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Nutraceuticals and its impact in the management of Parkinson's Disease - A Novel approach

Tathagata Dey[1], Kapil Raghuwanshi[2], Anitha L[3], Anil Kumar[4], Agilandeswari Devarajan[5], Bharath K S[6], Meenu Beniwal[7], Ajay Singh Amera[8], Deepthi D Kini[*9]

[1,3]Associate Professor, Department of Pharmaceutical Chemistry, East Point College of Pharmacy, Bangalore, Karnataka, India

[2]Assistant Professor, Department of Biochemistry, Chhindwara Institute of Medical Sciences, Chhindwara, Madhya Pradesh, India

[4]Head & Assistant Professor, Department of Chemistry (PG), Sahibganj College Sahibganj, Jharkhand, India

[5]Professor, Department of Pharmaceutics, MVM College of Pharmacy, Bangalore, Karnataka, India

[6]Assistant Professor, Department of Pharmacology, Chettinad School of Pharmaceutical sciences, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Kelambakkam - Tamilnadu, India.

[7]Assistant Professor, Department of Pharmaceutical Education and Research (DPER), Bhagat Phool Singh Mahila Vishwavidyalaya (BPSMV), Khanpur Kalan, Sonipat, Haryana, India.

[8]Director and Founder, Department of Pharmacology & Toxicology, Academic plus and Nysa Health Care Institute, Bhilwara- Rajasthan, India

*[*9]Professor, Department of Pharmaceutical Chemistry, East Point College of Pharmacy, Bangalore, Karnataka, India*

***Corresponding Author:** Dr. Deepthi D Kini, Professor, Department of Pharmaceutical Chemistry, East Point College of Pharmacy, Bangalore, Karnataka, India*

ABSTRACT

After Alzheimer's disease, Parkinson's disease (PD) is the second biggest aging-related condition worldwide. Dementia, cognitive impairment, and motor impairment are the results of a gradual degeneration of neurons that produce dopamine in the substantia nigra pars compacta and other areas of the brain. The sole goals of current therapeutic approaches, such L-dopa medication, are to reduce symptoms and slow the disease's development. Since PD currently has no known treatment, prevention is more crucial than ever. Numerous significant risk factors have been identified by more than ten years of research, including mitochondrial dysfunction and oxidative stress.The majority of current pharmaceutical treatments for Parkinson's disease (PD), the most prevalent neurological movement disorder in the world, focus on symptom relief and are frequently accompanied with unfavorable side effects during extended use. In spite of this, they continue to be the primary PD treatment because there aren't any better options. Many natural remedies derived from fruits, vegetables, and medicinal plants can be used to treat Parkinson's disease (PD). Apart from their widely recognized anti-oxidative and anti-inflammatory properties, these organic compounds also function as inhibitors in processes related to iron accumulation, protein misfolding, proteasomal breakdown maintenance, mitochondrial homeostasis, and various other neuroprotective mechanisms.The development of nutraceuticals—compounds obtained from whole food sources with potential therapeutic uses—has

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made it possible to employ several approaches to treat neurodegenerative illnesses like Parkinson's disease. Notably, because nutraceuticals are naturally produced chemicals and may thus have less adverse effects, they are able to market themselves as a "safer" approach. We will examine a few of the significant efforts that have been made to better understand the function of nutraceuticals in Parkinson's disease (PD) in this review. In general, these substances work by modifying signaling pathways, preventing oxidative stress, inflammation, and apoptosis, and controlling mitochondrial homoeostasis. Crucially, we will describe how the active ingredient in green tea, epigallocatechin-3-gallate, activates AMP kinase to give neuroprotection in Parkinson's disease (PD) and explain how its positive effects may be attributed to improving mitochondrial excellence of quality.

