Herbal Drug in Parkinson's Disease

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Abstract:

A neurological condition with multiple levels of intricacy is Parkinson's disease. It has long been distinguished by the loss of dopaminergic neurons in the substantia nigra and the conventional motor characteristics of parkinsonism linked to Lewy bodies. Nonetheless, it is now acknowledged that Parkinson's disease symptoms can vary widely and include non-motor characteristics that are clinically significant. Its disease also includes protein aggregates other than Lewy bodies, other neurotransmitters, and large areas of the nervous system. Although the exact origin of Parkinson's disease is still unknown, environmental influences are no longer thought to be the key contributing factor. Rather, a complex interaction between environmental and genetic factors that impact many basic cellular functions appears to be the cause of Parkinson's disease. Clinical difficulties associated with the intricacy of Parkinson's disease include the inability to make a conclusive diagnosis in the early stages of the illness and challenges managing symptoms later on. Moreover, the neurodegenerative process cannot be slowed by any treatment. One of the most prevalent nonmotor side effects of Parkinson's disease (PD) is sleep disturbance, which becomes more frequent as the condition worsens. There are many different reasons why people with Parkinson's disease experience sleep disturbances, and many individuals may have multiple contributing variables. These conditions can be roughly divided into two groups: those that affect sleep at night and those that show up during the day as excessive daytime sleepiness.

Key words : Parkinson disease, Mucuna pruriens, ginseng, Silymarin, Astragalus

Introduction:

The most prevalent neurodegenerative movement condition is Parkinson's disease (PD). Although bradykinesia/akinesia, stiffness, tremor, and postural instability are its primary motor symptoms, the clinical picture also includes other motor and non-motor symptoms (NMSs). Although certain tests can aid in the differential diagnosis from other types of parkinsonism, the diagnosis is primarily clinical.[1](1) One prevalent and intricate neurological condition is Parkinson's disease. Although Parkinson's disease was originally described in detail about 200 years ago, the notion of the illness is still being developed. Fundamentally, Parkinson's disease is a neurodegenerative condition in which dopaminergic neurons in the substantia nigra pars compacta (SNpc) die early and prominently.

Classical parkinsonian motor symptoms are the hallmark of a movement disease caused by the ensuing dopamine shortage in the basal ganglia.[2](2) The second most prevalent neurodegenerative illness affecting the elderly in the US is Parkinson's disease. According to estimates, there are 100 to 200 cases of Parkinson disease for every 100,000 people over 40. Among neurodegenerative diseases, Parkinson's disease has historically been distinct due to the availability of an efficient treatment based on dopamine replacement.[3](3) James Parkinson describes the clinical illness that now bears his name in his work "An Essay on the Shaking Palsy," which was written about 190 years ago. Even though bradykinesia, increased tone, loss of postural reflexes, and resting tremor are well-known hallmarks of Parkinson's disease, making the diagnosis can still be difficult. It is important to differentiate idiopathic Parkinson's disease from other types of parkinsonism since the prognosis and course of treatment will differ.(4) [4]A depletion of dopamine-producing cells in the substantia nigra results in Parkinson's disease (PD), a movement disability. Clinically and pathologically, it is more complicated than this, though. A substantial symptom burden is composed of non-motor characteristics such as cognitive impairment, depression, hallucinations, autonomic abnormalities, and sleep issues, in addition to the well-described motor characteristics of bradykinesia, stiffness, tremor, and postural instability.[5]

Overview of Parkinson disease:

The purpose of this summary of Parkinson's disease is to provide context for the discussion of the medications used to treat it elsewhere in this supplement. Parkinson's disease is a prevalent neurological illness that worsens quality of life

and causes substantial disability. The pathologic presentation of Parkinson's disease involves the loss or malfunctioning of dopaminergic neurons in the substantia nigra pars compacta, despite the fact that the exact origin of the condition is unknown. Bradykinesia, stiffness, and asymmetric resting tremor are examples of clinical symptoms that are indicative of difficulties with coordinated movement. The clinical diagnosis of Parkinson's disease is based on these symptoms and how they react to levodopa. (7)[6] James Parkinson made reference to sleep disturbance in his first account of Shaking Palsy. With the realization that sleep disturbances are a significant clinical concern and offer a chance to learn more about the pathophysiology of this neurodegenerative disease, the issues surrounding sleep have recently come under closer examination, despite the fact that they are frequently eclipsed by the varied motor manifestations of Parkinson's disease (PD).(8)[7] Numerous sleep disturbances, which are prevalent and severely reduce quality of life, are linked to Parkinson's disease. Asking medical professionals about sleep issues on a regular basis can improve their ability to identify and treat them. This article reviewed sleep disturbances and their special considerations in Parkinson's disease. (9)[8] The prevalence of pain in patients with Parkinson's disease (PD) varies depending on the disease stage, co-morbidities, and assessment instruments. Pain is a prevalent non-motor symptom of PD. Early onset age, prolonged illness duration, motor problems, concurrent depressive symptoms, female gender, and related medical conditions are risk factors for discomfort in Parkinson's disease. Musculoskeletal pain is the most prevalent type of pain in people with Parkinson's disease (PD), although other types include nocturnal pain, orofacial pain, fluctuation-related pain, chronic body pain (central or visceral), pain with discoloration, oedema, or swelling, and radicular/neuropathic pain.(10)[9]

Symptoms and diagnosis:

Movement is the main symptom of Parkinson's disease, a degenerative neurological condition. Symptoms might differ greatly from person to person and frequently appear gradually. Usually, they are divided into two categories: non-motor (associated to other body functions) and motor (connected to movement).

