

HERBAL DRUGS FOR NEUROPROTECTION IN ISCHEMIC STROKE***Nihar Ranjan Kar**

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Balasore, Odisha, India.**ABSTRACT**

Ischemic stroke is a leading cause of disability and mortality worldwide. Due to the limited effectiveness and likely detrimental effects of conventional therapies claiming long-term brain benefits, alternative neuroprotective drugs need to be studied. Ischemic stroke therapy alternatives derived from natural plant herbs and pharmaceuticals are gaining attention due to their wide range of bioactive components and long tradition of medical use. In this review article, comprehensive overviews of many natural plant herbs and their derivatives that have shown promise in the treatment of ischemic stroke have been provided. This review also discusses the mechanisms of action and clinical applications of herbal drugs used for

neuroprotection, as well as the preclinical and clinical evidence supporting their use in the treatment of ischemic stroke. This review also highlights the use of certain recently developed herbal drugs in the treatment of ischemic stroke. The main motto of this review focuses on the effective treatment of ischemic stroke by plant-based medications.

KEYWORDS: Ischemic stroke, Pathophysiology, Etiopathology, Conventional Therapies, Limitations, Recent neuroprotective herbal drugs.

INTRODUCTION

Ischemic stroke occurs when cerebral blood arteries get blocked, cutting off blood flow to the brain and leading to oxidative stress, excitotoxicity, inflammation, and, ultimately, neuronal cell death. The goal of contemporary therapies is to restore blood flow to the affected region of the brain as quickly as possible, and they include the use of thrombolytic medications and mechanical thrombectomy. However, there are risks associated with these therapies, and they may not be suitable for everyone. The immediate treatment of strokes has improved, but there is still a critical need for neuroprotective drugs that may reduce brain damage and speed up

recovery. Traditional medicine has a long history of using herbal medicines and plant-based therapies for the treatment of a variety of illnesses, including stroke. This has led to a greater interest in finding neuroprotective medications that do not rely on chemicals. Many bioactive components are found in herbal treatments and plant-based therapies. It's possible that some of these compounds are neuroprotective.^[1] Neuroprotective compounds obtained from several plant herbs and medicines may help patients with ischemic stroke. It is of the utmost importance to understand pathophysiology of the ischemic brain injury, so that novel medications might be developed to prevent or lessen the ailment. Neuroprotective mechanisms such anti-inflammatory, anti-apoptotic, and antioxidative processes are investigated in this study as prospective target therapies in ischemic stroke. Treatment for ischemic stroke depends on our knowledge of neuroprotective medications and their abilities to decrease oxidative stress, regulate inflammation, keep the blood-brain barrier intact, and boost neuronal survival. Traditional and alternative medications for the treatment of ischemic stroke are explored, including antioxidants, anti-inflammatory compounds, and neurotrophic drugs. Many different types of neuroprotective pharmaceuticals, both natural and manufactured, are covered, including antioxidants, anti-inflammatory agents, NMDA receptor antagonists, and others.^[2]

Ischemic Stroke: An Overview

Ischemic stroke, which is brought on by the occlusion or constriction of a brain-supplying artery as a result of atherosclerosis, embolism, or thrombosis, is responsible for around 85% of all cases of stroke. Neurons are damaged and become dysfunctional when blood flow is interrupted, setting off a chain reaction that worsens the condition. Energy exhaustion, excitotoxicity, oxidative stress, inflammation, and apoptosis are all examples of these processes. Because of how rapidly these incidents may develop, immediate medical intervention is crucial for preserving brain tissue and preventing long-term damage.^[3]

Pathophysiology of Ischemic Stroke^[4]

Ischemic strokes go through the following phases in their pathogenesis, which can be represented below,

a) Ischemia: Ischemia happens when a part of the brain doesn't get enough blood. Stroke may occur when a blood clot (thrombus) either forms naturally inside a blood vessel or is carried by embolisation to the brain.

b) Cellular energy failure: Without a steady supply of oxygen and glucose, neurons in the brain quickly run out of the cellular fuel known as adenosine triphosphate (ATP). By switching from aerobic to anaerobic metabolism, lactic acid and other potentially toxic byproducts are produced.

