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REVIEW ARTICLE

Neuroprotective Herbal Remedies: Efficacy, Safety and Clinical Perspectives

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Abstract

Strategies to maintain the structure and function of neurons are known as neuroprotection, and they are crucial in the fight against neurodegenerative diseases such as multiple sclerosis, Parkinson's disease, and Alzheimer's. Herbal therapies such as *Ginkgo biloba*, curcumin, *Bacopa monnieri*, *ashwagandha*, and ginseng are well-known for their possible neuroprotective benefits. These herbs are all rich in bioactive components that have been shown to have neuroprotective properties. These include antioxidant activity, anti-inflammatory effects, and improved cerebral blood flow. There is clinical evidence to suggest their effectiveness in controlling symptoms of neurodegenerative disorders and enhancing cognitive function. But cautious thought must be given to safety issues and possible negative consequences, such as gastrointestinal issues and drug interactions. Subsequent studies ought to concentrate on determining and describing active ingredients, carrying out thorough clinical trials, evaluating long-term safety, and combining these medicines with contemporary medical procedures. The focus of further research should be on identifying and characterizing active compounds, conducting comprehensive clinical trials, assessing long-term safety, and integrating these medications with modern medical practices.

Major Findings: *Ginkgo biloba*, turmeric bacopa monnieri *ashwagandha* and ginseng shows neuroprotective benefits through anti oxidant, anti inflammatory effects and improved cognitive function. These herbs demonstrate potential in managing neurodegenerative diseases, but concerns like gastrointestinal issues, drug interactions and bleeding risks require careful considerations.

Keywords: Antioxidant Activity, Cognitive Function, Herbal Medicines, Neuroprotection, Neurodegenerative Diseases

1. Introduction

The term "neuroprotection" describes tactics and interventions meant to prevent harm or degeneration to the nervous system's structure and functionality. Research in this area is essential to the fight against neurodegenerative illnesses, which are typified by the progressive loss of neurons and their activities. These disorders include multiple sclerosis, Parkinson's disease, and Alzheimer's disease.

Numerous strategies are included in neuroprotection, such as dietary changes, lifestyle adjustments, and pharmaceutical therapies. Delaying the start and progression of neurological injury and improving the general health of the nervous system are the main objectives[1].

2. Mechanisms of Neuroprotection

The different bioactive components found in herbal remedies have led to their recognition for their potential neuroprotective qualities. This chapter offers a thorough review of popular herbal remedies that have been shown to have neuroprotective properties. These remedies include ginseng (*Panax ginseng*), *B. monnieri*, ashwagandha (*Withania somnifera*), *G. biloba*, and turmeric (*Curcuma longa*). The active ingredients, methods of action, and supporting data on the herb's neuroprotective properties are covered in each area (Table 1). All the photographic representation of the neuroprotectives are mentioned in Figure 1.

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2.1 *Ginkgo biloba*

Drawn from the leaves of the *Ginkgo* tree, *G. biloba* is one of the herbal supplements with the most science behind it, used to support neuroprotection and improve cognitive function. Its reputation is based on claims that it can enhance memory and cognitive function, especially in cases of age-related cognitive decline.

2.1.1 Active Components

Flavonoids and terpenoids, such as ginkgolides and bilobalide, are the main active ingredients in *G. biloba*. These substances are thought to have antioxidant and anti-inflammatory qualities, which aid in the neuroprotective effects (Table 1)[2].

2.1.2 Mechanisms of Action

2.1.2.1 Antioxidant Activity

The terpenoids and flavonoids in *G. biloba* help shield neurons from oxidative damage by reducing oxidative stress and neutralizing Reactive Oxygen Species (ROS)[3].

2.1.2.2 Anti-inflammatory Effects

The extract lessens neuroinflammation, a major contributing factor to neurodegenerative disorders, by inhibiting inflammatory mediators and cytokines[4].

2.1.2.3 Brain blood flow

G. biloba promotes overall cognitive performance by enhancing endothelial function and decreasing platelet aggregation, which improves blood flow in the brain[5].

