GSC Biological and Pharmaceutical Sciences
eISSN: 2581-3250 CODEN (USA): GBPSC2
Cross Ref DOI: 10.30574/gscbps
Journal homepage: https://gsconlinepress.com/journals/gscbps/

(REVIEW ARTICLE)

Check for updates

Exploring the neuroprotective potential of herbal plants: A comprehensive review

Vishal D. Lahane [1] and Vinayak A. Katekar [2,*]

[1] *Department of Pharmacology, P R Pote College of Pharmacy, Amravati, India.*
[2] *Department of Quality Assurance, Shraddha Institute of Pharmacy, Washim, Maharashtra, India.*

GSC Biological and Pharmaceutical Sciences, 2024, 27(03), 141–148

Publication history: Received on 02 May 2024; revised on 08 June 2024; accepted on 11 June 2024

Article DOI: https://doi.org/10.30574/gscbps.2024.27.3.0175

Abstract

Neuronal damage resulting from traumatic brain injuries, strokes, and various neurological conditions poses significant challenges to modern medicine. In recent years, there has been a growing interest in the exploration of herbal plants as potential allies in safeguarding and supporting the nervous system. Among these botanical candidates, Ginkgo Biloba and turmeric have emerged as the most extensively researched herbs due to their promising neuroprotective properties. This review paper aims to provide a comprehensive overview of the neuroprotective activity of these herbal plants, shedding light on their mechanisms of action and therapeutic potential. The choice of research methodology in this field is multifaceted, with studies employing in vitro models using cell cultures, animal experiments utilizing mice and rats, and, in some instances, human clinical trials. These diverse research methods have enabled a deeper understanding of how herbal compounds interact with nerve cells, ensuring a rigorous evaluation of their safety profiles, and exploring their applicability as therapeutic interventions. This review paper synthesizes and critically analyzes the available body of evidence, encompassing both preclinical and clinical studies, to present a comprehensive perspective on the neuroprotective effects of Ginkgo Biloba and turmeric. The findings not only illuminate the potential of these herbal remedies in mitigating neuronal damage but also highlight the need for further research to unlock their full therapeutic potential. In an era where the demand for natural and alternative approaches to neurological disorders is on the rise, this review serves as a valuable resource for researchers, healthcare professionals, and the wider community seeking insights into the promising realm of herbal neuroprotection.

Keywords: Neuroprotection; Curcumin; Neuroprotection; Ginkgo Biloba; Traumatic brain injuries T

1. Introduction

An important and quickly expanding area of study in the fields of natural medicine and pharmacology is the study of herbal plants' neuroprotective properties. The potential of several herbs and plant constituents to promote and safeguard the health of the nervous system has been investigated[1].

The loss of the central nervous system (CNS) in neurodegenerative conditions results in either diminished functioning or sensory impairment[1]. Neurodegenerative disorders include Multiple Sclerosis (MS), Parkinson's disease, Alzheimer's disease, and others [2].

Numerous illnesses that impact the nervous system, such as traumatic brain injuries, neurodegenerative diseases, strokes, infections, and other conditions, can result in neuronal damage. Depending on where and how much neuronal damage occurs, the effects might be severe and diverse. There are several common problems linked to neuronal damage, including cognitive impairment, motor impairment, sensory loss, emotional and behavioral changes, neurodegenerative diseases, stroke, traumatic brain injury, and neuropathic pain. The utilization of distinctive, precisely defined chemical molecules is a component of modern pharmacotherapy. The biggest challenge confronting researchers is creating a

* Corresponding author: Vinayak A. Katekar

Copyright © 2024 Author(s) retain the copyright of this article. This article is published under the terms of the Creative Commons Attribution Liscense 4.0.

medication or treatment that can cross the blood-brain barrier, simultaneously affect many disease pathways, and have minimal adverse effects when taken at higher concentrations in humans. Therefore, researchers anticipate a paradigm shift from monotherapy—which employs isolated medications to target a specific cellular pathway—to multitherapy, which focuses on a number of targets and has a better chance of being effective. In order to do this, natural compounds derived from known phytochemicals that have Potential therapeutic abilities are being used[3]. The majority of our understanding of phytochemicals comes from conventional medicine and ancient herbal knowledge that has been used for thousands of years in developing nations like India. As a result, the use of herbal products has seen a substantial increase in popularity in Western countries in recent years. In order to provide better treatments, there is rising support for combining contemporary drugs with established therapies.