Motor Symptoms:

Tremors (Shaking) : Often starting in one hand or finger, tremors are a common early sign. They may diminish with purposeful movement.

Bradykinesia (Slowness of Movement) : This leads to difficulty initiating or completing movements, making simple tasks more time-consuming and challenging.

Muscle Rigidity : Stiffness in muscles can cause discomfort and limit the range of motion.

Postural Instability : Balance problems and a stooped posture increase the risk of falls.

Masked face – Reduced facial expressions, giving a mask-like appearance. Soft or slurred speech – Known as hypophonia. Gait changes – Shuffling walk, reduced arm swing, difficulty starting or stopping movement.

Non-Motor Symptoms (often overlooked but common):

Sleep disturbances – REM sleep behavior disorder, insomnia, excessive daytime sleepiness. Cognitive impairment – Memory problems, confusion, eventually may lead to Parkinson’s dementia.

Mood disorders – Depression, anxiety, apathy. Autonomic dysfunction : Constipation ,low blood pressure (orthostatic hypotension) Urinary urgency or incontinence ,Sexual dysfunction, Loss of smell (anosmia) – One of the earliest signs.

Fatigue – Extreme tiredness not always relieved by rest.

Pain – Muscle cramps or discomfort.

Early Signs:

-Slight tremor in a hand or finger

-Small or cramped handwriting (micrographia)

-Stooped posture

-Decreased arm swing on one side

How is the diagnosis made?

Parkinson disease is currently diagnosed using clinical symptoms from history and examination, as well as the development of motor fluctuations and the responsiveness to dopamine drugs over time.30 Asymmetrical motor manifestations of the disorder (Table 3) include resting tremor, hypophonia (soft voice), masked facies (first manifested as decreased blink rate), micrographia (small handwriting), rigidity (stiffness), bradykinesia (slow movement), shuffling steps, and balance issues. A common symptom is resting tremor, which typically affects one upper limb, though 20% of patients do not have it. Thirty percent of patients may first exhibit tremor in a lower leg, along with resting tremors of the lips, mouth, or even tongue.

What drugs should be avoided?

Drugs that inhibit dopamine receptors may cause neuroleptic malignant syndrome, cause parkinsonism, or significantly aggravate motor symptoms in Parkinson disease patients. These include antiemetics like prochlorperazine and metoclopramide; antihypertensives like methyldopa; neuroleptics like haloperidol, thioridazine, chlorpromazine, promethazine, fluphenazine, risperidone, and olanzapine; and antihypertensives like tetrabenazine. Those on monoamine oxidase B inhibitors should not take meperidine. (18)[10]

Clinical diagnosis of PD:

Bradykinesia, stiffness, and rest tremor are the hallmarks of Parkinson's disease. Not all of these might be present. Although early postural instability, especially in those with a history of falls, is more predictive of progressive supranuclear palsy (PSP), postural instability may be a characteristic. In Parkinson's disease, the clinical symptoms are typically asymmetrical. Although post-mortem studies have revealed an alternate diagnosis in up to 25% of PD patients identified by general neurologists, the clinical diagnosis may frequently seem clear-cut. Notably, individuals identified in expert movement disorder clinics have significantly lower diagnostic errors, supporting the case for early patient referral to movement disorder specialists. (5)[11]

Step-by-Step Diagnostic Process:

1. Clinical Evaluation
2. Medical History
3. Response to Levodopa
4. Imaging Tests (to rule out other conditions)
5. Exclusion of Other Causes

Pathophysiology:

The loss of dopaminergic cells in the substantia nigra and the ensuing dopamine depletion of the striatum are the pathological hallmarks of both Parkinson's disease and MPTP-induced Parkinsonism. The most distinctive symptom of idiopathic Parkinson's disease is rest tremor. In terms of the course of the disease, those with tremor-dominant Parkinson's disease (PD) have a better prognosis than those with the kinetic/rigid form. According to a number of research, the pathogenesis of akinesia/rigidity-dominant PD and human tremor-dominant PD are different.(11)[12] The distribution of Lewy bodies serves as the basis for this pathological stage. The pathological hallmark of Parkinson's disease is Lewy bodies. These immune-reactive inclusions of a-synuclein are composed of many neurofilament proteins and proteolysis-related proteins. Among these is ubiquitin, a heat shock protein that is crucial in directing the degradation of other proteins. Certain familial types of Parkinson's disease (PD) that also exhibit lewy bodies are caused by mutations in the a-synuclein gene. In juvenile cases, mutations in the parkin protein result in a parkinsonian syndrome without lewy bodies, indicating that the parkin protein is crucial for the formation of lewy bodies.(5)[11] A slow and selective loss of neurons is a hallmark of Parkinson's disease (PD), a degenerative illness. Axial symptoms include postural instability and abnormalities of gait, while motor symptoms include kinesia, rigidity, and tremor (the so-called cardinal symptoms). (12)[13]