KEY-WORDS: Parkinson's disease , Nutraceuticals, Scutellaria baicalensis, Safflower

INTRODUCTION:

In 1817, James Parkinson penned and published the first account of Parkinson's disease (PD). Idiopathic paralysis agitans, another name for Parkinson's disease (PD), is a common central nervous system (CNS) neurological condition. About 1% of those over 65 suffer from Parkinson's disease. It usually starts between the ages of 40 and 70, and it seldom happens before the age of 20. A kind of Parkinson's disease known as young-onset Parkinson's disease manifests before the age of twenty. Parkinson-like symptoms can also be seen in other diseases including Huntington's and Wilson's.[1-3] Parkinson's disease (PD) is a gradual and contingent on age neurodegenerative illness that primarily impairs the brain's Substantia nigra (SN) region's dopaminergic neuronal system, progressively leading to the system's degradation.[4] In a patient with Parkinson's disease (PD), this decline results in motor abnormalities such as tremor, bradykinesia, akinesia, postural instability, slurred speech, etc. Current studies have also shed light on the prevalence of non-motor problems in people with Parkinson's disease (PD) who began their treatment at an advanced stage.[5] It mostly consists of sadness, anxiety, constipation, sleep disorders, and cognitive impairment. At least 0.3% of people globally and more than 3% of those over 80 are known to have Parkinson's disease (PD). Global incidence of Parkinson's disease (PD) varies from 5 to over 35 new cases per 100,000 people year, which likely reflects the glaring differences in the study participants' demographics or methods.[6] Parkinson's disease (PD) is uncommon before the age of 50, but from the sixth to the ninth decade of life, occurrences rise five to ten times. among general, it was seen that the predicted 0.3% global frequency increased quickly to more than 3% among those over 80.[7] The symptoms of Parkinson's disease (PD) gradually begin to manifest and get worse over time. As they do, there are certain repercussions that come with them, such as first trouble walking and talking, memory loss, sadness, changes in thinking and behavior, sleep issues, and exhaustion. Men are 50 percent more likely than women to be affected by Parkinson's disease (PD), which can affect

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both sexes.One of the main risk factors for Parkinson's disease (PD) is age. The disease normally manifests symptoms around age 60, although 5–10% of PD patients have "early-onset," which usually starts before age 50. The latter is more common and is associated with certain gene abnormalities.Parkinson's disease (PD) is brought on by a malfunction of the neurons or nerve cells that produce dopamine (DA) in the part of the brain that controls movement.[8] Early signs of Parkinson's disease (PD) include difficulties rising from a chair and a change in speech tempo that is either too quick or too slow.[9] People with Parkinson's disease (PD) typically have a Parkinsonism gait, which involves leaning forward, reduced arm swinging, tiny, rapid steps as if rushing ahead, and difficulty beginning or maintaining movement. When Parkinson's disease (PD) worsens, one side of the body or limb is frequently affected first, and then both sides.[10]The loss of norepinephrine-producing nerve endings in patients with Parkinson's disease (PD) accounts for the main chemical messenger of the sympathetic nervous system, norepinephrine controlling blood pressure and heart rate, as well as other non-motor symptoms like fatigue, reduced food digestion, and a sharp drop in blood pressure when rising from a seated or lying-down position. [11–14]

Currently, the majority of PD patients' therapy approaches are symptomatic, and the majority of pharmaceutical therapies have unfavorable side effects. In fact, pharmaceutical replacement of dopamine with L-Dopa is still the gold standard for treating Parkinson's disease (PD), even though it has been linked to significant drug-induced dyskinesia and declining efficacy with chronic use. These shortcomings of the gold standard therapy underscore the pressing need for new potent PD disease-modifying medications.Nutraceuticals have lately gained attention as one of the various other strategies to slow the disease's progression that have been explored in recent years. Due to their potential health advantages when regularly and optimally ingested as part of a diverse diet, functioning foods and nutritional supplements—common sources of nutraceuticals—are starting to receive international notice. As a result, there is a push in both science and the food business to utilize these advantages in order to prevent and even treat age-related chronic illnesses like Parkinson's disease.[15]

The words "nutrition" and "pharmaceutical" combine to form the phrase "nutritraceutical." The phrase refers to items that are separated from herbal goods, dietary supplements (nutrients), certain diets, and processed meals like cereals, soups, and drinks that serve as medications in addition to being nutritional supplements. The goods referred to as "nutraceuticals" are regulated in the United States as medications, food additives, and dietary supplements. Although the definition of the phrase varies depending on the country, it is commonly understood to refer to a substance that has been separated from food and is often offered in medical forms unrelated to food.[16]

