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Review Article

Neuroprotective Activity of Medicinal Plants: Comprehensive Review of Phytochemicals, Neuronal Survival Mechanisms, Pharmacological Evidence, Safety Evaluation, Clinical Potential

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Abstract

Neurodegenerative disorders and neuronal injuries resulting from oxidative stress, inflammation, excitotoxicity and mitochondrial dysfunction represent significant global health challenges. Medicinal plants possessing neuroprotective properties are increasingly investigated as potential therapeutic agents for prevention and management of neurological diseases. This systematic review evaluates phytochemicals responsible for neuroprotection, mechanisms underlying neuronal survival including antioxidant defense, modulation of neurotransmission, inhibition of apoptosis and regulation of neuroinflammatory pathways, along with pharmacological evidence and safety considerations. Flavonoids, alkaloids, terpenoids, phenolic acids and glycosides contribute to preservation of neuronal integrity and synaptic function. Experimental studies demonstrate improvement in cognitive performance and reduction in neuronal degeneration. Although clinical data remain limited, plant-derived neuroprotective compounds show promising therapeutic potential requiring further standardization and controlled clinical evaluation.

Keywords: Neuroprotection; Medicinal plants; Neuronal survival; Oxidative stress; Phytochemicals.

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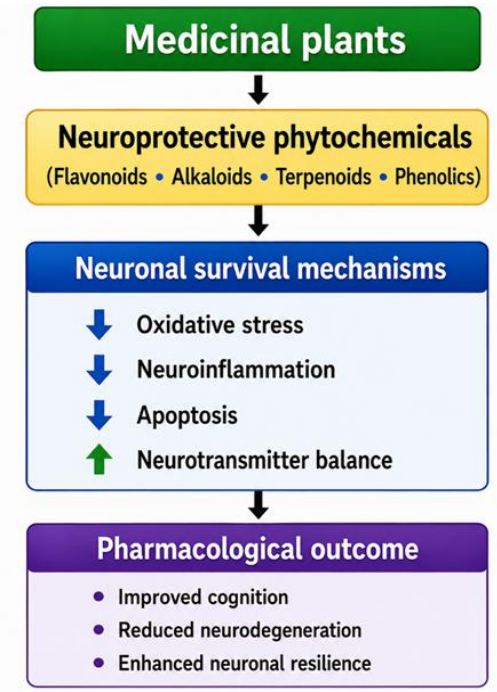
Graphical Abstract



Highlights

✓Multi-target medicinal phytochemicals mitigate oxidative stress and neuroinflammation.

✓Chhattisgarh medicinal plants exhibit strong neuroprotective and cognitive benefits.

✓Phytochemicals regulate Nrf2, NF-κB, PI3K/Akt, BDNF and related pathways.

✓Traditional ethnomedicine integrated with modern research advances neurotherapeutics.

✓Plant-derived compounds offer promising disease-modifying strategies for CNS disorders.

Introduction

Neurological disorders, including Alzheimer's disease (AD), Parkinson's disease (PD), stroke, traumatic brain injury (TBI), epilepsy and other neurodegenerative conditions, represent one of the leading causes of disability, cognitive impairment and mortality worldwide. These disorders are characterized by progressive neuronal loss, impaired synaptic transmission, cognitive decline and irreversible motor

