



A Review On Herbal Medicines As Neuroprotective Agent

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REVIEW ARTICLE

Abstract: Herbal medicines make up a significant component of the trend toward alternative medicine. Herbal medicine is becoming ever more popular in today's world as people seek out natural remedies. Herbal medicines have been used since the dawn of civilization to maintain health and to treat various diseases. Neurodegeneration refers to any pathological condition in which the nervous system or neuron loses its function, structure, or both. Neuronal death happening as a result of progressive disease of long-term and is becoming a major health problem in the 21st century. Many neurodegenerative diseases are caused by genetic mutations, most of which are located in completely unrelated genes. In many of the different diseases neurons degenerated are not changed resulting in a cognitive loss, many neurodegenerative disorders, such as Alzheimer's disease, cerebrovascular impairment, seizure disorders, head injury, parkinsonism. The common pathology of neurodegeneration includes deposition of misfolded proteins such as amyloid- β in Alzheimer's disease, α -synuclein in Parkinson's disease, Neuroprotection refers to the ability for a therapy to prevent neuronal cell death by intervening in and inhibiting the pathogenetic cascade that are able to protect the central nervous system against neuronal injury and neurodegenerative disorders. The past decade has viewed an intense interest in herbal plants having long-term health-promoting or medicinal qualities. To compete with the growing pharmaceutical market, there is an importance to use and scientifically authenticate more medicinally useful herbal products. Comprehensive research and discovery have demonstrated that natural products, medicinal herbs, plant extracts, and their metabolites, have great potential as the neuroprotective agent. Thus the herbal plants can be appreciated source of the drug against neurodegenerative disorders which will require high-throughput screening. This review will provides a general idea of herbal plants and their phytoconstituents against neurodegenerative infections and other related disorders, focusing on their mechanism of action and therapeutic potential.

Keywords: Alzheimer's disease, Antioxidant, Herbal medicine, Neurodegenerative diseases, Neuroprotective.

I. INTRODUCTION

Plants had been used for medicinal purposes long before recorded history. Ayurveda is a medical system primarily adept in India that has been known for nearly 5000 years. It embraces diet and herbal remedies, while highlighting the body, mind and spirit in disease prevention and treatment. Herbal medicine is also called phytomedicine. It refers to using a plant's seeds, roots, leaves, bark, berries, or flowers for medicinal purposes. Herbalism has a long tradition of use outside of conventional medicine. It is becoming more mainstream as improvements in analysis and quality control along with advances in

clinical research show the value of herbal medicine in the treating and preventing disease [3-6].

Neurodegenerative disorders are considered by progressive dysfunction and loss of neurons prominent to the distinct connection of functional systems defining clinical demonstrations. Neurodegeneration is a process involved in both neuropathological conditions and brain aging. It is known that brain pathology in the form of theneurodegenerative and cerebrovascular disease is a leading cause of death all over the world, with an incidence of about 2/1000 and an 8% total death

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rate[12]. Studies have proved that common pathology of neurodegeneration is removal of proteins with altered physicochemical belongings in the human brain. These pathological conformers are called as misfolded proteins such as accumulation and aggregation of amyloid- β in Alzheimer's disease, α -synuclein in Parkinson's disease, huntingtin protein in Huntington's disease [8]. In addition, it has been recognized that protein elimination pathways, like the ubiquitin-proteasome system and the autophagy-lysosome pathway, stress response proteins and chaperones have a high impact on the pathogenesis. People use herbal medicines to try to maintain or improve their health. Many people believe that products labeled "natural" are always safe and good for them. This is not necessarily true. Herbal medicines do not have to go through the testing that drugs do. Some herbs, such as comfrey and ephedra, can cause serious harm. Some herbs can interact with prescription or over-the-counter medicines[13]. The currently available drugs for the treatment of Alzheimer's disease are symptomatic only and do not modify the progression of the original disease and produce adverse reactions in patients thereby having limited scope for the treatment of patients with Alzheimer's syndrome [5]. Research is also intensifying at other substances and treatments that prevent the formation of beta-amyloid plaques, nerve growth factor to keep neurons healthy such as statins, antioxidants and folic acid, anti-inflammatory drugs. The previous era has also witnessed a strong interest in herbal medicines that have long-term health-promoting abilities. Herbal remedies for neurodegenerative disease is becoming more popular in the recent years as they show the prospect to slow down the brain's degeneration. The benefits derived from using herbal treatments have been very capable as they are not only as actual as remedy drugs but also have fewer side effects. The use of some medicinal herbs has been plugged to extend beyond that of modern instruction drugs and may be used as a substitute for pharmaceutical drugs or can be used in conjunction. In this present review articles are the summary have been made to present the mechanistic role of few herbal medicines in the

