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Review Article

A Systemic Review on Neuroprotective Activity of Various Herbal Plants

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ABSTRACT

Inflammation is the body's reaction to an injury, illness, or foreign particles. It is a multifaceted process involving blood vessels, tissues, and signaling pathways. Synthetic medications, such as NSAIDs and glucocorticoids, are widely used to treat inflammation. Neuroinflammation is a defense mechanism that protects the central nervous system (CNS) from infection and injury. It is caused by infections, autoimmune diseases, traumatic brain damage, and neurodegenerative disorders such as Alzheimer's and Parkinson's disease. Plant organs such as the leaves, stems, roots, fruit, flowers, and seeds, are used as alternative medicines in traditional medicine. The chemically derived compounds, such as rosmarinic acid, curcumin, ginsenoside, polyphenols, 6-shogaol, and resveratrol, that are found in the herbal plants *Zingiber officinale*, *Ginkgo-biloba*, *Curcuma longa*, *Camellia sinensis*, *Rosmarinus officinalis*, *Crocus sativus*, *Ferula asafoetida*, *Thymus vulgaris*, *Boswellia serrata*, and *Coriandrum sativum* have been shown to have anti-inflammatory properties.

INTRODUCTION

Inflammation is the response shown by body cells or tissues to injury, infection, or any foreign particles. It is a complicated process that includes blood vessels, tissues, and various signaling pathways. Inflammation is caused by the release of chemicals within the body that trigger an immune system to fight against infection or to heal damaged tissue. The inflammatory process ends once the injury or infection is healed. The symptoms of inflammation include local redness, heat, swelling, pain, and function loss. There are

two types of inflammation: acute and chronic. Acute inflammation induces an increase in vascular permeability, capillary infiltration, and leukocyte emigration. Chronic inflammation has been linked to the invasion of mononuclear immune cells, macrophages, monocytes, neutrophils, fibroblast activation, proliferation, and fibrosis. The most commonly used synthetic drugs are NSAIDs, which includes ibuprofen and naproxen, and glucocorticoids such as cortisone and prednisone.[1] Neuroinflammation is a defence process that protects the CNS from

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infection and damage, but in some situations, it can cause neuronal damage or malfunction. It is caused by infections, autoimmune diseases, traumatic brain injury, and neurodegenerative disorders such as Alzheimer's or Parkinson's disease. Acute neuroinflammation is caused in response to injury or infection and involves the activation of immune cells and the release of inflammatory mediators. Chronic neuroinflammation is associated with neurodegenerative diseases such as Alzheimer's and Parkinson's disease. Autoimmune neuroinflammation results from attacking healthy brain tissue, as seen in multiple sclerosis. The mediators associated with neuroinflammation are microglia, astrocytes, oligodendrocytes, and T cells. Microglia, the CNS's resident macrophages, are the key effector cells in mediating neuroinflammation, which is characterized by a variety of inflammatory and neurodegenerative illnesses. Once the brain injury or infection occurs, neuroinflammatory mediators get activated and secrete interleukin-1 beta, nitric oxide (NO), tumor necrosis factor alpha, and reactive oxygen species. The synthetic drugs used in the treatment of neuroinflammation include statins such as atorvastatin, lovastatin, fluvastatin, and simvastatin. Melatonin, derived from the penial gland, provides neuroprotection for brain and spinal cord trauma. Traditional medicine used plant organs such as leaves, stems, roots, flowers, fruits, and seeds as alternative and supplementary therapies. Medicinal plants include a wide range of biologically active components that can be employed as crude material or pure compounds to cure a number of diseases [2]. Allopathic drugs have a single active component that is effective in a specific pathway, whereas plants have several components that work together to target a complex pathway. Chemically derived compounds found in herbal plants, such as resveratrol, curcumin, ginsenoside, polyphenols, withanolides, rosmarinic acid, and others, have been shown to

have a therapeutic effect on neuroinflammation. Nowadays, most allopathic pharmaceuticals have toxicity and adverse effects; hence, herbal remedies are frequently used.

