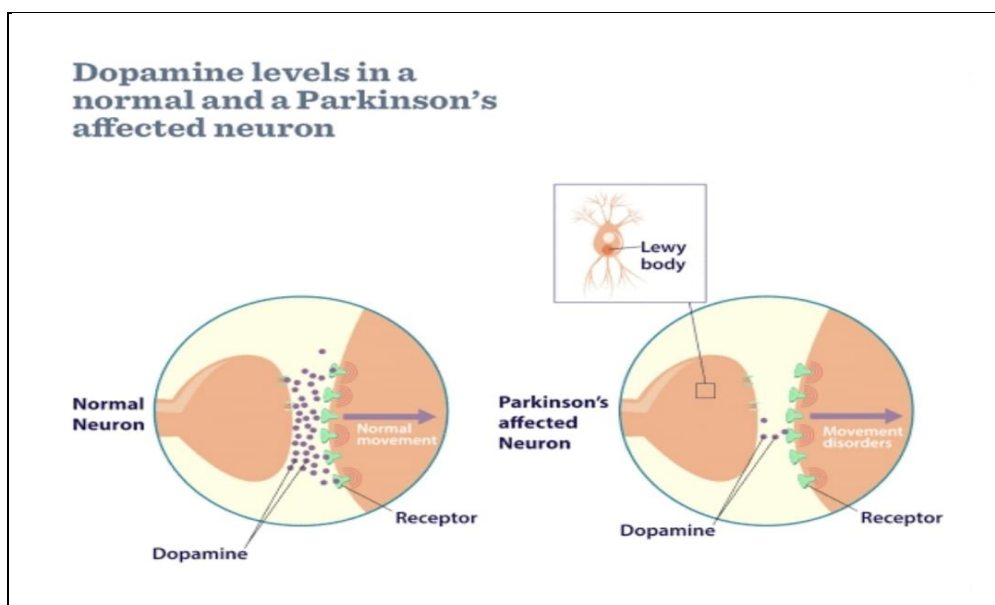
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INTRODUCTION

Parkinson's disease (PD) is an age-related neurodegenerative disorder that pathological feature is basically related on the progressive degradation of dopamine production in substantia nigra. The clinical manifestation includes bradykinesia (especially having difficulties in initiating movement), hypokinesia (lose of facial expression), rigidity, rest tremor (pill-rolling movement of the forearm) and non-motor features including depression, psychosis autonomic dysfunction .[1]

Parkinson's disease (PD) is a neurodegenerative disease with prominent motor impairments that include resting tremor, rigidity, bradykinesia and postural abnormality. Epidemiological studies show that the prevalence of PD in industrialized countries is usually estimated at 0.3% of the whole population and at ~1% in people over 60 years of age[2]

On the contrary, prevalence rate and incidence rate is slightly lower in Asian countries. It was reported that a standardized all-age prevalence of was 51.3 to 176.9 per 100,000 and the standardized incidence rates were 8.7 per 100,000 person-years[3]



AIM&OBJECTIVE

AIM:-To Study the Herbal drug in treatment of Parkinson's disease

OBJECTIVE:-

- To study Herbal drugs may aim to alleviate the motor symptoms of Parkinson's disease, such as tremors, bradykinesia, and rigidity.
- To study Some herbal compounds may have neuroprotective properties, potentially slowing down the progression of the disease or protecting against further damage to dopaminergic neurons
- To study Antioxidant effects Herbal drugs with antioxidant properties can help reduce oxidative stress in the brain, which is associated with Parkinson's disease
- To study Anti-inflammatory effects Herbal remedies may target inflammation in the brain, which is believed to play a role in the development and progression of Parkinson's disease
- To study Side effect management: Herbal drugs may be used to manage side effects of conventional Parkinson's medications, such as dyskinesias or gastrointestinal issues.

COMMON SYMPTOMS[4-6]

- Tremor or the involuntary and rhythmic movements of the hands, arms, legs and jaw
- Muscle rigidity or stiffness of the limbs – most common in the arms, shoulders or neck
- Gradual loss of spontaneous movement, which often leads to decreased mental skill or reaction time, voice changes, decreased facial expression, etc.
- Gradual loss of automatic movement, which may lead to decreased blinking, decreased frequency of swallowing and drooling
- A stooped, flexed posture with bending at the elbows, knees and hips
- Unsteady walk or balance
- Depression or dementia