A substance that has physiological benefits or offers protection against chronic illnesses might be classified as a nutraceutical product. Nutraceuticals can be used to maintain the body's structure and function, prevent chronic illnesses, promote health,

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and slow down the aging process. They can also lengthen life expectancy.[17] Unlike medicines, nutraceuticals are compounds that often do not have patent protection. It is possible to treat or prevent illnesses with both pharmaceutical and nutraceutical chemicals, but only pharmaceutical compounds have official government approval.[18]Any product bearing or containing one or more of the following nutritional components is regarded as a dietary supplement: A nutritional element that humans can utilize to supplement their diet by increasing their daily consumption, be it a mineral, vitamin, amino acid, medicinal herb or other plant, concentration, metabolite, constituent, extract, or combinations of these ingredients[19] Among these dietary supplements that are utilized for reasons other than nutrition are nutraceuticals. Ginseng, Echinacea, green tea, glucosamine, omega-3, lutein, folic acid, and cod liver oil are a few well-liked nutraceuticals. The majority of nutraceuticals have several different medicinal uses. These days, there is a lot of interest in nutraceuticals because of their possible benefits in terms of nutrition, safety, and therapy.[20]

SIGN AND SYMPTOMS OF PARKINSON'S DISEASE[21]

1.Problems with sleep

Parkinson's patients frequently have issues with their sleep and nights. Parkinson's disease patients are more prone to develop insomnia because of specific symptoms that interfere with sleep. Tremor, stiffness, discomfort, and restless legs syndrome are a few of them. People who experience sleep disturbances may also experience daytime fatigue and drowsiness.

2. **Losing sense of smell** A person suffering from Parkinson's disease can observe that their perception of odor has diminished or completely vanished. Someone could find it difficult to smell, for instance, their favorite cuisine. Smell loss can occasionally begin years before other symptoms appear.

3. Smaller handwriting

People with Parkinson's disease may notice that their motions are less powerful and smaller than they once were due to brain abnormalities. This may cause someone's handwriting to progressively grow smaller as they write or to become smaller than it was before.

4. Problems with bladder or bowels

The most prevalent bladder symptoms in Parkinson's patients are indications of an overactive bladder, such as sudden, overwhelming urges to use the restroom or frequent urination during the night.

5. Experiencing depression

If you have been feeling extremely down or as like there is a "emptiness" in your emotions for a long period, you could have depression. Sometimes depression sets in months before other symptoms become apparent. Another sign of "non-motor fluctuations" is depression. Put differently, the degree of non-motor symptoms associated with Parkinson's disease may vary based on when you take your

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medication. When levodopa's effects "wear off" before the next dose is scheduled, this is what occurs.

6. Experiencing anxiety

In the initial phases of the disorder, anxiety, especially uneasy sensations like concern or dread, can affect people with Parkinson's disease. Anxiety might result from any worries a person may have about managing a chronic illness. Anxiety is commonly characterized by a sensation of impending doom, persistent concern or trouble focusing, perspiration, palpitations (a beating or racing heart), dyspnea, vertigo, or shaking.

7. Feeling fatigued

A state of exhaustion that persists even after resting is called fatigue. Up to half of Parkinson's patients experience it. One day you could feel quite capable and fit, and the next you might be too tired to accomplish anything. Chemical alterations in the brain are assumed to be the source of fatigue in Parkinson's patients. It could also be connected to additional signs or characteristics of the illness, such stiffness, tremor, or stress. Cognitive or mental exhaustion may also be a sign of Parkinson's disease. Long periods of time without a break may be difficult for some people to focus on.

8. Noticing tremor and uncontrollable movement

An uncontrolled movement affecting a specific bodily area is called a tremor. Usually beginning in the hand, a Parkinson's tremor "spreads" to the arm's limbs or, on the same side of the body, to the foot. While a tremor cannot be cured, it can be managed with the help of a Parkinson's nurse or expert.