Neuroinflammatory activity and pharmacological action of various herbal plants

1. Zingiber officinale Roscoe

Zingiber officinale Roscoe is commonly referred to as ginger. It is a semiwoody perennial herb that grows to be 3 to 4 feet tall from its root stock. The plant's leaves and petals are used medicinally, and it grows swiftly. It is a member of the zingiberaceae family and is considered to be one of the most significant plants due to its numerous medicinal, nutritional, and traditional uses. The herb is used in traditional medicine around the world to treat a number of illnesses. Rheumatism, stomach disorders, diabetes, wounds, snake bites, baldness, toothaches, respiratory problems, arthritis, bleeding, rash, and so on.[3] Ginger has a variety of chemically active substances, from non-volatile components to volatile ones. These sesquiterpenes, which include bisapylene, zingiberene, and zingiberol, are the main active components of ginger oil [4]. 6-Shogaol, an active ginger component, protects dopaminergic neurones in Parkinson's disease models by inhibiting neuroinflammation.[5]



Fig no. 1: Zingiber officinale

2. Ginkgo biloba

Ginkgo biloba is often known as ginkgo or ginkgo. It belongs to the Ginkgoaceae family. Since it resembles the maidenhair fern, it is frequently referred to as the “maidenhair tree” and is also known as a living fossil. Leaves could be either pale yellow, bright yellow, or dark green in color. They are fan-shaped, leathery, and smooth in texture. Ginkgo contains numerous bioactive chemicals, including terpenoids, flavonoids, bioflavonoids, organic acids, and polyphenols. Ginkgo leaf can be taken orally to prevent acute mountain sickness and aging, manage gastric acidity, enhance liver and gallbladder activity, regulate bacterial flora, and manage blood pressure. It is administered orally to treat allergies, asthma, bronchitis, and other disorders of the central nervous system [6]. Ginkgo biloba leaf extract can have antioxidant benefits that lower platelet activating factor, enhance membrane fluidity, and inhibit glucocorticoid production. In lipopolysaccharide-activated primary microglia cells, Ginkgo biloba extract EGb 761 exhibited anti-neuroinflammatory action. EGb 761 was effective in reducing neuroinflammatory activity by targeting the COX/PGE2 pathway.[7]



Fig no.2: Ginkgo biloba

3. Rosmarinus officinalis

The aromatic plant *Rosmarinus officinalis* is a member of the Lamiaceae family. Rosemary is an evergreen bushy shrub that grows up to one meter tall. It has erected stems, whitish-blue blooms, and small, dark green leaves with backward-turned

borders. It is used as an antispasmodic to treat renal colic, menstrual cramps, and respiratory diseases. It has been used for several purposes, including analgesic, antirheumatic, carminative, cholagogue, diuretic, expectorant, antiepileptic, and reproductive benefits [8]. Rosemary extract contains phenolic and volatile components, including carnosol, carnosic acid, and rosmarinic acid, as well as alpha-pinene and (-)-bornyl acetate [9]. The study was conducted for rosemary extract's neuroprotective effects on MnCl₂-induced neurotoxicity in rats. The histological structure of the brain was preserved after treating manganese-exposed rats with rosemary extract. These results demonstrate that rosemary's antioxidant, anti-inflammatory, and anti-apoptotic characteristics can influence changes in histone acetylation in manganese-exposed rats' brain cells.[10]



Fig no. 3: Rosmarinus officinalis

4. Crocus sativus

Crocus sativus L. belongs to the family Iridaceae (synonym: kesar) and consists of the dried red stigma. This herbaceous perennial plant grows 10 to 25 cm tall from its bulbs. The leaves range from five to eleven per bud and are relatively slender, measuring 1.5 to 2.5 mm, and are dark green in color. *Crocus sativus* flowers occur in the early autumn, around the end of September, and are purple in color, and the style terminates with a single stigma made of three filaments of vivid red color [11]. Saffron includes around 150 volatile

and aroma-producing chemicals, primarily terpenes, terpene alcohol, and their esters. *C. sativus* has a variety of therapeutic properties, including antihypertensive, anticonvulsant, antitussive, antigen ototoxic and cytotoxic effects, anxiolytic aphrodisiac, antioxidant, antidepressant, antinociceptive, anti-inflammatory, and relaxing activity. It also boosts memory and learning abilities while increasing blood flow to the retina and choroid [12]. Saffron has the ability to cure neurodegenerative diseases (NDs) caused by oxidative stress, inflammation, and decreased mitochondrial activity, such as Alzheimer's disease, Parkinson's disease, multiple sclerosis, and cerebral ischemia. [13]