In recent years, greater attention has been given to ancient medicine. In traditional medicine, a large number of plants have been used to treat neurodegenerative illnesses such as Alzheimer's disease (AD) and other memory-related disorders.[4] Traditional herbalism and natural medicine are both interested in the use of herbal plants for neuroprotective action. In order to stop or delay the progression of Neurodegenerative illnesses and cognitive decline, neuroprotection refers to methods and substances that support maintaining the structure and functionality of neurons (nerve cells) in the brain and nervous system. In recent years, there has been growing interest in exploring the ability of plants and their bioactive compounds as a source of neuronal protection. These naturally occurring compounds have shown promise in attenuating neuronal damage, enhancing neuronal survival, and maintaining memory function.[5] Herbal plants are taken into consideration for their potential to protect neurons for several reasons, including historical and traditional use, complex chemical composition, natural source, multifaceted benefits, and the ability to target many pathways. Herbal treatments for a range of illnesses, including cognitive and neurological diseases, have been used for a very long time in numerous civilizations. Oftentimes, traditional herbal knowledge offers insights regarding plants that could be neuroprotective. Plant organs, such as leaves, stems, roots, flowers, fruits, and seeds, have been utilized as alternative and supplementary treatments in herbal medicine. Some plants have neuroprotective properties, such as resveratrol, curcumin, ginsenoside, polyphenols, triptolide, etc.3 Many different bioactive substances, including flavonoids, alkaloids, terpenoids, and polyphenols, are frequently found in herbal plants. Plant compounds known as phytochemicals, include polyphenols, flavonoids, alkaloids, and terpenoids, which exhibit antioxidant, anti-inflammatory, and anti-apoptotic activities, and have shown to be neuroprotective. They have the power to alter numerous cellular processes related to the health and viability of neurons. Numerous plant-derived bioactive compounds have been studied extensively for their potential neuroprotective effects, including resveratrol from grapes, curcumin from turmeric, quercetin from onions, and ginkgo biloba extracts.[6,7] These substances may have anti-inflammatory, antioxidant, and other advantageous properties that could help with neuroprotection. Herbal plants are products of nature, and many who support herbal medicine contend that natural substances are more readily absorbed by the body and have fewer side effects than synthetic pharmaceuticals. Some herbal plants may have potential neuroprotective benefits among their many other physiological effects. For instance, several herbs may strengthen antioxidant defenses, and support the immune system, and blood circulation, all of which may promote overall brain health. Complex and linked pathways, such as oxidative stress, inflammation, mitochondrial dysfunction, and protein misfolding, frequently play a role in neurodegenerative disorders. Due to their multi-target effects, herbal substances may target many of these pathways at once. When referring to a substance's capacity to prevent nerve cells (neurons) from deterioration or injury, which is frequently linked to disorders like neurodegenerative diseases, oxidative stress, inflammation, and more, we are referring to herbal plants or their constituents. These substances may stimulate brain healing, increase neuronal survival, and regulate a number of cellular processes. The goal of the discipline of neuroprotection is to provide methods and interventions that will protect the nervous system's health and functionality, notably from various neurodegenerative diseases like Alzheimer's, Parkinson's, and stroke. Plants have long been a source of bioactive compounds with various pharmacological properties, and their neuroprotective potential has gathered attention because of their potential to alter various cellular pathways implicated in neurodegeneration[8, 9]. The preservation of the structure and function of neurons against insults resulting from cellular damage brought on by a number of agents or neurodegenerative disorders is known as neuroprotection. Traditional medicine has received increased attention in recent years. Through methods that include preventing protein-based deposit buildup, oxidative stress, and neuroinflammation, as well as treating deficiencies of neurotransmitters like acetylcholine and dopamine, medicinal herbs provide neuroprotective properties[10].

2. Plants with Neuroprotective activity

2.1. Ginko Biloba

One of the herbs with the most research on it for potential neuroprotective properties is ginkgo biloba. Researchers have looked at the antioxidant and anti-inflammatory characteristics of its active ingredients, including terpenoids and flavonoids, which may be beneficial to brain health. Standardized Ginkgo biloba extract (GBE), obtained from dried