2.1.3 Clinical Evidence

Ginkgo biloba has been shown in numerous clinical trials to enhance cognitive function in people with mild to moderate Alzheimer's disease and age-related cognitive decline. According to a meta analysis, *G. biloba* extract considerably enhanced senior patients daily life and cognitive functioning[6].

2.2 Turmeric (*Curcuma longa*)

The rhizome of *C. longa* is the source of turmeric, which is widely used as a spice and in traditional medicine. Curcumin, the primary active ingredient in turmeric, is responsible for many of the plant's health advantages, including neuroprotection.

2.2.1 Active Components

The main bioactive ingredient in turmeric, curcumin, gives it its yellow hue. Numerous biological actions are demonstrated by it, such as anti-inflammatory, antioxidant, and neuroprotective properties[7].

2.2.2 Mechanisms of Action

2.2.2.1 Antioxidant Activity

Curcumin protects neurons from oxidative stress by scavenging free radicals and raising the amounts of antioxidant enzymes including catalase and Superoxide Dismutase (SOD)[8]. Curcumin's anti-inflammatory effects include lowering neuroinflammation linked to neurodegenerative disorders by preventing the activation of NF-κB and other inflammatory pathways[9]. Amyloid beta reduction: Research has demonstrated that curcumin inhibits the development and aggregation of amyloid-beta plaques, a hallmark of Alzheimer's disease[10].

2.2.3 Clinical Evidence

Curcumin may help with cognitive performance and lessen the symptoms of neurodegenerative illnesses, according to clinical research. For instance, a randomized controlled study indicated that supplementing with curcumin enhanced memory and attention in healthy elderly individuals[11].

2.3 *Bacopa monnieri*

Brahmi or *B. monnieri*, is a traditional plant used in *Ayurvedic* medicine for its adaptogenic and cognitive-enhancing qualities. Its effects on memory and cognitive function are especially well-known.

2.3.1 Active Components

Bacosides, the active ingredients in *B. monnieri*, are thought to be in charge of the plant's neuroprotective properties. It has been demonstrated that bacosides promote cognitive performance and neuronal health[12].

2.3.2 Mechanisms of Action

2.3.2.1 Neurotrophic Effects

Bacopa monnieri promotes the expression of Nerve Growth Factor (NGF) and Brain-Derived Neurotrophic Factor (BDNF), two factors that assist the growth and survival of neurons[13].

B. monnieri demonstrates antioxidant activity, which lowers oxidative stress and shields neurons from harm[14].

2.3.2.2 Memory Enhancement

The herb enhances neuroplasticity and synaptic transmission, two factors crucial to learning and memory functions[15].

2.3.3 Clinical Evidence

Bacopa monnieri has been found to improve memory and cognitive performance. After 12 weeks of supplementation, *B. monnieri* was found to increase memory performance and cognitive function in a study involving healthy older volunteers[16].

2.4 Ashwagandha (*W. somnifera*)

Withania somnifera, often known as *ashwagandha*, is an adaptogenic plant that is used in traditional Indian medicine to improve general health and reduce stress. It is well recognized for having possible benefits on cognition and neuroprotection.

2.4.1 Active Components

Withanolides, the main active ingredients in *ashwagandha*, have a number of pharmacological benefits, such as stress relief and neuroprotection[17].

2.4.2 Mechanisms of Action

2.4.2.1 Antioxidant Activity

Research has demonstrated that the withanolides found in *ashwagandha* can lower oxidative stress and strengthen antioxidant defences, which in turn protects neural cells[18].

2.4.2.2 Anti-inflammatory Effects

By blocking pro-inflammatory cytokines, *ashwagandha* inhibits inflammatory pathways and helps lower neuroinflammation[19].

2.4.2.3 Stress Reduction

The herb enhances the body's stress response and lowers cortisol levels, which can have a good impact on mental and cognitive health[20].