Fig no. 4: crocus sativus

5. *Ferula asafoetida*

The herbaceous plant *Ferula asafoetida* belongs to the Umbelliferae family. It is oleo gum resin that is extracted from the plant's root and rhizome. This perennial plant can grow up to 12 feet tall in the wild and has round leaves about 30-40 cm in size. The stem leaves have broad sheathing petioles. Flowering stems are 2.5–3 m tall, 10 m thick, and hollow. These flowering stems have a number of schizogenous ducts in the cortex that produce resinous gum. It is composed of up to three primary components, which are resin (40-64%), gum (25%), and essential oil (10-17%). Ferulic acid and its esters, coumarins, sesquiterpene coumarins, and other terpenoids are all present in the resin fraction. There are recognized antifungal, anti-diabetic, anti-inflammatory, anti-mutagenic,

and antiviral properties of this oleo-gum-resin [14]. *Ferula* protects nerve cells by lowering cytokines like interleukin (IL)-6, interleukin (IL)-1b, and tumor necrosis factor (TNF)- α . As a result, the effects of *Ferula* plants and their active compounds can be utilized to prevent or treat illnesses of the neurological system. Members of this genus help to build and improve the antioxidant system, lower oxidative stress, and block or reduce inflammatory factors in the neurological system. [15]



Fig no. 5: *Ferula asafoetida*

6. *Coriandrum sativum*

Coriandrum sativum L. commonly known as coriander (synonym: dhanya), belongs to the Apiceae family. The plant's height ranges from 20 to 140 cm, depending on agro-climatic environments. The leaves are oval and slightly lobed, with top parts that are linear and split. The plant contains monoterpenes, α -pinene, limonene, γ -terpinene, p-cymene, borneol, citronellol, camphor, geraniol, coriandrin, dihydrocoriandrin, coriandrins, flavonoids, and essential oils. The seeds, leaves, flowers, and fruit of this plant have been shown to have antioxidant, anti-diabetic, anti-mutagenic, anti-helminthic, sedative-hypnotic, anticonvulsant, diuretic, cholesterol-lowering, protective against lead toxicity, antifungal, anti-feeding, anticancer, anxiolytic, hepatoprotective, and anti-protozoal properties [16]. All purified crocus sativus compounds were tested for anti-neuroinflammatory and neurotrophic activities. Compounds showed

moderate anti-neuroinflammatory activity by inhibiting NO production from BV-2 cells. [17]



Fig no. 6: Coriandrum sativum

7. *Thymus vulgaris*

Thymus vulgaris is a flowering plant usually known as thyme from the mint family Lamiaceae that is endemic to southern Europe, ranging from the western part of the Mediterranean to southern Italy. It is a bushy, woody evergreen subshrub with small, strongly scented gray-green leaves and clusters of either purple or pink blossoms in early summer. The essential oil (EO) from *T. vulgaris* included a high concentration of oxygenated monoterpenes but low concentrations of monoterpene hydrocarbons, sesquiterpene hydrocarbons, and oxygenated sesquiterpenes. Thymol was the most common chemical among the essential oil components. Thyme is regarded to be an antiseptic, antibiotic, medicine, astringent, medicinal drug, carminative, disinfectant, medicinal drug, and tonic [18]. *Thymus vulgaris* EO's neuroprotective effects may be due to its high antioxidant levels, as demonstrated in a scopolamine-induced neurotoxicity approach in zebrafish. EO therapy before exposure to scopolamine boosted reactive oxygen species (ROS) scavenging defenses in the brain, which were connected with enhanced cognitive functioning during this experimental model. [19]



