REVIEW ARTICLE

Current Evidence on Memory-Enhancing Compounds and Herbs: A Comprehensive Review

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DOI: 10.18811/ijpen.v11i01.06

Abstract

Memory and cognitive function play vital roles in our daily lives, and the pursuit of effective strategies to enhance these cognitive abilities has long been a topic of interest. The current review aims to provide a comprehensive overview of memory-enhancing compounds and herbs, focusing on their potential benefits, mechanisms of action, and limitations. Numerous compounds and herbs have been studied for their cognitive benefits, with some promising results. *Ginkgo biloba*, a well-known herb with antioxidant properties, has been investigated for its potential to improve memory and cognitive function, particularly in the elderly. *Bacopa monnieri*, a herb used in traditional Ayurvedic medicine, has demonstrated positive effects on memory and attention in several clinical studies. *Panax ginseng*, commonly used in traditional Chinese medicine, has also shown potential as a cognitive enhancer, with evidence suggesting improvements in cognitive performance, attention, and working memory. The aroma of rosemary, a culinary herb, has been found to have memory-enhancing properties, although further research is needed to fully elucidate its mechanisms. The current article reviews the data from experimental and clinical findings for several Indian herbal medicines, including *Withania somnifera, Ginkgo biloba, Centella asiatica, Bacopa monnieri, Panax ginseng, Rosmarinus officinalis, Glycyrrhiza glabra, Convolvulus pluricaulis*, Acorus calamus and *Phyllanthus emblica*; all of which have demonstrated prospects for addressing memory disorders. While these compounds and herbs hold promise, their efficacy and safety profiles vary; therefore, rigorous clinical trials and standardized protocols, are desired to establish their effectiveness, optimal dosages, and long-term effects.

Highlights

- Certain herbs and compounds can significantly enhance the brain's ability to process, store, and retrieve information.
- These herbs have been traditionally used in various cultures and are now supported by modern scientific studies.
- These memory-enhancing herbs protect brain cells from oxidative stress and inflammation.
- Phytochemicals found in these herbs hold potential for preventing or slowing the advancement of dementia.
- The neurotransmitters (acetylcholine, GABA, etc.) play critical roles in memory formation and cognitive processes.
- Despite the diverse phytotherapeutic benefits of these herbs, further clinical trials are necessary to validate their safety and effectiveness at standardized doses.

Keywords: Cognition, Dementia, Memory, Memory-enhancing herbs, Neuroprotection, Neurotransmitters, Nootropics

International Journal of Plant and Environment (2025); **ISSN:** 2454-1117 (Print), 2455-202X (Online)

Introduction

Maintaining a sharp and focused memory has become increasingly crucial in today's fast-paced world. With an overload of information everywhere, effective survival depends on memory, one of the most vital functions of our brain. A person's ability to gather sensory inputs, experiences, bits of knowledge, etc., keep them for brief or extended periods, and then retrieve them as needed later is known as memory (Zlotnik & Vansintjan, 2019).

Memory impairment is the hallmark symptom of Alzheimer's disease (AD). According to the cholinergic hypothesis, memory is impaired due to the gradual degeneration of cholinergic neurons in the basal forebrain. This degeneration leads to reduced acetylcholine (ACh) levels, a neurotransmitter crucial for cognitive functions (Shiksharthi *et al*., 2011). In addition, stress, aging, and emotions are other factors that can cause memory loss.

In recent years, growing interest has been shown in the potential of plants and herbs to boost memory and positively impact the nervous system. Plants are the chemical factories of nature, offering a vast variety of chemical blends. Plants produce distinctive, intricate, and biologically diverse compounds with neuroprotective, anti-inflammatory, and antioxidant properties, with minimal to no negative effects (Wahid *et al*., 2022). These organic compounds have long been recognized for having the potential to improve cognitive abilities, boost brain health, and maybe lessen age-related memory loss. Humans have effectively used these medicinal plants to address a range of health conditions including dementia, amnesia, and AD. The plants have also been found effective in lowering amyloid protein deposits in the brain and mitigating oxidative stress, which aids in memory restoration (Fig. 1) (Malík & Tlustoš, 2023). The chemical composition of plants and their effectiveness has been studied, and validated through clinical trials.