c) Excitotoxicity: Glutamate and other neurotransmitters are released as part of a chain reaction inside the cell brought on by its lack of energy. Glutamate may be neurotoxic when it accumulates to hazardous levels in the brain, a phenomenon known as excitotoxicity.

d) Ion imbalance and cytotoxic edema: The concentrations of ions (such as sodium and potassium) within and outside of cells are also altered by ischemia. This causes cytotoxic edema and cell swelling from excess intracellular water.

e) Inflammatory response: When brain tissue is damaged, it sets off an inflammatory response. Immune cell infiltration worsens tissue damage and ups the production of inflammatory mediators.

f) Blood-Brain Barrier disruption: The blood-brain barrier, a protective barrier that regulates the circulation of chemicals between the bloodstream and the brain, may be compromised, allowing potentially harmful medications to enter the brain.

Etiopathology of Ischemic Stroke^[5]

Multiple risk factors contribute to the development of ischemic stroke. The most common reasons include, among others are,

a) Atherosclerosis: Atherosclerosis is a disease in which fatty plaques form within the artery walls. The formation of blood clots when these plaques rupture poses a threat to the brain's ability to receive oxygen and nutrients.

b) Cardioembolism: In the case of a cardioembolic stroke, a clot forms in the heart and then travels via the bloodstream to the brain, where it obstructs an artery.

c) Small vessel disease: The tiny blood arteries in the brain are vulnerable to injury from conditions like hypertension, which may cause microclots or vascular constriction.

d) Other cardiovascular conditions: Damage to these arteries may result in the formation of microclots or the narrowing of brain blood vessels due to conditions like hypertension.

e) Diabetes mellitus: Diabetes-related vascular impairment increases the risk of blood clot formation.

f) Smoking, alcohol abuse, and drug use: Some lifestyle choices may raise stroke risk.

g) Genetics and family history: Some people have a higher heritability for developing stroke.

Treatment of Ischemic Stroke^[6]

When treating an ischemic stroke, time is of the essence in reducing brain damage and increasing survival rates. Common forms of treatment include,

a) Thrombolytic therapy: Intravenous administration of tissue plasminogen activator (tPA) is the standard treatment for eligible patients during the first few hours following the start of stroke. By dissolving the clot that caused the stroke, tPA is able to restore blood flow to the brain.

b) Mechanical thrombectomy: To restore blood flow, the clot must be surgically removed from the artery. This method is often used in conjunction with thrombolytic therapy since it improves outcomes for patients with severe arterial occlusions.

c) Anticoagulants and antiplatelet therapy: Anticoagulants or antiplatelet drugs may be given beyond the acute phase to prevent more clots emerging, depending on the underlying etiology of the stroke.

d) Blood pressure management: It helps in keeping blood flow to the brain while preventing the excessive pressure that might cause bleeding in damaged brain tissue.

e) Cholesterol Management: To treat high cholesterol and reduce the risk of atherosclerosis, statins are commonly used medications.

f) Brain Edema management: To treat brain edema, doctors may provide drugs such as mannitol or hypertonic saline to reduce intracranial pressure in extreme cases.

g) Neuroprotective Agents: Neuroprotective interventions are being researched for their potential to mitigate early-stage stroke-related brain cell damage.

h) Rehabilitation Therapy: After the first phase of recovery after a stroke, most patients participate in rehabilitation in an effort to regain functional independence and improve their quality of life.

It can be remembered that the best way to deal with ischemic strokes is to prevent them from happening in the first phase. Maintaining healthy lifestyles, managing risk factors like high blood pressure and diabetes, and scheduling regular checkups are all effective ways to reduce your chance of having a stroke. If anybody is experiencing stroke symptoms, immediately emergency service helpline no is called to save life as it is being given in maximum of countries. It should be remembered that, "Time is Brain," and that getting quick treatment for an ischemic stroke may dramatically improve outcomes.