Fig no.7: Thymus vulgaris

8. *Curcuma longa*

Turmeric is a spice obtained from the rhizomes of *Curcuma longa*, a ginger family member (Zingiberaceae). Rhizomes are horizontal stems that grow underground that produce shoots as well as roots. The vibrant yellow shade of turmeric derives mostly from lipid-soluble, polyphenolic pigments known as curcuminoids. Turmeric contains the flavonoid curcumin, as well as volatile oils such as tumerone, atlantone, and zingiberone. Other components include carbohydrates, proteins, and resins. Curcumin, which makes about 0.3-5.4 percent of raw turmeric, is the most extensively studied active component. Turmeric rhizome has well-established therapeutic characteristics and has been used by healthcare experts as an anti-inflammatory, anti-diarrheal, hepatoprotective, anti-diabetic, hypolipidemic, and anti-cancer drug [20]. Curcumin administered orally to rats significantly reduced lipid peroxidation, brain lipids, and increased glutathione, a non-enzymic antioxidant. This suggests that curcumin's antioxidative and hypolipidemic properties are responsible for its protective role against ethanol-induced brain injury. [21]



Fig no.8: Curcuma longa

9. Salvia officinalis

Salvia officinalis also known as garden sage or common sage is a perennial, evergreen shrub with woody stems, grayish leaves, and blue to purple flowers. It belongs to the Lamiaceae family and is native to the Mediterranean region. Common sage is a fragrant and therapeutic plant with well-known pharmacological effects. *Salvia officinalis* leaves are used as medicine for their digestive, carminative, antispasmodic, sedative, analgesic, tonic, and diuretic properties, as well as for functional gastrointestinal diseases. The main components found in sage oils were 1,8-cineole, camphor, α -thujone, β -thujone, borneol, and viridiflorol. The essential oil comprises cineole, borneol, and thujone [22]. Studies on the ethanolic extract of the *Salvia officinalis* plant at two doses (200 mg/kg and 400 mg/kg) revealed dose-dependent efficacy against Alzheimer's disease. [23]



Fig no. 9: Salvia officinalis

10. Glycyrrhiza glabra

Glycyrrhiza glabra, or liquorice, is an annual herbaceous plant that belongs to Fabaceae family, with long, cylindrical, elastic roots and runners. The plant's roots and dried runners have long been used medicinally because they contain vital phytoconstituents that include triterpenoids, saponins, glycyrrhizin, flavonoids, or isoflavonoids, chalcones, coumarins, lignins, amino acids, gums, and volatile oils. The main active constituent is glycyrrhizin, in addition to glycyrrhitinic acid and related derivatives, belonging to the class of triterpenoids, and glabridin is the most prevalent isoflavanone. Liquorice root extracts provide numerous health benefits, including treating throat infections, tuberculosis, respiratory and liver illnesses, and providing antibacterial, anti-inflammatory, and immunodeficiency support [24]. The active component glycyrrhizin has been found to have neuroprotective properties against scopolamine-induced neurological disorders. In addition, flavonoids derived from liquorice have been demonstrated to have neuroprotective properties against brain cell death caused by seizures. [25]



Fig no.10: Glycyrrhiza glabra

11. Melissa officinalis

Melissa officinalis commonly known as lemon balm, a perennial bushy plant in the Lamiaceae (previously Labiatae) family, grows upright and can reach a height of approximately 1 m. These delicate, hairy leaves are 2 to 8 cm long, heart-

shaped. It's also known as 'lemon balm' because to its lemon-like flavour and scent. Lemon balm extracts include a variety of useful phenolic components, including phenolic acids, cholinergic acid, flavonoids (including apigenin and luteolin), rosmarinic acid, metrilic acid, caffeic acid, and triterpenes including ursolic and oleanolic acid. Lemon balm has been used for a variety of medical applications, including tonic, antispasmodic, carminative, diaphoretic, surgical wound dressing, sedative-hypnotic, memory boosting, and stress-induced headache treatment [26]. Lemon balm extract has capacity to disrupt the synthesis of β -amyloid, which contributes to Alzheimer's disease, has been attributed to the presence of rosmarinic acid. It has the potential to be a natural and therapeutic choice for people suffering from Alzheimer's disease due to its numerous brain-health benefits. [27]