treatment and controlling of neurodegenerative disorders

Advantages of Herbal Drugs

- ❖ Lowest cost
- ❖ enriched tolerance
- ❖ potency and efficiency
- ❖ complete availability
- ❖ More safety
- ❖ fewer side-effects
- ❖ biodegradable

Disadvantages of Herbal Drugs

- ❖ Not able to cure rapid infection and accidents
- ❖ Risk with self-dosing
- ❖ Difficulty in standardizations

Preparation and Usage of Herbal Drugs

The usage of herbal drugs in the correct way provides effective and safe treatment for many disorders. The effectiveness of the herbal drugs is typically personal to the patient. The strength of the herbal drugs varies based on the growing conditions, genetic distinction, timing and method of harvesting, revelation of the herbs to air, light and humidity, and type of preservation of the herbs[2]. Some of the plants that make up herbal drugs are cultured and processed in the country and others are imported from around the world. Raw materials for herbal drugs may be derived from sensibly cultivated plants or collected in the remote. Herbal drugs are available in several forms and often require preparation before their use [7]. They can be generally purchased in bulk form as dried plants, plant parts or tentatively packed for herbal drinks and decoctions. Decoctions are made by boiling the herb in water, then straining out of the plant material. More intense forms of herbal drugs are available in the form of hydro alcoholic tinctures and fluid extracts. Methods of preparation may differ because of the nature of the plants active chemical constituents [4].

Overview of herbal neuroprotective agents and their mechanical pathway

Neuroprotective treatments are practices designed to interrupt the cellular, biochemical, and metabolic explanation of injury during or following contact to



ischemia; they incorporate a rapidly expanding array of pharmacologic interventions. Neuroprotective agents refer to constituents that are accomplished of preserving brain function and structure by reducing and preventing oxidative stress, mitochondrial dysfunction, and inflammation, various forms of neurotoxicity and protein deficiencies [13]. Exact examples of things that can cause neurodegeneration include: traumatic brain injuries, drug abuse, pharmaceutical medications, strokes, and dementia but the most common cause of neurodegeneration is oxidative stress and to prevent the effects of any neurodegeneration, considering neuroprotective agents may be beneficial for long-term brain health. Direction of a neuroprotective agent may help minimize the effects of chronic conditions that could: kill brain cells, decrease brain volume, and lead to long-term functional impairment [16]. There are more than 120 traditional medicines that are being used for the therapy of Central nervous system disorders in Asian countries [10]. Protein aggregation, inflammation, excitotoxicity, oxidative stress, and neurotoxicity have been implicated in the pathophysiology of NDs. In the Indian system of medicine the following medicinal plants have shown promising activity in neuro-psycho-pharmacology.

Allium sativum

Allium sativum belongs to the family *Amaryllidaceae*, generally known as garlic, is one of the most extensively mentioned herbs found in the old medical literatures mainly for its medicinal abilities in prevention and treatment of cardiovascular and other metabolic diseases, , thrombosis, hypertension, dementia, atherosclerosis, hyperlipidemia, cancer and diabetes [14, 15]. Allicin and alliin are the principal bioactive compounds of *Allium sativum*. S-allyl cysteine (SAC) is the major constituent of aged garlic extract (AGE) which is extensively studied [16, 17]. S-allyl cysteine has both direct and indirect antioxidant activity. Apart from decreasing lipid peroxidation and DNA fragmentation, it also reduces protein oxidation and nitration. In 1-methyl-4-phenyl pyridinium (MPP) and 6-hydroxydopamine (6-OHDA) models of Parkinsonism, S-allyl cysteine protected dopamine levels, oxidative damage and