2.4.3 Clinical Evidence

According to clinical investigations, taking supplements of *ashwagandha* can boost general wellbeing, lessen stress, and improve cognitive performance. One study found that taking *ashwagandha* extract significantly improved participant's cognitive function and reduced their stress levels[21].

2.5 Ginseng (*Panax ginseng*)

In traditional medicine, ginseng especially *P. ginseng* is a commonly used adaptogen with a lengthy history. It is praised for possible advantages to cognition and neuroprotection.

2.5.1 Active Components

Panax ginseng's main active ingredients are called ginsenosides. Numerous biological effects of these saponins, such as neuroprotection and cognitive improvement, have been demonstrated[22].

2.5.2 Mechanisms of Action

2.5.2.1 Antioxidant Activity

Ginsenosides reduce oxidative damage to neurons and scavenge Reactive Oxygen Species (ROS) to demonstrate their antioxidant qualities[23].

2.5.2.2 Neurotrophic Effects

Panax ginseng supports neuronal health and cognitive function by enhancing the expression of neurotrophic factors including BDNF and NGF[24].

2.5.2.3 Cognitive Enhancement

By regulating neurotransmitter systems and boosting brain activity, the herb enhances memory and cognitive function[25].

2.5.3 Clinical Evidence

The effects of *P. ginseng* on cognitive function have been supported by numerous investigations. For example, clinical research showing enhancements in mood and cognitive function in individuals taking *P. ginseng* supplements[26].

3. Safety and Side Effects of Herbal Neuroprotectives

Although the potential neuroprotective benefits of herbal medications are becoming more widely acknowledged, it is important to understand their safety profiles and potential side effects in order to

utilize them wisely. The safety and adverse effects of several popular herbal neuroprotectives, like as ginseng (*P. ginseng*), *G. biloba*, turmeric (*C. longa), B. monnieri,* and *ashwagandha* (*W. somnifera)*, are thoroughly reviewed in this chapter. Comprehending these facets is crucial for their secure and efficient implementation in medical practice.

3.1 *Ginkgo biloba*

3.1.1 Safety Profile

When used at authorized quantities, *G. biloba* is usually regarded as safe for the majority of individuals. However, because of possible interactions and adverse effects, its safety profile needs to be carefully considered.

3.1.2. Adverse Reactions

3.1.2.1. Gastrointestinal Problems

Nausea, diarrhea, and cramping in the stomach are examples of common gastrointestinal side effects. Most of the time, these effects are minor and fleeting[27].

3.1.2.2. Risk of Bleeding

Ginkgo biloba may make bleeding more likely, especially in people who are using anticoagulants or antiplatelet drugs. Ernst and Pittler's meta-analysis brought attention to the possibility of bleeding issues when using *G. biloba*, particularly at high dosages[28].

3.1.2.3. Allergic Reactions

In certain instances, allergic reactions have been documented, resulting in skin rashes and itching. Although uncommon, these reactions need to be watched[29].

3.1.2.4. Drug Interactions

The safety and effectiveness of some drugs, including as anticoagulants and antidepressants, may be impacted by *G. biloba* interactions. Ishihara *et al.*'s study covered important drug interactions and advised caution when taking *G. biloba* with other prescription drugs[30].

3.2 Turmeric (*C. longa*)

3.2.1 Safety Profile

Turmeric's major ingredient, curcumin, is generally well-tolerated and regarded as safe in moderation. On the other hand, negative effects may result with high dosages.

3.2.2 Side Effects

3.2.2.1. Gastrointestinal Distress

Abdominal discomfort, diarrhea, and nausea are among the gastrointestinal symptoms that high dosages of curcumin may produce. Certain people have experienced these effects, according to several studies, including those by Hewlings and Kalman[31].

3.2.2.2 Blood Thinning

Due to its anticoagulant qualities, curcumin may make bleeding more likely, especially in people on blood thinners. Panahi *et al.*'s analysis highlighted the need for vigilance in patients who are having surgery or on anticoagulants[32].