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How to cite this article: Kashyap, S., Bist, R. (2025). Current Evidence on Memory-Enhancing Compounds and Herbs: A Comprehensive Review. International Journal of Plant and Environment. 11(1), 48-60

Submitted: 25/11/2024 **Accepted:** 26/02/2025 **Published:** 28/03/2025

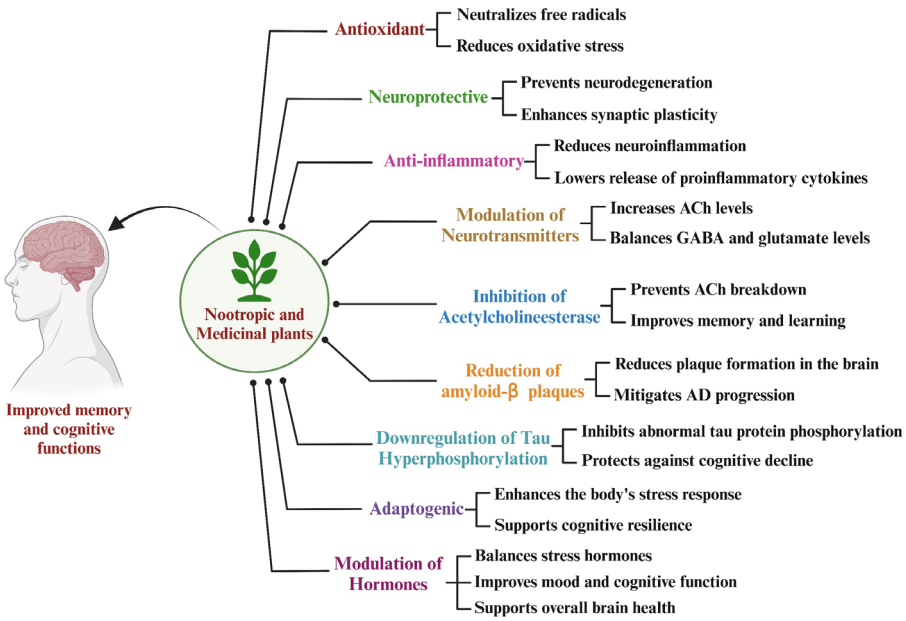

Fig. 1: Diagrammatic representation of the role of various phytoconstituents found in nootropic and medicinal plants in cognition and memory enhancement.

In conventional healing practices like the Ayurveda of India and Traditional Chinese medications (TCM), several plants and herbs have been used for centuries for treating central nervous system (CNS) disorders as well as for their memory-enhancing properties (Howes & Houghton, 2003). One of the rejuvenating specialities of Ayurveda is Rasayana therapy which employs several memory-improving and revitalizing botanicals such as *Clitoria ternatea*, *Terminalia chebula*, *Bacopa monniera*, *Nardostachys jatamansi*, *Acorus calamus*, and others (Singh, 2013).

Cognitive enhancers include supplements, functional foods, and medications designed to improve cognition, enhance memory, and support various mental functions. The herbs that operate on brain cells are referred to as "nootropic herbs/drugs," with their distinct constituents known as 'smart drugs', 'brain boosters' or 'cognitive enhancers' (Frati *et al*., 2015). These substances regulate specific brain pathways that involve neurotransmitters and neuromodulators that unequivocally impact cognitive processes.

An alternative approach to address memory loss and cognitive decline involves promoting neurogenesis (generation of new nerve cells) in adults, which is involved in memory formation (Lazarov & Marr, 2010). While there is a wealth of information regarding medicinal plants with potential neurological benefits, only a few have undergone rigorous scientific validation. Plants that promote neurogenesis include *Bacopa monnieri, Acorus tatarinowii, Ginkgo biloba, Radix Astragali, Salvia miltiorrhiza, Hericium erinaceus, Cuscuta japonica, Banisteriopsis caapi, Lycium barbarum, Curcuma longa, and Centella asiatica* (Krishnapriya *et al*., 2022).