Ginkgo leaves, is used as a medicinal medication to treat dementia, including Alzheimer's disease (AD), and memory loss[11]. Ginko Biloba has a variety of chemical components, including tri-lactonic diterpenes and ginkgolides A, B, and C. There are also flavonoids such as proanthocyanidins, trilactonic sesquiterpene, isorhamnetins, and quercetin. Major antioxidants are known to be flavonoids. Additionally, in preclinical AD models, GBE demonstrated neuroprotection and anti-inflammatory properties [12]. In vitro investigations using human brain tissues that have undergone oxidative damage due to exposure to hydroxyl ($OH^{\bullet}$) or superoxide ($O2^{\bullet}$) free radicals produced by Co^{60} irradiation revealed a protective effect of Ginkgo biloba extract. Inhibiting the oxidative damage brought on by H2O2/FeSO4 with EGb 761 extract efficiently protected rat cerebellar granule cells from apoptotic cell death[13]. The flavonoid components of G. biloba, namely kaempferol, and quercetin, which decreased ROS in the body in both in vitro and in vivo models, are linked to the antioxidant activity in the extract[14]. It can be deduced from several in vitro and in vivo investigations that Ginkgo biloba's components have neuroprotective qualities. These characteristics could help defend neurons against oxidative stress and inflammation, two factors linked to a number of neurodegenerative diseases. As potential methods of action, it is possible to explore PAF antagonistism, free radical scavenging, interactions with neurotransmitters, and even the production of growth factors. Clinical research indicates that the Ginkgo biloba leaf extract may be clinically effective in the treatment of mild and moderate dementia[15]. The potential advantages for cognitive function and its capacity to ward off neurodegenerative illnesses have received the majority of attention in studies on Ginkgo Biloba's neuroprotective action. Cognitive Improvement, Neurodegenerative Diseases, Anti-Inflammatory and Antioxidant Effects, Blood Flow, and Vasodilation are some of the research fields. According to certain studies, it may have somewhat beneficial effects on cognitive function, especially in elderly persons. The precise mechanisms underlying these effects are not entirely known, and outcomes have been inconsistent.

2.2. Turmeric

Turmeric has long been used in Asia as a spice and traditional herbal treatment. Epidemiological evidence suggests that consuming curry with turmeric enhances cognitive function in elderly Asians[16]. The main yellow polyphenol found in turmeric (Curcuma longa) rhizomes is curcumin. According to research, curcumin has the potential to protect the brain by attaching to redox-active metals[17]also, according to numerous studies, curcumin must be paired with a bioavailability enhancer such as piperine because it does not easily enter the blood-brain barrier[18]. When coupled with prepared turmeric extract and essential oils, Al-induced cognitive deficits and toxicity in mice might be reduced. Demethoxycurcumin (DMC), bisdemethoxycurcumin (BDMC), and curcumin (CUR) are three of the phenolic, yellowish curcuminoids found in turmeric. Turmeric extract combined with essential oil is a promising therapeutic strategy for the prevention and treatment of neurodegenerative diseases, since it may considerably lower neuroinflammation and oxidative stress and improve memory in mice exposed to aluminum[19]. The neuroprotective potential of curcumin in PD also is related to its antioxidant properties. also it has shown that curcumin restored ROS intracellular accumulation in human cell line SH-SY5Y exposed to 6-OHDA.[20,21] When rats were treated for AD with Cur-NLCs, their capacity for learning and memory greatly increased. The results suggest that pre-treatment of AD rats with Cur NLCs may be able to reduce the deficits induced by an A injection by maintaining favorable conditions for neuronal activity. Curcumin Nanostructured lipid carrier therapy for AD mice also decreased the number of amyloid plaques, which relieved the symptoms of the condition. Our results suggest that curcumin may even be helpful after the onset of a disease. When utilized as a neuroprotective agent, the availability of curcumin in the brain presents a challenge. Orally consumed curcuminoids are swiftly broken down by the liver after entering the body. In the liver and intestinal mucosa, phase I metabolism transforms curcuminoids into tetrahydrocurcumin (THC) and hexahydrocurcumin (HHC). Curcumin glucuronide and curcumin sulphate are produced by substantial conjugation of curcuminoids and their reductive metabolites with glucuronic acid and sulfate in phase II metabolism[22]. The porosity of the blood-brain barrier and curcumin's poor absorption limit its therapeutic potential. Free curcumin can be supplied to target tissues to have the desired therapeutic effects by improving its bioavailability in the brain and plasma.