3.2.2.3 Skin Rashes or Hives

These are examples of allergic reactions to turmeric, albeit they are uncommon. It is advisable to keep an eye out for allergic reactions, especially in people who have a history of allergies[33].

3.2.2.4 Drug Interactions

Curcumin may interact with drugs that the liver metabolizes, thereby changing how effective such drugs are. This interaction is especially pertinent to medications that impact the activity of liver enzymes[34].

3.3 *B. Monnieri*

3.3.1 Safety Profile

Although *B. monnieri* is generally well-tolerated, it can have negative effects and interact with other drugs, just like any other herbal product.

3.3.2 Side Effects

3.3.2.1 Gastrointestinal Symptoms

Nausea, diarrhea, and cramping in the stomach are among the most typical gastrointestinal side effects of *B. monnieri*. These effects were mentioned in a research by Stough *et al.*, however they were often minor and fleeting[35].

3.3.2.2 Fatigue

Some people may feel drowsy or fatigued, which might interfere with day-to-day activities. Although less frequent, this side effect needs to be watched[36].

3.3.2.3 Thyroid Function

Although the effects of *B. monnieri* on thyroid hormone levels are not well-documented, they may have an

impact. *Bacopa* users with thyroid conditions should use it with caution and speak with their doctors[37].

3.3.2.4 Drug Interactions

B. monnieri may interact with drugs that influence the central nervous system, among other prescriptions. Morgan and Stevens study addressed the possibility of interactions and suggested close observation[38].

3.4 *Ashwagandha* (*W. somnifera*)

3.4.1 Safety Profile

Because of its adaptogenic properties, *ashwagandha* is frequently utilized, and when taken as prescribed, it is usually safe. But it's important to take into account any possible interactions and adverse effects.

3.4.2 Side Effects

3.4.2.1 Gastrointestinal Disturbances

Diarrhea, nausea, and discomfort in the abdomen are examples of common gastrointestinal side effects. These effects were generally moderate, according to research by Chandrasekhar *et al*[39].

3.4.2.2 Drowsiness

For certain people, *ashwagandha* may result in drowsiness or sedation. Higher dosages are more likely to have this effect, which could affect day-to-day functioning[40].

3.4.2.3 Thyroid Function

Ashwagandha may affect the amounts of thyroid hormone in susceptible people, which may result in hyperthyroid symptoms. Individuals with thyroid conditions should keep an eye on their thyroid function and speak with medical professionals[41].

3.4.2.4 Drug Interactions

Medication for diabetes, hypertension, and sedatives may interact with *ashwagandha*. These interactions were covered in a research by Rani *et al.*, which also recommended caution for anyone taking these drugs[42].

3.5 Ginseng (*P. ginseng*)

3.5.1 Safety Profile

Because of ginseng's cognitive and adaptogenic properties, it is popularly utilized; nonetheless, its safety profile and possible adverse effects should be taken into account.

3.5.2 Side Effects

3.5.2.1 Insomnia

Sleep difficulties or insomnia are frequently reported side effects of ginseng. This is especially noticeable in sensitive people or at large dosages. This impact was noted in a research by Kennedy *et al.* and may need changing the dosage[43]. Ginseng may result in gastrointestinal distress, including nausea, diarrhea, and upset stomach. The majority of these symptoms are moderate and under control[44].

3.5.2.2 Hormonal Effects

Ginseng may alter hormone-sensitive conditions and have estrogen-like effects. These possible consequences were mentioned in a review by Lee *et al.*, which advised caution in people with hormone-sensitive disorders[45].

3.5.2.3 Drug Interactions

Ginseng may interact with antihypertensives, anticoagulants, and antidiabetic medicines, among other prescriptions. In particular, the combination with anticoagulants may make bleeding more likely. Poon *et al.*'s work emphasized these relationships and suggested close observation[46].