lipid peroxidation. It also increased manganese and copper/zinc superoxide dismutase activity and prohibited behavioural changes. AGE, directly and indirectly, activates expression of important genes needed for neuronal survival [18, 19]. Allyl-containing sulfides in garlic cause the up regulation of neuroprotective proteins such as mitochondrial uncoupling proteins. Allicin also activates transient receptor potential ion channels in the plasma membrane of neurons [20, 21].

Curcuma longa

Curcuma longa belongs to the family Zingiberaceae is a gold-coloured Spice that has been used as a traditional medicine. Curcumin, the principal constituent of turmeric, has several known neuroprotective actions [33]. In Alzheimer's disease, it has been shown that curcumin has the ability to bind A β peptides, prevent aggregation of new amyloid deposits and promote disaggregation of existing amyloid deposits [34]. Scientific studies also reported that curcumin and its analogues demethoxycurcumin and bis-demethoxycurcumin can protect cells from A β -induced oxidative stress [35]. Curcumin has the ability to inhibit A β oligomerization and fibril formation, enhance A β uptake by macrophages and inhibits the peroxidase activity of A beta-heme complex [36]. *In vitro* and *in vivo* studies suggest that curcumin has various mechanisms, which supports the concept of it interacting with multiple cellular signalling pathways and modulating numerous molecular targets. It exerts anti-inflammatory, anti-tumour, antioxidant and antiangiogenic properties through the modulation of numerous biochemical mediators (Hewlings et al., 2017; Peddada et al., 2019). Peroxisome proliferator-activated receptor- γ (PPAR- γ) ligands play an antiangiogenic role in AMD. Curcumin, a PPAR- γ agonist, may therefore play a role in mitigating AMD progression through the down-regulation of the proinflammatory functions of microglia. Recently, Saberi et al. (2019) reported that curcumin activates PPAR- γ that, in turn, down-regulates matrix metalloproteinases production. It is well-known that matrix metalloproteinase-9 causes extracellular matrix degradation and stimulates RPE cell migration



to Bruch's membrane, and thus contributes to AMD pathogenesis. It has also been shown that curcuma extract and its curcuminoids provide significant protection against photooxidative damage and apoptosis in human retinal pigment epithelial cells laded with A2E in a dose-dependent manner [14]. Curcuminoids, polyphenol compounds from turmeric attenuate mitochondrial dysfunction induced oxidative stress and inflammatory responses to inflammatory cytokines, COX-2, and iNOS. Curcuminoids also bind to A β plaques to inhibit amyloid accumulation and aggregation in the brain [37, 38].

Ginkgo biloba

Ginkgo biloba belongs to the family *Ginkgoaceae*. The therapeutic benefits of ginkgo extracts have long since been known, with a established history of use in traditional Chinese medicine. More recently, clinical studies have discovered the potential benefits of ginkgo for a wide range of pathological disorders, including neuroprotective activities [17]. About its chemical composition, two main groups of bioactive metabolites are reflected responsible for ginkgo medicinal effects: terpene lactones and ginkgo flavones (quercetin, kaempferol and iso-rhamnetin glycosides as the main flavonoids, together with biflavonoidsginkgetin. The pharmacologically active ginkgo leaf extracts are available as standardised preparations EGb 761 and LI1370. Free radical quenching properties, reduction of platelet aggregation and improved blood flow of ginkgo extracts are attributed to the antioxidant and radical scavenging properties of ginkgo flavonoids and terpenoids, along with the potent platelet activating factor inhibition of ginkgolides [9]. In addition, flavonoids probably reduce oxidative damage to lipid membranes. Therefore, due to vascular factors and oxidative damage are hypothesized as potential mechanisms in AMD pathology, an interest in using ginkgo extract has aroused for AMD treatment. Presently, ginkgo extract is measured safe within the daily dose range. It is worth stating, however, the increased risk of bleeding because ginkgolides are potent platelet activating factor antagonists. *In vitro* and *in vivo* experiments have shown the beneficial

effects of EGb 761 on functional retinal impairment, retinal microcirculation and retinal tissue protection from oxidative stress [20]. Preliminary clinical studies have considered the efficacy of ginkgo extracts, including two randomized controlled trials with positive effects on vision in patients. According To many research on ginkgo clinical efficacy should be carried out.