2.3. Brahmi (*Bacopa monnieri)*

it is a very well-known perennial, creeping herb from the Indian Ayurveda system; It contains different bioactive phytoconstituents used in the therapeutic management of several life-threatening Diseases. This herb was used by Ancient Vedic scholars due to its pharmacological effect, especially as a nerve tonic and nootropic booster. It has been used in Ayurveda for therapeutic purposes since the dawn of humanity. It is employed in the management of tumors, ulcers, asthma, and epilepsy. It is referred to as a "MedhyaRasayan" drug, which is used to improve memory. According to "Ayurveda," the Indian traditional medical system, "Medhyarasayanas" possess natural therapeutic properties that support memory, reestablish intellectual deficiencies, and enhance mental capacity. Since over three thousand years ago, clinical Ayurveda specialists in India have used intellect (Medhya)[29]. On measuring the concentration of compounds in ethanolic extracts by HPLC active components of Brahmi were found to be substances from the saponin group. The results showed that mixtures of at least five saponin glycosides, including bacoside A3, bacopaside II, bacopasaponin C isomer, bacopasaponin C, and bacopaside l, are present in combinations containing 5.04 0.40% (w/w) of ethanolic

extraction of the aerial part of Brahmi plants[23].Bramhi has the potential to reduce intracellular ROS. The quantity of intracellular ROS in Brahmi-treated cells was measured to determine whether the antioxidant properties of Brahmi extract contribute to cortical cell survivability in culture conditions. The amount of intracellular ROS, measured as the ratio of ROS/cell viability, decreased in cells treated with 100 g/ml Brahmi for 48 h compared to untreated cells. This finding implies that Brahmi can lessen the intracellular oxidative stress experienced by cultured cortical neurons, which may result in a longer lifespan for the neurons in the culture medium. Brahmi appears to improve the survival of cortical neurons in culture in addition to preventing the damage that A25-35 causes to neurons. It is conceivable that compounds in Brahmi extract extend the longevity of neurons in culture media in some way by encouraging cell survival or delaying cell death. Brahmi has a therapeutic potential possibly as an alternate therapy for reducing the progression of Alzheimer's disease. According to studies, Brahmi extract has the ability to treat neurodegenerative diseases linked to oxidative stress and amyloid-induced memory loss as well as prevent memory loss due to aging [23]. *Bacopa monnieri* has been shown to influence neurotransmitter systems in the brain, particularly acetylcholine. By enhancing cholinergic transmission, *Bacopa monnieri* may support cognitive processes and potentially offer neuroprotection. In India, some pharmaceutical companies have formulated syrups of Bramhi with other herbs as neurotoxic and which are being used on large scales. Brahmi's effects have been investigated in a variety of human clinical investigations, most of which have concentrated on its capacity to improve cognition. Bramhi has a notable beneficial impact on the retention of freshly acquired knowledge [24]. Bacosides A and B are the active ingredients in *B. monnieri* that have been shown to have cognitive benefits. Triterpenoid saponins are also responsible for enhancing nerve impulse transmission. By promoting kinase activity, neuronal synthesis, the recovery of synaptic activity, and nerve impulse transmission, the bacosides also assist in the repair of injured neurons. When acetylcholinesterase activity is suppressed, the cholinergic system performs better, which improves working memory, attention, and memory retrieval in senior persons. Due to its biological activity, Brahmi, also known as *Bacopa monnieri*, may be used as a memory-enhancing alternative source for the development of new neurological agents. Recent studies have demonstrated the efficacy of Brahmi as a medication for enhancing mental health as well as the prevention and treatment of age-related cognitive decline[25].Numerous convulsive models were used to test the anticonvulsant effects of the strong nootropic medication *Bacopa monnieri* in albino rats. In this study, formulations of *Bacopa monnieri* (*Bramhi Ghrita*) and Saraswatarishta, two of the most widely used dosage forms of this well-known medicine, were assessed for their anti-convulsion effectiveness against phenytoin, and various stages were recorded on the eighth day of the experiment on all four groups. In comparison to the control, Bramhi Ghrita had a more significant impact on the phases of extension and recovery. In comparison to the control, both formulations dramatically shortened the rat's MES-induced convulsions' length and time to recover. Activity is predicted by the inhibition of MES-induced convulsions. in opposition to tonic-clonic convulsions. Brahmi Ghrita and Saraswatarishta have promising anti-convulsive activity with better restorative effects [26]. Fresh whole plant BM extract was found in clinical trials to improve different elements of cognitive function in both children and adults. It was traditionally applied to infants in order to "open the gate of Brahma" and enhance their intelligence. Today, it is administered to students for the same reason numerous studies have shown that BM has positive effects on both humans and animals. As a result, BM has been made available on the market in India and other nations, where it is used to treat memory and attention issues either by itself or in combination with other phytocomplexes[27]. The commercial medication demonstrated a remarkable nootropic efficacy, especially in younger patients[28]. The alcohol and hexane components of *B. monnieri* have anti-oxidant capabilities that prevent the lipid peroxidation impact. It shows great potential in enhancing many neuro-pharmacological illnesses, aggravation, and other issues. Conventional treatments for treating a variety of ailments make heavy use of the methanolic and ethanolic extracts of *B. monnieri*. Additionally, the most significant phytochemical obtained from this plant and used to make a variety of therapeutic drugs is known as bacoside A. The anticancer, antidiabetic, alleviating, antibacterial, antioxidant, and memory-enhancing effects of Brahmi are proven [30]. Other academic research also demonstrated the antioxidant activity of *B. monnieri* through other ways. i.e., by preventing the activities of glutathione peroxidase (GPX), catalase, and superoxide dismutase (SOD).The superoxide anion can be restrained by the methanolic extract. It has been reported in numerous studies that *B. monnieri* crude water extract suppresses epilepsy. Sedative effects are produced by the plant extract. It is known that drugs that stimulate the neurotransmitter GABA have anticonvulsant, analgesic, and sedative effects [31.32].

