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Review Article

Review: Neuroprotective Effect of Herbal Extract

Shravani Dhanve*, Dipali Patil, Tanvi Bhosale, Mayuri Bhadalekar, Nilesh Chougule

Ashokrao Mane Institute of Pharmacy, Ambap, Kolhapur, Maharashtra, India. 416112.

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ABSTRACT

One of the biggest health issues of the twenty-first century is neurodegeneration, which is the name for the state of neuronal death caused on by a long-term, degenerative disease. Neurodegenerative disorders (NDs) include epilepsy, Parkinson's, Alzheimer's, and Huntington's, pose a significant threat to global health, affecting millions worldwide. Traditional herbal medicine has garnered attention for its potential therapeutic benefits in preventing and managing these diseases. This review highlights the neuroprotective properties of six herbal plants such as *Curcuma longa* (Turmeric), *Lavandula angustifolia* (Lavender), *Rosmarinus officinalis* (Rosemary), *Cardiospermum halicacabum* (Balloon Vine), *Careya arborea* (Wild Guava), and *Withania somnifera* (Ashwagandha). These plants exhibit antioxidant, anti-inflammatory, and anti-apoptotic activities, inhibiting neurodegeneration and promoting neuronal survival. Their bioactive compounds, such as curcumin, linalool, and withanolides, demonstrate potential in preventing cognitive decline, neuroinflammation, and oxidative stress. This review provides an overview of some popular neuroprotective plants and their therapeutic roles in managing NDs, highlighting their pharmacological properties, mechanisms of action, and the current understanding of their efficacy.

INTRODUCTION

As many persons with mental illnesses suffer severely from stigma and discrimination related to their health, neurological disorders are frequently not regarded as common illnesses, even though the majority of the public relies on traditional medicine for primary healthcare. Additionally,

speaking, breathing, movement, mood, and memory are all impacted by nervous disorders. The neurological disorder affects the brain and spinal cord [1]. Neurodegeneration is the cause of neurodegenerative diseases (ND), which are characterized by a progressive loss of neurons.

***Corresponding Author:** Shravani Dhanve

Address: Ashokrao Mane Institute of Pharmacy, Ambap, Kolhapur, Maharashtra, India. 416112.

Email ✉: shravanidhanve@gmail.com

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The neurological system may stop functioning with this condition. It is a long-term illness that harms the brain. Alzheimer's disease, Parkinson's disease, epilepsy, spinocerebellar ataxia, and Huntington's disease, myasthenia gravis disease, and stroke are examples of neurodegenerative diseases [2]. People who suffer from these acute or chronic disorders often experience a decline in their cognitive and intellectual abilities as a result of the CNS's neurons breaking down and deteriorating. The symptoms of NDs typically appear gradually and worsen over time, and include several functional losses, learning difficulties, motor coordination issues, and mostly short-term memory loss [3]. Neurodegeneration is a process that occurs in both aging of the brain and neuropathological diseases. With an incidence of roughly 2/1000 and an overall death rate of 8%, brain pathology in the form of cerebrovascular and neurodegenerative diseases is recognized as a major cause of death worldwide [4]. The substance that can maintain brain function and structure, they are referred to as neuroprotective medications. These chemicals can minimize and prevent oxidative stress, mitochondrial dysfunctions, inflammation, various forms of neurotoxicity (including excitotoxicity), and protein shortages. Currently, the oldest and most widely used medicinal system in the world is thought to be herbal remedies [5].

Plant parts like leaves, fruits, flowers, seeds, roots, stalks, and bark have been utilized in complementary and alternative medicine. Medicinal herbs contain a wide range of active compounds or phytochemicals, including flavonoids, alkaloids, isoprenoids, polyphenols, and tannins. Antioxidant-rich herbs have neuroprotective qualities as well. With some significant, well-known medicinal herbs derived from plants acting as neuroprotective agents, this article provides a quick summary of neurodegenerative disease and therapy options.

These herbal plants helps to protect neurons damage by various mechanism such as oxidative stress, excitotoxicity, inflammation, apoptotic, Neurotrophic. The goal of these substances or systems is to maintain the nervous system's composition and functionality [6].