9. Slowness of movement

Parkinson's disease patients may move more slowly, a condition known as "bradykinesia," which might cause them to take longer to complete tasks. For instance, your gait may become uncoordinated, your pace may decrease, or you may find it difficult to walk. Daily chores like traveling to the bus stop or paying for goods at the register may take longer to complete.

10. Stiffness, inflexibility and cramps

Parkinson's disease results in cramping, rigid muscles, and inflexibility. We call this rigidity. This can make certain jobs more difficult, such writing, buttoning things, and tying shoe laces. Muscles can't stretch or relax if they are rigid. For example, it may be very apparent if you have trouble turning over or getting in and out of bed.

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FIG 1: Sign & Symptoms of Parkinson's disease

ETIOLOGY OF PARKINSON'S DISEASE

Genetic and environmental variables are involved in Parkinson's disease (PD), which is a complex illness. The primary risk factor for Parkinson's disease (PD) is age, with a median age of onset of 60 years old. In the age range of 70 to 79 years, the disease's incidence increases with age, reaching 93.1 (per 100,000 person-years). Furthermore, there were intercultural disparities, wherein a greater incidence has been documented in Europe, North America, and South America in contrast to African, Asian, and Arabic nations.

1. Cigarette smoking

With regard to Parkinson's disease (PD), cigarette smoking has been well examined, with generally reliable findings.[22] Larger cohort studies concur with the majority of epidemiological research, which are case-control studies that indicate a lower chance of acquiring Parkinson's disease (PD). [23] Smoking and Parkinson's disease (PD) were shown to be inversely correlated in a major meta-analysis that included eight cohort studies and forty case-control studies from twenty different countries. The pooled relative risk for current smokers was 0.39.[24–26]Having a pooled odds ratio ranging from 0.23 to 0.70, two other meta-analyses also found an inverse relationship between smoking and Parkinson's disease (PD), suggesting a preventive mechanism against the disease.[27] Additionally, they found that the risk of Parkinson's disease (PD) was negatively correlated with the number of pack years and years of smoking, with heavy or long-term smokers having a far lower chance of getting PD than nonsmokers.[28–30]

2. Caffeine

Numerous research examining the impact of caffeine on Parkinson's disease development have found that coffee users had a lower chance of getting Parkinson's disease.[31] Adenosine A2A receptor antagonist caffeine is thought to be protective against Parkinson's disease (PD) and has demonstrated neuroprotective effects in a mouse model of the disease. Coffee consumers have been shown to have a 25% lower chance of acquiring Parkinson's disease (PD).[32] Numerous retrospective investigations, in addition to two sizable prospective epidemiological studies, have

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demonstrated that coffee users had a lower relative risk of Parkinson's disease (PD) of 0.45 to 0.80 when compared to non-drinkers.[33] Coffee users have a considerably lower chance of getting Parkinson's disease (PD) according to a meta-analysis that included eight case-control studies and five cohort studies (RR 0.69). Those who regularly consume tea have also been linked to a decreased risk of Parkinson's disease (PD).[34, 35]

3. Pesticides, herbicides, and heavy metals

1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) was originally linked to nigrostriatal degeneration in 1983 when a number of individuals who had injected themselves with a medicine tainted with MPTP began to exhibit classic Parkinson's disease symptoms.[36] MPTP is converted into the neurotoxic MPP+ (1-methyl-4-phenylpyridinium), a mitochondrial complex-I inhibitor that specifically destroys substantia nigra dopaminergic cells. The notion that PD may be brought on by an environmental toxin originated with the discovery that MPTP is a cause of nigral degeneration.[37] Subsequent research has demonstrated a correlation between pesticides and Parkinson's disease (PD); a case-control study found a higher risk of late-onset Parkinson's disease among males who had professional pesticide exposure. Both the insecticide rotenone and the herbicide paraquat, which physically resembles MPP+, are selective complex-I inhibitors that cause dopaminergic depletion in animal models of Parkinson's disease. Other epidemiological studies have looked at the connection between exposure to these substances and the chance of acquiring Parkinson's disease. It has also prompted research on surrogate indicators, such as the link between rural life, farming, and well water use and Parkinson's disease risk. Investigations on the connections between welding and exposure to heavy metals (such as iron, copper, lead, aluminum, and zinc) and Parkinson's disease (PD) have shown conflicting results.38

