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A -Comprehensive Review of Integrating Medicinal Plant Constituents into Neurological Disorder Therapeutics

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Abstract

Neurological diseases are disorders of the nervous system that gradually destroy the structure and function of the central or peripheral nervous system, affecting various parts of the brain. It affects a great number of individuals globally and is one of the main causes of death. Many disorders, particularly neurological diseases that have resisted conventional medical treatment have been treated with plant-based medications. Alzheimer's disease (AD) and Parkinson's disease (PD) are two of the most common neurological disorders (NDDs) and have a significant socioeconomic impact. Over many ages, people have looked to natural herbal remedies for a solution for non-divertic disorders. Numerous therapeutic plants and their secondary metabolites have been shown to be able to reduce the symptoms of NDDs. The main mechanisms that have been found to underpin phytochemicals' neuroprotective effects and potential to maintain neurological health as we age include inhibition of acetylcholinesterase and monoamine oxidase, antioxidant, anti-inflammatory, antithrombotic, and antiapoptotic properties, as well as neurotrophic activities. This article examines the molecular targets of some of the main herbal products that have the potential to cure non-communicable diseases (NDDs). Numerous investigations proved that plant extracts or their bioactive components were effective against non-disease-causing bacteria. Millions of individuals worldwide suffer from age-related NDDs, and herbal products may provide new avenues for therapy.

Keywords: *Neurological disorders; Alzheimer's disease (AD), Parkinson's disease (PD), plant constituents, pharmacological activities, therapeutics*

1. Introduction

Memory loss and tremors are common symptoms of neurological disorders, which can be either acute or chronic pathological conditions with weak neuronal cell death **[1].**The increased mortality and morbidity in developed nations, along with shifting demography and life expectancy, make these illnesses noteworthy **[2].** By shielding neurons from inflammation and other harmful agents, neuroprotection seeks to lessen neuronal damage or apoptosis, such as a stroke, an injury, or long-term pathological disorders. These conditions include Huntington's disease (HD), Alzheimer's disease (AD), Parkinson's disease (PD), multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), psychological disorders, and mental illnesses that cause loss and damage to neurons **[3].** NDDs are associated with ageing, heredity, behaviour, the environment, and extra concomitant neurological disorders **[2].** Phytochemical substances with therapeutic qualities are found in the stems, roots, leaves, fruits, and seeds of plants **[2]**.

Herbal medicines have been used worldwide for centuries to treat various ailments. Natural products have drawn a lot of interest and contributed to the development of new drugs **[2&4]**. Natural products have been shown to have positive benefits in numerous research studies. They are essential for

preserving the neuronal chemicals in the brain because they work by inhibiting different receptors' actions in distinct ways **[4].** Approximately 80% of people on the planet rely on medicinal plants to meet their basic medical needs, according to the World Health Organisation (**WHO**) **[4].**

History:

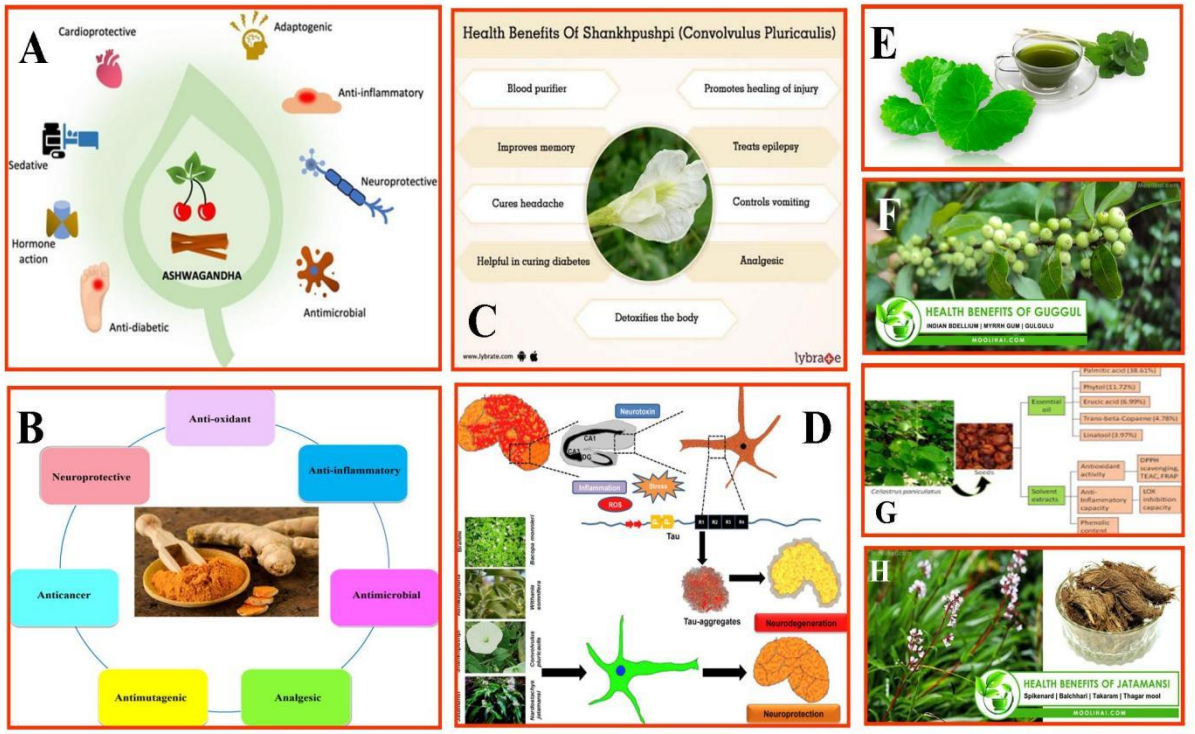
However, the history of Indian traditional medicine predates 5000 years; the Samhitas of Charaka and Sushruta include 341 and 395 herbal remedies, respectively, from 1000 BCE onwards **[5].** The collection, storage, and appropriate application of traditional medicine in the then-known world, however, was documented by the Greek physician Dioscorides and the Roman physician Dioscorides, who both made significant contributions to the coherent development of traditional medicine use in the ancient Western world **[7].** Fifty percent of the top 50 drugs available in pharmacies in Europe are natural products (NPs) marketed as dietary, herbal, or both supplements. Ayurveda, an ancient Indian medicine system, is deeply connected to the use of medicinal plants in India **[6].** Its roots can be traced back to the ancient Vedas, particularly the Atharvaveda, which contains knowledge on health and healing. According to Ayurveda, good health is determined by the equilibrium of the three doshas (Vata, Pitta, and Kapha), which are the basic energies that control different bodily physiological and psychological processes **[10].** Ayurvedic treatments frequently entail restoring this balance through a comprehensive approach that includes nutrition, lifestyle, and herbal remedies **[8].** It is believed that imbalances of these doshas are the underlying cause of ailments **[11].**

Background of medicinal plants:

Throughout recorded history, people have relied on nature to cure their illnesses, and one of the most significant sources of medicinal plants is the kingdom of plants **[15].** Secondary phytochemical metabolites are largely responsible for the therapeutic qualities of plants **[9].** Adaptive small-molecule organic molecules that support an organism's survival but are not directly engaged in growth and development are referred to as secondary metabolites, or natural products **[12].**

Depending on their metabolic origins, secondary metabolites are divided into several chemical classes, such as terpenoids, alkaloids, phenylpropanoids, and related phenolic compounds. They can also be broadly categorised as nitrogen-containing or non-nitrogen-containing metabolites **[14].** Evidence now available supports the use of natural molecules in human health, and secondary metabolites are a rich source of new compounds due to their vast diversity **[16].** Actually, there is increasing interest in the possible application of secondary metabolites in the management and prevention of NDDs. A number of secondary metabolites, such as those that protect neurons against oxidative and ER stress, neuroinflammation, excitotoxicity, and proteinopathies, may be protective in NDDs **[13].**

FIG: Neuroprotective benefits of different medicinal plants:



A. **Ashwagandha** (*Withaniasomnifera*), B.Turmeric (*Curcuma longa*) , C.**Shankhpushpi** (*Convolvulus pluricaulis*), .**Brahmi** (*Bacopa monnieri*),E.**Gotukola** (*Centella asiatica*),F,Guggulu ,G.**Jyotishmati** (*Celastruspaniculatus*), H.**Jatamansi** (*Nardostachysjatamansi*)

Self-designed by author

Ashwagandha (*Withaniasomnifera*)

