International Journal of Zoology and Applied Biosciences **ISSN: 2455-9571**
Volume 10, Issue 6, pp: 383-388, 2025 (Special Issue)
https://doi.org/10.55126/ijzab.2025.v10.i06.SP077 **http://www.ijzab.com**

Research Article

NEUROPROTECTIVE EFFECTS OF HERBAL MEDICINES

***Mohini Rangala, Kada Lakshmi Monica, Modalavalasa Anusha, Ashish Gardi, Gundapuneni Srinidhi and Boddu Yamini devi**

Department of Pharmacognosy, Vignan Institute of Pharmaceutical Technology, Near VSEZ, Duvvada, Visakhapatnam-530049, Andhra Pradesh, India.

Article History: Received 10th September 2025; Accepted 15th November 2025; Published 30th November 2025

ABSTRACT

The brain, as the central regulator of all bodily systems, requires robust protection against aging and neurodegenerative diseases. This review explores the neuroprotective potential of traditional medicinal herbs, particularly those from the Indonesian *Cabe Puyang* Manuscript. Among 31 herbs identified, 12 including *Zingiber officinale*, *Centella asiatica*, and *Moringa oleifera*—demonstrated strong central nervous system activity due to their antioxidant and anti-inflammatory properties. Neurodegenerative conditions such as Alzheimer's, Parkinson's, and dementia are characterized by progressive neuronal loss and the accumulation of misfolded proteins like amyloid-β and α-synuclein. Herbal bioactive compounds offer promising neuroprotection by reducing oxidative stress, inhibiting pathogenic enzymes, and promoting neuronal growth. Additionally, herbal medicines show therapeutic potential in managing autoimmune disorders like multiple sclerosis and in mitigating damage from ischemic stroke through multi-targeted mechanisms, including modulation of mitophagy. Gut microbiota dysbiosis, a newly recognized factor in Alzheimer's disease, may also be regulated through herbal interventions. Phytochemicals such as flavonoids, alkaloids, phenylpropanoids, and isoprenoids found in traditional and Ayurvedic herbs contribute to cognitive health by countering oxidative damage and inflammation. Collectively, these findings highlight the therapeutic potential of natural products and traditional herbs in preventing and managing neurodegenerative diseases, warranting further research and drug development efforts.

Keywords: Neuroprotection, Herbal medicine, Neurodegenerative diseases, Phytochemicals; Oxidativestress.

INTRODUCTION

Herbal medicines have served as primary therapeutic agents for nervous system disorders innumerous cultures for centuries (Abdolmaleki A *et al*, 2000). Their renewed scientific interest arises from their complex phytochemical compositions that target multiple cellular processes. Unlike single-target synthetic drugs, herbs such as Ginkgo biloba, Curcuma longa, Panax ginseng, and Bacopamonnieri exert pleiotropic effects including antioxidant, anti-inflammatory, anti-apoptotic, and neurotrophic actions (Sarkar B, *et al* 2024; Sahu D, *et al*, 2021). Herbal plants are often used for cognitive enhancement, mood stabilization, and the management of chronic neurological disorders (Abdolmaleki A *et al*, 2000; Roy S *et al*, 2017). Their active constituents flavonoids, terpenoids, alkaloids, and polyphenols interact with neuronal pathways, protect against toxicinsults, and preserve neural viability (Nahar L *et al*. 2025). Importantly, many bioactive compounds found in herbal medicines are believed to be safer and more bioavailable than synthetic pharmaceuticals, resulting in fewer adverse effects. Herbal extracts have shown efficacy in treating age-related cognitive decline and depression, which are closely associated with neurodegeneration (Moise G, *et al* 2024).