Overview of neurodegenerative disease:

1] Epilepsy disease:

A chronic neurological disorder called epilepsy is characterized by frequent, unplanned seizures that are caused by abnormal brain electrical activity. affecting more than 70 million individuals globally [7,8]. The hallmark of epilepsy is a persistent propensity to experience epileptic seizures, which can lead to subsequent neurologic, cognitive, psychosocial, and social repercussions [9].

2] Huntington's disease:

Oxidative stress and the death of basal ganglia neurons are hallmarks of Huntington's disease, a progressive neurodegenerative illness. It is a hereditary autosomal dominant syndrome linked to dementia, emotional instability, and muscle dysfunction. Lack of focus, sadness, short-term memory loss, and issues with speech, language, and movement are all included [10].

3] Amyotrophic lateral sclerosis disease:

The most basic form of motor neuron disease, also referred to as amyotrophic lateral sclerosis (ALS), is a clinical condition that is simple to identify. Muscle weakness and atrophy in the arms, legs, trunk, and bulbar area are caused by a rapidly progressing degeneration of upper and lower motor neurons. Additionally, there is spasticity in the bulbar, arm, and leg areas. Breathlessness, difficulty speaking and eating, loss of arm and hand function, and loss of ambulation are examples of clinical symptoms. Respiratory insufficiency and aspiration pneumonia are frequent fatalities. Symptoms and signs typically begin at one location and spread to adjacent areas, frequently resulting in mortality within three to



five years of the commencement of symptoms [11].

4] Myasthenia gravis disease:

Myasthenia gravis (MG) is a chronic autoimmune illness that damages the nerve-muscle connection [12]. MG, a classic autoimmune disease, has been linked to several types of autoantibodies (abs) against certain neuromuscular endplate proteins. MG can be classified as seronegative if no antibodies against the nicotinic acetylcholine receptor (AChR), muscle tyrosine kinase (MuSK), or low density lipoprotein receptor type 4 (LRP4) are found using the methods now in use, and seropositive if such antibodies are found. Agrin, cortactin, collQ, acetylcholinesterase (AChE), Kv1.4, titin, and ryanodine receptor antibodies are among the various muscle antibodies that may be found in some MG patients; however, their pathophysiological significance has not yet been established. 7–9 While abs directed against MuSK or LRP4 are detectable in around 6% and 2% of generalized MG patients alone, depending on demographic variance, abs against the nicotinic type of AChR are present in up to 80% of patients with generalized MG[13].

5] Parkinsons disease:

More than 6.5 million people worldwide suffer from Parkinson's disease (PD), the most prevalent movement condition and the second most common neurodegenerative illness, accounting for 2-3% of the population over 65 [14]. Parkinson's disease (PD) is a progressive neurodegenerative disorder that primarily affects movement control. It occurs when nerve cells in the brain, particularly those in a region called the substantia nigra, become damaged or die. These nerve cells produce dopamine, a neurotransmitter that is essential for coordinating smooth and controlled movements. As dopamine levels decrease, people with Parkinson's disease experience a range of motor and non-motor symptoms. Motor deficits such as muscle rigidity, bradykinesia, rest tremor, loss of

postural reflexes, freezing phenomenon, and flexed posture are hallmarks of Parkinson's disease (PD), a clinical condition. There have been reports of non-motor symptoms such dementia, sleep difficulties, anxiety, sadness, and exhaustion in addition to motor deficits [15,16,17].

6] Alzheimer's disease:

Alzheimer's disease (AD), the most common type of dementia, affects at least 27 million individuals and is responsible for 60–70% of dementia cases[18]. Cognitive decline, personality changes, and memory issues or deficiencies are progressive and irreversible. Memory problems initially arise in the early stages of the illness, and as it worsens, motor and sensory function are also impacted. AD starts to show symptoms beyond the age of 65[19,20,21]. The development and accumulation of extracellular amyloid plaques from amyloid β precursor protein (APP) and intracellular neurofibrillary tangles (NFTs) with an aberrantly phosphorylated tau protein are the neuropathological hallmarks of AD. These are accompanied by the loss of synapses and pyramidal neurons, resulting in severe cognitive decline and behavioral issues such as aggression, depression, and wandering. Tau is a protein involved with microtubules in neurons that is controlled by the phosphorylation of several protein kinases [22]. The main enzyme responsible for acetylcholine synthesis is choline acetyltransferase (ChAT). It has been shown that notable neocortical deficiencies in ChAT lead to reduced choline absorption, Ach release, and loss of cholinergic perikarya from the nucleus basalis of Meynert. Additionally, it impacts Ach functions like Learning and memory. This led to the "cholinergic hypothesis of AD"[24].