4. Genetics

Even though PD is often an idiopathic condition, family history is reported in 10-15% of cases, and Mendelian inheritance accounts for roughly 5% of cases.[39] Moreover, a person's risk of Parkinson's disease (PD) is partly determined by poorly characterized polygenic risk factors. In the order that they were discovered, the genes that have been linked to Parkinson's disease (PD) are given "PARK" names.[40]

PD has been associated with 23 PARK genes thus far. Autosomal dominant inheritance is exhibited by mutations in the PARK genes (e.g., SCNA, LRRK2, and VPS32)[41] or autosomal recessive inheritance (e.g., PRKN, PINK1, and DJ-1). Some of these genes (PARK5, PARK11, PARK13, PARK18, PARK21, and PARK23) may or may not be involved; other genes (PARK3, PARK10, PARK12, PARK16, and PARK22) are thought to be risk factors.[42–44]

PATHOPHYSIOLOGY OF PARKINSON'S DISEASE

Pathophysiologically characterized as dopaminergic neuronal loss or degradation in the SN, Lewy body (LB) is a pathologic feature of dopaminergic neurons that is improved in Parkinson's disease (PD). It might take several years to show any

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symptoms of a pathologic alteration. The absence of dopamine-producing neurons severely compromises motor function. Numerous proteins, such as ubiquitin alpha-synuclein and ubiquitin, are present in LB aggregation and impede optimum neuron activity. According to recent recommendations, neuropathology is a result of both aging and environmental stress. A persistent low-stage mental disorder called "inflammation" is brought on by environmental pollution (such as pesticides), the strain of aging, or medication abuse. This inflammatory process is the reason behind the gradual cellular aging of brain neurons.[45] Information regarding the PD's pathophysiology are mentioned below

FIG 2: Pathogenesis of Parkinson's disease

Gene mutations encoding for proteins found in the central nervous system (CNS) cause neurons to degrade. Alpha-synuclein protein, in particular, exhibits aberrant self-aggregation. One of the key components of LB, the cellular aggregation that defines Parkinson's disease, is this rigid alpha-synuclein. Additionally, atypical protein-disrupting systems, such as the ubiquitin-proteasome apparatus, become more challenging. Numerous malfunctioning mechanisms, including diseases of the mitochondria or specific oxidative stress brought on by reactive oxygen species (ROS), which causes neuronal degeneration, can lead to Parkinson's disease (PD).

Role of substantia nigra, dopaminergic transmission, and D1, D2 receptors in Parkinson’s disease

Shortcomings in movement are brought on by a dopaminergic imbalance in the new neurodegenerative illness Parkinson's disease (inhibitory D2 and excitatory D1 receptors). K+ channels, however, improve these. Dopamine: When PD patients have substantia nigra degeneration, the nigrostriatal pathway is destroyed. Reduced striatal dopamine as a result is the neurochemical underpinning of Parkinson's disease (PD).[46] The development of Parkinson's disease (PD) motor symptoms appears to be dependent upon and adequate for the impairment in striatal dopaminergic transmission. Levodopa is derived from dopamine. Dopamine does not pass across the BBB on its own. Active transportation of levodopa occurs into the brain, where it is processed into dopamine. Medication decarboxylated dopamine in the brain's outer regions. It needs a high dose of levodopa as a result. Levodopa metabolism in the gastrointestinal tract (GIT) and peripheral tissues improves levodopa bioavailability in the central nervous system (CNS) and decreases in response to carbidopa. Levodopa

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should thus have a greater effect on the central nervous system when given in combination with carbidopa.[47]

NUTRACEUTICALS ROLE IN THE MANAGEMENT OF PARKINSON'S DISEASE

1. Erythrina velutina

This plant's ethanol extract has neuroprotective properties. It has been demonstrated to eliminate free radicals and lessen the neurotoxicity that 6-OHDA causes in SH-SY5Y cells, which raises the possibility that it might be utilized to treat Parkinson's disease. [48]

2. Resveratrol

A polyphenolic substance found in many plants, especially berries and grapes, is called resveratrol. In animal models of Parkinson disease, resveratrol has been demonstrated to aid with motor impairments, oxidative stress, and the loss of TH neurons.[49] Resveratrol reduces the expression of TNF-α and COX-2 genes and prevents mitochondrial growth and chromatin condensation.