Curcuma longa

Curcumin, a hydrophobic polyphenolic compound extracted from the rhizome of *Curcuma longa*, has been traditionally utilized in Indian and Chinese medicine as well as incorporated into dietary practices. Over the last few decades, it has gained attention as a potential therapeutic agent for several neurodegenerative diseases, including Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD), multiple sclerosis (MS),

*Corresponding Author: Mohini Rangala, Assistant Professor, Department of Pharmacognosy, Vignan Institute of Pharmaceutical Technology, Visakhapatnam, Andhra Pradesh, India, 530049, Email: mohinirangala8555@gmail.com

amyotrophic lateral sclerosis (ALS), and prion-related conditions. Curcumin demonstrates a wide range of biological properties—anti-inflammatory, antioxidant, neuroprotective, immunomodulatory, antiproliferative, and antimicrobial—that directly target major pathological processes such as oxidative stress, neuroinflammation, mitochondrial dysfunction, and protein aggregation. These mechanisms highlight its potential role as a disease-modifying nutraceutical rather than a merely palliative therapy.

Despite its promising pharmacological profile, curcumin's clinical utility has been restricted by poor aqueous solubility, low systemic stability, rapid metabolism, limited bioavailability, and insufficient blood–brain barrier (BBB) penetration. To overcome these challenges, advanced drug delivery systems have been extensively investigated, including liposomes, micelles, dendrimers, cubosomes, polymeric nanoparticles, and solid lipid nanoparticles. Further innovations such as cell membrane–camouflaged and ligand-functionalized nanoparticles enhance BBB penetration and enable targeted neuronal delivery, thereby improving curcumin's stability, uptake, and therapeutic performance. Owing to its natural origin, safety, affordability, and absence of severe side effects, curcumin continues to stand out as an attractive candidate for long-term neuroprotective intervention, particularly when coupled with nanotechnology-driven delivery strategies (Genchi G et .al 2024).

Ginkgo biloba

Its extract (EGb 761) has long been used to improve cerebral and peripheral blood flow and to manage dementia. Rich in flavonoids and terpenoids, EGb 761 exerts neuroprotective and vasotropic effects. Experimental studies demonstrate that its mechanisms include modulation of cerebral blood flow, neurotransmitter systems, cellular redox state, nitric oxide levels, platelet-activating factor antagonism, and free-radical scavenging. Additional actions involve interaction with neurotransmitters and induction of growth factors. Clinical trials support a favorable risk–benefit profile of EGb 761 in treating mild to moderate dementia, though side effects have also been noted (Ahlemeyer B, *et al* 2003).

Bacopa monnieri

Bacopa monnieri (Brahmi), a perennial creeping herb widely used in Ayurveda, has long been recognized for its neuroprotective and cognition-enhancing effects. Rich in diverse bioactive phytoconstituents, (Table1) including bacosides, bacopasides, bacopasaponins, stigmasterol, and betulinic acid, *B. monnieri* extract (BME) demonstrates significant pharmacological potential in the management of neurological disorders. Experimental and clinical studies suggest that BME exerts its neuroprotective effects through multiple mechanisms, such as antioxidant defense, anti-inflammatory activity, anti-apoptotic pathways, mitochondrial protection, modulation of tau protein phosphorylation, inhibition of amyloid-beta aggregation, and maintenance of ion homeostasis. These actions are particularly relevant in preventing or slowing the progression of Alzheimer's disease and other age-related neurodegenerative conditions. Moreover, *B. monnieri* shows promise as a nootropic, enhancing learning, memory, and cognitive performance.

Despite abundant evidence supporting its efficacy, limitations remain due to the incomplete characterization of individual phytoconstituents, bioavailability challenges, and insufficient large-scale clinical validation. Future studies integrating advanced phytochemical analysis, in silico modeling, and well-designed clinical trials are required to establish its therapeutic utility and optimize its use in neurodegenerative disease management. Given its safety, multi-targeted action, and affordability, *B. monnieri* holds great promise as a candidate for drug discovery and development in neurological health (Fatima U, *et al* 2022).

Table 1. Bioactive Phytoconstituents of *Bacopa monnieri* and Their Neuroprotective Mechanisms.