Herbal plants used against nervous disorder:

1] curcuma longa –

Kingdom: Plantae

Phylum: Magnoliophyta

Class: Liliopsida



Order: Zingiberales
Family: Zingiberaceae
Genus: Curcuma
Species: Curcuma longa



Fig 1: Curcuma Longa

Turmeric, also called *Curcuma longa* (*C. longa*), is a belong to the Zingiberaceae family and is widely grown in Asia [24]. The primary components of turmeric include tigmastero, ketone, sesquiterpene alcohol, and curcuminoids, or curcumin. A and β -pinene, camphene, limonene, terpinene, linalool, curcumene, tigmasterol, and others are also found in turmeric [25]. Curcumin has a number of biological and therapeutic properties, including anti-inflammatory and antioxidant properties. In recent years, there has been a lot of interest in curcumin's potential as a treatment for neurodegenerative illnesses. Dopamine, norepinephrine, and 5-HT levels in the central nervous system can all be increased by the water-soluble extract of curcumin [26]. The neuroprotective effects of curcumin in PD also are related to its antioxidant properties [27]. Turmeric has been shown to bind $A\beta$ peptides in Alzheimer's disease, inhibit the formation of new amyloid deposits, and cause the disintegration of preexisting amyloid deposits. [28]. In addition, studies shows that curcumin and its derivatives demethoxycurcumin and bis-demethoxycurcumin may protect cells from oxidative stress induced on by $A\beta$ [29]. Curcumin can improve $A\beta$ uptake by macrophages, prevent $A\beta$ oligomerization and fibril formation, and stop the beta-heme complex's peroxidase activity [30]. Turmeric contains

polyphenol chemicals called curcuminoids, which reduce oxidative stress and inflammatory reactions to inflammatory cytokines like COX-2 and iNOS caused by mitochondrial dysfunction. In order to prevent amyloid buildup and coagulation in the brain, curcuminoids also attach to $A\beta$ plaques [31, 32].

2] *Lavandula angustifolia*-

Kingdom: Plantae
Phylum: Magnoliophyta
Class: Magnoliopsida
Order: Lamiales
Family: Lamiaceae
Genus: Lavandula
Species: *L. angustifolia*



Fig 2: Lavandula angustifolia

Researches reveal that *Lavandula angustifolia* can put down and glutamate-induced neurotoxicity by inhibition cholinesterase [33]. *Lavandula angustifolia* extract has been shown to help with cognitive impairment [34]. It contains tannins, coumaric acid, glycolic acid, valeric acid, ursoilic acid, anthocyanin, sugars, minerals, and essential oil. Decrease the glutamate induced neurotoxicity by inhibiting cholinesterase, so it helps in prevention of cognitive dysfunction and provide neuroprotection. Lavender oil has reported to possess anti-apoptotic properties that could help prevent cell death and protect the neurons affected in Huntington's disease [35,36].

The mechanisms of action of lavender are complex and involve several biological systems, primarily related to its effects on the central nervous system, inflammation, and its antimicrobial properties. The primary mechanisms through which lavender exerts its effects are :

1. Central Nervous System Effects (Sedation and Anxiety Reduction) :

- **GABAergic Mechanism:** By interacting with the brain's GABA (gamma-aminobutyric acid) receptors, lavender is thought to provide sedative and anxiolytic (anxiety-reducing) effects. The primary inhibitory neurotransmitter in the brain is GABA, and substances that increase its activity can lessen anxiety, encourage calmness, and facilitate sleep. It has been demonstrated that lavender essential oil, in particular its linalool component, increases GABA receptor activation and inhibits GABA breakdown.
- **Direct Modulation of Serotonergic and Dopaminergic Systems:** According to research, lavender may also have an impact on the dopamine and serotonin pathways, which are critical for mood regulation and the stress response. Lavender's capacity to lower anxiety and enhance wellbeing is a result of these interactions[37].