and sensory dysfunction.[1] Although substantial advances have been made in neuroscience and pharmacotherapy, currently available neuroprotective drugs mainly provide symptomatic relief and are largely ineffective in preventing or reversing disease progression. Consequently, there is increasing interest in identifying multi-target therapeutic agents capable of preserving neuronal function and delaying neurodegeneration.[2] The pathophysiology of neurological disorders is complex and multifactorial, involving interconnected molecular and cellular mechanisms. Excessive production of reactive oxygen species (ROS) and oxidative stress, mitochondrial dysfunction, chronic neuroinflammation, glutamate-mediated excitotoxicity, calcium dysregulation, protein misfolding and aggregation, apoptosis and impaired neurogenesis collectively contribute to progressive neuronal damage.[3] In Alzheimer's disease, extracellular amyloid-β plaque deposition and intracellular hyperphosphorylated tau accumulation disrupt neuronal integrity and synaptic communication, whereas Parkinson's disease is characterized by degeneration of dopaminergic neurons and α-synuclein aggregation. Similarly, ischemic stroke and traumatic brain injury trigger inflammatory cascades, oxidative damage and neuronal apoptosis, further exacerbating neurological dysfunction. These overlapping pathogenic mechanisms highlight the need for therapeutic approaches capable of simultaneously targeting multiple signaling pathways.[4] Medicinal plants have been utilized for centuries in Ayurveda, Siddha, Unani and indigenous tribal medicine to enhance memory, improve cognitive function and manage neurological disorders. Modern pharmacological investigations have confirmed that numerous plant-derived phytochemicals, including flavonoids, polyphenols, alkaloids, terpenoids, saponins, lignans and phenolic acids, possess potent antioxidant, anti-inflammatory, anti-apoptotic and neurodegenerative activities. These bioactive compounds modulate key neuroprotective signaling pathways, including Nrf2/ARE, NF-κB, PI3K/Akt, MAPK, BDNF/TrkB, SIRT1 and AMPK**,** thereby reducing oxidative stress, suppressing neuroinflammation, preserving mitochondrial integrity, enhancing synaptic plasticity, promoting neuronal regeneration and improving cognitive performance. Furthermore, several phytochemicals inhibit acetylcholinesterase activity, attenuate β-amyloid and α-synuclein aggregation and enhance endogenous antioxidant defense systems, making them promising candidates for the development of disease-modifying neurotherapeutics.[5] India is recognized as one of the world's richest reservoirs of medicinal plant biodiversity and Chhattisgarh, often referred to as the "Herbal State of India," possesses extensive forest resources and a rich ethnomedicinal heritage preserved by tribal communities such as the Gond, Baiga, Halba, Kanwar, Maria and Muria.[6] These communities traditionally employ numerous medicinal plants for memory enhancement, epilepsy, anxiety, insomnia and age-related neurological disorders. Several species abundantly distributed in the forests of Bastar, Kanker, Dantewada, Surguja, Koriya, Kabirdham and Bilaspur-including *Bacopa monnieri* (Brahmi), *Centella asiatica* (Mandukaparni), *Withania somnifera* (Ashwagandha), *Curcuma longa* (Turmeric), *Mucuna pruriens* (Kaunch), *Tinospora cordifolia* (Guduchi), *Convolvulus pluricaulis* (Shankhpushpi), *Celastrus paniculatus* (Jyotishmati), *Acorus calamus* (Vacha), *Ocimum tenuiflorum* (Tulsi), *Terminalia chebula* (Haritaki), *Terminalia bellirica* (Bibhitaki), *Phyllanthus emblica* (Amla), *Asparagus racemosus* (Shatavari) and *Azadirachta indica* (Neem)-have demonstrated significant neuroprotective effects through antioxidant, anti-inflammatory, cholinesterase inhibitory, anti-apoptotic and neurorestorative mechanisms in experimental studies.[7] Recent advances in molecular pharmacology, nanotechnology, artificial intelligence and systems biology have accelerated the scientific validation of medicinal plants by identifying their molecular targets, improving phytochemical standardization and enhancing bioavailability through novel drug delivery systems.[8] Integrating traditional ethnopharmacological knowledge with modern biomedical research provides a promising strategy for discovering safe, effective, and multi-target neuroprotective agents. Therefore, this review comprehensively summarizes the phytochemical constituents, molecular mechanisms, pharmacological evidence and therapeutic potential of medicinal plants, with particular emphasis on important medicinal species of Chhattisgarh, for the prevention and management of neurological disorders.[9] Figure 1 illustrates the general mechanism by which medicinal plant extracts protect neurons from neurotoxic injury. Through antioxidant, anti-inflammatory and anti-apoptotic actions, these phytochemicals reduce neuronal damage and maintain neuronal survival and synaptic function.