The Role of Drugs in Clinical Practise: An Overview of Their Action Mechanisms^[7]

a) Tissue plasminogen activators (tPA): These are kind of thrombolytic drugs that convert plasminogen into the enzyme plasmin, therefore dissolving fibrin clots. If administered soon after the onset of symptoms, it may be effective in treating acute ischemic stroke by dissolving the clot and restoring blood flow. Examples- alteplase, reteplase, and tenecteplase.

b) Anticonvulsants and others- Seizures produced by a stroke are extremely rare, but repeating seizures can be deadly. Medicines used to treat recurrent convulsive seizures are also used to treat seizures caused by a stroke. Benzodiazepines, most commonly diazepam and lorazepam, are the first-line treatments for ongoing seizures.

c) Anti-Platelet Agents

i) Aspirin: It is an antiplatelet medication that reduces the risk of a blood clot by stopping platelets from sticking together. It's widely used to lessen the likelihood of subsequent strokes.

ii) Clopidogrel: It is another antiplatelet drug that works by inhibiting platelet ADP receptors, hence preventing clot formation. In combination with aspirin, it is used by certain high-risk patients.

d) Anticoagulants

i) Warfarin: It is an anticoagulant that works by counteracting vitamin K's clotting-inducing properties. It is used to prevent blood clots in patients with atrial fibrillation and other conditions that need anticoagulation.

ii) Direct Oral Anticoagulants - These cutting-edge anticoagulant medications, such dabigatran, rivaroxaban, apixaban, and edoxaban, target specific blood clotting components and are used to treat a broad variety of illnesses requiring anticoagulation.

It should be kept in mind that each patient's have unique medical background, stroke severity, and underlying health concerns which may play a part in identifying the most appropriate drugs and treatment approaches. Stroke treatment should only ever be administered by after advice of a registered medical practioner.

Existing Treatment Limitations

The first line of defence against an acute ischemic stroke is thrombolytic treatment, which makes use of drugs like tissue plasminogen activator (tPA). Although tPA shows promise, it

is not regularly employed because to its narrow therapeutic window and the potential of hemorrhagic effects. Moreover, waiting too long for assistance or having certain underlying problems might rule some individuals out as ideal candidates for thrombolytic therapy.^[8]

Mechanical thrombectomy, in which the clot is physically removed, has emerged as a promising option for appropriate individuals, albeit it is not without limitations, such as the necessity for early identification and the availability of trained locations. Reperfusion injury, which occurs when blood flow is restored to the brain, may exacerbate preexisting damage even if the procedure is effective.^[9]

Once the first critical time has gone, rehabilitation and secondary prevention become the pillars of post-stroke treatment. While these approaches are useful, there is a severe lack of novel therapy options that may address both the acute and chronic phases of ischemic stroke from a neuroprotection standpoint.^[10]

Necessity and Efficacy of Herbal Medicines (Why Herbal Drugs?)

Herbal remedies produced from plants have been valued for their effectiveness, safety, and adaptability by traditional medical practises for a very long time. These natural products include a wide variety of bioactive compounds, some of which have been utilized in mitigation of majority of ailments including neurological disorders. Among all ailments, they also have been investigated to have neuroprotective activity after getting positive evidences after their preclical and clinical studies. Another advantage of natural herbs is their capacity to target many pathways at once makes them an exciting new alternative for treating ischemic stroke.^[11]

Neuroprotective Effects of Herbal Medicines

The historical use of herbal medicines in alternative medical systems provides a basis for their evaluation as potential neuroprotective agents in ischemic stroke. Plants have evolved a vast range of chemical compounds as defence mechanisms against predators, diseases, and environmental stresses. The antioxidant, anti-inflammatory, and anti-apoptotic actions of many of these phytochemicals are very helpful in understanding the aetiology of ischemic stroke.^[12]

It has been shown that some herbal extracts may inhibit inflammation, neutralise free radicals, and control the signalling pathways that determine whether or not cells live or die.

In addition, a number of plant-based compounds have shown efficacy in fostering angiogenesis and accelerating neuronal regeneration, both of which are critical for brain tissue repair after ischemic injury.^[13]

Mechanisms of Neuroprotection in Herbal Medicines

The complex cascades of events that make up the pathophysiology of ischemic stroke include excitotoxicity, oxidative stress, inflammation, and apoptotic cell death. Herbal drugs provide a multifaceted approach to neuroprotection since several pathways are involved in these processes.^[14]

The levels of pro-inflammatory cytokines including interleukin-1 beta and tumour necrosis factor-alpha are lowered by curcumin and resveratrol, while the levels of anti-inflammatory mediators are raised. By inhibiting glutamate-induced excitotoxicity and lowering calcium input to neurons, flavonoids in ginkgo biloba have been proven to prevent excessive neuronal cell death.^[15]