4. Future Directions and Research Opportunities in Herbal Neuroprotection

Although the neuroprotective effects of herbal medications have been shown, there is still much that can be done to better understand the mechanisms, safety, and effectiveness of these treatments. This chapter examines potential avenues for future research and directions in the field of herbal neuroprotection, emphasizing areas that may result in advances in scientific knowledge and clinical applications.

Table 1. Herbs and their active constituents[2-46]

S. No.	Name of Herb	Scientific Name	Active Constituent
1	Maidenhair tree	*G. biloba*	Ginkgolides and Bilobalides
2	Turmeric	*C. longo*	Curcumin
3	*Brahmi*	*B. monnieri*	Bacosides
4	*Ashwagandha*	*W. somnifera*	Withanolides
5	Ginseng	*P. quinquefolius*	Ginsenosides

Herb	Name
	*G. biloba*
	Turmeric
	*B. monnieri*
	*Ashwagandha*
	Ginseng (*P. ginseng*)

Figure 1. Herbs used in neuroprotection.

5. Advances in Phytochemical Research

5.1 Identification of Active Compounds

Subsequent investigations ought to concentrate on identifying and characterizing the active ingredients in herbal neuroprotectives. New phytochemicals with potential neuroprotective benefits can be isolated and identified using methods including Nuclear Magnetic Resonance (NMR) spectroscopy, mass spectrometry, and high-throughput screening. These methods have been applied in recent research to find new chemicals in plants such as *B. monnieri* and *G. biloba*[47,48].

5.2 Understanding Mechanisms of Action

Research should concentrate on thorough mechanistic studies to comprehend how these compounds affect neuroinflammatory pathways, oxidative stress, and neurotrophic factors. For instance, current studies are examining how curcumin from turmeric modulates neuroinflammatory pathways and enhances neurogenesis[49].

6. Clinical Trials and Efficacy Studies

6.1 Design of Robust Clinical Trials

Large-scale, carefully planned Randomized Controlled Trials (RCTs) should be a part of future research to offer high-caliber proof of the effectiveness of herbal neuroprotectives. Small sample sizes and brief study durations are 2 methodological flaws that plague many of the clinical studies conducted nowadays. It will be essential to have better trial designs with longer follow-up times and standardized outcome measures[50].

6.2 Comparative Effectiveness Research

Comparative efficiency Studies that contrast herbal neuroprotectives with traditional therapies or a placebo can reveal important details about the relative safety and effectiveness of each. Research ought to compare the effectiveness of these herbal remedies with well-known neuroprotective medications, as those prescribed for Parkinson's or Alzheimer's[51].

6.3 Safety and Toxicology Studies

6.3.1 Long-term Safety Assessments

Studies on the long-term safety of herbal neuroprotectives are necessary to assess their long-term use. Finding possible long-term side effects and combinations with other drugs should be the main focus of research. Extensive research on the safety characteristics of herbs such as *ashwagandha* and ginseng can yield valuable information on their long-term usage[52].

6.3.2 Toxicology Profiling

To evaluate the possibility of toxicity at various dosages and usage durations, toxicology studies ought to be carried out. Thorough toxicological analyses, incorporating both *in vitro* and *in vivo* models, can aid in determining any possible hazards linked to elevated dosages or extended utilization of herbal neuroprotectives[53].

7. Integration with Modern Medicine

7.1 Synergistic Approaches

Research on the potential benefits of combining herbal neuroprotectives with traditional therapies is a promising field. Research ought to look into how these combos can improve treatment results and lessen adverse effects. For instance, curcumin and traditional anti-inflammatory medications together may increase treatment effectiveness in neurodegenerative diseases[54].

7.2 Personalized Medicine

The usage of herbal neuroprotectives could be optimized by personalized medicine techniques, taking into account each person's unique genetic profile, lifestyle, and medical problems. Studying biomarkers and pharmacogenomics can assist customize herbal remedies to each person's needs, increasing their safety and efficacy[55].