3. Peganum harmala

Peganum harmala reduced muscular stiffness, prevented the brain's oxidation of proteins and lipids, and prevented the degeneration of dopaminergic neurons. The capacity of this herb to lower angiotensin II activity is assumed to be the source of its neuroprotective qualities. This keeps dopaminergic neurons safe and lessens oxidative stress. [50]

4. **Scutellaria baicalensis**

A chemical substance known as baicalein is extracted from the dried roots of the Scutellaria baicalensis plant. In tests for rotenone-induced neurotoxicity, baicalein stopped the accumulation of ROS, apoptosis, ATP depletion, and mitochondrial membrane rupture in PC12 cells.[51] Treatment with baicalein increases levels of 5-hydroxytryptamine and dopamine while preventing the basal ganglia's dopamine levels from declining.

5. Safflower

It is commonly used in China as a traditional therapy for cerebrovascular problems and has been shown to contain flavonoids. It raised the expression of the DJ-1 protein, the DA transporter, and the DA levels. Safflower may prevent α-synuclein overexpression or aggregation in addition to reactive astrogliosis.[52]

6. Ginseng

It is believed that ginsenosides (Araliaceae) Rb1 and Rg1 are the main chemicals that give ginseng its medicinal qualities. In SNK-SH cells (a neuroblastoma cell line), the ginsenosides Rb1 and Rg1 both reduced MPTP-induced cell death, according to a prior research. By upregulating Bcl-2 and Bcl-xl expression, downregulating Bax and iNOS expression, and preventing caspase-3 activation, Rg1 shields cells against MPTP-induced apoptosis.[53] Research indicates that ginsenosides provide protection by reducing intracellular reactive oxygen species (ROS), increasing antioxidant

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activity, preserving complex I activity, and increasing intracellular adenosine triphosphate (ATP) levels.

Mice given 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) had better motor function and more dopaminergic neurons in the substantia nigra (SN) and striatum when they were given Rg1. In addition, the ginsenoside Rb1 has the ability to disaggregate fibrils and inhibit α-synuclein polymerization.[54]

7. Pueraria lobata

It has been demonstrated that purerarine inhibits both the accumulation of potentially dangerous proteins such as ubiquitin-conjugated proteins and proteasomal dysfunction. Conversely, Puerarin decreases caspase-3 activity and the ratio of BCL-2/Bax. Puerarin restores DA and its metabolites while shielding TH-positive neurons from 6-OHDA-mediated damage.[55]

8. Juglandis semen

Aqueous extract of Juglandis semen (walnut) has been shown to have neuroprotective properties. Because it can inhibit the monoamine oxidase B (MAO-B) enzyme, which raises oxidative stress in Parkinson's disease patients, walnut is considered to have neuroprotective properties. Additionally, walnuts offer mitochondrial defense and antioxidant qualities. [56]

9. Ginkgo biloba

Chinese trees called ginkgo biloba have long been utilized to relieve lung and heart-related illnesses. Ginkgolic acid, terpenoids, and flavonoids are three of G. biloba's most prevalent ingredients.[57] Long-term usage of EGb761 reduced the loss of dopaminergic nerve terminals induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) in a PD rat model. EGb761, administered either before or after the therapy, was demonstrated to offer protection against the dopaminergic neurotoxicity resulting from MPTP. Furthermore, in the 6-hydroxydopamine (6-OHDA) Parkinson's disease (PD) model, EGb761 reduced the neurotoxicity of levodopa. This indicates that EGb761 may lessen the neurotoxicity of levodopa.[58]