Phytoconstituent	Mechanism of Action	Therapeutic Relevance
Bacoside A (incl. A3)	Enhances synaptic activity, improves neurotransmission, modulates kinase activity	Memory enhancement, learning improvement, protection against cognitive decline
Bacopaside I & II	Antioxidant and anti-apoptotic effects; reduces ROS and neuroinflammation	Neuroprotection in Alzheimer's disease, Parkinson's disease, and age-related cognitive loss
Bacopasaponin C	Inhibits amyloid-beta aggregation, modulates tau phosphorylation	Potential therapeutic agent in Alzheimer's disease
Stigmasterol	Modulates membrane fluidity, antioxidant effects, supportscholesterol metabolism	Neuroprotection, reduction of oxidative stress
Betulinic acid	Anti-inflammatory, anti-apoptotic, mitochondrial protection	Defense against neurotoxicity and mitochondrial dysfunction
Luteolin	Potent flavonoid antioxidant, reduces microglial activation and cytokine release	Anti-neuroinflammatory effects in neurodegenerative disorders
Monnieraside I–III	Antioxidant activity, supports synaptic plasticity	Cognitive enhancement, learning and memory improvement

Panax ginseng

As the global population ages, the management of neurodegenerative diseases has become a critical public health priority. Among natural products, *Panax ginseng* (C.A. Mey.), a widely used traditional Chinese herbal medicine, has shown remarkable neuroprotective potential owing to its pharmacologically active constituents, particularly ginsenosides. Extensive studies demonstrate that ginseng exerts protective effects against Alzheimer's disease, Parkinson's disease, Huntington's disease, stroke, and depression through mechanisms such as antioxidant activity, anti-apoptosis, anti-inflammatory effects, and regulation of neurotransmission. Importantly, ginseng has been reported to promote neuronal survival as well as peripheral nerve regeneration, thereby supporting both central and neuromuscular health. Although ginsenosides have shown promising efficacy in preclinical models, their clinical application is limited by poor bioavailability and restricted blood–brain barrier permeability. Current research highlights two important areas for advancement: the correlation between ginsenoside structure and activity, and a better understanding of their metabolic transformation in vivo. While numerous formulations, including oral and injectable Chinese patent medicines, are already in clinical use, systematic post-marketing evaluation and large-scale, high-quality clinical studies remain scarce. Emerging drug delivery strategies, including nanotechnology-based systems, may offer solutions to enhance brain bioavailability and therapeutic outcomes. Collectively, ginsenosides (Huang X, *et al* 2019) and their metabolites (Table2) (Huang X *et al* 2019) represent promising candidates for the development of safe and effective neuroprotective agents, though further mechanistic exploration and clinical validation are essential.

Table 2. Major Ginsenosides and Their Neuroprotective Mechanisms.

Phytoconstituent	Mechanism of Action	Therapeutic Relevance
Rb1	Antioxidant, anti-apoptotic, enhances synaptic plasticity, regulates cholinergic system	Improves memory, protects against Alzheimer's disease and cerebral ischemia
Rg1	Anti-inflammatory, promotes neurogenesis, regulates HPA axis, mitochondrial protection	Enhances learning and cognition, alleviates depression, protects against AD and PD
Rd	Inhibits excitotoxicity, reduces calcium influx, stabilizes mitochondrial function	Protects against ischemic stroke, Huntington's disease, and neuronal apoptosis
Re	Antioxidant, vasodilatory, reduces oxidative stress and lipid peroxidation	Prevents neuronal injury in AD and vascular dementia
Compound K	Major intestinal metabolite of protopanaxadiol-type ginsenosides; anti-inflammatory, antioxidant	Improved BBB permeability, strong candidate for clinical use in neurodegenerative diseases