The adaptogenic herb ashwagandha has been employed in ancient Ayurvedic medicine for its neurological effects **[17].** Ashwagandha (Indian Ginseng) is a nightshade (Solanaceae family) plant, and the root is the most commonly used portion. According to Ayurvedic science, Ashwagandha promotes happiness by promoting physical and mental health **[18].** It has been shown to alleviate stress by modifying the body's response to stress hormones, resulting in a more balanced physiological response **[30].** Ashwagandha may also improve cognitive function by reducing oxidative stress **[22].** Its antioxidant qualities could shield nerve cells from oxidative damage, which has been related to neurodegenerative illnesses **[28].** Its anxiolytic actions may regulate neurotransmitters, resulting in nervous system relaxation **[20].** The anti-inflammatory characteristics of ashwagandha may aid in reducing neuroinflammation, perhaps providing neuroprotective effects **[19].** It may potentially have antidepressant properties due to its influence on neurotransmitter levels **[18].** Its sedative qualities may help you sleep better **[21].**

Drug dose and use of consumption:

According to a pilot study, people with bipolar disorders who take 500 mg/day of ashwagandha in addition to their medications report improvements in their social cognition, response time, and auditory-verbal working memory **[24].** Although some people have diarrhoea or nausea after ingesting the root, Ashwagandha has the ability to pass across the ***blood-brain barrier*** and reduce brain inflammation **[24].**

Turmeric (*Curcuma longa*):

Turmeric, a traditional spice, has been discovered to have important neurological characteristics **[25].** Curcumin, its main ingredient, has anti-inflammatory properties that may aid in reducing inflammation in the brain, which is linked to neurological diseases **[23&24].** Curcumin's antioxidant capabilities protect cells, particularly neurons, from oxidative damage and may contribute to neuroprotection **[26].** It has been researched for its potential function in neurodegenerative illnesses such as Alzheimer's and Parkinson's. Turmeric may also help with cognitive function, neurotransmitter modulation, and oxidative stress reduction **[27].** Because it can pass the blood-brain barrier, it can interact with brain tissues and have neuroprotective effects **[29].** Curcumin may possibly have antidepressant properties due to its ability to modulate neurotransmitters and neurotrophic factors **[31&32].**

Drug dose and use of consumption:

Potent anti-inflammatory and antioxidant curcumin (10, 20, and 50 mg/kg, p.o. for 21 days) has been shown to improve memory impairment in Alzheimer's disease (AD) mice, inflammatory and apoptotic gene expression in rats infused with Aβ+ibotenic acid, and in a double transgenic AD model, diet containing low (160 ppm) and high (1000 ppm) doses of curcumin after administration for the 6-month period showed a significant improvement in cognitive function **[33].**

When compared to placebo, the daily dosage of 400 mg of curcumin considerably enhances the performance of healthy people over 60 on tests involving sustained attention and working memory **[34&35].** Another study among older people who live in the community shows that treatment with turmeric (1500 mg/day) does not cause cognitive decline in the treatment group but does cause cognitive loss in the placebo group **[35].**

Brahmi (*Bacopa monnieri*):

Brahmi, also known as Bacopa monnieri, is a traditional Ayurvedic medicinal herb with potential neurological effects. It is well-known for its memory-boosting abilities, antioxidant characteristics, and stimulation of neurotransmitter activity **[24].** It also possesses adaptogenic properties, which help the body adapt to stimuli and maintain homeostasis. Brahmi's anti-inflammatory effects may help reduce neuroinflammation, potentially lowering the risk of neurodegenerative illnesses **[34].** It may also influence serotonin levels, a neurotransmitter important for mood regulation **[17].** Brahmi may also improve synaptic transmission, promoting optimal cognitive performance. Its circulatory benefits may enhance blood flow to the brain, assisting in the delivery of nutrients and oxygen **[36].** It has shown promise against amyloid-beta plaques, which are linked to neurodegenerative illnesses like Alzheimer's. Brahmi is frequently used in Ayurvedic medicines to improve mental clarity and cognitive well-being **[22].**

Drug dose and research Evidence of use:

Brahim's alcoholic extract (20, 40, and 80 mg/kg) for cognitive functions and neurodegeneration prevented the reduction in cholinergic neuron density and improved escape latency in the Morris water maze test in an animal model of AD induced by bilateral intracerebroventricular administration of AF64A **[31].**

Shankhpushpi (*Convolvulus pluricaulis*)"