2. Anti-inflammatory and antioxidant properties

- **Inhibition of Pro-inflammatory Mediators:** Studies have demonstrated that lavender inhibits the synthesis of pro-inflammatory cytokines, including IL-1 β , TNF- α , and IL-6. This could reduce inflammation and its related effects. The reduction of nuclear factor-kappa B (NF- κ B), a transcription factor implicated in inflammation, is most likely the mechanism underlying this action.
- **Antioxidant Activity:** Flavonoids, phenolic acids, and terpenoids are among the substances having antioxidant qualities found in lavender essential oil. By scavenging free radicals, these substances minimize oxidative stress and protects cells from harm.

3. Neuroprotective Effects

Decrease in Excitotoxicity: Research has shown that lavender oil has neuroprotective properties, especially when it comes to oxidative stress and

excitotoxicity-related disorders. Its anti-inflammatory and antioxidant qualities, which are useful in protecting neurons from harm and degeneration, are primarily responsible for this. [38].

3] Rosmarinus officinalis-

Kingdom: Plantae

Phylum: Magnoliophyta

Class: Magnoliopsida

Order: Lamiales

Family: Lamiaceae

Genus: Rosmarinus

Species: Rosmarinus officinalis



1. Fig 3: Rosmarinus officinalis

Rosmarinus officinalis, Often referred to as rosemary, this perennial shrub is evergreen. Belonging to the Lamiaceae family [39]. In traditional medicine, rosemary has been used to treat a number of illnesses, such as headache, dysmenorrhea, stomachache, epilepsy, rheumatic pain, spasms, nervous agitation, memory enhancement, hysteria, sadness, and physical and mental exhaustion[40,41]. In the brain that breaks down acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), Rosmarinus officinalis has shown strong neuroprotective effects against neurodegenerative illnesses like Alzheimer's. The terpene and rosmarinic acid constituents in the plant's essential oil are probably what cause these anti-AChE and anti-BChE effects[42,43]. Rosemary may reduce Alzheimer's disease, memory loss, anxiety, and sadness by raising the brain's total choline levels[44]. Two other research demonstrate R. officinalis's neuroprotective properties. In the first, it was discovered that the polyphenols in

rosemary extract block stress proteins, which are involved in the neurodegenerative process[45]. According to the findings of the second study, rosemary stimulates the synthesis of a protein called nerve growth factor (NGF), which is essential for the development and upkeep of nerve tissue. Alzheimer's disease, dementia, and other neurodegenerative illnesses can be lessened by elevated NGF levels [46].

The pharmacological actions of rosemary are given to its bioactive components, such as essential oils like camphor, 1,8-cineole, and α -pinene, as well as rosmarinic acid, ursolic acid, and caffeic acid. The main ways that *Rosmarinus officinalis* produces its medicinal effects are given below:

1. Antioxidant Mechanism

- **Free Radical Scavenging:** Phenolic chemicals including rosmarinic acid, caffeic acid, and carnosic acid are the primary cause of rosemary's potent antioxidant qualities. These compounds neutralize free radicals and reduce oxidative stress, which is linked to aging, cardiovascular diseases, and neurodegenerative conditions. The antioxidants in rosemary inhibit lipid peroxidation and protect cellular components from oxidative damage.
- **Regulation of Antioxidant Enzymes:** In addition to its protective actions against oxidative damage, rosemary also increases the activity of endogenous antioxidant enzymes such as glutathione peroxidase (GPx), catalase (CAT), and superoxide dismutase (SOD).

2. Anti-inflammatory Mechanism

- **Inhibition of Pro-inflammatory Pathways:** Numerous pro-inflammatory enzymes, including lipoxygenase (LOX) and cyclooxygenase-2 (COX-2), which are involved in the synthesis of inflammatory mediators such as prostaglandins and leukotrienes, have been demonstrated to be

inhibited by rosemary. On the other hand, rosemary lowers inflammation by blocking these enzymes.