Normal aging results in the loss of dopaminergic neurons in the SNpc. However, since the pattern of dopaminergic neuronal loss in PD is different from that of normal aging, models of accelerated aging appear inadequate in understanding PD.(13)[14] The loss of dopaminergic neurons in the substantia nigra is a hallmark of Parkinson's disease. The Lewy body, a neuronal inclusion primarily composed of α-synuclein protein aggregations, is the pathologic hallmark of Parkinson disease. The Braak hypothesis is the model most frequently used to explain the neuropathological course of Parkinson's disease. This concept proposes that the medulla and olfactory bulb are where Parkinson disease begins (stages 1 and 2). This early pathology is linked to symptoms including diminished smell and rapid eye movement sleep behavior disorder, which occurs before the development of the movement disorder. In this condition, people lose their typical rapid eye movement sleep paralysis and physically play out their dreams while they sleep. (15)[15]

Pathophysiological Features:

1. Degeneration of Dopaminergic Neurons

2. Dopamine Imbalance in Basal Ganglia

3. Lewy Body Formation

4. Progression Beyond the Substantia Nigra

Biochemical Changes:

↓ Dopamine → Motor symptoms

Altered levels of other neurotransmitters:

↓ Serotonin → Depression

↓ Norepinephrine → Autonomic symptoms

↓ Acetylcholine → Cognitive decline

MOST COMMON SLEEP DISORDERS ASSOCIATED WITH PARKINSON'S DISEASE:

1) INSOMNIA

Insomania is defined as the chronic inability to initiate, sustain, consolidate, or generate an overall acceptable sleep quality despite having adequate sleep opportunities, resulting in daytime impairment.

2) EXCESSIVE DAYTIME SLEEPINESS

Excessive daytime sleepiness (EDS) is the difficulty to remain awake and alert during the day which leads to unintended episodes of sleep or drowsiness.

3) SLEEP RELATED BREATHING DISORDERS

Sleep related breathing disorders (SBD) include obstructive sleep apnea (OSA), central sleep apnea, sleep related hypoventilation and sleep related hypoxemia.

4) RESTLESS LEGS SYNDROME

Restless legs syndrome (RLS) is the urge to move the legs usually associated with leg discomfort.

5) CIRCADIAN RHYTHM DISORDERS

Circadian rhythm disorders are defined as chronic or recurring sleep disturbances caused by changes in the circadian system or a misalignment between the endogenous circadian rhythm and socially imposed sleep-wake cycles.

6) REM SLEEP BEHAVIOR DISORDER

Rapid eye movement sleep behavior disorder (RBD) is a parasomnia described as repeated

Treatment options for Parkinson disease:

In recent years, Parkinson's disease treatment options have expanded significantly. Pharmacological treatments, such as levodopa, dopamine receptor agonists, anticholinergic medicines, monoamine oxidase B inhibitors, and catechol-O-methyl transferase inhibitors, are still the mainstay of therapeutic intervention and are discussed. In addition, the classic and new roles of amantadine are discussed. Despite levodopa's high efficacy, "levodopa-sparing strategies" are promoted in early Parkinson's disease to prevent the development of difficult-to-manage motor fluctuations and dyskinesias. (16)[16] It is important to underline that Parkinson's disease treatment must be tailored to each individual patient; no "textbook" formula should be used. Instead, drugs should be used and titrated according to the patient's specific needs and clinical presentation.(16)[16] Alzheimer's disease (AD) and Parkinson's disease (PD) are the most frequent neurodegenerative illnesses seen in clinical practice. While dementia has long been associated with Alzheimer's disease, it can be classified into several clinical stages, ranging from prodromal Mild Cognitive Impairment (MCI) to mild, moderate, and severe dementia.(17)[17] Parkinson's disease is a neurodegenerative condition that affects multiple motor and nonmotor brain pathways.8,9 Parkinson's disease is characterized by two key pathologic processes: (a) premature selective death of dopamine neurons and (b) the buildup of Lewy bodies, composed of α-synuclein, which get misfolded and accumulate in numerous systems of patients. It is not apparent which step comes first. According to pathologic studies10, neurons degenerate gradually over many years, with each damaged region matching to a specific symptomatology in Parkinson's disease. When motor symptoms appear, pathological testing reveals 30-70% cell loss in the substantia nigra.11 The primary goal of therapy is to replenish dopamine with dopaminergic medicines and regulate the malfunctioning circuit. Dopamine deficiencies beyond the basal ganglia, as well as in serotonergic and noradrenergic systems, are associated with cognitive failure, mood disorders, and impulse control issues.(18)[10] Although there is no cure for Parkinson's disease (PD), treatment focuses on symptom management, improving quality of life, and delaying the condition's progression. Care is personalized to each individual and may include drugs, surgical procedures, and lifestyle changes.