Quercetin

In recent years, considerable attention has been given to the potential of nutraceuticals in supporting neuroprotection across the developing, adult, and aging nervous system. Among these, quercetin, a naturally occurring dietary flavonoid, has been one of the most extensively investigated. Evidence from in vitro experiments, animal models, and limited clinical studies indicates that quercetin provides protection against neurotoxic chemicals as well as in experimental models of neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, and ischemic brain injury. The precise mechanisms underlying these protective effects are not fully understood, but multiple hypotheses have been proposed. Quercetin is thought to act not only as a direct antioxidant but also by enhancing cellular defense mechanisms against oxidative stress. This includes activation of the Nrf2-ARE pathway and induction of paraoxonase-2 (PON2), an antioxidant and anti-inflammatory enzyme. Additionally, quercetin has been reported to modulate sirtuin-1 (SIRT1) activity, induce autophagy, and act as a phytoestrogen, thereby contributing to its neuroprotective capacity.

Beyond these mechanisms, further biological targets have been suggested, including modulation of signal transduction pathways, maintenance of proteasome function, preservation of mitochondrial integrity, and regulation of inflammatory processes. Despite these promising findings, one of the key challenges for clinical application is quercetin's limited bioavailability and restricted ability to cross the blood–brain barrier. Recent progress in novel drug delivery systems, such as nanoparticle-based carriers and liposomal formulations, has shown potential to improve central nervous system accessibility. Furthermore, the role of quercetin metabolites in neuroprotection is an emerging area of interest, though current evidence remains scarce and requires systematic investigation.

Overall, quercetin represents a promising nutraceutical candidate with multimodal mechanisms of action. However, further experimental and clinical research is

required to optimize its delivery, validate its efficacy, and fully establish its role in the prevention and treatment of neurodegenerative diseases (Costa LG, *et al* 2016).

Molecular mechanisms of Neuroprotection

Herbal medicines protect neural cells through several interconnected biological pathways:

Antioxidant Effects

Many herbs scavenge free radicals and upregulate endogenous antioxidant enzymes, mitigating oxidative stress a major driver of neuronal death in neurodegenerative disorders.

Anti-inflammatory Actions

Herbal compounds inhibit pro-inflammatory cytokines (e.g., IL-6, TNF-α, IL-1β) and downregulate microglial activation, thereby preserving neuronal Function.

Mitigation of Mitochondrial Dysfunction

Bioactive molecules such as polyphenols and saponins conserve mitochondrial membrane potential, stimulate biogenesis, and prevent apoptosis.

Protein Aggregation Inhibition

Certain herbs impede the aggregation of pathogenic proteins such as amyloid-β and α-synuclein, central to Alzheimer's and Parkinson's disease pathology (Dharmalingam K, 2025)

Modulation of Neurotransmitters

Herbal medicines adjust levels of acetylcholine, dopamine, and glutamate, helping to normalize synaptic transmission and cognitive performance.

Table 3. Major Neurodegenerative Diseases targeted.

Neurodegenerative Disease	Pathological Features	Key Herbal Medicines	Neuroprotective Effects
Alzheimer's Disease (AD)	- Amyloid-β plaques - Tau tangles - Synaptic dysfunction	- *Curcuma longa* (Curcumin) - *Ginkgo biloba* - *Bacopa monnieri*	- Reduces Aβ plaque burden - Improves memory and cognition
Parkinson's Disease (PD)	- Dopaminergic neuron loss - Lewy body formation (α-synuclein aggregates)	- *Mucuna pruriens* - *Panax ginseng* - Triptolide	Preserves dopaminergic neurons - Reduces α-synuclein toxicity - Mitigates motor deficits
Huntington's Disease (HD) & Others	Neuronal death - Inflammation - Mitochondrial dysfunction	Ginsenosides (*Panax ginseng*) - Polyphenols (e.g., Resveratrol)	Reduces inflammation - Preserves neuronal integrity - Shows efficacy in stroke & TBI models

Table 4. Herbal Medicines—Key Clinical and Preclinical Studies.