The Preclinical Investigation of Herbal Neuroprotectants

Herbal medications have been studied extensively for their neuroprotective effects in several animal models of ischemic stroke. The possible advantages and disadvantages of certain compounds have been shown by a number of research. Nonetheless, caution must be used when extrapolating findings from animal studies to human patients. Preclinical data analysis requires consideration of confounding variables such as species differences, dosing schedules, and experimental settings.^[16]

Clinical Trials and Their Challenges

Several herbal drugs are now under clinical trials as potential adjuvant treatment for ischemic stroke in humans, having advanced beyond the domain of preclinical research. Study objectives have mostly focused on gauging efficacy, safety, and acceptability.^[17]

The effectiveness of herbal treatments may vary from person to person owing to genetic and environmental variables, and there is a possibility that they may interfere with conventional pharmaceuticals. Some studies have yielded encouraging findings, while others have proved inconclusive or encountered difficulties in design or implementation. Standardising herbal formulations and maintaining quality control may help progress herbal neuroprotective treatment.^[18]

Rationale behind Use of Herbal Drugs for Neuroprotection

In recent years, there has been a rise in the study of herbal treatments as researchers seek natural therapies with neuroprotective properties. In this article, we discuss the preclinical evidence for several potential novel natural medications for treating ischemic stroke. Several substances, including curcumin, resveratrol, and quercetin, have showed promise in decreasing stroke-related brain damage.^[19]

Major advances have been made in the treatment of ischemic stroke using both natural plant remedies and pharmaceuticals in recent years. In this article, the most recent findings on the neuroprotective properties of herbs and supplements are thoroughly reviewed.

Herbal Drugs for Neuroprotection^[20,21,22,23]

New plants and herbal medications are being discovered and investigated all the time, making herbal medicine a vibrant field. In this part, recently found herbal treatments which shown promise in treating ischemic stroke have been discussed. Some of them may be natural substances with shown neuroprotective benefits and other may have been extracted from unrecognised plants or traditional medicines. So, some herbal drugs having neuroprotective action have been enlisted below,

1. *Bacopa monnieri* (Brahmi)

The medicinal herb *bacopa monnieri* is a member of the Plantaginaceae family. It lives in the tropics and subtropics anywhere there is plenty of water and dirt. Bacosides, alkaloids, and flavonoids are some of the active compounds found in *bacopa monnieri* that contribute to its neuroprotective effects. The primary method of action is a rise in the levels of certain neurotransmitters. These include acetylcholine, serotonin, and gamma-aminobutyric acid (GABA). It has been shown that the bacosides in *Bacopa* help in nerve cell renewal and the transmission of nerve impulses. *Bacopa monnieri* has been utilised as a nerve tonic and cognitive enhancer in Ayurvedic medicine for thousands of years due to its antioxidant properties, which help preserve brain cells from damage caused by free radicals. Neuroprotective properties are of interest to researchers presently because of their potential use in the treatment of neurodegenerative illnesses like Alzheimer's and Parkinson's. It may improve cognitive functioning and hence aid in learning and remembering. You may get *bacopa* in a variety of dietary supplements, including capsules, tablets, and even herbal teas.

2. *Ginkgo biloba* (Ginkgo)

One of the world's oldest living tree species, ginkgo biloba is harvested for its leaves. Neuroprotective effects of ginkgo biloba are attributed to its flavonoids and terpenoids. Flavonoids are powerful antioxidants that protect the brain from damage caused by free radicals and oxidative stress. Scientists think that the terpenoids improve blood flow, leading to increased delivery of oxygen and nutrients to brain cells. Ginkgo biloba's ability to reduce platelet aggregation and increase blood viscosity may potentially help treat conditions related with poor brain blood flow. Traditional medicine, particularly traditional Chinese medicine, has relied on ginkgo biloba preparations for thousands of years because of its neuroprotective properties. Ginkgo biloba extract is widely used as a dietary supplement because of its ability to improve memory and focus. They may be given for conditions such as mild cognitive impairment, dementia, and age-related memory loss. However, if you are already using any medications, it is essential to see a medical professional prior to utilising Ginkgo biloba.