1. Medications
2. Surgical Options
3. Supportive & Non-Pharmacological Therapies
4. Emerging & Experimental Therapies

Treatment Plan Considerations:

Early Stage: Treatment often begins with MAO-B inhibitors or dopamine agonists to control mild symptoms.

Moderate Stage: Levodopa becomes the primary therapy, often combined with adjunct medications such as COMT inhibitors or additional dopamine agonists to enhance effectiveness.

Advanced Stage: Management includes deep brain stimulation (DBS), strategies to address motor fluctuations, and targeted treatment for non-motor symptoms.

Levodopa and a peripheral decarboxylase inhibitor have been considered the gold standard for treating Parkinson's disease (PD) for the past 40 years. It continues to be the most effective medication treatment in many ways. But there is frequently a cost associated with the advantages attained. Side effects from long-term levodopa medication are often incapacitating. After starting levodopa, levodopa-induced dyskinesias occur at an average annual incidence of 10%, albeit this number is higher in patients with younger onset. While dyskinesias are primarily caused by the length of levodopa medication, motor fluctuations are most strongly correlated with the duration of the disease and the dose of levodopa exposure.19. Intermittent dopamine receptor activation appears to be linked to the onset of drug-induced dyskinesias in Parkinson's disease. (5)[11]

What has changed in the treatment of advanced Parkinson disease?

Levodopa's effectiveness in advanced Parkinson disease may wane and change during the day as the patient alternates between "on" and "off" drug periods. Due to levodopa's brief half-life, the variations in motor and non-motor

components are similar to those observed in levodopa plasma concentrations. The objective of treating fluctuations in people with severe Parkinson disease is to provide constant dopaminergic stimulation. To treat these patients, we now have surgical options such as levodopacarbidopa intestinal gel and deep brain stimulation. (18)[10]

Mechanism of action of herbal drug over Parkinson disease:

Herbal remedies have drawn interest due to their potential to help control Parkinson's disease (PD), mainly through neuroprotective, anti-inflammatory, and antioxidant processes. An outline of some well-known plants and their suggested modes of action is provided here.

Mucuna pruriens (Velvet Bean):

Mechanism : contains L-DOPA, a precursor to dopamine, which raises dopamine levels in the brain and may help reduce movement symptoms in Parkinson's disease. Parkinson disease (PD) sufferers have taken a liking to Mucuna pruriens, a legume that grows extensively across the tropics. Since the third century BC, it has been utilized in Ayurvedic therapy to treat neurological syndromes with symptoms resembling Parkinson's disease. Levodopa (LD),4 which is present in considerable amounts (4%–6%) in mucuna seeds, is thought to be the primary cause of its effect in Parkinson's disease. There is little information available on the LD bioavailability and associated therapeutic effects of Mucuna formulations in PD patients when compared to LD standard products. (19)[18]

As previously mentioned, the trial medication was MP powder made straight from roasted seeds without the use of any extra substances (such as additives) or pharmaceutical processing.6. The coauthor of this paper, J.L., a Bolivian neurologist with extensive experience using MP powder in impoverished PD patients, had proposed this inexpensive approach. In short, we toasted MP seeds for 15 minutes in a skillet, then we removed the teguments and ground them in a small grinder. Finally, we sieved the ground seeds to get the powder, which we then mixed with water. (20)[19]

Ginseng (Panax ginseng):

Mechanism : Ginsenosides Rb1 and Rg1 exhibit neuroprotective effects by reducing oxidative stress and apoptosis in dopaminergic neurons.

For thousands of years, ginseng, the root of the Panax ginseng plant, has been utilized as a common and extensive traditional herbal remedy in China, Japan, and Korea. It is now utilized as a natural medicine all over the world and has gained popularity as a functional health food. The body of research on P. ginseng's physiological and pharmacological effects on neurodegenerative illnesses is growing. Potential neuroprotective mechanisms mediated by ginseng or ginsenosides primarily include immune-stimulatory, anti-inflammatory, anti-oxidant, and anti-apoptotic properties as well as homeostasis maintenance. Publications discussing P. ginseng's diverse actions that suggest potential neurotherapeutic benefits in neurological conditions and neurodegenerative diseases, including Parkinson's disease, Alzheimer's disease, Huntington's disease, amyotrophic lateral sclerosis, and multiple sclerosis, are taken into consideration in this review. Ginsenosides, the pharmacologically active chemicals found in P. ginseng, have recently been shown to have positive benefits in both in vitro and in vivo models of Parkinson's disease. (21)[20]

Silymarin (Milk Thistle):

Mechanism : protects dopaminergic neurons from oxidative injury by acting as a strong antioxidant, scavenging free radicals and increasing glutathione levels. Extra Impacts: contributes to its neuroprotective qualities by regulating estrogen receptors and preventing neuroinflammation.