- **Downregulation of NF- κ B:** Rosemary compounds, particularly rosmarinic acid, suppress the activation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B), a key regulator of inflammatory responses. This results in reduced expression of pro-inflammatory cytokines, such as TNF- α , IL-6, and IL-1 β .
- **Modulation of MAPK Pathways:** It has been discovered that rosemary affects the signaling pathways of mitogen-activated protein kinase (MAPK), which are essential for inflammation. Rosemary lowers the synthesis of inflammatory cytokines and mediators by modifying MAPK.

3. Neuroprotective Mechanism

- **Acetylcholinesterase Inhibition:** It has been shown that rosemary inhibits acetylcholinesterase, the enzyme that degrades acetylcholine, a neurotransmitter crucial for memory and cognitive function. Rosemary may help enhance memory and protect against cognitive loss by stopping acetylcholine from degrading.
- **Anti-excitotoxicity:** Rosemary has been found to have neuroprotective effects against excitotoxicity, which is a process where excessive neurotransmitters like glutamate cause neuronal damage. This effect is believed to be related to rosemary's antioxidant and anti-inflammatory properties.
- **Regulation of Neurotrophic Factors:** It has been demonstrated that rosemary increases the expression of BDNF, a protein involved in neuronal survival and neurogenesis. This mechanism may support its role in cognitive health and neuroprotection[47,48,49].

4] *Cardiospermum halicacabum*-

Kingdom: Plantae



Phylum: Magnoliophyta
Class: Magnoliopsida
Order: Sapindales
Family: Sapindaceae
Genus: *Cardiospermum*
Species: *Cardiospermum halicacabum*



Fig 4: *Cardiospermum halicacabum*

Cardiospermum halicacabum is a member of the family Sapindaceae. This herbaceous plant is found in tropical and subtropical areas all over the world. The plains of Africa and America, as well as Bangladesh, India, and Pakistan, are home to this plant. Among its common names are balloon vine, heart vine, heart pea, love-in-a-puff, and heart seed.[50]. The essential chemical components extracted from this plant are 8-O-luteolin-7-O-glucuronide, chrysoeriol-7-O-glucuronide, apigenin, apigenin-7-O-glucuronide, and arachidic acid[51]. It shows neuroprotective activity. A degenerative brain disorder called dementia causes an ever-increasing limitation of daily tasks. Memory issues, linguistic problems, psychological and mental abnormalities, and difficulty in daily tasks are its hallmarks. The methanolic extract of *C. halicacabum* may enhance memory and reverse amnesia brought on by scopolamine treatment. Additionally, it markedly reduced the activity of acetyl cholinesterase across the whole brain[52]. The neuroprotective effects of *Cardiospermum halicacabum* (*C. halicacabum*) are primarily attributed to its bioactive compounds, which exert various mechanisms of action to protect neurons and the central nervous system (CNS) from

damage. Here's a detailed overview of the potential mechanisms of action:

1. **Antioxidant Mechanism**

- Many neurological diseases, such as Alzheimer's and Parkinson's, are significantly influenced by oxidative stress. Antioxidants found in abundance in *C. halicacabum* aid in scavenging free radicals and minimizing oxidative damage to neural cells. Research has demonstrated that *C. halicacabum* extracts can scavenge reactive oxygen species (ROS) and free radicals, lowering the risk of oxidative stress-induced brain damage[53].

2. **Anti-Inflammatory Action**

- Neurodegenerative diseases are characterized by persistent neuroinflammation. According to reports, *C. halicacabum* has anti-inflammatory qualities via inhibiting pro-inflammatory mediators and cytokines. The plant aids in stopping additional neuronal damage by lowering inflammation. In particular, the plant protects neurons from inflammation-induced damage by suppressing the production of cyclooxygenase-2 (COX-2) and other inflammatory enzymes[54].

3. **Neurotrophic Activity**

- Neurons cannot survive, multiply, or differentiate without neurotrophic factors, such as brain-derived neurotrophic factor (BDNF). In order to promote neurogenesis and the healing of injured neural tissue, *C. halicacabum* may increase the expression of neurotrophic factors. This process may lessen cognitive impairments and enhance brain function[55].