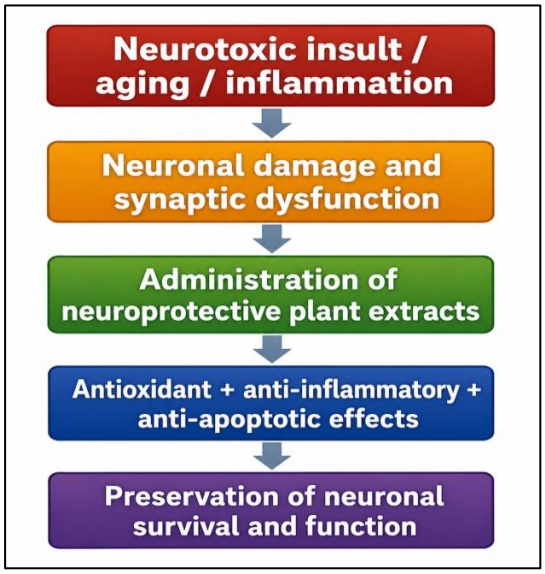


Figure 1: Neuroprotective mechanism of medicinal plant extracts against neuronal damage

(Schematic representation of the neuroprotective mechanism of medicinal plant extracts. Neurotoxic insults, aging and inflammation induce neuronal damage and synaptic dysfunction. Administration of neuroprotective plant extracts exerts antioxidant, anti-inflammatory and anti-apoptotic effects, ultimately preserving neuronal survival and functional integrity.)

Mechanisms of neuronal survival modulation

Medicinal plant neuroprotectants exert pharmacological effects through multiple molecular mechanisms that promote neuronal survival, reduce neurodegeneration and maintain central nervous system function. Figure 2 summarizes the major classes of plant-derived phytochemicals and their neuroprotective mechanisms. By reducing oxidative stress, improving mitochondrial function, preserving membrane integrity, regulating neurotransmission and activating neurotrophic signaling, these phytochemicals collectively support neuronal survival and brain health.

Table 1: Mechanisms of neuronal survival modulation by medicinal plant phytochemicals

Phytochemical class	Mechanisms of neuronal survival modulation	ReF.
Flavonoids	Scavenge free radicals, reduce oxidative stress and enhance synaptic plasticity.	10
Alkaloids	Regulate neurotransmitter balance and inhibit excitotoxic neuronal damage.	11
Terpenoids	Protect mitochondrial function and suppress neuroinflammatory responses.	12
Phenolic Acids	Inhibit lipid peroxidation, stabilize neuronal membranes and reduce oxidative injury.	13
Glycosides	Enhance neurotrophic signaling, promote neuronal survival and support neurogenesis.	14

