

Stereospermum Suaveolens DC. : Phytopharmacology and Future Perspectives in Neurodegenerative Disorders

Thodapu kavya¹, S.Amala², G.vasavi³, Baratam Sandhya Rani⁴, chandi vishala⁵, Kunda Daniel Raju¹, Baratam Harshitha¹, Dharmasoth Rama Devi^{6*}

¹Department of Pharmacology, Vignan Institute of pharmaceutical Technology, Duvvada, Visakhapatnam, Andhra Pradesh, India 530049

²Department of Pharmacology, Aditya College of pharmacy (A), Surampalem, East Godavari, Kakinada,

³JNTU-GV College of Pharmaceutical sciences, Andhra Pradesh, India 533437

⁴Department of Chemistry, Raghu College of pharmacy, Visakhapatnam District, Andhra Pradesh, India 531162

⁵Department of pharmacology, Srinivasa Rao College of pharmacy, P.M.palem, Visakhapatnam, Andhra Pradesh 530041

⁶Department of Pharmacognosy, Vignan Institute of pharmaceutical Technology, Duvvada, Visakhapatnam, Andhra Pradesh, India 530049

Author of correspondence: ramajoy90@gmail.com

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ABSTRACT

With growing aging populations, neurodegenerative disorders (NDDs) such as Parkinson's disease, Alzheimer's disease, Huntington's disease, amyotrophic lateral sclerosis, and cerebral ischemic injury are a significant burden on the world's health. There are few treatments to stop the degeneration of neurons, and treatment is mostly symptomatic. Thus, plants with multitarget neuroprotective properties have become prominent of interest. *Stereospermum suaveolens* DC. Patala (family Bignoniaceae), is an important medicinal tree and used in Ayurvedic medicines for inflammatory disorders, fever, pain, epilepsy and brain related disorders. Recent pharmacological studies have shown antioxidant, anti-inflammatory, antiapoptotic, and neuroprotective properties of *S. suaveolens*, which indicate its therapeutic potential in neurodegenerative disorders. It is critically summarized botanical profile, ethnomedicinal usage, phytochemical composition, pharmacological action, mechanisms of neuroprotective effect, molecular targets, present limitations, and future perspectives. Recent evidence suggests that *S. suaveolens* can potentially be a valuable source of novel neurotherapeutics.

Keywords: *Stereospermum suaveolens*, neurodegeneration, phytochemistry, Parkinson's disease, Alzheimer's disease, neuroprotection, oxidative stress.

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INTRODUCTION

The characteristic features of neurodegenerative disorders are progressive deterioration of the nervous system functions and irreversible loss of neurons causing cognitive, motor and behavioral deficits. The main pathological mechanisms involve oxidative stress and mitochondrial dysfunction, neuroinflammation, excitotoxicity, protein aggregation and apoptosis¹⁻⁵.

Although significant progress has been made in synthetic therapies, current medications like levodopa, Donepezil, and memantine only offer symptomatic relief, and have

limited disease-modifying effects, 6-8. As a result, medicinal plants possessing multi-target pharmacology have been targets of interest for alternative therapeutic agents.

Stereospermum suaveolens DC. of family Bignoniaceae is one among the 10 roots of Dashamoola in Ayurveda and is traditionally used for fever, inflammation, wounds, respiratory disorders and neurological disorders. In recent experimental research, the neuroprotective property was proven in certain models of Parkinson's disease and cerebral ischemia^{9,10}.

BOTANICAL PROFILE

Table 1. Botanical classification of *Stereospermum suaveolens*

Parameter	Details
Kingdom	Plantae
Division	Magnoliophyta

*Author for Correspondence: ramajoy90@gmail.com

Class	Magnoliopsida
Order	Lamiales
Family	Bignoniaceae
Genus	<i>Stereospermum</i>
Species	<i>Stereospermum suaveolens</i> DC.