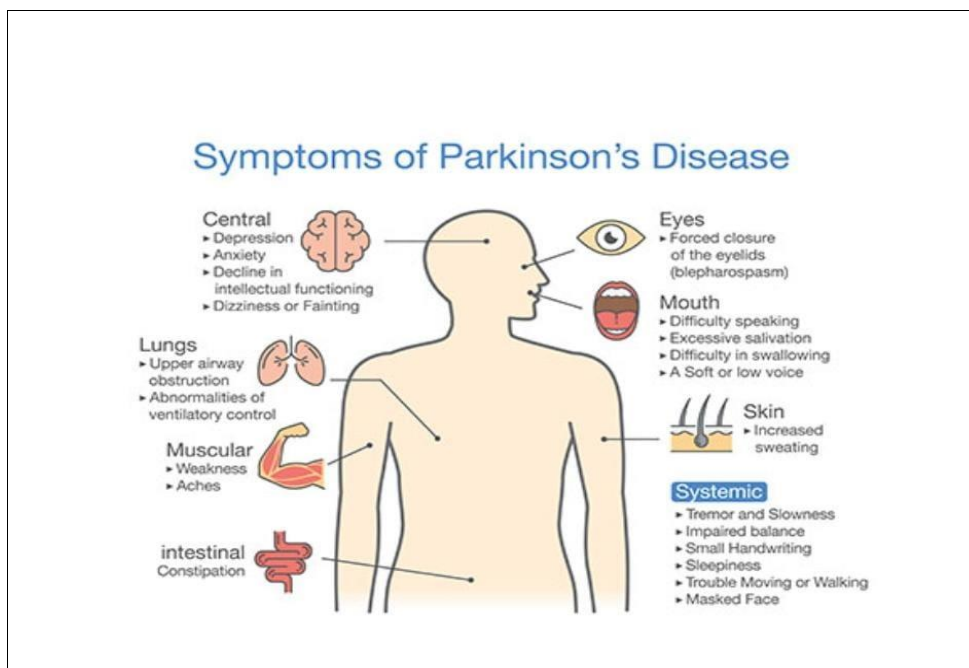


Fig.01

CAUSES OF PARKINSON'S DISEASE [7]

➤ Neurotransmitter Death

The brain's substantia nigra produce dopamine. If the dopaminergic neurons that secrete dopamine begin to die rapidly, the amount of dopamine in the body declines, resulting in Parkinson's symptoms.

➤ Gene Abnormality

The much more similar inherited cause of Parkinson's disease is a single genetic mutation in the LRRK2 gene.

➤ Environmental Cause

Some chemicals and metals have been related to Parkinsonism, according to recent study. Herbicides, insecticides, and fungicides used in crops, and also metals used in factories like lead, manganese, and trichloroethylene, all could cause the disease.

➤ Previous Head Injury

If a patient had suffered a serious head injury and went into shock in the previous, he or she is more prone to developing Parkinson's disease later in life.

➤ Presence of Alpha-synuclein within Lewy Body

Some microscopic marks remain in our brain cells as Lewy bodies, which are clumps of a specific substance. Within Lewy bodies, a crucial natural and widely spread protein called alpha-synuclein can deactivate the disease's cause.

CLASSIFICATION OF PARKINSONISM[8-14]

1. Idiopathic PD (Primary Parkinsonism)
2. Secondary Parkinsonism
3. Drug-induced Parkinsonism (DIP)
4. Vascular Parkinsonism
5. Other causes for secondary Parkinsonism
6. Parkinsonism plus syndrome

DIAGNOSIS

- Presently, the diagnosis of Parkinson's is primarily based on the common symptoms outlined above. There is no X-ray or blood test that can confirm the disease. However, noninvasive diagnostic imaging, such as positron emission tomography (PET) can support a doctor's diagnosis. Conventional methods for diagnosis include
 - The presence of two of the three primary symptoms
 - The absence of other neurological signs upon examination
 - No history of other possible causes of parkinsonism, such as the use of tranquilizer medications, head trauma or stroke
 - Responsiveness to Parkinson's medications, such as levodopa

TREATMENT OF PARKINSON'S DISEASES[15-17]

Pharmacologic treatments for Parkinson's disease motor symptoms are primarily dopamine based. Levodopa preparations, dopamine agonists, and monoamine oxidase-B (MAO-B) inhibitors are useful initial therapies. For young individuals with prominent tremors, anticholinergic agents (e.g., trihexyphenidyl) are useful, but caution is required because of the potential for adverse events, particularly relating to cognition.

More than 40% of individuals treated with oral dopamine agonists (ropinirole, pramipexole) experience impulse control disorders (e.g., gambling, compulsive spending, abnormal sexual and eating behaviors, compulsive medication use, and lobbyism). Individuals who discontinue the use of dopamine agonists, often due to impulse control disorders, experience withdrawal symptoms (e.g., anxiety, panic attacks, irritability, diaphoresis, pain, and drug cravings) 15% to 20% of the time. Due to this, sometimes the dopamine agonist cannot be discontinued despite serious associated adverse events such as impulse control disorders.

DRUG PROFILE[18-24]**SILYMARIN**

SOURCE OF SILYMARIN:-Silymarin is a pharmacologically active phytochemical extracted from seeds and fruits of *S. marianum*, commonly known as milk thistle. *Marianum* is an annual or biennial plant and is a member of plant family Asteraceae. The genus *Silybum* contains two species that are *S. marianum* and *Silybum eburneum*. Geographically this plant distributes around the globe. It is cultivated in the Mediterranean region, Sinai, and Afghanistan, and has been neutralized in other parts of the world. It has been used from ancient times where Theophrastus (4th century B.C.) was probably first to describe it under the name *Pternix*. The initial use of *S. marianum* was reported by Dioscorides for treatment of serpent bites. In 1898, the use of herb to relieve obstructions of the liver was documented by British herbalist Culpepp.