To treat Parkinson's disease (PD), a mucoadhesive lipophilic silymarin microemulsion (SLMMME) was created. Central Composite Design (CCD) was used to optimize the SLM microemulsion (ME). According to the design, the ratio of oil, surfactant, co-surfactant, and water was adjusted to attain the desired droplet size, zeta potential, and drug loading. The neurodegenerative condition known as Parkinson's disease (PD) is characterized by irregular gait, slowness of movement, rigidity, resting tremors, and balance issues. The irreversible loss of dopaminergic neurons in the substantia nigra (SN) and their connections to the striatum characterizes Parkinson's disease (PD), the second most common progressive and chronic neurodegenerative illness in the world. Consequently, movement abnormalities arise as the function of the nigrostriatal system declines.(22)[21]

Astragalus (Astragalus membranaceus):

Mechanism: Contains compounds like astragaloside IV and polysaccharides that reduce oxidative stress and promote the survival of dopaminergic neurons.

Research Findings: These compounds have shown potential in enhancing dopamine production and protecting against neurodegeneration.

Astragalus membranaceus has been utilized as a traditional herb in Asian countries for ages. It is also utilized in Chinese culture as a hmembranaceus has a wide spectrum of biochemical and pharmacological activities, including immunomodulatory, anti-hyperglycemic, and antiviral properties. More than 200 chemicals identified from A. membranaceus have a variety of biochemical and pharmacological actions, including immunomodulatory, anti-hyperglycemic, and antiviral properties. Flavonoids are one of the key bioactive components responsible for A. membranaceus' pharmacological effects, with over 200 molecules identified. Although total flavonoids isolated from A. membranaceus (TFA) have been shown in trials to have a number of health advantages, their therapeutic potential in Parkinson's disease has not been established.

Bacopa monnieri (Brahmi):

Mechanism: Exhibits antioxidant properties and may influence dopamine levels, potentially supporting cognitive function in PD.

A common medicinal herb used as a brain tonic is Bacopa monnieri (L.) Wettst. We examined the neuroprotective and neurorescue effects of Bacopa monnieri (L.) Wettst extract (BME) in a mouse model of Parkinson's disease (PD) produced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). The primary components of BM consist of bacosides, which are dammarane-type triterpenoid saponins with jujubogenin or pseudojujubogenin moieties as a glycone unit. Along with D-mannitol, apigenin, hersaponin, monnierasides I–III, cucurbitacins, and plantainoside B, the primary alkaloids are brahmine, nicotine, and herpestine. A class of twelve recognized analogs is known as bacosides. Recently, new saponins known as bacopasides I–XII have been discovered. The most researched BM component is bacoside A, which is a combination of bacoside A3, bacopaside II, bacopa saponin C, and a jujubogenin isomer of bacosaponin C. (24)[22]

One such creeping, semi-succulent herbal remedy is Bacopa monnieri, which has been thoroughly studied for its diverse pharmacological qualities in a range of animal models and cell lines, in addition to its potential to improve brain health. For example, B. monnieri extract has been shown to be useful in the treatment of inflammatory diseases such rheumatism, dropsy, bronchitis, and asthma. Bacopa has also been discovered to be a potent nervine, diuretic, and cardiotonic. Through clinical research, the neuroprotective effectiveness of brahmi supplementation was also investigated in both healthy and ill subjects. Supplementing with bacopa has been shown to improve learning abilities, memory, focus and attention, perceptivity, cognitive processing, and anxiety levels. (25)[23]

Gastrodia elata:

Mechanism: Contains gastrodin, which offers neuroprotection by reducing oxidative stress and inhibiting apoptosis in dopaminergic neurons.

Gastrodia elata can balance yin and yang, calm the liver, and suppress yang. It can also open channels and quench wind. The primary chemical components of Gastrodia elata, according to our pharmacological analysis, are B-sterol, tianmuin, tianmuoside, tianmu ether glycoside, and tianmu polysaccharide. Anticonvulsant, antioxidant, antidepressant, analgesic, sedative, antiepileptic, anti-inflammatory, and neuroprotective are only a few of its many pharmacological properties. Additionally, it is utilized to treat the aftereffects of traumatic brain injury and Parkinson's disease. Few research have been done on the use of Gastrodia elata and its active components in the treatment of neurodegenerative illnesses, particularly Parkinson's disease (PD), despite the fact that they are frequently used in clinical practice. hus, by thoroughly examining the pathophysiology of Parkinson's disease and the pharmacological effects of Gastrodia elata, the current study sought to uncover the pharmacological mechanism of this medication in the treatment of PD.(26)[24]