2.4. Ashwagandha (*Withania somnifera*)

Withania somnifera, an ancient plant relied on in traditional Ayurvedic treatment, has been shown to have neuroprotective properties among its many possible benefits for health. The term "neuroprotection" describes a substance's capacity to protect the nervous system, in particular nerve cells (neurons), against harm and deterioration. While some study indicates that ashwagandha may have neuroprotective properties, it's critical to remember that more research is required because the scientific data is not yet conclusive. The chemical compounds known as withanolides are principally liable for *Withania somnifera*'s medicinal effects. The antioxidant, anti-inflammatory, anti-cancer, hemopoietic, and rejuvenating attributes of WS and its constituents are the basis for its multimodal positive effects. Numerous neurological conditions, such as Alzheimer's disease, Parkinson's disease, Huntington's disease, anxiety

disorders, and cerebral ischemia, have been proven to gain benefits with WS[33]. The root extract of *Withania somnifera* Dunal, known as Ashwagandha, has shown anti-inflammatory, antioxidative stress, and neuroprotective properties that activate choline acetyltransferase, inhibit corticosterone release, and increase serotonin in the hippocampus. The proposed technique may be effective at reducing NO and modifying neurochemical mechanisms within neurotransmitter systems, thus offering a potential therapy for Neurodegenerative diseases [34, 35]. Included *Withania somnifera* root powder linctus (200 mg twice daily after meals) to the patient's existing insomnia treatment plan. After receiving treatment for two months, the patient stated that all of the restless leg syndrome symptoms (RLS) had vanished, going from three bouts per week to none at all when she was checked again after a month. When it was first described, this was the only instance where the use of *Withania somnifera* may have completely resolved refractory RLS in a case of Parkinsonism Disease. In addition, the motor problems and sleeplessness partially subsided. *Withania somnifera*, especially in situations of advanced and refractory PD, may be able to halt the course of symptoms due to its neuroprotective and pro-dopaminergic effects [36]. The reduction in motor symptoms after the addition of *Withania somnifera* is due to its neuroprotective effect and the resultant improvement in native dopamine activity [37]. Improvement in insomnia, however, has also been attributed to stimulation of $GABA_A$ receptors by *Withania somnifera*[38]. *Both physically and physiologically, developed PC12 cells resemble real brain neurons. In a concentration-dependent manner, a study showed that pretreatment of differentiated PC12 cells with an aqueous extract of W. somnifera root effectively protected dPC12 cells from both H2O2- and Ab-induced cytotoxicity*[39]*. A 6-hydroxydopamine-induced model in rats and a lithium-pilocarpine-induced seizures model of status epilepticus in rats revealed that W. somnifera root extract also had neuroprotective properties* [40].