3. *Withania somnifera* (Ashwagandha)

Ashwagandha is the name of more than one well-known medicinal herb. Its valuable medical characteristics have led to its cultivation in many countries outside its country of origin, India. Ashwagandha's protective effects on the nervous system may be shown in a variety of ways. One of its active ingredients, withanolides, has antioxidant and anti-inflammatory properties. Chemicals like these have been shown to reduce oxidative stress and inflammation in the brain, two factors that have been associated to neurodegenerative diseases. Ashwagandha helps in the growth and maintenance of nerve cells in addition to promoting neurogenesis and boosting brain plasticity. Also possibly controlled are the neurotransmitters dopamine and serotonin, which play key roles in both emotional and mental health. Ashwagandha has been used for millennia in Ayurvedic medicine for its positive benefits on brain health and cognitive performance. It may help reduce the harmful effects of stress, anxiety, and depression on the neurological system. The enhancements to memory and focus may also help those suffering from mild cognitive impairment or age-related memory loss.

4. *Curcuma longa* (Turmeric)

The root of the plant *Curcuma longa*, which is related to ginger, is used to make the spice turmeric. The spice turmeric gets its culinary and medicinal purposes from its main component, curcumin. The neuroprotective effects of curcumin have been well-documented.

Curcumin is a powerful antioxidant and anti-inflammatory, suggesting it may protect brain tissue from free radical damage and reduce inflammatory reactions. It may also be able to cross the blood-brain barrier and act on nerve cells directly. Curcumin may inhibit the formation of protein aggregates like amyloid-beta plaques, which are characteristic of neurodegenerative diseases like Alzheimer's. Turmeric is used to enhance cognitive abilities and treat neurological disorders in alternative medicine. There's speculation that doing so might improve cognition generally, including memory and attention span. In addition, it has become a popular natural therapy for mental health concerns including depression and anxiety due to its mood-boosting benefits.

5. *Hericium erinaceus* (Lion's Mane Mushroom)

It's possible to find the tasty Lion's Mane Mushroom wherever in the world. Its distinguishing characteristics are the long, white spines that resemble a lion's mane. Among the bioactive compounds in Lion's Mane Mushroom are the neuroprotective hericenones and erinacines. These substances stimulate the production of nerve growth factor (NGF) in the brain. NGF is essential for proper nerve cell maturation and survival. The increased synthesis of nerve growth factor facilitated by Lion's Mane Mushroom aids in the regeneration and adaptability of nerve cells. Lion's Mane Mushroom, long used in TCM, is extremely popular in Japanese cooking because of its antioxidant and anti-inflammatory properties. It's growing in popularity as a dietary supplement for the brain. Memory and concentration are two of the supposedly improved cognitive functions. Neurodegenerative disorders including Alzheimer's and Parkinson's have also been studied for potential treatment using this compound.

6. *Rhodiola rosea* (Radiola)

Rhodiola is a perennial plant that is adapted to cold, mountainous regions. Rhodiola is supposed to help the body adapt to stress and maintain its internal balance by acting as an adaptogen. Neurons may have easier access to mood-regulating neurotransmitters like serotonin and dopamine if this is the case. It's also possible that the HPA axis, which controls the body's stress response, might be impacted. The neuroprotective benefits of rhodiola are used to treat memory loss, depression, and cognitive fatigue.

7. *Huperzia serrata* (Huperzine A)

Huperzia serrata, a kind of club moss found in China, is the source of huperzine A. Huperzine A is an acetylcholinesterase inhibitor, meaning it helps prevent the breakdown of acetylcholine, a neurotransmitter important for learning, memory, and other cognitive

functions. The consequence is improved cholinergic neurotransmission, which aids cognitive processes. Huperzine A is used as a neuroprotective medication to enhance memory and cognitive function, especially in Alzheimer's disease and age-related cognitive decline.

8. *Centella asiatica* (Gotu kola)

Gotu kola is a plant that is indigenous to the Asian subcontinent. Gotu kola contains compounds with anti-inflammatory and antioxidant properties, such as asiaticoside and madecassoside. These compounds may play a role in neuroprotection by providing protection against oxidative and inflammatory stress. It has been shown that gotu kola may prevent cell death in the brain and improve cognitive abilities including memory and focus. It has also been reported to provide calming and anxiety-reducing effects.