Glycyrrhiza glabra

Glycyrrhiza glabra, belongs to family Leguminosae. *Glycyrrhiza glabra* commonly known as Yashtimadhu. The major flavonoid of *G. glabra* is Glabridin that possesses multiple pharmacological activities like anti-diabetic, antioxidant, antiviral, anticancer, anti-ulcer, immunomodulatory activity, antimicrobial activity, anti-inflammatory activity, and anticonvulsant. Liquorice expressively improved learning and memory but the research have indicated that its consumption improves the general intelligence rather than short-term memory. Glabridin significantly declines the level of MDA and it upraises the level superoxide dismutase and reduced glutathione in the brain [18]. A study indicated that organization of *G. glabra* restored the decreased levels of brain enzymes such as glutamate and dopamine and decreased AChE activity [19].

Hypericum perforatum

Hypericum perforatum is a member of the family Hypericaceae. *Hypericum perforatum*, is also known as hypericum or millepertuis. Even though it has a worldwide distribution, it is mainly native to Europe, western Asia, Europe and northern Africa. Hyperoside is the main active factor of H [22]. *perforatum*. Biapigenin, Hypericin, quercetin, Kaempferol are its other constituents. *Hypericum perforatum* extract has also been described to protect against enzymatic (NADPH-dependent) and non-enzymatic (Fe²⁺/ascorbate dependent) lipid peroxidation in the cerebral cortex. The extract also protects brain cells from glutamate-induced cytotoxicity by reducing glutathione loss, calcium overload and ROS-mediated cell death. *Hypericum perforatum* ethanolic extract may improve microglial viability by reducing amyloid-beta mediated toxicity in Alzheimer's



disease[19]. *Hypericum perforatum* inhibits acetylcholinesterase enzyme and MDA formation in the brain and increases the level of SOD, CAT, GPx. According to these findings, *Hypericum perforatum* also act as an antioxidant and have the ability to bind iron ions and have scavenging action for hydroxyl radical.

Melissa officinalis

Melissa officinalis L. belongs to the family Lamiaceae, and it is also known as lemon balm, are used in traditional medicine for its nerve calming and spasmolytic effects. The leaves produce calming and soothing effects through GABA_A benzodiazepine receptor [13]. Its extracts contain some compounds such as flavonoids such as quercitrin as well as apigenin, luteoline and phenolic acids. These derivatives inhibit enzymes monoamine oxidases and AChE, scavenge these free radicals and prevent apoptosis[19]. The inhibition of these enzyme leads to improvement of depression symptoms. Research also suggests that *Melissa officinalis* employ protective activities in the PC12 cell line and might protect neurons from oxidative stress.

Ocimum sanctum

Ocimum sanctum, belongs to family Labiatae, also known as 'Tulsi' in Hindi and 'Holy Basil' in English. The plant is also defined to contain saponins, tannins, alkaloids and glycosides, vitamin C, and maleic acid, citric and tartaric acid [11]. A research conducted by Kusindarta et al. directed that an ethanolic extract derived from leaves of *Ocimum sanctum* may stimulate and restores the expression of choline acetyltransferase in ageing human cerebral microvascular endothelial cells and could deliver nerve protection and increased production of Ach may enhance the memory and cognitive ability [18]. Scientific studies reveal that the hydroalcoholic extract of *Ocimum sanctum* exhibits strong antioxidant ability against DPPH and hydroxyl radicals which may be due to the high amount of flavonoids and polyphenols. It inhibits lipid peroxidation, DNA damage, ROS generation and membrane depolarization [23]. It also declines the lactate dehydrogenase leakage and conserved the

cellular morphology, restored superoxide dismutase and catalase enzyme levels thereby preventing neuronal damage.