7.3 Standardization and Quality Control

7.3.1 Development of Standards

To ensure consistency and dependability, consistent processes must be established for the preparation and quality control of herbal neuroprotectives. The development and validation of standards for the identification, measurement, and evaluation of the quality of herbal products ought to be the main emphasis of research[56].

7.3.2 Authentication Techniques

Sophisticated methods for herbal material identification and verification can guard against adulteration and

guarantee product purity. To confirm the authenticity of herbal neuroprotectives, methods including DNA barcoding, chromatography, and spectroscopy should be further developed and use[57].

7.4 Regulatory and Policy Frameworks

7.4.1 Harmonization of Regulations

Subsequent investigations ought to support the unification of regional regulatory frameworks for herbal neuroprotectives. As part of this, international standards for quality, safety, and efficacy are being established[58]. This will help ensure that herbal remedies are accessible to people worldwide.

7.4.2 Development of Policy

Innovation can be encouraged and treatment options can be enhanced by creating regulations that support research and development in herbal medicine. Research funding, commercial collaboration incentives, and expedited clearance procedures for herbal products that show promise are examples of supportive policies[59].

8. Awareness and Education

8.1 Education of Healthcare Professionals

It is essential to inform medical professionals about the advantages and restrictions of herbal neuroprotectives in order to successfully incorporate them into clinical practice. Research ought to concentrate on creating materials and training courses to help medical practitioners become more knowledgeable about herbal medicine[60].

8.2 Campaigns for Public Awareness

Educating the public on the possible advantages and disadvantages of herbal neuroprotectives can help people make well-informed decisions. Campaigns for public education should dispel prevalent myths about herbal remedies and present information based on research[61].

9. Conclusion

More and more people are realizing the potential benefits of herbal neuroprotectives for neurodegenerative diseases and cognitive wellness. Studies have indicated that a number of herbal remedies, such as ginseng, *B. monnieri, G. biloba*, turmeric, and *ashwagandha*, have been shown to have neuroprotective effects *via* a variety of pathways, including the regulation of oxidative stress, neuroinflammation, and neurotrophic factors[62,63]. Even with the encouraging preclinical data and historical application, many herbal treatments have not yet received full scientific validation.

Future research has to concentrate on a few important topics in order to progress the subject. First, in order to comprehend these herbs modes of action and therapeutic potential, it is crucial to identify and characterize unique active chemicals inside them utilizing cutting-edge phytochemical approaches[64, 65]. Extensive and meticulous clinical trials are required to verify the effectiveness of these plant-based neuroprotectives and determine their long-term safety profiles [66,67].

Furthermore, extensive toxicological analyses and long-term safety research are necessary to guarantee that these herbal remedies do not pose unanticipated hazards when taken regularly or in conjunction with other medical interventions[68,69]. In order to solve the current problems with product variation and authenticity, established methods and quality control techniques would improve the consistency and dependability of herbal goods[70,71].

Herbal neuroprotectives could be optimized for therapeutic efficacy and tailored to the specific needs of each patient by being combined with contemporary medical treatments and investigating personalized medicine approaches[72,73]. Global access to these medicines and their safe use will be facilitated by harmonizing regulatory systems across various locations[74].

Ultimately, in order to make well-informed decisions on herbal neuroprotectives, it is imperative that the public and healthcare professionals receive more education and understanding. Better integration of these treatments into clinical practice might be supported by efficient training initiatives and public awareness efforts that close the knowledge gap between traditional applications and scientific data[75,76].

In conclusion, even if the topic of herbal neuroprotection has a lot of promise, further study, the creation of regulations, and public awareness campaigns are necessary to fully realize its potential. By focusing on these areas, we can improve the efficacy and security of herbal neuroprotectives, aid in the

treatment of neurodegenerative illnesses, and promote better cognitive health.

10. Author Contribution

Krushika Patel and Anuvarsh Nair: Conceptualization; writing, review and editing. Cyril Sajan and Varunsingh Saggu: Supervision and review. All authors have read and agreed to the published version of the manuscript.

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