Stereospermum suaveolens is a medium to large sized deciduous medicinal tree which is widely distributed in the tropical and sub-tropical regions of the Indian Subcontinent and Southeast Asia, such as India, Sri Lanka, Nepal, Bangladesh and neighbouring Southeast Asian countries. Adapts to a wide range of ecological conditions; it is common in moist deciduous forests, riverbanks, plains and hilly areas. The tree grows to 15-25 m tall, but can reach as much as 30 m under suitable conditions. Enlarged, straight, cylindrical trunk with gray to pale brown bark which is rough and fissured with age. The leaves are large, opposite, imparipinnately compound, made up of several ovate to lanceolate leaflets with a smooth margin. The tree is also attractive and fragrant, with tubular flowers of yellowish to pinkish-purple colour in terminal panicles during the flowering season; this accounts for the tree's ornamental and medicinal values. The fruits are long, slender, cylindrical capsules which can be quite long, and they have many flattened seeds for wind dispersal.

Various organs of the plant like roots, stem bark, leaves, flowers and sometimes fruits have been widely used in traditional medicine systems like the Ayurvedic, folk and indigenous healing systems. Of these, roots and bark are most common for the treatment of inflammatory conditions, fever, respiratory diseases, pain and metabolic disorders, and leaves and flowers are used for wound healing, antioxidant effects and as general tonics.

ETHNOMEDICINAL IMPORTANCE

Stereospermum suaveolens DC. or Patala is used extensively in traditional medicine in Ayurveda and indigenous medicine for treatment of fever, inflammation, pain, respiratory ailments, vomiting, diarrhoea, edema, liver disorders, wounds, blood related disorders, neurological disorders such as epilepsy and nervous debility. It is one of the important ingredient of classical Dashamoola formulation and mentioned in Ayurvedic books as Shothahara (anti-inflammatory), Jwarahara (antipyretic), Vedanasthapana (analgesic) and Rasayana (rejuvenative) properties. These include roots, bark, leaves, flowers, and fruits, with the leaves being used chiefly for treating hiccups and the fruits primarily for asthma; the roots and leaves for dyspepsia, loss of appetite, and piles; and the fruits and roots for general weakness, among other indications, thus highlighting its wide ethnopharmacological applications in systemic and nervous ailments¹³⁻¹⁶.

The phytochemical studies of *S. suaveolens* DC. have identified various secondary metabolites present in different plant parts such as roots, bark, leaves, flowers and heartwood that are bioactive. The roots are reported with lignans (cycloolivil), naphthoquinones (lapachol and

dehydro- α -lapachone), and phytosterols (β -sitosterol) which are attributed antioxidant, anti-inflammatory, and neuroprotective properties. The leaves are high in flavonoids glycosides including scutellarein derivatives, dinatin, dinatin-7-glucuronide and other polyphenolic constituents. Furthermore, the presence of other compounds such as quinones, phenolic acids, fatty acids, tannins, glycosides, and terpenoid compounds have been detected from various extracts of *S. suaveolens*. The sum of these phytoconstituents gives rise to its various pharmacological properties such as antioxidant, anti-inflammatory, cytoprotective and neuroprotective properties which are relevant to neurodegenerative disorders^{17,21}.

PHARMACOLOGICAL ACTIVITIES OF DIFFERENT PLANT PARTS OF STEREOSPERMUM SUAVEOLENS DC.

Various organs of *Stereospermum suaveolens* DC such as roots, bark, leaves, flowers, fruits and stem wood have been extensively explored for their pharmacologic properties. Based on the traditional use and modern experimental studies, the plant has been reported to have a wide variety of biological activities including antioxidant, anti-inflammatory, analgesic, antipyretic, hepatoprotective, antimicrobial, antidiabetic, immunomodulatory and neuroprotective activities.

Root

The roots of *S. suaveolens* are one of the most therapeutic parts and traditionally incorporated in classical Ayurvedic formulation Dashamoola. Methanolic and ethanolic root extract has exhibited strong antioxidant activity with its ability to reduce lipid peroxidation and increase endogenous antioxidant enzymes like super oxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH). The antioxidant activity is primarily believed to be due to lignans, flavonoids and quinone derivatives in the roots.²²

Root extracts have also been shown to have high neuroprotective activity in experimental Parkinsonism in 6-Hydroxydopamine (6-OHDA) induced rats. The treatment was found to be relevant in the treatment of neurodegenerative disorders due to its ability to significantly improve locomotor deficits, reduce oxidative damage and protect dopaminergic neurons.²³