The current study reviews the understanding of medicinal plants and their active phytoconstituents (Table 1). These plants have a long history of use in traditional medicine for enhancing cognitive function. Their potential benefits may help alleviate memory loss and other dementia-related problems.

Withania somnifera (Ashwagandha)

W. somnifera, described as a Rasayana or "adaptogen," is an established therapeutic in the Indian Ayurveda and has been utilized for more than 3000 years (Santhanu & Senthil, 2021). *W. somnifera* is also referred to as Ashwagandha, winter cherry, or Indian ginseng.

Ashwagandha is a well-known herb used as a brain revitalizer for AD. It is a nervine stimulant that revives cells, increases energy, improves cognitive activity, boosts memory, and improves general health and longevity. It also possesses anxiolytic, antioxidant, neuroprotective, antidepressant, anti-inflammatory, antimicrobial, antidiabetic, antiarthritic, antistress, and cardioprotective properties (Kumar *et al*., 2015).

The main biologically active compounds of ashwagandha are withanolides, which are steroidal chemicals found primarily in the roots. It contains numerous other secondary bioactive metabolites, including amino acids, flavonoids, phenolic compounds, withanosides, withaferins, sitoindosides, glycowithanolides, alkaloids, withanine, pseudo-withanine, anferine, and saponins. Ashwagandha roots are the most commonly utilized part of the plant for their stimulant and tonic properties (Dar *et al*., 2015). *W. somnifera* nanoparticles possessing such properties have also been developed to enhance bioavailability, ensure targeted delivery, and minimize side effects. Compared to its solution counterpart, these nanoparticles also prolong therapeutic activity, making them a promising advancement in herbal medicine (Madhu *et al*., 2021; Parashar *et al*., 2023).

Standardized extracts of ashwagandha exhibit multi-dimensional neuromodulatory effects. These effects can be ascribed to its potential to modify cell adhesion molecules, cytoskeletal elements, neurotrophic factors, and synaptic proteins. Ashwagandha has been shown to strongly regulate the

Table 1: Pharmacological effects of various memory-enhancing herbs in improving cognition and overall brain health. Abbreviations. AChE-Acetylcholinesterase; BDNF-Brain-derived neurotrophic factor; ROS-Reactive oxygen species; LPO-Lipid peroxidation; MAPK-Mitogen-activated protein kinase; PKC-Protein kinase C; SOD-Superoxide dismutase; CAT-Catalase; TNF-a-Tumor necrosis factor-a; IL-6-Interelukin-6; IL-1β-Interleukin-1β.