10. Curcuma longa

Evidence of Curcuma longa's anti-inflammatory, chemotherapeutic, antioxidant, wound-healing, anti-proliferative, and antiparasitic qualities has been demonstrated.[59] Curcumin, the polyphenolic fraction's active component, is most likely to blame. Curcumin prevents DA depletion, MPTP-induced loss of TH-positive neurons, and decreases cytokines, total nitrite, and inflammatory markers such inducible nitric oxide synthase in the striatum of MPTP-induced animal models. [60]

11. Flavonoids

A class of naturally occurring polyphenol phytochemical known as flavonoids has long been employed as a therapeutic agent. The primary metabolite of baicalein (Lamiaceae) is baicalin, a flavonoid obtained from Scutellaria baicalensis.[61] The neuroprotective properties of baicalein were demonstrated to be genuine in an in vivo model of Parkinson's disease using the neurotoxin 6-OHDA, which demonstrated protective effects on dopaminergic dysfunction and lipid peroxidation. Two flavones

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that shield dopaminergic neurons from inflammatory neurotoxicity include lutein and apigenin.[62]

12. **Passion flower**

Another name for passion flowers is Passiflora incarnata. It has been used to treat muscular spasms, epilepsy, anxiety, and other illnesses.[63] Consequently, research has been done on the biological effects of passion flowers on Parkinson's disease patients. Passionflower extract decreased the amount of jaw movements elicited by tacrine, a common animal model of Parkinson's disease tremors.[64]

12. Tinospora cordifolia

It is beneficial against stress, throat cancer, and has anti-inflammatory and antiandrogenic qualities. It also enhances memory and learning. T. cordifolia shown not to be hazardous in an acute toxicity study. Recent extensive study has demonstrated its strong antioxidant activity. Since antioxidants are known to stop or shield neurodegeneration, the goal of the current study was to evaluate T. cordifolia ethanol extract's (TCEE) anti-Parkinson's effectiveness. [65]

13. St. John's Wort

Naphthodianthrones, phloroglucinols, flavonoids, and essential oils are among the active components of St. John's wort. Consequently, the active components exhibit neuroprotective and antioxidative qualities. We examined the effects of two standardized extracts of St. John's Wort on rotenone-induced neurotoxicity in rats over an extended period of time.[66] By reducing Bax levels, St. John's wort reduced neuronal damage and stopped the apoptotic process. Additionally, St. John's wort extract was administered to rats that had intrastriatal 6-hydroxydopamine (6-OHDA) lesions. This prevented dopaminergic neuron damage and reduced striatal malondialdehyde levels, as well as normalized tumor necrosis factor alpha (TNF-α) and glial fibrillary acidic protein (GFAP) expression. Additionally, it increased catalase activity and decreased glutathione (GSH) content.[67]

14. Centella asiatica

A medical plant called Centella asiatica seems to aid with inflammation, rheumatoid arthritis, and physical and mental exhaustion. Plant leaves include monoterpenes such as α-pinene, β-pinene, δ-terpinene, and bornyl acetate. It has been demonstrated that these monoterpenes suppress the action of acetylcholinesterase (AChE).[68] In vivo, an ethanolic plant extract of C. paniculatus demonstrated sedative and antidepressant effects. In neuroblastoma cells transfected with amyloid precursor protein (APP) constructs, compound 5 inhibited the development of Ab. Additionally, b-proteolytic secretase's activity on its substrate was decreased by toxinsin. Similarly, rats with scopolamine-induced amnesia may benefit from P. tenuifolia (BT-11) dried root extract (80% ethanol-water) in terms of learning and memory.[69]

15. Valeriana officinalis

Herbal remedies for insomnia, anxiety, and restlessness have long included Valeriana officinalis, often known as Valerian. Valeriana is a sedative and antispasmodic. It has been demonstrated that valerian inhibits rotenone-induced cell death in SH-SY5Y