Tribulus terrestris:

Mechanism : may improve motor function and lessen α-synuclein aggregation in PD mice via modifying acetylcholinesterase activity and lowering inflammation. In many cultures, Tribulus terrestris L., also referred to as puncture vine, caltrop, goat's head, and yellow vine, is a member of the Zygophyllaceae family. It can be found in both tropical and mildly temperate regions. Phytopathologists and Ayurvedic practitioners employ T. terrestris as a remedy herb with success. Since it contains steroidal saponins, alkaloids, flavonoids, steroidal glycosides, cinnamic acid, and phytosterol, phytochemical investigation revealed its therapeutic value against neurodegeneration. Flavonoids and saponins, which are abundant in Tribulus terrestris (T.T.), have been shown to have antioxidant and neuroprotective properties. The purpose of the current study was to examine T. terrestris methanol extract's (TTME) potential anti-Parkinson's effects. TTME was thought to have antioxidant properties and to improve Parkinson's disease (PD) by modifying α-synuclein and acetylcholinesterase (AChE).(27)[25]

Common herbal drug used in Parkinson disease :

Recent years have seen a significant increase in interest in herbal remedies, which are utilized in China to treat Parkinson's disease (PD) according to contemporary pharmacological theories or traditional Chinese medicine. In addition to provide future references for fundamental and clinical research, we compiled and examined the anti-Parkinsonian properties of herbal medications and herbal formulations studied in PD models. All of the herbal remedies and formulations underwent both in vitro and in vivo testing in PD models. Based on their pharmacological activity or genera, the pertinent chemicals and herbal extracts with anti-Parkinsonian properties were evaluated. Eleven herbal formulations and 38 herbal medications in all were examined. By modifying several important events or signaling pathways linked to the pathophysiology of Parkinson's disease, the pertinent drugs, herbal extracts, and formulations have been shown to be efficacious on PD models. (28)[26]

A common herbal drug used as complementary therapy in Parkinson's disease (PD) are:

GREEN TEA (CAMELLIA SINENSIS):

Tea is one of the most popular beverages in the world. Tea plant Camellia sinensis (family Theaceae) originated in Southeast China and spread to India, Sri Lanka, and many other tropical and subtropical nations. The tea plant is grown in over 30 countries worldwide. It thrives in tropical and subtropical climates with regular rainfall, good drainage, and slightly acidic soil.(30)[27] Many studies have demonstrated that many natural products have anti-Parkinson's disease qualities due to their antioxidant and anti-inflammatory effects, prevention of metal ion accumulation, and modulation of Parkinson's disease-related pathways.[39-41] Tea was high in phytochemicals with excellent antioxidant capabilities, and its capacity to prevent the development of Parkinson's disease was particularly intriguing. (31)[28]
Parkinson's disease is a neurological condition that affects the motor system and has a gradual start. persons over 50 are typically affected by PD; when persons under 50 are impacted, it's typically referred to as early-onset PD. The English doctor Dr. James Parkinson is credited with giving the illness its name. In his 1817 essay "An essay on the shaking palsy," which was later reproduced in the journal of neuropsychiatry and clinical neurosciences in 2002, Parkinson provided the first detailed description of the symptoms. (32)[29]
The possible neuroprotective properties of green tea, especially its active component epigallocatechin-3-gallate (EGCG), in Parkinson's disease (PD) have attracted attention. Several studies indicate that green tea may help manage Parkinson's disease symptoms and reduce the disease's course, however clinical evidence is still being gathered.
Potential Benefits of Green Tea in Parkinson’s Disease:

1. Slower Progression to Dementia
2. Neuroprotective Effects
3. Modulation of Dopamine Metabolism
4. Antioxidant and Anti-inflammatory Properties

The leaves of Camellia sinensis (L.) O. Kuntze (Theaceae) are used to make green tea. According to a recent study, drinking Chinese and Japanese teas, such as oolong and green tea, can lower your risk of Parkinson's disease. In SH-SY5Y cells, green tea extracts can reduce the activation of nuclear factor-κB (NF-κB) and cell death caused by 6-OHDA. By inhibiting the ROS–nitrogen monoxide (NO) pathway, polyphenolic catechins from green tea show protective effects on SH-SY5Y cells and the PD rat model. (28)[26]

Curcumin (turmeric):

Curcumin may have neuroprotective benefits for Parkinson's disease (PD), according to recent studies. According to studies, curcumin has anti-inflammatory and antioxidant properties that can penetrate the blood-brain barrier and shield dopaminergic neurons from PD-related damage. Furthermore, a lower risk of Parkinson's disease progression has been linked to South Asian dietary patterns, which frequently involve a higher intake of curcumin.