Herbal Medicine	Study model	Main Findings	References
Curcumin	Human/Animal	Reduced Aβ plaques, improved memory	Genchi G, et al (2024)
Ginkgo biloba	Human/Animal	Cognitive boost, antioxidant effects	Ahlemeyer B, et al (2003)
Bacopa monnieri	Cell/Animal	Inhibited apoptosis (↑Bcl-2)	Fatima U, et al (2022)
Quercetin	Human/Animal	Reduce oxidative stress	Costa LG, et al (2016)
Withania somnifera	Rodent	Reduced neuroinflammation	Wongtrakul J (2021)

Comparing Research Methods by Different Authors

Researchers employ various approaches in assessing neuroprotective efficacy: Vitro Cellular Models: Studies use neuronal cell lines to evaluate direct toxicity, anti-apoptotic effects, and mechanistic pathways such as Bcl-2 modulation. In Vivo Animal Studies: Rodent models are commonly used to study cognitive, motor, and behavioral outcomes following herbal administration, with biochemical assays to validate neuronal survival and inflammation. Clinical Trials: Randomized, double-blind, placebo-controlled trials test herbal extracts for cognitive and motor benefits in humans. For example, Azargoonjahromi *et al*. (2024) assessed curcumin's efficacy in reducing amyloid plaque and improving cognition in AD patients. Ginkgo biloba extracts have

yielded variable success in improving cognitive function in mild dementia. Advanced Techniques: Nanocarrier systems (nanoparticles, nanogels) are increasingly used to enhance bioavailability and targeted delivery of phytochemicals (Table 4).

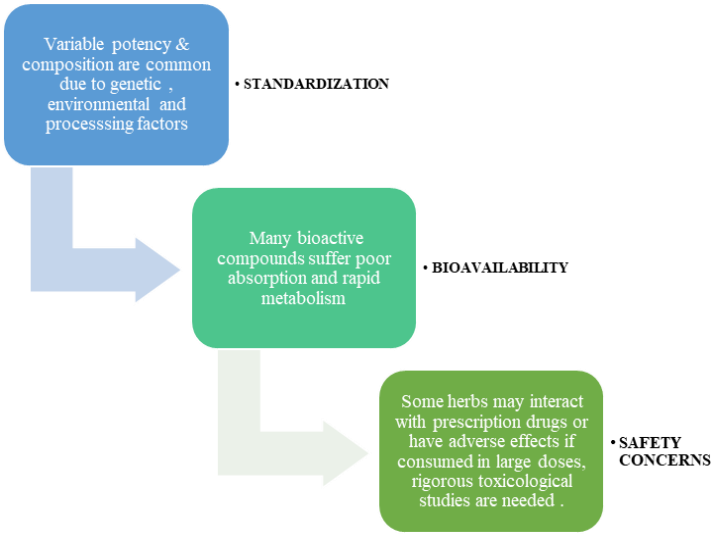

Figure 1. Safety, Standardization and Limitations.

CONCLUSION

Herbal medicines present a multifaceted approach to neuroprotection by targeting oxidative stress, inflammation, mitochondrial dysfunction, protein aggregation, and neurotransmitter balance. Substantial progress in understanding their cellular and molecular actions is evident, with enhanced outcomes in animal and clinical models. Nevertheless, bioavailability, safety, and standardization issues must be addressed before widespread clinical adoption. Future research must bridge these gaps to unlock the full potential of herbal therapies for neurodegenerative diseases.

ACKNOWLEDGMENT

The authors express sincere thanks to the head of the Department of Pharmacognosy, Vignan Institute of Pharmaceutical Technology, Near VSEZ, Duvvada, Visakhapatnam-530049, Andhra Pradesh, India for the facilities provided to carry out this research work.

CONFLICT OF INTERESTS

The authors declare no conflict of interest

ETHICS APPROVAL

Not applicable

FUNDING

This study received no specific funding from public, commercial, or not-for-profit funding agencies.

AI TOOL DECLARATION

The authors declares that no AI and related tools are used to write the scientific content of this manuscript.

DATA AVAILABILITY

Data will be available on request

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