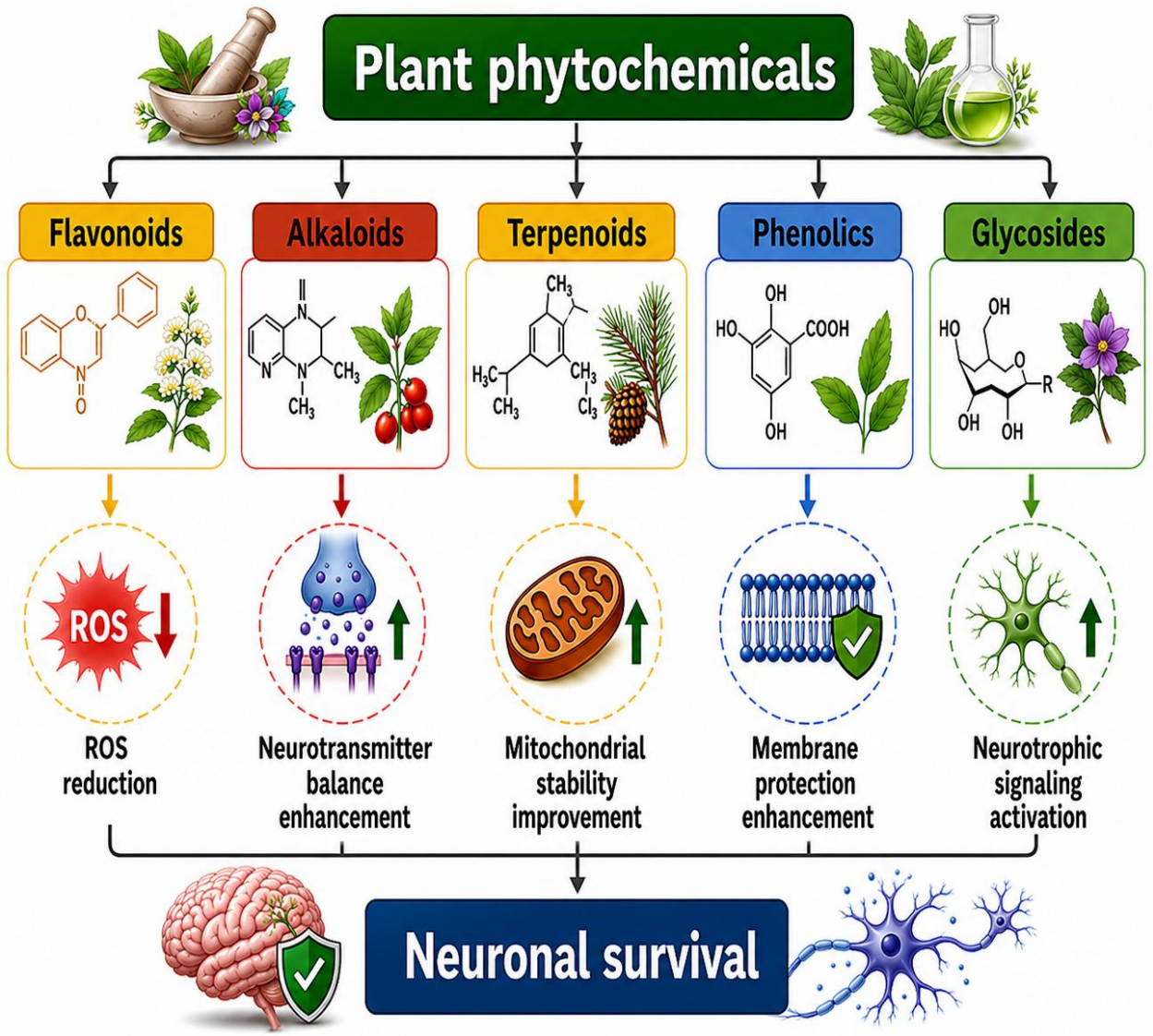


Figure 2: Major classes of neuroprotective plant phytochemicals and their mechanisms of action

(Schematic illustration of the major classes of neuroprotective plant phytochemicals and their principal biological actions. Flavonoids reduce reactive oxygen species (ROS), alkaloids enhance neurotransmitter balance, terpenoids improve mitochondrial stability, phenolics protect neuronal membranes and glycosides activate neurotrophic signaling. Together, these complementary mechanisms promote neuronal survival and maintain neural function.)