Fig no. 11: Melissa officinalis

12. Boswellia serrata

Boswellia serrata, also referred to as Salai or Salai guggul, in the family Burseraceae (Genus *Boswellia*). *Boswellia serrata* is a medium-to-large deciduous tree with a maximum height of 18 meters. The bark has a thick, ashy to reddish inner layer and an exterior layer that flakes and is papery thin. The leaves are 20–45 centimetres, alternating, exstipulate, and imparipinnate [28]. *Boswellia serrata*'s resinous component contains four primary pentacyclic triterpenic acids that

block pro-inflammatory enzymes: β -boswellic acid, acetyl- β -boswellic acid, 11-keto- β -boswellic acid, and acetyl-11-keto- β -boswellic acid. *Boswellia serrata* extract has anti-inflammatory effects on mice macrophages and human peripheral blood mononuclear cells (PBMCs) via inhibiting the kinases of mitogen-activated protein (MAP), Nitric oxide, TNF-alpha, and interleukin-1beta (IL-1beta). Incensole acetate, a novel anti-inflammatory present in *Boswellia* resin, inhibits nuclear factor-kappa B activation. Boswellic acids function as direct 5-Lipoxygenase inhibitors to efficiently limit the generation of 5-Lipoxygenase products in standard in vitro test settings [29].



Fig no. 12: Boswellia serrata

13. Camellia sinensis:

Camellia sinensis plant's leaves and buds are used to make Chinese tea. It is a genus of flowering plants that use twigs and branches in place of leaves, and it is a member of the family Theaceae. The length of the leaves is 4–15 cm, and their width is 2–5 cm [30]. About 4% of fresh leaves contain caffeine and other similar chemicals, such as theobromine. Gallate and epigallocatechin's are the main chemical components of catechins. Anti-aging, anti-Parkinson's, anti-cardiac, anti-cancer, and anti-diabetic actions are among the additional health benefits [31]. The tea (*Camellia sinensis*) floral hot water extract's anti-inflammatory

qualities. Pharmacological studies showed that tea flower extract (TFE) could be a useful treatment for paw oedema brought on by croton oil [32]. Furthermore, TFE therapy markedly decreased the levels of nitric oxide (NO), tumour necrosis factor (TNF)- α , and interleukin (IL)-1 β mRNA in patients by reversing the histologic damage and plasma alanine aminotransferase (ALT) increase. These results indicate that tea blossoms have potent anti-inflammatory properties on both the acute and immune systems in vivo, and can be utilised as a functional natural diet [33].



Fig no. 13: Camellia sinensis

CONCLUSION:

Inflammation is a complex process that can have a serious influence on the body, causing a variety of symptoms and illnesses. Neuroinflammation, in particular, can cause considerable harm to the central nervous system. Traditional medicinal herbs such as *Zingiber officinale* (ginger), *Ginkgo biloba*, *Rosmarinus officinalis* (rosemary), and *Curcuma longa* (turmeric) have been found to have neuroinflammation-reducing properties due to their diverse bioactive components. These herbs have anti-inflammatory and neuroprotective qualities, which can help treat disorders including Alzheimer's and Parkinson's disease. Herbal components have been shown to reduce inflammatory mediators and enzymes, including TNF- α , interleukins, and COX-2. This suggests natural alternatives to manufactured medications, which may have toxicity and bad effects. Furthermore, *Camellia sinensis* (Chinese tea) and *Ferula asafoetida* (asafoetida) have been

demonstrated to have anti-inflammatory properties, lending support to the possible efficacy of herbal treatments in the treatment of neurological inflammation. Overall, the study of numerous herbs with anti-neuroinflammatory effects reveals that traditional medicinal plants may be promising treatments for neuroinflammation and related disorders.

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