Curcumin's Mode of Action : Curcumin's protective qualities begin with its ability to pass the blood-brain barrier thanks to its lipophilicity. Curcumin has a variety of brain protective qualities, including resistance to harmful metals and ROS. Toxic metal ions can interact inappropriately with brain tissues, resulting in neurological impairment. Curcumin, as a flavonoid, has antioxidant effects that may be stronger than traditional antioxidants such as vitamins C and E. The brain is more vulnerable to oxidative injury than other body tissues because it absorbs a greater quantity of oxygen (about 20%). Excess oxygen causes ROS, such peroxide, to build up over time, which lowers mitochondrial density, lowers total ATP production, and makes it harder to maintain intracellular ion concentrations, all of which eventually cause neuron death. It is believed that curcumin's anti-ROS qualities stem from its capacity to donate a H ion from the beta-diketone molecule.(29)[30] The main ingredient in turmeric, curcumin, has been investigated for possible neuroprotective benefits in Parkinson's disease (PD). Although preclinical research has shown encouraging findings, there is still a dearth of clinical data.

Bacopa monnieri (Brahmi):

Bacopa monnieri has been used in India's traditional Ayurvedic medicinal system to improve memory, cognitive abilities, and longevity. It has been utilized as an antioxidant to prevent brain cells from oxidatively deteriorating. The neurodegenerative illness known as Parkinson's disease (PD) is typified by the development of filamentous intraneuronal inclusions called Lewy Bodies and the death of dopaminergic neurons in the substantia nigra [6][5]. PD symptoms can be studied using a variety of genetic models in flies and mice, such as those based on the expression of α-synuclein (αS) (mutant or wild type). [7-9]. When transgenic Drosophila overexpress either the wild type or the mutant version of αS, Lewy Bodies (LB) form, which causes dopaminergic neurons to be lost and, as a result, behavioral abnormalities [6, 10]. In this regard, PD model flies that expressed human αS in their brains were used to study the effects of Bacopa monnieri leaf extract.(34)[31] Approximately one percent of those over 60 suffer with Parkinson's disease (PD), the second most prevalent neurological illness. The primary cause of PD-related symptoms is the death of dopamine-producing neurons. Tremors, bradykinesia, and muscle rigidity result from the death of dopaminergic neurons since the neurotransmitter dopamine is linked to motor function. Moreover, PD also affects cognition, mental state, sleep, personality, and behavior leading to depression and anxiety.(33)[32]

Extract Preparation:

The entire plant material obtained was shade-dried and pulverized. The plant material was percolated with circulating 95% ethanol (200 ml) for 3-4 rounds. The residue was extracted twice, following the same technique. The extract was filtered and concentrated under decreased pressure in the Buchi rotavapour, leaving a greenish-black sticky residue. Finally, the extract was freeze-dried and employed in further research. (35)[33]

- Ashwagandha: (Withania somnifera)

A mainstay of Ayurvedic medicine, ashwagandha (Withania somnifera) has drawn interest for its possible neuroprotective qualities, especially in relation to Parkinson's disease (PD). Several preclinical and case studies indicate that ashwagandha may help manage Parkinson's disease symptoms, even if there is currently little clinical proof in humans.

Potential Mechanisms in Parkinson’s Disease:

1. Oxidative Stress Reduction

2. Neuroprotection and Dopaminergic Support

3. Inflammation Modulation

4. Case Report on Non-Motor Symptoms

In PD models, ashwagandha has shown promise in reducing oxidative damage. The injection of ashwagandha resulted in decreased markers of lipid peroxidation and increased levels of antioxidants including glutathione and dopamine metabolites in mice treated with MPTP, a neurotoxin used to cause symptoms similar to Parkinson's disease. Better motor functions, such performance on the rotarod test, were linked to these modifications.
Action: Adaptogen with anti-inflammatory and neuroprotective properties.

Use: May help reduce stress, anxiety, and oxidative damage.

- Mucuna pruriens:

Mucuna pruriens (MP, also known as vLidou in Chinese and lacuna bean in English) is a tropical leguminous plant indigenous to Africa and tropical Asia, including southern China and eastern India. All of its components have important therapeutic effects. MP produces seed pods containing serotonin and mucunain, which frequently cause human skin to itch when touched, earning MP notoriety. MP seeds have been used in Indian traditional medicine to cure a variety of ailments, including aging, rheumatoid arthritis, diabetes, and neurological diseases, as well as as a tonic and aphrodisiac for male fertility. One of the primary sources of L-DOPA is the MP plant, which naturally has a comparatively high quantity of the chemical (~5% of dry weight) [202, 203]. Early in 2004, Manyam et al. found that MP cotyledon powder treatment is more effective than synthetic levodopa treatment at restoring the endogenous levodopa, dopamine, norepinephrine, and serotonin content in the substantia nigra [204]. More significantly, a human investigation by Lieu et al. showed that, in comparison to regular levodopa treatment, the water extract of MP seed powder shows less occurrence in the treatment of dyskinesia. (37)[34]

Mechanism of Action:

Mucuna pruriens includes a variety of bioactive chemicals, including L-DOPA, ursolic acid, and betulinic acid, which may contribute to its neuroprotective properties. These chemicals are known to have antioxidant, anti-inflammatory, and neuroprotective characteristics, which could assist Parkinson's sufferers. Mucuna pruriens has shown promise as a supplemental treatment for Parkinson's disease, providing a plant-based supply of L-DOPA with possible benefits such as quick beginning of action and extended "on-time." However, due to the diversity in supplement quality and potential side effects, patients should check with their healthcare practitioners before introducing Mucuna pruriens into their treatment plan.