4. **Modulation of Neurotransmitter Systems**

- Neuronal systems such as acetylcholine, dopamine, and serotonin have been demonstrated to be impacted by *C. halicacabum*. Neurodegenerative diseases are frequently linked to changes in these neurotransmitter systems. The plant extract

may help preserve cognitive function and guard against conditions like Parkinson's disease, which is characterized by dopamine depletion, by modifying neurotransmitter levels and receptor functioning[56].

5. Inhibition of Apoptotic Pathways

- In neurodegenerative illnesses, apoptosis, or programmed cell death, is a major factor in the degeneration of neurons. It has been discovered that *C. halicacabum* increases the expression of anti-apoptotic proteins like Bcl-2 while inhibiting important apoptotic pathway components like caspases and Bax. This neuroprotective effect may be attributed to the suppression of apoptosis, which shields neurons from cell death.[57]

5] *Careya arborea*-

Kingdom: Plantae

Phylum: Tracheophyta

Class: Magnoliopsida

Order: Ericales

Family: Lecythidaceae

Genus: *Careya*

Species: *arborea*



Fig 5: *Careya arborea*

The wild guava, or *Careya arborea* roxob, is a medium-sized deciduous tree with thin, peeling bark strips and a dark gray tint. It is widely accessible in Malaysia, the Philippines, Sri Lanka, and India. Big tropical trees with woody skins that produce big fruits are members of the Lecythidaceae family. There are roughly 20 genera and 450 species of tropical trees in this family. The family is primarily found in South

America, with a few genera also found in Africa and Asia. It contains various chemical constituents such as alkaloids : careyarine , careyiene ,arboreine flavonoids: quercetin, kaempferol, gallic acid, ellagic acid ; phenolic acids: ferulic acid,cinnamic acid ,vanillic acid ; terpenoids : careyol, α -Pinene, β -Pinene, limonene .This plant is used for the treatment of various disorder such as tumors, bronchitis, epileptic episodes, and skin disorders. Additionally, it is used to treat ear pain, diarrhea, and dysentery with bloody stools. It also shows various pharmacological activities such as neuroprotective ,anti-microbial, antioxidant ,anticancer[58-60]. Effects of anticoagulants i.e. The bark's methanolic extract significantly increased the active prothrombin and thrombin times and shown anticoagulant efficacy similar to that of warfarin [61]. The mechanism of this plants are linked with chemical constituents present in this plant which give pharmacological properties.

1. Antioxidant Activity:

- The plant has substances that scavenge free radicals, which are known to put neurons under oxidative stress. One of the main causes of neurodegenerative illnesses like Parkinson's and Alzheimer's is oxidative stress. *Careya arborea* may improve cellular health, shield neurons from harm, and boost brain function by lowering free radicals.
- Flavonoids and phenolic compounds in the plant have been shown to have potent antioxidant properties that help mitigate oxidative damage to brain cells, which can be crucial in neuroprotection.

2. Anti-inflammatory Properties:

- Neurodegenerative disorders are largely caused by chronic neuroinflammation. The bioactive chemicals found in *Careya arborea* may help regulate the brain's immunological response by lowering the synthesis of mediators and pro-inflammatory cytokines

that lead to neurodegeneration, including as TNF- α , IL-6, and nitric oxide.

- The general neurological health could be improved and brain tissue damage could be lessened by this anti-inflammatory impact.

3. Neurotransmitter Modulation:

According to certain research, *Careya arborea* may have an impact on neurotransmitter levels, which are critical for mood management, cognitive function, and motor control. These neurotransmitters include serotonin and dopamine. Numerous neurological conditions, such as depression and Parkinson's disease, are linked to changes in neurotransmitter systems. The plant may protect the central nervous system by altering the balance of neurotransmitters.

4. Neurogenesis and Synaptic Plasticity:

Careya arborea may also have neuroprotective effects via enhancing synaptic plasticity, which is the capacity of synapses to become stronger or weaker over time, and promoting neurogenesis, which is the formation of new neurons. Memory, learning, and general brain function may all be enhanced by this, particularly in diseases that cause cognitive decline. [62].