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cells.[70] The standardization of superoxide dismutases-SOD and catalase mRNA expression in Drosophila melanogaster, which indicates that valerian's effects are, at least partially, due to the plant's antioxidant properties due to its phenolic and flavonoid constituents, further supports the effectiveness of valerian extract in reducing rotenone toxicity in this species. [71]

16. Mucuna pruriens

Every part of mucuna pruriens (Mp) has medicinal properties. They are said to have anti-microbial, anti-inflammatory, analgesic, and anti-epileptic qualities. They demonstrated that Mp is a more effective long-term treatment for Parkinson's disease than regular L-DOPA medication, which overuse can result in severe dyskinesia. The stem, leaf, and seed of MP have important neuroprotective qualities. Seeds are frequently used as anti-PD medications because they contain higher levels of L-DOPA than other plant components. [72]

17. Withania somnifera

In experiments, the environmental toxins paraquat (PQ) and maneb (MB) have been used to selectively destroy dopaminergic neurons, which causes Parkinson's disease (PD). In a rat model of Parkinson's disease produced by MB-PQ, an ethanolic root extract of Withania somnifera (Ws) was found to greatly reduce characteristic Parkinson's disease symptoms such as sluggish movement, decreased dopamine in the substantia nigra, and various forms of oxidative damage. [73]

18. **Bacopa monnieri**

The antiparkinsonian effectiveness of B. monnieri has been investigated in vitro as well as in animal models of neurodegenerative disease. The anti-Parkinsonian effect of B. monnieri is due to its antioxidant and neuroprotective qualities, which also cause a reduction in the aggregation of synuclein proteins and the selective degeneration of dopaminergic neurons.[74] B. monnieri has been shown to have anti-Parkinsonian effects in worms by reducing synuclein aggregation, preventing dopaminergic neurodegeneration, and restoring lipid content.[75]

CONCLUSION

The notion that nutrition has a role in preventing disease is not new. In fact, the fundamental tenet of Chinese herbal medicine—that "medicine and diet share the same origins"—emphasizes the possibility that human health may be positively impacted by scientific diet strategies. A good diet and active lifestyle are key components of a healthy aging approach that can help avoid most age-related disorders, including cancer, cardiovascular disease, and neurological diseases. Numerous studies have demonstrated this. Actually, a lot of people all around the world have adopted this idea for centuries and have included a variety of nutraceuticals in their diets. This idea should be promoted and used in a clinical context in addition to being supported as a part of everyday living to prevent disease.

Dietary plans and nutraceuticals offer more for patients than only enhance their quality of life.As previously mentioned, B-complex vitamins and vitamin C when

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used in conjunction with L-dopa medication therapy have favorable benefits, such as less side effects and improved absorption of L-dopa. These nutraceuticals may enable a reduced drug dosage, further mitigating any dose-dependent adverse effects, and they may improve the effectiveness of modern pharmacological therapy. Positive synergistic effects between clinical medication treatment and nutraceuticals have a lot of promise. Therefore, future research should examine the benefits of nutraceuticals in conjunction with medication therapy rather than focusing on determining the neuroprotective effects of nutraceuticals alone. Furthermore, enhanced drug therapy may be developed through design and application of co-drugs linking nutraceuticals and therapeutic drugs, e.g., by linking stilbene compounds to L-dopa or even by linking curcuminoids to L-dopa. This strategy of linking nutraceuticals to drugs may contribute to new drug designs as well as to more well-designed experimental studies and clinical trials. Even if they are appealing and advantageous, nutraceuticals cannot treat Parkinson's disease. There is not enough experimental data to support the creation of pharmaceuticals that are effective from nutraceuticals. It goes without saying that well-planned, placebo-controlled human intervention studies are necessary to validate experimental results. Numerous nutraceuticals covered in this study have been demonstrated to be both therapeutic and preventive for Parkinson's disease. However, there are still a lot of unanswered questions, particularly about the precise therapeutic target, the appropriate intake amount, and the pharmacokinetics and pharmacodynamics of these nutraceuticals, all of which make it difficult to use them in a clinical environment. To encourage the introduction of more nutraceuticals into therapeutic use, high-quality research is required.

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