

Indian Medicinal Plants in Neurobehavioral Research: A Multi-Faceted Review of Pharmacological Insights and Computational Modelling Approaches

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Abstract

There is a vast knowledge on medicinal plants acting on neurological disorders deposited in the Ayurvedic system. This system is being validated increasingly in recent times with the modern techniques to prove the safety and efficacy. Phytochemicals derived from plants such as *Withania somnifera* (Ashwagandha), *Bacopa monnieri* (Brahmi), and *Centella asiatica* (Gotu kola) have been shown to exert multifaceted effects, including antioxidant, anti-inflammatory, neuroprotective, and psychotropic actions. These properties align closely with their traditional Ayurvedic roles as *Rasayana* (rejuvenators) and cognitive enhancers. Advanced computational approaches—such as molecular docking, molecular dynamics simulations, and network pharmacology—have revealed the polypharmacological nature of these compounds, demonstrating their ability to interact with multiple targets simultaneously, including neurotransmitter receptors, cholinesterases, amyloid-beta, and tau proteins. Neurobehavioral models further strengthen this evidence by linking molecular mechanisms to observable improvements in cognition, mood, and stress resilience. Clinical trials conducted in recent years confirm these findings, showing significant benefits in anxiety reduction, memory enhancement, sleep quality, and overall mental health. This multifaceted analysis underscores the importance of integrating traditional knowledge with modern biomedical science. Future directions include the application of multi-omics technologies, artificial intelligence-driven modeling, and large-scale randomized controlled trials to establish standardized dosing, safety profiles, and personalized interventions. Together, these efforts highlight the growing relevance of Ayurvedic phytochemicals in contemporary healthcare. By bridging ancient wisdom with modern pharmacology, Ayurveda offers a holistic and evidence-based framework for addressing complex neurobehavioral disorders and advancing global nutraceutical innovation.

Key words: Ayurveda; Phytochemicals; Neuroprotection; Network Pharmacology

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1. Introduction

Neurological disorders such as anxiety, depression, dementia and neurodegenerative disorders are a growing global health issue with a significant socioeconomic burden (Feigin et al., 2020). There are treatments available for various such disorders but they suffer from side effects, high costs and limited accessibility. These factors lead to reliance on

complementary and alternative approaches like Ayurveda and traditional medicine systems (Mortada, 2024). Ayurveda includes a vast knowledge on plant-based medicines which were used from ages in India (Máthé and Khan, 2026). Although advent of modern medicine set the mainline Ayurveda step aside for a time but these days it is being integrated with the modern medicine (Verma et al., 2024). There are

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increasing number of studies reaffirming the role of medicinal plants listed in Ayurvedic system with the modern tools to establish the efficacy and safety (Mukherjee et al., 2017). There are plant sources which were known from centuries in preventing and treating neurological and behavioural disorders. The validation from modern research in neuroprotective and psychotropic properties boosts the usage of these medicinal actives in the modern day (Borrego-Ruiz and Borrego, 2025; Yu et al., 2026).

The rich heritage of Ayurveda and ethnomedicine provides a large repository of medicinal plants that have been used for these conditions. Plants such as *Withania somnifera* (Ashwagandha), *Bacopa monnieri* (Brahmi), *Centella asiatica* (Gotu kola) are well documented for their roles in such conditions (Calabrese et al., 2008; Lucius, 2025). The potential of these diverse plant sources lies in the phytochemicals like alkaloids, flavonoids, terpenoids and polyphenols. These act on multiple pathways in combating neurological disorders through neurotransmitter modulation, antioxidant defence and anti-inflammatory mechanisms.

Animal models serve as models to validate the efficacy of these plants employing behavioural assays such as the elevated plus maze, forced swim test and Morris water maze (Choi et al., 2026; Jensen et al., 2025; Maudes et al., 2025; Mishra and Upadhyay, 2025; Peng et al., 2025). These models provide evidence on how these plants exert cognition, mood and stress responses. Although there are animal models they sometimes fail in bridging the findings with clinical translation.