6] *Withania somnifera*-

Kingdom: Plantae

Phylum: Angiospermophyta

Class: Magnoliopsida (Dicotyledons)

Order: Solanales

Family: Solanaceae

Genus: *Withania*

Species : *Withania somnifera*

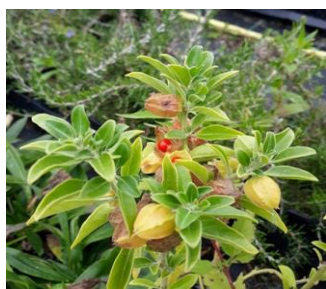


Fig 6: *Withania somnifera*

Ashwagandha is a belong to the Solanaceae family. Ashwagandha is also known as winter cherry, poison gooseberry, and Indian ginseng. In India's central and northwestern regions, ashwagandha is grown. The states that produce the most ashwagandha in India include Madhya Pradesh, Gujarat, Haryana, Maharashtra, Punjab, Rajasthan, and Uttar Pradesh. Yemen, China, and Nepal are also home to it. Ashwagandha may improve neurogenesis and memory and contains adaptogenic qualities that lower stress and anxiety. It also exhibits promise in preventing oxidative damage to neurons and regulating neuroinflammatory pathways[63]. The chemical components that are biologically active are saponins with an extra acyl group (sitoindoside VII and VIII), steroidal lactones (withanolides, withaferins), alkaloids (isopellertierine, anferine), and withanoloides with a glucose at carbon 27 (sitoindoside XI and X). Iron is also rich in *Withania somnifera*[64]. One herbal remedy that has neuroprotective properties is *Withania somnifera*. The chemical molecule Withanoside IV is responsible for the health benefit. It has been shown that in rats induced with Ab (25–35), oral administration of Withanoside IV reduced axonal, dendritic, and synaptic loss as well as memory impairments. Following injection, withanoside IV is converted to sominone, which promotes neurite and synaptic repair. Rat cortical neurons were cultivated with Ab (25–35) for four days in an in vitro investigation. Sominone and withanoside were then added to the medium. Axons and dendrites were found to have significantly increased. A hydrophobic substance, sominone easily penetrates the blood-brain barrier [65]. Ashwagandha extract has been demonstrated to raise antioxidant activity and inhibit lipid peroxidation by raising the brain's levels of free-radical scavenging enzymes. Other components extracted from the aqueous methanol extract of *Withania somnifera* roots, including withaferin

and sitoindosides VII–X, have been shown to reduce AChE activity in the brain [66].

Numerous studies have suggested that *Withania somnifera* may have neuroprotective properties that could help shield the brain from neurodegenerative conditions like Parkinson's disease, Alzheimer's disease, and stress-induced cognitive loss. Below are some of the proposed neuroprotective mechanisms of *Withania somnifera*:

1. Antioxidant Activity:

- Alkaloids and withanolides, two strong bioactive substances found in *Withania somnifera*, have strong antioxidant qualities. Neuronal injury and neurodegeneration are greatly affected by oxidative stress. *Withania somnifera* protects neurons from oxidative stress-induced damage by scavenging free radicals and lowering oxidative damage, maintaining brain health and function.
- It has been demonstrated that withanolides in particular lower lipid peroxidation and replenish cellular antioxidant enzymes such as glutathione peroxidase (GPx), catalase, and superoxide dismutase (SOD), hence reducing oxidative damage to brain cells. [67].

2. Anti-inflammatory Effects:

- Chronic inflammation in the brain is a hallmark of many neurodegenerative disorders. The anti-inflammatory compounds in *Withania somnifera* aid in controlling the brain's immunological response by reducing the activation of microglia, the immune cells that live there, and the release of pro-inflammatory cytokines including TNF- α , IL-1 β , and IL-6.
- *Withania somnifera* lowers the progression of inflammatory-related neurodegenerative

disorders and helps prevent damage to neural tissue by regulating neuroinflammation[68].