2.5. Gotu Kola (*Centella asiatica*)

Southeast Asian countries like India, Sri Lanka, China, Indonesia, and Malaysia, as well as South Africa and Madagascar, are dwelling to the tropical medicinal plant *Centella asiatica* (L.) Urban (Syn. *Centella coriacea* Nannfd., *Hydrocotyle asiatica* L., *Hydrocotyle lunata* Lam., and *Trisanthus cochinchinensis* Lour.)[41]. *Centella asiatica*, sometimes referred to as gotu kola or Indian pennywort, is a medicinal herb that has been utilized for many years in several forms of conventional medicine, most notably Ayurveda and traditional Chinese medicine. Among other potential health advantages, it is well known for its neuroprotective capabilities. *C. asiatica* has been reported to be endowed with a wide range of biological activities desired for human health, such as wound healing, in addition to its neuroprotective effects [42, 43, 44]. Several biological elements, which include flavonoids, terpenoids, essential oils, alkaloids, carbohydrates, and amino acids, have been found in CA by scientific studies [45]. CA has been applied to increase intelligence and promote cognitive function since ancient times and now, it has been experimentally proven through 28 human samples that CA may improve mood and enhance memory[46]. A 14-day oral administration of *C. asiatica* aqueous extract in doses of 100, 200, and 300 mg/kg has been reported to improve cognitive functioning in normal rats in a dose-dependent manner also Streptozotocin-induced cognitive impairment was substantially reversed by pretreatment with the extract for 21 days[47,48]. Rats memory and cognition were improved by *C. asiatica* aqueous leaf extract, which additionally influenced the dopamine, 5-hydroxytryptamine (5-HT), and noradrenaline systems in the rat brain in vivo[49]. Recent research investigations additionally discovered and proven that *C. asiatica* serves as an antioxidant, minimizing the effect of oxidative stress in vitro and in vivo, in addition to previous discoveries. At the in vitro level, *C. asiatica* promotes dendritic arborization and elongation while also protecting against apoptosis in the neurons. Studies conducted in animals indicate a protective effect of *C. asiatica*'s entire extract and specific components against an array of neurological disorders. The majority of in vivo studies on neuroprotective effects have been on epilepsy, learning and memory augmentation, neurotoxicity, Alzheimer's disease, Parkinson's disease, and other mental diseases like depression and anxiety[50]. A study involving feeding 7-day-old rat pups fresh juice from *C. asiatica* leaves at doses of 2, 4, and 6 mL/kg body weight for 2, 4, and 6 weeks revealed a substantial boost in dendritic length and dendritic branching points. Only the neurons of rats treated for longer periods (4 and 6 weeks) with 4 and 6 mL *C. asiatica*/kg body weight/day showed significant increases, suggesting that the effects were dose- and duration-dependent [51, 52].

3. Conclusion

It's vital to keep in mind that much of the study is still in its early phases, even though there is encouraging research about the neuroprotective potential of numerous herbal plants and their chemicals. To determine the safety and effectiveness of these herbal remedies for neuroprotection and to comprehend their potential role in controlling neurodegenerative diseases and boosting general brain health, more thorough investigations, including clinical trials, are required. After thorough research and clinical trials, these herbs may be used as supplementary treatment as well as formulated dosage forms to protect and enhance neuronal health.

While there's promising research regarding the neuroprotective potential of various herbal plants and their compounds, it's important to note that much of the research is still in its early stages. The effects can vary, and more comprehensive

studies, including clinical trials, are needed to establish the safety and efficacy of these herbal treatments for neuroprotection and to understand their potential role in managing neurodegenerative disorders and promoting overall brain health.

Compliance with ethical standards

Acknowledgments

We would like to thank the authors for their contributions to the excellent outcome of this review.

Disclosure of conflict of interest

The authors declare no conflicts of interest.

References

[1] MATTSON MP. Metal-Catalyzed Disruption of Membrane Protein and Lipid Signaling in the Pathogenesis of Neurodegenerative Disorders. Annals of the New York Academy of Sciences. 2004; 1012:37-50

[2] Saxena S, Caroni P. Selective neuronal vulnerability in neurodegenerative diseases: from stressor thresholds to degeneration. Neuron. 2011; 71:35-48.

[3] Virmani A, Pinto L, Binienda Z, Ali S. Food, nutrigenomics, and neurodegeneration— neuroprotection by what you eat! Molecular neurobiology. 2013; 48:353-362

[4] Mohammad Reza Khazdair. Neuroprotective potency of some spice herbs, a literature review.Journal of Traditional and Complimentary Medicine.2019;2225-4110

[5] Kuresh A youdim. Interaction between flavonoids and the blood-brain barrier: in vitro studies.J. Neurochem.2003:1471-4159

[6] Tarun Belwal. Dietary Anthocyanins and Insulin Resistance: When Food Becomes a Medicine.Nutrients.2017: 9(10): 1111

[7] Birks J, Grimley Evans J. Ginkgo biloba for cognitive impairment and dementia. Cochrane Database Syst Rev. 2009 ;(1): CD003120.