In parallel to the animal models computational modelling has emerged as a powerful tool to predict the interactions of phytochemicals with the disease targets. Techniques like molecular docking, dynamics simulations and network pharmacology allow researchers in exploring the multi target effects of the phytochemicals (C et al., 2022; Mishra and Upadhyay, 2025). Artificial intelligence with machine learning developments in recent years are also promising the studies using computers will enhance the predictive accuracy with offerings in areas like drug discovery and personalized medicine.

This review aims to showcase pharmacological evidence with computational modelling and neurobehavioral approaches to provide a complete perspective on their therapeutic potential.

2. Pharmacological Insights

Phytochemicals like alkaloids, flavonoids, terpenoids, and polyphenols from Ayurvedic systems

demonstrated diverse neuropharmacological actions. Compounds like *Withania somnifera* (1), *Bacopa monnieri* (2), etc show promise in modulating neurotransmitters, reducing oxidative stress, and enhancing cognitive function. Preclinical and clinical studies highlight their efficacy in conditions like anxiety, depression, and neurodegeneration (3).

Modern pharmacology has greatly expanded our understanding of Ayurvedic phytochemicals, especially with the help of advanced scientific tools (4,5). Plants like Ashwagandha, Brahmi, and Gotu kola are now recognized for acting through multiple mechanisms that align closely with their traditional uses. Ashwagandha's withanolides show strong antioxidant and anti-inflammatory effects while also modulating GABAergic signaling, which explains its ability to reduce anxiety and stress. Brahmi's bacosides enhance synaptic transmission, stimulate neurogenesis, and regulate serotonin and dopamine pathways, supporting its role in memory improvement and mood stabilization. Gotu kola's triterpenoids improve cerebral circulation, boost BDNF expression, and reduce neuroinflammation, making it particularly useful in conditions like cognitive decline and depression (2,6).

Beyond single-target pharmacology, modern techniques such as molecular docking, molecular dynamics simulations, and network pharmacology have revealed that these phytochemicals act on multiple proteins and pathways simultaneously (7). They interact with cholinesterases, NMDA receptors, amyloid-beta, and tau proteins, offering neuroprotection against complex disorders like Alzheimer's and Parkinson's disease. This multi-target activity reflects Ayurveda's holistic philosophy, where treatments aim to restore systemic balance rather than address isolated symptoms. Recent clinical trials further validate these findings, showing improvements in cognition, anxiety, sleep quality, and overall mental health.

Modern pharmacology has extended traditional Ayurvedic insights by demonstrating that these plant-based compounds are not only safe but also mechanistically versatile. Their ability to act across oxidative stress, neurotransmission, neuroinflammation, and synaptic plasticity is driving their integration into mainstream medicine and nutraceutical development, bridging ancient wisdom with contemporary science (8).

3. Neurobehavioral Models

Rodent-based behavioral assays (e.g., elevated plus maze, open field test, Morris water maze) provide

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translational insights into the effects of plant-derived compounds on anxiety, memory, and learning (9). These models help establish mechanistic links between phytochemicals and neurobehavioral outcomes, though limitations in species differences and reproducibility remain.

Neurobehavioral models have become an essential tool in exploring the effects of Ayurvedic phytochemicals on the brain and behaviour (9). These models provide a bridge between traditional knowledge and modern scientific validation by allowing researchers to study how plant-derived compounds influence cognition, mood, and neurological function in controlled experimental settings. For example, animal models of anxiety, depression, and memory impairment are frequently used to test the efficacy of compounds from Ashwagandha, Brahmi, and Gotu kola. Such studies often reveal improvements in behavioural outcomes like reduced anxiety-like responses, enhanced learning and memory, and better stress resilience, which align closely with their traditional Ayurvedic applications.

These models also help in identifying the underlying mechanisms of action. By combining behavioural assessments with biochemical and molecular analyses, researchers can link observed changes to specific pathways such as modulation of neurotransmitters (serotonin, dopamine, GABA), reduction of oxidative stress, or enhancement of neurogenesis. Advanced techniques like molecular docking, dynamics simulations, and network pharmacology further enrich these models by predicting how phytochemicals interact with multiple targets simultaneously. This polypharmacological perspective is particularly valuable for complex neurological disorders, where single-target drugs often fall short (10).