S. No.	*Scientific Name*	*Common Name (Local Name)*	*Family*	*Chemical Constituents*	*Plant part used*	*Uses and Specific Cognitive Effects*	*References*
1.	*Withania somnifera*	Ashwagandha, Indian ginseng, Winter cherry	Solanaceae	Withanolides, sitoindosides, alkaloids	Roots	Neuroprotective, anti-inflammatory, immunomodulatory, inhibits AChE, decreases cortisol, stimulates BDNF, regenerates axons and dendrites, reverses amyloid-β toxicity	Singh *et al.*, 2011; Kumar *et al.*, 2012
2.	*Ginkgo biloba*	Ginkgo	Ginkoaceae	Terpenoids, flavanoids, kaempferol, ginkgolides	Leaves	Neuroprotective, antioxidant, inhibits amyloid-β induced neurotoxicity and tau hyperphosphorylation, stimulates neurogenesis, free radical scavenger, reduces ROS, LPO	Biernacka *et al*., 2023
3.	*Centella asiatica*	Gotu kola, Thankuni	Apiaceae	Asiatic acid, asiaticoside,	Whole plant	Neuroprotective, anti-inflammatory, antioxidant, sedative, antidepressant, increases neuronal dendritic arborization and axonal regeneration, inhibits AChE and overactivated p38 MAPK pathway, protects from amyloid- β neurotoxicity	Orhan et al., 2013; Sabaragamuwa *et al.*, 2018
4.	*Bacopa monnieri*	Brahmi	Plantaginaceae	Bacosides A and B, saponins	Whole plant	antioxidant, anti-inflammatory, hepatoprotective, free radical scavenger, prevents age-related neurodegeneration, inhibits AChE, enhances PKC activity	Rastogi *et al.*, 2012; Aguiar & Borowski, 2013
5.	*Panax ginseng*	Ginseng	Arialaceae	Ginsenosides (Panaxosides)- Rg1, Rg2, Rg3	Roots	Neuroprotective, anti-neuroinflammatory, hypotensive, vasorelaxant, decreases ROS and malondialdehyde levels, suppresses MAPK activation, inhibits tau aggregation	Chen *et al.*, 2019; Shin *et al.*, 2020
6.	*Rosmarinus officinalis* (*Salvia rosmarinus*)	Rosemary	Limiaceae	Rosmarinic acid, carnosic acid, carnosol	Leaves	Antioxidant, anti-inflammatory, free radical scavenger, increases SOD and CAT, reduces TNF-α, IL-6, and IL-1β levels, inhibits AChE, decreases amyloid-β plaques and phosphor tau	Lipton *et al*., 2016; Song *et al*., 2016
7.	*Glycyrrhiza glabra*	Licorice, Yashtimadhu	Fabaceae	Glycyrrhizin, glycyrrhetinic acid	Roots	Anti-inflammatory, hepatoprotective, antioxidant, antibacterial, antiviral, antifungal, inhibits neuronal cell death and ROS production, prevents mitochondrial lipid peroxidation	Thangavelu and Geetha, 2011; Rodino *et al.*, 2015
8.	*Convolvulus pluricaulis*	Bindweed, Shankhpushpi	Convolvulaceae	Triterpenoids, flavonol glycosides, anthocyanins	Whole plant	Antioxidant, neuroprotective, increases ACh content, stimulates dendritic arborization, downregulates tau protein level, slows brain aging	Nahata *et al.*, 2008; Sharma *et al.*, 2010
9.	*Acorus calamus*	Sweet flag, Calamus	Acoraceae	α-Asarone, β-Asarone, isougenol	Rhizomes	Neuroprotective, antioxidant, anti-inflammatory, immunosuppressive, antihyperglycaemic, antifungal, AChE inhibitor, free radical scavenger	Sharma *et al.*, 2014; Joshi, 2016
10.	*Phyllanthus emblica*	Indian gooseberry, Amla	Phyllanthaceae	L-Ascorbic acid (Vitamin C) phyllanthin'	Fruit	Antioxidant, anti-inflammatory, antidiabetic, immunomodulator, anti-cholinesterase	Variya *et al.*, 2016; Yadav *et al.*, 2017

dopaminergic, cholinergic, antioxidant, and gamma-aminobutyric acid (GABA)ergic systems (Yenisetti *et al*., 2016). In a study, chronic administration of *W. somnifera* root extract (100 and 200 mg/kg) restored acetylcholinesterase (AChE) levels in the striatum, brain, and hippocampal regions of mice. In another study, *W. somnifera* root extract (50, 100, and 200 mg/kg; p.o.) improved persistence in mice in a passive avoidance task (Halder *et al*., 2021). Studies have shown that rats on administration of aqueous extracts of *W. somnifera* had elevated ACh levels and increased choline acetyltransferase (ChAT) activity, which may account for some of the factors that improve memory and cognitive function. Several clinical trials provided evidence for the cognitive potential of ashwagandha extract in alleviating memory impairment in propoxur-treated rats (Yadav *et al*., 2010), improving performance in cognitive tasks, cognitive flexibility, psychomotor speed, visual memory, reaction time, stress response, and executive function (Remenapp *et al*., 2022). In a double-blind, clinical study, patients with mild cognitive impairment (MCI) were administered a 100% aqueous extract of *Withania* roots for eight weeks. This treatment improved the speed of information processing, immediate and general memory, executive functioning, and attention (Choudhary *et al*., 2017).