Furthermore, the root extract showed cerebroprotective activity in global cerebral ischemia/reperfusion injury models through decreases in infarct volume as well as antioxidant and preservation of neuronal architecture.²⁴

In addition, the roots have demonstrated anti-inflammatory and analgesic effects in animal models by blocking paw

edema (caused by carrageenan) and acetic acid-induced writhing.²⁵

Stem Bark

The barks of *S. suaveolens* are traditionally used for treating fevers, inflammation, and gastrointestinal ailments. Pharmacological examinations showed that significant antipyretics and pyretics effects were obtained in the yeast induced pyrexia models; the extracts of the bark showed a significant reduction of the elevated body temperature similar to the standard drugs.²⁶

Methanolic bark extracts also exhibited anti-inflammatory properties by inhibiting inflammatory mediators such as prostaglandins and cytokines. The activity is thought to be due to polyphenols and tannins present in the bark.²⁷

Moreover, the antimicrobial activities of the bark extracts against Gram-positive and Gram-negative bacteria, and fungal pathogens were observed, justifying its traditional use in infectious diseases.²⁸

Leaves

The anti-inflammatory and antiarthritic properties of the leaf extracts of *S. suaveolens* have been found to be highly effective in experimental animal model. The leaf extract was very effective in significantly decreasing the edema and inflammatory cytokines and joint swelling in arthritis models. It is thought that flavonoids – specifically scutellarein derivatives – mediate these effects.²⁹

The antioxidant activity of the leaves is also high, as shown by DPPH radical scavenging, reducing power assay and inhibition of oxidative stress markers.³⁰

In addition, the extracts of the leaves have antimicrobial properties against the pathogenic microorganisms such as *Staphylococcus aureus*, *Escherichia coli* and *Candida albicans*.³¹

Flowers

Reportedly, the flowers of *S. suaveolens* are anti-inflammatory and have free radical scavenging properties due to the flavonoids and phenolic compounds found in them. Flowers have been also used in traditional medicine for respiratory disorders and fever in experimental studies, which have demonstrated their ability to inhibit oxidative stress markers and reduce inflammatory responses.³²

Fruits and Seeds

The fruits and seeds are rich in various secondary metabolites such as terpenoids and glycosides with antimicrobial and antioxidant properties. The extracts of the seeds have been found to be inhibitory against bacterial strains and can also help to provide systemic immunity.³³

Whole Plant Extract

S. suaveolens whole plant extract has been shown to have immunomodulatory effects, including the activation of macrophages and the regulation of immune responses. These extracts were also found to have hepatoprotective activity against liver toxicity that was induced by chemicals by reducing the level of liver enzymes and oxidative damage.³⁴

Furthermore, hydroalcoholic extracts demonstrated antidiabetic activity through decreasing blood glucose level and antioxidant defense in diabetic animal models.³⁵

Table. Pharmacological activities of different parts of *Stereospermum suaveolens*

Plant Part	Extract Used	Pharmacological Activity	Major Findings
Root	Methanol/Ethanol	Neuroprotective	Protection against Parkinsonism and cerebral ischemia
Root	Methanol	Antioxidant	Increased SOD, CAT, GSH
Root	Ethanolic	Analgesic, Anti-inflammatory	Reduced pain and edema
Bark	Methanol	Antipyretic	Reduced fever
Bark	Methanol	Antimicrobial	Activity against bacteria and fungi
Leaves	Hydroalcoholic	Anti-inflammatory	Reduced cytokines and edema
Leaves	Methanol	Antioxidant	Free radical scavenging
Flowers	Ethanolic	Anti-inflammatory	Reduced oxidative stress
Fruits/Seeds	Methanol	Antimicrobial	Inhibited microbial growth
Whole Plant	Hydroalcoholic	Hepatoprotective, Antidiabetic	Organ protection and glucose regulation

CHALLENGES AND LIMITATIONS

Although there are some promising pharmacological evidences, the therapeutic development of *Stereospermum suaveolens* DC. for neurodegeneration diseases is challenged by various factors. A significant drawback is the absence of detailed phytochemical standardization, which may result in different amounts of active ingredients from different geographical locations and extraction techniques. To assure reproducibility and quality control, however, advanced metabolomic profiling and analytical validation are required.^{36,37}

One challenge is the lack of knowledge of the exact molecular mechanisms involved in its neuroprotective effects. Initial studies indicate antioxidant, anti-inflammatory and antiapoptotic properties, but in-depth target-based research, employing systems pharmacology and molecular interaction studies are still lacking.