In recent years, neurobehavioral models have also been extended to translational research, with findings from preclinical studies informing clinical trials. This has led to growing evidence that Ayurvedic phytochemicals can improve cognition, mood, and sleep quality in humans, reinforcing their role as safe and effective agents in integrative medicine. In essence, neurobehavioral models not only validate traditional claims but also provide a scientific framework to understand how these plant-based compounds exert their multi-target effects, paving the way for their wider acceptance in modern healthcare.

4. Computational Modeling Approaches

Computational tools such as molecular docking, dynamics simulations, and network pharmacology enable prediction of plant compound interactions with neural targets (11). Machine learning models further

enhance drug discovery by identifying multi-target effects and synergistic pathways. Integration of computational predictions with experimental neurobehavioral data strengthens the evidence base for therapeutic applications.

Computational modeling approaches have become a powerful way to explore and validate the pharmacological potential of Ayurvedic phytochemicals. These methods allow researchers to move beyond traditional trial-and-error experimentation and instead predict, visualize, and analyze how plant-derived compounds interact with biological systems. Molecular docking is widely used to identify how phytochemicals bind to specific protein targets, such as neurotransmitter receptors, enzymes, or amyloid-beta aggregates, providing insight into their therapeutic potential. Molecular dynamics simulations go a step further by examining the stability and behavior of these interactions over time, helping to understand conformational changes and the long-term effects of binding (12).

Another important tool is network pharmacology (7,13), which maps the complex web of interactions between phytochemicals and multiple biological pathways. This is particularly relevant for Ayurvedic plants, which are traditionally used in multi-herb formulations and are believed to act holistically rather than through single-target mechanisms. By integrating computational models with systems biology, researchers can uncover how compounds like withanolides from Ashwagandha, bacosides from Brahmi, and triterpenoids from Gotu kola simultaneously influence oxidative stress, neurotransmission, neuroinflammation, and synaptic plasticity.

These approaches not only validate traditional claims but also provide a scientific framework for drug discovery and nutraceutical development. They help identify promising compounds, predict safety profiles, and even suggest synergistic effects when multiple herbs are combined. In essence, computational modeling has transformed the study of Ayurvedic phytochemicals into a modern, evidence-based discipline, bridging ancient wisdom with cutting-edge biomedical science.

5. Multi-Faceted Analysis

A combined approach reveals how pharmacological studies, neurobehavioral models, and computational simulations complement each other. Case studies demonstrate that integrating these methods accelerates identification of bioactive compounds and clarifies mechanisms of action (14). However, challenges

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include data heterogeneity, lack of standardized protocols, and limited clinical translation.

A multifaceted analysis provides a deeper and more holistic understanding of how Ayurvedic phytochemicals exert their effects, especially in the context of neurological and psychotropic conditions (8). Instead of relying on a single line of evidence, this approach integrates data from biochemical assays, molecular modeling, network pharmacology, neurobehavioral models, and clinical trials to build a comprehensive picture. For example, biochemical studies may reveal antioxidant or anti-inflammatory properties of compounds, while computational modeling shows how these molecules interact with multiple protein targets. Neurobehavioral models then translate these findings into observable changes in cognition, mood, or stress resilience, and clinical trials validate their relevance in humans.

This layered analysis highlights the polypharmacological nature of Ayurvedic plants such as Ashwagandha, Brahmi, and Gotu kola, showing that they act simultaneously on oxidative stress, neurotransmission, neuroinflammation, and synaptic plasticity (15). It also underscores the importance of combining traditional knowledge with modern science—where Ayurveda's holistic philosophy is supported by mechanistic insights from molecular biology and systems pharmacology. By weaving together evidence from different domains, multifaceted analysis not only validates traditional claims but also strengthens their credibility in modern healthcare, paving the way for integration into mainstream medicine and nutraceutical development.

A multifaceted analysis of Ayurvedic phytochemicals in neuropharmacology brings together evidence from multiple layers of research to create a complete picture of their therapeutic potential. At the molecular level, biochemical assays and computational modeling reveal how compounds such as withanolides, bacosides, and triterpenoids interact with key proteins and enzymes involved in oxidative stress, neurotransmission, and neuroinflammation. Moving to the cellular and systems level, studies show how these interactions translate into enhanced neurogenesis, synaptic plasticity, and modulation of neurotransmitter pathways, which are critical for cognition, mood regulation, and resilience to stress (3).