Shankhpushpi is an herb used in traditional Ayurvedic medicine for its putative neurological and cognitive-enhancing qualities **[37].** It is well-known for its memory- and learning-enhancing properties, as well as its use as a nervine tonic **[24].** Shankhpushpi includes antioxidants that aid in the neutralisation of free radicals, thereby lowering oxidative stress in the brain. It also has anxiolytic properties, relaxing the nervous system by influencing neurotransmitters **[23].** Its anti-inflammatory qualities aid in the reduction of chronic inflammation in the brain, which contributes to neuroprotection. The antioxidant capabilities of Shankhpushpi, as well as its possible modification of neurotransmitter activity, contribute to its neuroprotective effects. It may potentially have antidepressant qualities due to its effect on serotonin levels **[36].** More research, however, is required to fully understand its mechanisms of action and therapeutic applications **[34].**

Drugs and their bioactive compounds:

Shankhpushpi leaves are used as nerve tonics, raising intellectual ability and improving cognitive and memory function. Shankhpushpi leaves are traditionally used to treat depression and mental health disorders. Glycosides, flavonoids, coumarins, anthocyanins, and alkaloids are the main bioactive ingredients. Other compounds that have been extracted from the plant include glucose, hydroxycinnamic acid, octacosanol tetracosane, and sitosterol glycoside **[38].**

Jyotishmati (*Celastruspaniculatus*):

Jyotishmati (Celastrus paniculatus) is an herb used in traditional Ayurvedic medicine because of its possible benefits for the nervous system and for improving cognitive function **[38].** It is thought to improve learning and memory as well as have adaptogenic qualities that help the brain adjust to stimuli. It has nootropic potential, which improves cognitive performance without stimulating or sedating the user **[33].** The antioxidant activity of jyotishmati lowers the risk of neurodegenerative diseases by shielding nerve cells from oxidative stress **[15].** Additionally, it possesses anti-inflammatory qualities that help to maintain cognitive resilience by reducing chronic inflammation in the brain and regulating the stress response **[14].** In addition to helping with pain relief, its analgesic qualities may also have antidepressant benefits **[13].** Its potential to enhance blood flow to the brain is also investigated. To completely comprehend its mechanics, though, more research is required **[13].**

Dose confirmation and improvement:

Examined the effects of 400 mg/kg of seed oil on Wistar rats for 14 days; the oil improved memory and learning in the radial arm maze and reduced AChE enzyme activity in the hippocampus, frontal cortex, and hypothalamus.When seeds were extracted aqueously, methanolically, with chloroform, and with petroleum ether, rats' cognition improved at dosages of 200 and 300 mg/kg for 14 days. The methanolic extract also showed memory-enhancing action at doses of 100, 200, and 400 mg/kg **[15].**

Gotukola (*Centella asiatica):*

Centella asiatica, often known as Gotukola, is a traditional herb used in Ayurveda and Chinese medicine due to its potential neurological qualities and effects on improving cognitive function **[39].** It is thought to have anxiolytic qualities, reduce neuroinflammation, neutralise free radicals, improve memory and learning, and increase the synthesis of nerve growth factor **[40].** Additionally, it increases blood flow, promotes microcirculation, and facilitates the delivery of brain cells. Additionally, gotu kola may support the body's ability to adjust to stressors that impact cognitive function. Additionally, by adjusting serotonin and dopamine levels, which are essential for mood control, it might have antidepressant effects **[40].** The ability of gotu kola to support nerve regeneration—a critical component of nerve system wound healing—has been investigated. However, prior to implementing Gotu, it is imperative that you speak with a healthcare provider **[51].**

Dose confirmation and drug use evidence:

It was reported that the aqueous extract of gotukola (100, 200, and 300 mg/kg) was administered for 21 days in male Wistar rat models by inducing streptozotocin-induced cognitive impairment and oxidative stress on days 1 and 3. Their cognitive behaviour was assessed, and the results showed that the cognitive behaviours of rats treated with gotokola extract improved significantly **[51].** The gotukola extract was given orally for 14 days at doses that have been shown to dose-dependently improve cognitive functions

in normal rats. Following the administration of the extract at doses of 200 and 300 mg/kg, the greatest reaction was seen **[40&41].**

Jatamansi (*Nardostachysjatamansi*):

The plant jatamansi, botanically known as Nardostachys jatamansi, has a rich history in conventional Ayurvedic treatment **[41].** Potential neurological benefits of this substance include enhanced cognition, neuroprotection, anxiolytic and antidepressant effects, reduced stress, better sleep, anti-seizure effects, anti-inflammatory effects, nerve regeneration, and antioxidant actions in the brain **[40].** Because of its antioxidant qualities, jitamansi helps shield nerve cells from oxidative stress and free radical damage. Its sedative properties enhance the quality of sleep and encourage relaxation **[51].** It is best to speak with a healthcare provider, particularly if you are using medication or already have medical conditions **[40].**