Table 2: Medicinal plants with neuroprotective activity

Plant name	Family	Part used	Extraction method	Major assays	Phytochemical	Ref.
Acorus calamus	Acoraceae	Rhizome	Methanolic	Memory enhancement test	β-asarone	15
Allium sativum	Amaryllidaceae	Bulb	Hydroalcoholic	Neurotoxicity protection assay	Allicin	16
Aloe vera	Asphodelaceae	Leaves	Aqueous	Oxidative stress neuronal model	Aloin	17
Andrographis paniculata	Acanthaceae	Aerial parts	Methanolic	Neuroinflammation assay	Andrographolide	18
Bacopa monnieri	Plantaginaceae	Whole plant	Hydroalcoholic	Morris water maze test	Bacosides	19
Camellia sinensis	Theaceae	Leaves	Polyphenol extract	Neuronal antioxidant assay	Catechins	20
Centella asiatica	Apiaceae	Leaves	Ethanolic	Cognitive function test	Asiaticoside	21
Cinnamomum verum	Lauraceae	Bark	Essential oil	Neurobehavioral assay	Cinnamaldehyde	22
Clitoria ternatea	Fabaceae	Roots	Methanolic	Memory retention study	Triterpenoids	23
Convolvuluspluricaulis	Convolvulaceae	Whole plant	Aqueous	Learning performance test	Alkaloids	24
Curcuma longa	Zingiberaceae	Rhizome	Ethanolic	Neurodegeneration inhibition	Curcumin	25
Eclipta alba	Asteraceae	Leaves	Methanolic	Neuroprotective screening	Wedelolactone	26
Emblica officinalis	Phyllanthaceae	Fruits	Aqueous	Antioxidant neuronal assay	Vitamin C	27
Ginkgo biloba	Ginkgoaceae	Leaves	Standardized extract	EEG cognitive analysis	Ginkgolides	28
Glycyrrhiza glabra	Fabaceae	Roots	Hydroalcoholic	Neuroinflammatory model	Glycyrrhizin	29
Hypericum perforatum	Hypericaceae	Aerial parts	Methanolic	Neurotransmitter modulation assay	Hypericin	30
Lavandula angustifolia	Lamiaceae	Flowers	Essential oil	Neurobehavioral sedation test	Linalool	31
Melissa officinalis	Lamiaceae	Leaves	Hydroalcoholic	GABA modulation assay	Rosmarinic acid	32
Moringa oleifera	Moringaceae	Leaves	Ethanolic	Cognitive impairment test	Quercetin	33
Nelumbo nucifera	Nelumbonaceae	Seeds	Methanolic	Neuroprotective assay	Neferine	34
Panax ginseng	Araliaceae	Roots	Standardized extract	Neurotrophic activity test	Ginsenosides	35
Phyllanthus niruri	Phyllanthaceae	Whole plant	Aqueous	Oxidative neuronal model	Phyllanthin	36
Tinospora cordifolia	Menispermaceae	Stem	Methanolic	Neuroimmune modulation test	Tinosporaside	37
Withania somnifera	Solanaceae	Roots	Hydroalcoholic	Neuroregeneration assay	Withanolides	38
Zingiber officinale	Zingiberaceae	Rhizome	Ethanolic	Neuroinflammation inhibition	Gingerols	39

Discussion

The systematic evidence suggests that medicinal plants provide neuroprotection through multifactorial molecular mechanisms. Antioxidant phytochemicals such as flavonoids and phenolic acids reduce oxidative stress and prevent lipid peroxidation, thereby preserving neuronal membrane integrity. Anti-inflammatory compounds including terpenoids and alkaloids suppress microglial activation and pro-inflammatory cytokine release, mitigating neuronal injury. Several plants such as *Bacopa monnieri*, *Ginkgo biloba* and *Withania somnifera* demonstrate cognitive enhancement and neurodegenerative potential in experimental models. Modulation of neurotransmitter systems, particularly cholinergic and GABAergic pathways, contributes to improved synaptic transmission and behavioral outcomes. Although herbal neuroprotective agents are generally well tolerated, excessive doses or prolonged use may lead to gastrointestinal disturbances or herb-drug interactions. Standardization of extracts and clinical validation are essential for therapeutic application.

Conclusion

Medicinal plants represent valuable sources of neuroprotective agents capable of mitigating neuronal injury through antioxidant defense, anti-inflammatory modulation, mitochondrial stabilization and enhancement of neurotrophic signaling. Phytochemicals such as flavonoids, alkaloids, terpenoids, phenolics and glycosides play central roles in neuronal survival mechanisms. Preclinical evidence strongly supports neurotherapeutic potential, whereas clinical data remain limited and heterogeneous. Future research should focus on phytochemical standardization, pharmacokinetic evaluation, long-term safety assessment and large randomized clinical trials. Integration of traditional herbal knowledge with modern neuroscience may facilitate development of effective plant-derived neuroprotective therapeutics.

Ethics approval and consent to participate: This manuscript is a narrative review and does not involve original research involving human participants, animals, or identifiable human data. Consequently, ethical approval and informed consent were not required.

Clinical Trial No: This manuscript is a review article and does not report the results of a clinical trial. Therefore, clinical trial registration and registration numbers are not applicable.

Consent for publication: This manuscript is a review article and does not report the results of a clinical trial. Therefore, clinical trial registration and registration numbers are not applicable.

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Authorship contribution statement

Kishan Lal Bharti: Conceptualization, review and editing of the manuscript.

Ashish Kumar: Literature review, data collection, manuscript review and editing.

Shiv Kumar Bhardwaj: Original drafting of the manuscript

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