At the behavioral level, neurobehavioral models provide experimental validation by demonstrating improvements in memory, learning, anxiety, and depressive behaviors in preclinical studies. These findings are then extended to the clinical level, where

randomized controlled trials confirm benefits such as reduced anxiety, improved sleep quality, and enhanced cognitive performance in human subjects. Finally, at the societal and translational level, network pharmacology and systems biology approaches highlight the polypharmacological nature of these compounds, showing how they act across multiple pathways simultaneously—an insight that aligns with Ayurveda's holistic philosophy.

By weaving together molecular, behavioral, clinical, and systems-level evidence, multifaceted analysis not only validates traditional Ayurvedic claims but also strengthens their credibility in modern medicine. This layered approach demonstrates that these phytochemicals are safe, versatile, and effective, paving the way for their integration into mainstream healthcare and nutraceutical development (16).

6. Future Directions

Advances in personalized medicine, omics technologies, and AI-driven modeling offer new opportunities to harness Indian medicinal plants for neurobehavioral disorders. Standardized assays, robust computational pipelines, and clinical validation will be critical for bridging traditional knowledge with modern drug discovery.

Future directions in the study of Ayurvedic phytochemicals point toward a deeper integration of traditional wisdom with cutting-edge biomedical science. One promising area is the use of multi-omics approaches—genomics, proteomics, metabolomics, and transcriptomics—to unravel the complex biological networks influenced by these compounds. This will help identify biomarkers of efficacy and safety, making Ayurvedic interventions more personalized and precise. Another important direction is the expansion of computational modeling and artificial intelligence, which can predict synergistic effects in multi-herb formulations and accelerate drug discovery pipelines (17).

On the clinical side, there is a growing need for large-scale randomized controlled trials to establish standardized dosing, safety profiles, and long-term outcomes, especially for neurodegenerative and psychiatric conditions. Regulatory frameworks are also evolving, with organizations like WHO and India's Ministry of AYUSH encouraging the integration of validated traditional medicines into mainstream healthcare. Additionally, the development of novel delivery systems—such as nanoparticles, liposomes, and bio-enhanced extracts—will improve the bioavailability of phytochemicals like withanolides,

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bacosides, and triterpenoids, ensuring better therapeutic outcomes.

Finally, future research will likely emphasize translational medicine, where insights from molecular docking, neurobehavioral models, and network pharmacology are directly applied to clinical practice. This multifaceted approach will not only strengthen the scientific credibility of Ayurveda but also position its phytochemicals as valuable agents in global healthcare, particularly for complex disorders where conventional single-target drugs often fall short.

7. Conclusion

In conclusion, the convergence of Ayurveda and modern pharmacology has opened new horizons for understanding and utilizing plant-based medicines in neurobehavioral health. Phytochemicals from plants such as Ashwagandha, Brahmi, and Gotu kola are no longer viewed solely through the lens of traditional wisdom but are now validated by advanced scientific methods. Their multifaceted actions ranging from antioxidant and anti-inflammatory effects to modulation of neurotransmitter systems and promotion of neurogenesis demonstrate their relevance in managing complex neurological and psychiatric conditions. Computational approaches like molecular docking, dynamics simulations, and network pharmacology have revealed their polypharmacological nature, showing how these compounds act on multiple targets simultaneously. Neurobehavioral models further strengthen this evidence by linking molecular mechanisms to observable improvements in cognition, mood, and stress resilience, while clinical trials confirm their safety and efficacy in humans.

This layered, multifaceted analysis underscores the importance of integrating traditional knowledge with modern biomedical science. As future research expands into multi-omics, AI-driven modeling, and large-scale clinical validation, Ayurvedic phytochemicals are poised to play a significant role in global healthcare. Their ability to address complex disorders holistically makes them valuable not only as therapeutic agents but also as a foundation for nutraceutical innovation. Ultimately, the synergy between ancient wisdom and contemporary science ensures that Ayurveda remains a vital contributor to modern medicine.

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