Research evidence for the drug:

Jatamansi may help cure dementia because it has been shown to repair age-induced forgetfulness in rats. Its historical use as a cognitive enhancer may be explained by its neurotrophic properties and acetylcholinesterase (AChE) activity **[42].** Research on its ethanol extracts revealed that it preserved neurological characteristics in flies that expressed Aβ42 and prevented Aβ-induced cell death in SH-SY5Y cells **[38].**

Guggulu:

Guggulu, a classic component of Ayurvedic medicine, has been associated with possible neurological effects **[32].** Its anti-inflammatory properties may lessen neuroinflammation, shield nerve cells from oxidative damage, and maintain their integrity **[33].** In addition, guggulu has the potential to improve memory, regulate stress reactions, and affect brain neurotransmitter levels **[31].** Moreover, it might have antidepressant properties that impact mood and mental clarity. Because of its capacity to improve blood flow to the brain, it supports the supply of nutrients and oxygen, which benefits brain health in general **[27].** However, additional study is required to completely comprehend its modes of action and neurological impacts **[28].** Before using Guggulu as part of your regimen, it is best to speak with a healthcare provider, especially if you are taking medication or already have a medical issue **[50].**

Bio-Active compounds:

Guggulu, an oleogum resin, is present in the cracks and incisions of several plant species. It is made up of water-soluble gum, volatile oils, and resins soluble in alcohol. Mucilage, carbohydrates, and proteins are examples of water-soluble substances **[49].** Commiphoric acids, heéromyrrhols, and commiphorinicacids are examples of compounds that dissolve in alcohol **[50].** Guggulsterols, sesquiterpenoids, and terpenes are examples of volatile substances. Both phenols and non-phenolic acids are present in guggulu **[43].**

Saffron (*Crocus sativus):*

The spice saffron, which comes from the flower of the Crocus sativus plant, has long been used for its supposed health benefits, which include neurological ones **[44].** The neuroprotective characteristics of this compound stem from its antioxidant actions, which include the neutralisation of free radicals **[49].** This may help maintain the structure and function of nerve cells. The anti-inflammatory properties of saffron may lessen neuroinflammation and provide neuroprotection **[48].** Additionally, it might enhance learning and memory while perhaps lowering anxiety. Additionally, it may prevent neurodegenerative illnesses like Alzheimer's by preventing beta-amyloid plaques from aggregating **[39].** Because of its vasodilatory properties, the brain may get more blood, promoting general neurological health **[29].** Potential antidepressant effects of saffron may be mediated through modulation of mood-regulating neurotransmitters, including dopamine, norepinephrine, and serotonin **[19].**

Research evidence:

The results of this double-blind, placebo-controlled study suggest that saffron is safe and effective in treating mild to moderate AD, at least in the short term **[44&48].** Forty-six patients with probable AD were screened for a 16-week, double-blind study of parallel groups of patients with mild to moderate AD. The patients received saffron in the form of capsules of about 30 mg/day (15 mg twice per day) or capsule placebo (**Two capsules per day**) **[46].** There is a need for larger confirmatory randomised controlled trials. A similar clinical experiment compared the effectiveness of saffron extract and memantine in reducing moderate-to-severe cognitive decline in 68 patients who were given 30 mg/d of saffron extract or 20 mg/d of memantine over a 12-month period **[47]**.

4. Conclusion

Plants are a rich source of bioactive compounds that have been shown to enhance human health. However, because of neurodegenerative diseases, the pharmaceutical business faces difficulties like excessive costs, danger, and inefficiency. Ayurvedic and Chinese medicine systems are receiving more attention for treating complicated illnesses, leading to a shift in medication research that centers on herbal formulations. Herbal formulations are the subject of much research, offering an improved quality method. Strong scientific evidence supports the use of herbs as a therapy for Alzheimer's disease, since recent mechanistic studies have demonstrated that they improve neuron development, reduce inflammation, and minimize oxidative stress damage. For medicinal usage, standardization of herbal medications is essential, yet pharmacopoeia and formal monographs are lacking. Trials, quality control protocols, scientific proof of herb-drug interactions, and epidemiological research on botanicals that may prevent disease are among the top priorities for standardization.

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Conflict of interest:

None.

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