9. *Sarcenesh ashoka* (Ashoka)

The Ashoka tree, as its name implies, is native to India. Ashoka bark extract's antioxidant properties have been demonstrated to be neuroprotective. It could protect nerve cells by scavenging free radicals, which would reduce oxidative stress. Ashoka is utilised as a neuroprotective agent to enhance overall brain health and mental clarity in traditional medicine.

10. *Mucuna pruriens* (Velvet Bean)

L-DOPA, a precursor to the neurotransmitter dopamine, is found in the seeds of the tropical and subtropical leguminous *Mucuna pruriens* plant. L-DOPA is able to cross the blood-brain barrier and play a role in dopamine synthesis in the brain. *Mucuna pruriens* improves cognitive function, motor abilities, and memory because it protects nerve cells from damage.

Recent Herbal Drugs and their derivatives used in Ischemic Stroke Management.^[24,25,26,27]

Name	Biological Source	Mechanism Of Action	Uses
Saffron (<i>Crocus sativus</i>)	<i>Crocus sativus</i> flower	Antioxidant, anti-inflammatory, anti-apoptotic	Alzheimer's disease, Parkinson's disease, cognitive decline
Coriander (<i>Coriandrum sativum</i>)	<i>Coriandrum sativum</i> seeds	Antioxidant, anti-inflammatory, neuroprotective	Alzheimer's disease, Parkinson's disease, cognitive decline
Fenugreek (<i>Trigonella foenum-graecum</i>)	<i>Trigonella foenum-graecum</i> seeds	Antioxidant, anti-inflammatory, neuroprotective	Alzheimer's disease, Parkinson's disease, cognitive decline
Rosemary	<i>Rosmarinus officinalis</i>	Antioxidant, anti-	Alzheimer's disease,

(Rosmarinus officinalis)	leaves	inflammatory, neuroprotective	Parkinson's disease, cognitive decline
Scutellaria baicalensis	Scutellaria baicalensis root	Antioxidant, anti-inflammatory, neuroprotective	Alzheimer's disease, Parkinson's disease, cognitive decline
Eleutherococcus senticosus	Eleutherococcus senticosus root	Adaptogenic, neuroprotective	Stress, fatigue, cognitive decline
Nigella sativa	Nigella sativa seeds	Antioxidant, anti-inflammatory, neuroprotective	Alzheimer's disease, Parkinson's disease, cognitive decline
Green tea	Camellia sinensis	Antioxidant, anti-inflammatory, neuroprotective	Alzheimer's disease, Parkinson's disease, cognitive decline
Echinacea	Echinacea purpurea	Antioxidant, anti-inflammatory, neuroprotective	Alzheimer's disease, Parkinson's disease, cognitive decline
Grape seed extract	Vitis vinifera	Antioxidant, anti-inflammatory, neuroprotective	Alzheimer's disease, Parkinson's disease, cognitive decline
Scutellaria baicalensis	Scutellaria baicalensis (Chinese skullcap)	Anti-inflammatory, antioxidant, anti-apoptotic	Alzheimer's disease, Parkinson's disease, multiple sclerosis
Eleutheroside B	Eleutherococcus senticosus (Siberian ginseng)	Anti-stress, adaptogenic, neuroprotective	Fatigue, stress, anxiety, depression
Cyanidine-3-glucoside	Vaccinium myrtillus (bilberry)	Antioxidant, anti-inflammatory, neuroprotective	Age-related macular degeneration, glaucoma
Carnosic acid	Rosmarinus officinalis (rosemary)	Antioxidant, anti-inflammatory, neuroprotective	Alzheimer's disease, Parkinson's disease, multiple sclerosis
Epigallocatechin-3-gallate	Camellia sinensis (green tea)	Antioxidant, anti-inflammatory, neuroprotective	Alzheimer's disease, Parkinson's disease, multiple sclerosis
Luteolin	Matricaria recutita (chamomile)	Antioxidant, anti-inflammatory, neuroprotective	Alzheimer's disease, Parkinson's disease, multiple sclerosis
Resveratrol	Vitis vinifera (grape)	Antioxidant, anti-inflammatory, neuroprotective	Alzheimer's disease, Parkinson's disease, multiple sclerosis
Chamomile	Matricaria recutita	Anti-oxidant, anti-inflammatory, and neuroprotective	Reduces anxiety and improves sleep
St. John's wort	Hypericum perforatum	Anti-depressant, anti-oxidant, and neuroprotective	Improves mood and sleep
Caffeine	Coffee beans, tea leaves, kola nuts	Blocks adenosine receptors, which increases alertness and cognitive function	Improves cognitive function, memory, and reaction time
Epigallocatechin	Green tea leaves	Acts as an antioxidant and	May help prevent