CHEMISTRY OF SILYMARIN:- Silymarin is a mixture containing isomer flavonolignans (silybin, isosilybin, and silychristin), small number of flavonoids (taxifolin), fatty acids, and other polyphenolic compounds. It is a lipophilic agent extracted from seeds of *S. marianum*. Silybin comprises 50–70% of silymarin having greatest degree of biological activity. Seeds of *S. marianum* also contain other flavonolignans including isosilybin, dehydrosilybin, desoxysilychristin, desoxysilydianin, silandrin, silybinome, silyhermin, and neosilyhermin. Flavonolignans present in the mixture of silymarin contain flavonoid moiety links to a molecule of lignin moiety (coniferyl alcohol). It has been documented that silybin is a mixture of diastereoisomers namely silybin A and silybin B. Silybin also known as silibinin contains 1,4-dioxane ring in addition to flavonoid moiety and is a most active anti-hepatotoxic agent. It has been reported that the presence of 2,3-double bond in the C-ring of flavonoid structure results in increasing antioxidant activity of silybin.

NEUROPROTECTIVE POTENTIAL OF SILYMARIN:-Silymarin is a polyphenolic flavonoid with strong antioxidant activities and is in clinical practice for management of hepatic disorders. Free radicals scavenging, elevating cellular glutathione level, and improving activity of superoxide dismutase are key mechanisms attributed to antioxidant activities of silymarin. Through inhibition of oxidative stress, silymarin possesses neuroprotective effects and it can be used in the management of neurodegenerative disorders including Alzheimer's disease, PD stroke, and traumatic brain Injury.

SAFETY PROFILE OF SILYMARIN:-Being a phytochemical Silymarin generally possesses favorable safety profile, although allergic reactions including anaphylactic reactions have been reported. Other ADRs include mild laxative effects, nausea, epigastric discomfort, arthralgia, pruritus, urticaria, and headache. Silymarin also leads to inhibition of cytochrome P450 system and thus affecting the clearance of other drugs including chemotherapeutic agents.

LOW SOLUBILITY OF SILYMARIN:-Low solubility of silymarin has been documented, i.e., 0.04 mg/ml and this is one of the basic reason of low oral bioavailability of silymarin from GIT. Studies also reflect that, however, silymarin has low aqueous solubility, it possesses lipophilic properties.

ANTI-PARKINSON'S TARGETS OF SILYMARIN:- As stated earlier in this review that neuro-inflammation is a consequence or a cause of nigral cell loss and thus plays one of the most crucial roles in pathophysiology of PD. Beside antioxidant properties silymarin also inhibits neuro-inflammation by several mechanisms. Silymarin exerts its anti-inflammatory

Drugs use in Parkinson;s disease				
PLANT NAME	FAMILY	COMMON NAME	PLANT PART USE	CHEMICAL CONSTITUENTS
Blepharis Maderaspatensis	Acanthaceae	Nethirs poondu	Dry Seed	Steroids-gomisin-D
Smilax perfoliata	Smilacaceae	Ram damtena	Dry root	Steroidal Sapogenins
Smilax zeylanica	Smilacaceae	Rough blind weed,hill lotus	Dry root	Alpha, beta hydroxy acids
Plantago ovata	plantaginaceae	Flax seed	Husk fiber	Mucilage, cyano genetic glyco cydes-linamarin lotaustralin

Fig.Herbal drugs used in Parkinson's disease

Fig.02

Conclusion

Parkinson's disease (PD) is a complex neurodegenerative disease, manifested by the progressive functional impairment of the midbrain nigral dopaminergic neurons. Due to the unclear underlying pathogenesis, disease-modifying drugs for PD remain elusive. In Asia, such as in China and India, herbal medicines have been used in the treatment of neurodegenerative disease for thousands of years, which recently attracted considerable attention because of the development of curative drugs for PD. In this review, we first summarized the pathogenic factors of PD including protein aggregation, mitochondrial dysfunction, ion accumulation, neuroinflammation, and oxidative stress, and the related recent advances. Secondly, we summarized 32 Chinese herbal medicines (belonging to 24 genera, such as Acanthopanax, Alpinia, and Astragalus), 22 Chinese traditional herbal formulations, and 3 Indian herbal medicines, of which the ethanol/water extraction or main bioactive compounds have been extensively investigated on PD models both in vitro and in vivo. We elaborately provided pictures of the representative herbs and the structural formula of the bioactive components (such as leutheroside B and astragaloside IV) of the herbal medicines. Also, we specified the potential targets of the bioactive compounds or extractions of herbs in view of the signaling pathways such as PI3K, NF-κB, and AMPK which are implicated in oxidative and inflammatory stress in neurons. We consider that this knowledge of herbal medicines or their bioactive components can be favorable for the development of disease-modifying drugs for PD.

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