Nigella sativa

Nigella sativa L. (*N. sativa*) belonging to *Ranunculaceae* family, is an annual herbaceous and which widely grown in the Mediterranean countries, Eastern Europe, Western Asia and Middle East [4]. The *Nigella sativa* seeds have been added as a spice to range of Persian foods such as, sauces, bread, pickle, and salads. Chemical components of *Nigella sativa* seeds include carbohydrate, oil, protein, and fiber. The fixed oil chemical compositions of *N. sativa* are linoleic acid, oleic acid, Eicosadienoic acid, Stearic acid, Palmitic acid, Arachidic acid Linoleic acid and Myristic acid [14]. The major phenolic compounds of *Nigella sativa* seeds are p-cymene, Thymoquinone and thymol *Nigella sativa* as a medicinal plant is recognized for its potent anti-oxidative effects. It has been reported that *Nigella sativa* have defensive effects on the renal damage. *Nigella sativa* seeds could expressively ameliorate the spatial cognitive deficits caused by chronic cerebral hypo perfusion in rats. Furthermore, Antioxidant effects of *Nigella sativa* oil on the patients with rheumatoid arthritis exhibited [11]. *Nigella sativa* also improved inflammatory responses and condensed oxidative stress in patients with rheumatoid arthritis. In the other clinical trial, 40 healthy volunteers were divided into the treatment with capsules of *Nigella sativa* (500 mg) and placebo (500 mg) twice daily for 9 weeks. *N. sativa* enhanced memory, attention and cognition compared to the placebo group. Neuroprotective effects of *Nigella sativa* and thymoquinone on various nervous system disorders such as Alzheimer disease, epilepsy and neurotoxicity have been revised [22].

Withania somnifera

Withania somnifera belongs to the family *Solanaceae*, generally known as Ashwagandha is considered as the Indian ginseng. The major ingredients of Ashwagandha root are two withanolides, withaferin A and withanolide D [23]. Active glyco-withanolides of *Withania somnifera*



have important antioxidant activity. Ashwagandha is also reported as a Nervine tonic that rejuvenates the cells and boosts energy. According to Rajasankara, oral treatment of PD mice with *Withania somnifera* root extract (0.1 g/kg body weight) for 7 day or 28 day prominent dopamine, 3,4-dihydroxy phenyl acetic acid and homovanillic acid levels in the corpus striatum [19]. Additionally, it was reported that *Withania somnifera* treatment increased the level of anti-apoptotic proteins and decreased the level of the pro-apoptotic proteins in the Maneb-Paraquat-induced dopaminergic neurodegeneration model of PD. Ashwagandha extract has shown to avoid the lipid peroxidation and increase the antioxidant activity by increasing the free-radical scavenging enzymes levels in the brain.

II. CONCLUSION

The neurodegenerative diseases remain a challenge in the modern medicine because of their complex pathogenesis. Protein misfolding and their addition inside or outside of neurons is the key pathological feature in several neurodegenerative diseases including Alzheimer's, Parkinson's Huntington's disease. Medicinal herbs as potential source of therapeutics aids has achieved a significant role in health care system all over the world for human lives not only in the contaminated condition but also as potential material for keeping proper health [17]. It is clear that the herbal industry can make great strides in the world. With the increased use of herbal products, the future worldwide labeling practice should adequately address quality aspects. Standardization of methods and quality control data on safety and efficacy are required for understanding of the use of herbal drugs [16]. A major factor delaying the development of the medicinal plant based industries in developing countries has been the lack of information on the social and economic benefits that could be resulting from the industrial utilization of medicinal plants. Further research is required to exploit the compounds responsible for the observed biological activity [17]. Our review has recognized several herbal medicines such as such as *Allium sativum*, *Ginkgo biloba*, *Terminalia chebula* with potential therapeutic effects for

neurodegenerative diseases. It is anticipated that the information provided through this review should help the researcher to provide some evidence and conceptual detail of the benefit of a wide range of herbs as neuroprotective agents.

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