gallate (EGCG)		anti-inflammatory, and protects neurons from damage	Alzheimer's disease and Parkinson's disease
Silymarin	Milk thistle	Protects liver cells from damage, and may also have neuroprotective effects	May help protect against neurodegenerative diseases
Cacao	Theobroma cacao	Antioxidant, anti-inflammatory, neuroprotective	Stroke, Alzheimer's disease, Parkinson's disease
Coffee	Coffea arabica	Antioxidant, anti-inflammatory, neuroprotective	Alzheimer's disease, Parkinson's disease, stroke
Coenzyme Q10	Ubiquinone	Antioxidant, neuroprotective	Alzheimer's disease, Parkinson's disease, stroke
Fish oil	Salmon, tuna, mackerel	Omega-3 fatty acids, neuroprotective	Alzheimer's disease, Parkinson's disease, stroke
L-theanine	Green tea	Antioxidant, anti-stress, neuroprotective	Improves cognitive function and protects against neurodegenerative diseases
Panax quinquefolius	Panax quinquefolius	Adaptogenic, antioxidant, neuroprotective	Alzheimer's disease, Parkinson's disease, multiple sclerosis
Eleutherococcus senticosus	Eleutherococcus senticosus	Adaptogenic, antioxidant, neuroprotective	Alzheimer's disease, Parkinson's disease, multiple sclerosis
Reishi mushroom	Ganoderma lucidum	Antioxidant, anti-inflammatory, neuroprotective	Alzheimer's disease, Parkinson's disease, multiple sclerosis
Chaga mushroom	Inonotus obliquus	Antioxidant, anti-inflammatory, neuroprotective	Alzheimer's disease, Parkinson's disease, multiple sclerosis
• Skullcap (Scutellaria lateriflora)	leaves and flowers	○ sedative, antispasmodic, and neuroprotective.	anxiety, insomnia, and seizures
• Panax Notoginseng	Sanqi or Tianqi ginseng (Chinese medicine)	○ blood circulation and stroke.	Stroke management
• vinpocetine	Derived from periwinkle plant	○ improves blood circulation	Stroke management
• Hawthorn	Crataegus species	○ improve blood flow and reduce brain damage	Supports ischemic stroke
• Bilberry	Vaccinium myrtillus	○ antioxidant	protects brain cells from ischemic damage
• Garlic	Allium sativum	○ anticoagulant	reduce blood clotting, potentially beneficial in

			preventing ischemic stroke
• Angelica sinensis	Dong Quai(traditional Chinese medicine)	○ Neuroprotective	protect against cerebral ischemia and reduce inflammation
• Ginger	Zingiber officinale	○ anti-inflammatory and antioxidant	reduce oxidative stress and inflammation
• Uncaria rhynchophylla	Gou-teng(Chinese medicine)	○ Neuroprotective	improve cerebral blood flow and reduce oxidative stress
• Ligusticum wallichii	Chuanxiong(traditional Chinese medicine)	○ neuroprotective	support post-stroke recover
• Nattokinase	Derived from fermented soyabeans	○ anticoagulant	prevent blood clot formation in conditions
• Astragalus membranaceus	traditional Chinese herb	○ immune-enhancing properties	promote neurological recovery after stroke
• Panax Ginseng	Asian Ginseng	○ Neuroprotective and anti-inflammatory effect	reduce oxidative stress and inflammation
• Salvia officinalis	Sage	○ Neuroprotective	reduce oxidative stress

CONCLUSION

Herbal medications have been used for centuries in traditional medicine, and they have several mechanisms of action, making them a good candidate for neuroprotection in ischemic stroke. Stroke is a devastating illness, but it may be treatable in the future thanks to research into plant compounds as complementary therapies in stroke therapy. However, further research, especially in the form of well-designed clinical trials, is required to evaluate the safety, efficacy, and optimal dosage of these herbal neuroprotective chemicals. This research project will investigate the current knowledge of many herbal drugs and their potential importance in the treatment of ischemic stroke.

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