Many phytoconstituents are poorly bioavailable, have very low aqueous solubility and are unclear on how they penetrate the blood–brain barrier, which will further limit their clinical translation. These pharmacokinetic limitations could be overcome by new drug delivery systems, such as those involving the use of nanoparticles.^{40, 41}

Moreover, most studies available focus on in vitro experiments or animal studies, and there are few long-term studies or pharmacokinetic data or clinical trials in humans. Comments on the future development of *Stereospermum suaveolens* as a potential phytotherapeutic agent in the treatment of Parkinson's Disease and Alzheimer's Disease that aim to overcome these limitations are necessary.

FUTURE PERSPECTIVES

Stereospermum suaveolens DC. has shown a potential antioxidant, anti-inflammatory, neuroprotective and cytoprotective action in preclinical studies, but the therapeutic effects of this plant in neurodegenerative diseases are understudied. Future studies should focus on the isolation, purification and structure elucidation of individual neuroactive phytoconstituents like lignans, flavonoids, naphthoquinones, iridoid derivatives for the identification of lead compounds responsible for their neuroprotective activity. Phytochemical standardization and batch to batch quality control should be done using advanced analytical platforms such as HPLC, LC–MS/MS, GC/MS, NMR, metabolomics, and chemometric profiling.^{44–46}

Mechanistic studies should include elucidating the molecular pathways involved in neuroprotection, specifically the pathways that mediate oxidative stress, the Nrf2/ARE pathway; pathways that mediate inflammation, the NF- κ B pathway; pathways that mediate mitochondrial apoptosis, autophagy pathways; pathways that mediate protein aggregation such as α -synuclein and amyloid- β ; and pathways that modulate neurotransmitters, including monoamine oxidases (MAO); acetylcholinesterase

(AChE). Multitarget interactions of phytoconstituents can be explored by network pharmacology, molecular docking, molecular dynamics simulations and systems biology approaches to boost mechanism-based drug discovery.^{47–50}

In order to establish efficacy in several different neurodegenerative disease models, further preclinical study in disease-specific models of Parkinson's disease, Alzheimer's disease, Huntington's disease, amyotrophic lateral sclerosis and cerebral ischemia is required. Additionally, blood–brain barrier permeability, pharmacokinetics, pharmacodynamics, long-term safety and toxicity profiling are required for translational development. The delivery system of nanotechnology, like phytosomes, polymeric nanoparticles, liposomes and nanoemulsions, can be useful for brain targeting and increase the bioavailability of poorly soluble phytoconstituents^{51,52}.

The therapeutic potential of *S. suaveolens* continues to grow with the possibilities of artificial intelligence, machine learning-based bioactivity prediction, omics-based biomarker discovery, and personalized phytomedicine strategies. Conclusively, well-designed clinical trials with standardized extracts or isolated bioactive compounds should be performed to prove its therapeutic relevance and safety in human neurodegenerative disorders. Therefore, with its high level of medicinal potential, *Stereospermum suaveolens* could be a promising plant for the future development of drugs for complex neurodegenerative diseases.^{53,54}

CONCLUSION

Stereospermum suaveolens DC. is a promising medicinal plant with tremendous neurotherapeutic potential. With an abundance of phytochemicals and multiple targets for its pharmacological activity, such as antioxidant, anti-inflammatory, mitochondrial protective and antiapoptotic properties, it is an ideal candidate for use in neurodegenerative disorders. Its therapeutic significance is further confirmed by experimental evidence in models of cerebral ischemia and Parkinson's disease. Further research with standardized extracts, molecular characterization and clinical validation is, however, necessary for therapeutic application.

CONFLICT OF INTEREST: Authors declare no conflict of interest

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