3. Neurogenesis and Synaptic Plasticity:

- *Withania somnifera* has been shown to stimulate neurogenesis, particularly in the hippocampus, a part of the brain crucial for memory and learning. Plant compounds encourage the production of brain-derived neurotrophic factor (BDNF), an essential protein that supports the growth, maintenance, and survival of neurons.
- Learning, memory, and emotional control are among the cognitive processes that are supported by the stimulation of neurogenesis and synaptic plasticity, which is the strengthening of synapses in response to sensation [69].

4. Reduction of Amyloid Plaques and Tau Tangles:

- According to research, *Withania somnifera* may help reduce the production of tau tangles and amyloid-beta plaques, two pathological indicators of Alzheimer's disease. *Withania somnifera* helps avoid the neuronal damage and cognitive loss commonly connected to Alzheimer's by preventing the aggregation of tau and amyloid-beta proteins.[70].

Marketed Herbal Formulations of Neurological Disease:

Herb	Disease	Mechanism	Herbal Formulation
Ashwagandha (<i>Withania somnifera</i>)	Alzheimer's Disease	anti-inflammatory, antioxidant, inhibits the production of A β ,	1.NeuroShield (by NOW Foods)



		and stops brain cell death [71,72]	2. Brain Shield (by Jarrow Formulas) 3. Ashwagandha Neuro Protect (by Source Naturals) 4. Cognitive Support (by Gaia Herbs) 5. Neuro Optimize (by Double Wood Supplements)
Ginkgo biloba	Alzheimer's Disease	antioxidant, enhances mitochondrial performance, and increases blood flow to the brain [73,74]	1. Ginkgo Smart (by NOW Foods) 2. Ginkgo Biloba Extract (Nature's Bounty)
Saffron (Crocus sativus)	Alzheimer's Disease	anti-amyloidogenic, anti-inflammatory, antidepressant, immunomodulation, neuroprotection [75,76]	1. Nature's Bounty Saffron 100mg tablet 2. NOW Foods Saffron 50mg tablet 3. Natrol Saffron 50mg Softgels
Zingiber officinale	Epilepsy	Inhibits NO production Elevated intracellular cGMP level Block calcium channel [77,78]	1. NOW Foods Ginger 550mg tablet 2. Jarrow Formulas Ginger 500mg tablet
Turmeric (Curcuma longa)	Alzheimer's Disease	anti-inflammatory, antibacterial, reduces the death of brain cells, and prevents the production of A β [79,80]	1. Solgar Curcumin 500mg tablet 2. Gaia Herbs Turmeric Supreme 400mg tablet
Ginseng	Epilepsy	blocks L-type Ca ²⁺ channels, NMDA-dependent Ca ²⁺ influx, and status epilepticus-induced Ca ²⁺ influx, as well as hippocampal neurons. [81,82,83]	1. Herb Pharm Ginseng Liquid Extract 2. Solgar Ginseng 400mg tablet
Shankpushpi (Convolvulus pluricaulis)	Alzheimer's Disease	enhances cognitive performance, reduces aging in the brain, and has anti-inflammatory and	1. Himalaya Shankpushpi Tablets (500mg) 2. Organic India Shankpushpi Powder (100g)

		antioxidant properties[84,85]	
Cat's claw (Uncaria tomentosa)	Alzheimer's Disease	decreases gliosis, prevents plaque and tangles, and enhances memory [86,87,88]	1. NOW Foods Cat's Claw 2. Gaia Herbs Cat's Claw

CONCLUSION

The increasing prevalence of neurodegenerative diseases necessitates innovative and effective treatment approaches. Traditional herbal medicine offers promising neuroprotective potential, demonstrated through various bioactive compounds found in plants such as *Curcuma longa*, *Lavandula angustifolia*, *Rosmarinus officinalis*, *Cardiospermum halicacabum*, *Careya arborea*, and *Withania somnifera*. These herbs have strong anti-inflammatory, anti-apoptotic, and antioxidant qualities that help reduce oxidative stress and neuroinflammation while also preventing cognitive decline. While further research is needed to fully elucidate the mechanisms and optimize the clinical applications, current evidence suggests that incorporating these herbal remedies could support conventional therapies, offering a complementary strategy for managing neurodegenerative diseases. Future studies should focus on the standardization of herbal extracts, dosage optimization, and comprehensive clinical trials to validate their efficacy and safety.

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