[8] Kim, S. R., Lee, D. Y., Chung, E. S., Oh, U. T., Kim, S. U., Jin, B. K., & Lee, M. Y. (2004). Neuroprotection of nigral dopaminergic neurons by cinnamon through activation of peroxisome proliferator-activated receptor γ. NeuroSignals, 13(3), 150-162.

[9] Baharuldin, M. T., Radzi, N. I. M., Safri, S. N. A. M., Rajab, N. F., & Mohd Yusof, N. A. (2020). Flavonoids and Their Neuroprotective Effects on Experimental Models of Parkinson's disease: A Systematic Review. Biomolecules, 10(6), 869.

[10] Ali Esmail Al-Snafi. Medicinal Plants with neuroprotective effects. GSC Biological and Pharmaceutical Sciences, 2021, 17(01), 213–231

[11] Vellas B. Long-term use of standardised *Ginkgo biloba* extract for the prevention of Alzheimer's disease (GuidAge): a randomised placebo-controlled trial. Lancet Neurol. 2012;11(10):851–9.

[12] Sandeep Kumar Singh. Neuroprotective and Antioxidant Effect of *Ginkgo biloba* Extract Against AD and Other Neurological Disorders. Neurotherapeutics. 2019 Jul; 16(3): 666–674.

[13] Wei, T., Ni, Y., Hou, J., Chen, C., Zhao, B., and Xin, W. (2000). Hydrogen Peroxide-Induced Oxidative Damage and Apoptosis in Cerebellar Granule Cells: protection by Ginkgo Biloba Extract. *Pharmacol. Res.* 41 (4), 427–433.

[14] Xin, W.Mechanisms of Apoptosis in Rat C

[15] erebellar Granule Cells Induced by Hydroxyl Radicals and the Effects of EGb761 and its Constituents. *Toxicology* 148 (2-3), 103–110.

[16] Barbara Ahlemeyer. Neuroprotective Effects of Ginkgo biloba Extract. Phytomedicines of Europe. ACS Symposium Series; American Chemical Society: Washington, DC, 1998:210-220

[17] T. P. Ng. Curry consumption and cognitive function in the elderly. American Journal of Epidemiology.2006:164(9); 898–906.

[18] M. Garcia-Alloza. Curcumin labels amyloid pathology in vivo, disrupts existing plaques, and partially restores distorted neurites in an Alzheimer mouse model. Journal of Neurochemistry. 2007 (102): 1095–1104

[19] C. A. Martins. Curcumin in combination with piperine suppresses osteoclastogenesis in vitro.Journal of Endodontia. 2015(41):10:1638–1645

[20] David Banji. Neuroprotective Effect of Turmeric Extract in Combination with Its Essential Oil and Enhanced Brain Bioavailability in an Animal Model. BioMed Research International.2021: 6645-720

[21] Wang, X. Curcumin attenuates 6-hydroxydopamine-induced cytotoxicity by anti-oxidation and nuclear factor-kappa B modulation in MES23. 5 cells.Biochem Pharmacol.2009:178-193

[22] Soroor Sadegh Malvajerd. Neuroprotective Potential of Curcumin Loaded Nanostructured Lipid Carrier in an Animal Model of Alzheimer's Disease: Behavioral and Biochemical Evidence. Journal of Alzheimer's Disease . 2019:69: 671–686

[23] Y. M. Tsai.Curcumin and its nano-formulation: the kinetics of tissue distribution and blood-brain barrier penetration. International Journal of Pharmaceutics.2011:416:331–338

[24] N.Limpeanchob Neuroprotective effect of Bacopa monnieri on beta-amyloid-induced cell death in primary cortical culture.Journal of Ethnopharmacology.120:1:112-117.

[25] Roodenrys.Chronic effects of Brahmi (Bacopa monnieri) on human memory, Neuropsychopharmacol., 27: 279-281.

[26] Natthawut Charoenphon. Brahmi (Bacopa monnieri): Up-to-date of memory boosting medicinal plant: A review. Indian J. Agric. Res., 50 (1) 2016: 1-7.

[27] S.Giramkar.Anticonvulsant potential of commonly practiced formulations of Brahmi (Bacopa monnieri Linn.) in Wistar rats.Journal of Pharmacy research.2013:7:9:787-791.

[28] Shukia B. Effect of Brahmi Rasayan on the central nervous system. J Ethnopharmacol1987; 21: 65-74.

[29] Dave UP. Evaluation of BR-16 A (Mentat) in cognitive and behavioral dysfunction of mentally retarded children: A placebo-controlled study. Indian J Pediatr 1993; 60: 423-8.