Kapoor (Camphor) :

In Ayurveda, camphor (Cinnamomum camphora), also referred to as kapoor, is a volatile substance that has long been utilized for its medicinal qualities. Although camphor is not a main treatment for Parkinson's disease (PD), it has been used in Ayurvedic traditions to help manage some of the symptoms of PD. Parkinson's disease (PD), known in Ayurveda as Kampavata, is typified by bradykinesia, stiffness, tremors, and postural instability. Because of its possible neurostimulant qualities, camphor (Cinnamomum camphora), sometimes referred to as kapoor in Ayurveda, is used.

Role of Camphor in Ayurvedic Management of Parkinson's Disease :

CNS Stimulation : Camphor is classified as a central nervous system stimulant, with effects ranging from modest excitement to generalized seizures. Its lipid-soluble nature allows it to pass through the blood-brain barrier, potentially activating nerve endings and delivering symptom alleviation.

Therapeutic Applications : Camphor is used in a number of Ayurvedic remedies for Kampavata control. One clinical research, for example, focused on the use of camphor in conjunction with other medications to treat Parkinson's disease symptoms. Many cultures have long utilized camphor (Cinnamomum camphora), a waxy, aromatic substance, for its therapeutic and fragrant qualities. It is referred to as Kapoor in Ayurveda and is used because it may help manage some Parkinson's disease (PD) symptoms.

Safety and efficacy of herbal drug in Parkinson's disease (PD):

Numerous herbs have shown promise in preclinical and early clinical trials, making the safety and effectiveness of herbal remedies for Parkinson's disease (PD) a hot study topic. The majority of herbal therapies lack extensive, high-quality randomized controlled trials (RCTs), and the evidence is highly inconsistent. An outline of the most researched herbs and their safety/effectiveness profile is provided below:

1. Mucuna pruriens (Velvet Bean)

Main compound : Natural levodopa source.

Efficacy : Similar to synthetic levodopa in alleviating motor symptoms

Clinical evidence : A few small RCTs indicate quicker onset and extended duration of effect compared to regular levodopa/carbidopa.

Safety : Generally tolerated well, but standardization is a problem. Potential for dopaminergic side effects (e.g. dyskinesia) still exists.

2. Ginkgo biloba

Key actions: Antioxidant, neuroprotective.

Efficacy: Limited data; certain animal studies demonstrate cognitive benefits and decreased oxidative stress.

Clinical trials : Inconclusive in PD; more extensively studied in Alzheimer's.

Safety : Generally safe but may enhance risk of bleeding, particularly with anticoagulants.

3. Withania somnifera (Ashwagandha)

Key actions: Adaptogen, antioxidant, anti-inflammatory.

Efficacy: Some animal models demonstrate enhanced motor performance and neuroprotection.

Human studies: Very limited data in PD.

Safety: Generally safe at usual doses; high doses may produce GI upset or sedation

4. Bacopa monnieri (Brahmi)

Key actions: Cognitive enhancer, antioxidant.

Efficacy: Used to treat cognitive dysfunction in PD; limited PD-specific trials.

Safety: Typically well absorbed; may produce nausea or loose stools.

5. Curcumin (Turmeric)

Primary actions: Powerful antioxidant and anti-inflammatory.

Efficacy: Promising in animal models (decreases α-synuclein aggregation, oxidative stress). Human studies: Deficient in PD.

Safety: High doses can induce GI distress; bioavailability is problematic (usually piperine is added).

Discussion:

For ages, traditional medical systems including Ayurveda, Traditional Chinese Medicine, and Kampo have used herbal medicines to treat neurological conditions. Herbal medicines are being investigated more and more for their dopaminergic, antioxidant, anti-inflammatory, and neuroprotective properties in Parkinson's disease, a neurodegenerative condition brought on by a progressive loss of dopaminergic neurons.

Conclusion:

Although certain herbal therapies show promise in reducing Parkinson's disease symptoms, the research is inconclusive. Assessing the effectiveness and safety of herbal therapies is challenging due to variations in herbal medications, dosage, and research methodologies. Therefore, to draw definitive conclusions, well planned, exacting clinical trials are required. To maintain safety and avoid potential interactions with conventional therapies, people who use herbal therapy must consult medical professionals.

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