[30] Shinomol GK. Exploring the role of Brahmi (Bacopa monnieri and Centella asiatica) in brain function and therapy. Recent patents on endocrine, metabolic & immune drug discovery. 2011 Jan 1;5(1):33-49.

[31] Shailja Choudhary. Shanker G. Anxiolytic profile of standardized Brahmi extract. Indian J Pharmacol. 2000;32(152):5. Brahmi(Bacopa monnieri)-a potential ayurvedic cognitive enhancer and neuroprotective herb. International Journal of Ayurveda and Pharma Research. 2021:9:5:41-49.

[32] Shanmugasundaram ER.An Ayurvedic herbal formula for the control of epilepsy. Journal of ethnopharmacology. 1991 1;33(3):269-76.

[33] Shanker G. Anxiolytic profile of standardized Brahmi extract. Indian J Pharmacol. 2000;32(152):5

[34] Rajat Sandhir. Neuroprotective Potential of Withania somnifera (Ashwagandha) in Neurological Conditions.Science of Ashwagandha:Preventive and therapeutic potential.2017:373-387.

[35] Bhatnagar, M. Neuroprotective effects of Withania somnifera dunal.: A possible mechanism. Neurochem. Res. 2009, 34, 1975–1983.

[36] Ratheesh, G. Role of medicinal plants in neurodegenerative diseases. Biomanuf. Rev. 2017:2:1–16.

[37] Kaustubh Chaudhary. Withania somnifera as an Adjunctive Treatment for Refractory Restless Legs Syndrome in Parkinson's Disease: A Case Report.Cureus.2021:13:12

[38] Prakash J. Withania somnifera alleviates parkinsonian phenotypes by inhibiting apoptotic pathways in dopaminergic neurons. Neurochem Res. 2014: 39:2527-36.

[39] Candelario M. Direct evidence for GABAergic activity of Withania somnifera on mammalian ionotropic GABAA and GABAρ receptors. J Ethnopharmacol. 2015:171:264-72.

[40] S. Kumar. In vitro Protective Effects of Withania somnifera (L.) Dunal Root Extract against Hydrogen Peroxide and b-amyloid(1–42)-induced Cytotoxicity in Differentiated PC12 Cellsptr_3261. Phytotherapy research.2010:24: 1567–1574.

[41] Kulkarni SK. Neuroprotection by Withania somnifera root extract against lithiumpilocarpine-induced seizures. Ind Drugs 1998:35: 208–215.

[42] S. S. Jamil. "Centella asiatica (Linn.) Urban: a review. Natural Product Radiance.2007:6:2:158–170.

[43] R. Tenni. Effect of the triterpenoid fraction of Centella asiatica on macromolecules of the connective matrix in human skin fibroblast cultures.Italian Journal of Biochemistry. 1988: 37:2: 69–77.

[44] L. Suguna. Effects of Centella asiatica extract on dermal wound healing in rats.Indian Journal of Experimental Biology. 1996: 34:12,:1208–1211.

[45] B. S. Shetty. Biochemical analysis of granulation tissue in steroid and Centella asiatica (Linn) treated rats. Pharmacologyonline. 2008:2: 624–632.

[46] Jamil SS. Urban L. Centella asiatica L. urban a review. Nat Prod Rad 2007; 6: 158-70.

[47] D Dhingra. Indian journal of experimental biology. 2008; 46: 212-218.

[48] Kumar, M.Effect of different extracts of Centella asiatica on cognition and markers of oxidative stress in rats. J. Ethnopharmacol. 2002:79:253–260.

[49] Rao, S.B. Centella asiatica treatment during postnatal period enhances learning and memory in mice. Physiol. Behav. 2005: 86:449–457.

[50] Nalini, K. Effects of Celastrus paniculatus on passive avoidance performance and biogenic amine turnover in albino rats. J. Ethnopharmacol. 1995:47:101–108.

[51] Ogeswaran Loknathan. Recent Updates in Neuroprotective and Neuroregenerative Potential of Centella asiatica. Malays J Med Sci. 2016 ; 23:1) 4–14.

[52] Rao MGK. Centella asiatica (L.) leaf extract treatment during the growth spurt period enhances hippocampal CA3 neuronal dendritic arborization in rats. Evid-Based Compl and Alt. 2006;3:3:349–357.

[53] Rao KGM. Enhancement of amygdaloid neuronal dendritic arborisation by fresh leaf juice of Centella asiatica (Linn) during growth spurt period in rats. Evid Based Complement Alternat Med. 2009; 6:2:203–210.