Ashwagandha is generally regarded as safe, but an overdose may lead to gastrointestinal issues and vomiting. The usage of ashwagandha is not suggested for pregnant women or individuals with thyroid disorders (Meher *et al*., 2016). Although the nootropic effects of ashwagandha show promise for improving cognitive decline, comprehensive clinical data remains lacking to fully support its therapeutic applications. This is due to small-scale clinical studies and a lack of rigorous methodology, creating a gap in scientific validation. Large-scale, well-controlled human trials are essential to confirm its efficacy, determine optimal dosages, and establish its safety profile for widespread medical use.

Ginkgo biloba

G. biloba is a living fossil Indigenous to Japan and China, commonly known as ginkgo or maiden-hair tree. Ginkgo is widely employed in treating dementia, AD, cerebrovascular disease, cancer, amnesia, tinnitus, cardiovascular diseases, and other age-associated conditions. The major bioactive compounds of *G. biloba* extract are found in leaves and roots. These chemical constituents include flavonoids (kaempferol, quercetin, and isorhamnetin) and terpenoids (ginkgolides and bilobalide) (Beek & Montoro, 2009). These compounds exhibit astringent properties and inhibit bacterial and fungal growth. Among these, ginkgolides possess antioxidant, neuroprotective, and cholinergic activities along with neural stem cells (NSCs) regenerative potential (Ren *et al*., 2019). Bilobalide, the active component of *G. bilioba*, possesses neuroprotective potential and is able to cross the blood-brain barrier (BBB) (Madgula *et al*., 2010).

A standardized extract of *G. biloba* called EGb 761, with a recommended daily dose of 120 to 300 mg, (24% flavonoids and 6% terpene lactones) is used to treat several adverse health conditions including anxiety, depression, headaches, memory problems, and confusion (Diamond *et al*., 2000). Currently, EGb 761 is in Phase III of clinical trials as a possible medication to prevent AD (Ramassamy *et al*., 2007).

Experimental evidence has demonstrated that standardized *Ginkgo* extract exhibits various pharmacological effects including neuroprotective effects, antioxidant effects, anti-inflammatory effects, and lowering the expression of caspase-3 to mitigate mitochondrial-initiated apoptosis. It has also been shown to directly inhibit the aggregation of amyloid-β in AD (Luo *et al*., 2002), inhibit membrane lipid peroxidation, and exhibit anti-platelet activating factor activity for vascular diseases (Ramassamy *et al*., 2007). Studies suggest that *G. biloba* extracts have counteracted the toxicity induced by nitric oxide, and inhibited AChE activity in the brain indicating an increase in ACh levels. Additionally, these extracts have demonstrated the ability to reduce scopolamine-induced amnesia while significantly improving memory retention in rats and short-term memory in mice (Gong *et al*., 2006). Ginkgo promotes blood circulation to the CNS, optimizing oxygen and nutrient delivery to the brain. Additionally, it neutralizes reactive oxygen species (ROS) and enhances cognition and memory (Singh et al., 2017). Another investigation revealed that EGb761 influences monoaminergic neurotransmission by inhibiting the transport of serotonin (5-hydroxytryptamine (5-HT)), dopamine, and norepinephrine into synaptic terminals in a dose-dependent manner in mice (Fehske *et al*., 2009).

In a multicenter, placebo-controlled study, the clinical efficacy of *G. biloba* extract was investigated. In this study, 216 patients with AD-type presenile and senile primary degenerative dementia and multi-infarct dementia (MID) were given an oral dose of 240 mg of *G. biloba* daily for 24 weeks. When compared to the placebo group, the treatment group showed significant improvement and also the dose was well tolerated (Kanowski *et al*., 1997). In another placebo-controlled clinical trial, 61 young subjects were provided neuropsychological tests before and after the 30-day administration of 120 mg *G. biloba* extract. The statistical data showed that *G. biloba* treatment significantly improved working memory and information processing speed (Stough *et al*., 2001).

Despite this, the evidence for expected clinical advantages for people with AD or dementia remains inconclusive. Also, there is currently no evidence to support the safety of ginkgo in newborns, pregnant and breastfeeding mothers.

Centella asiatica

C. asiatica is commonly known as Gotu kola, Asiatic pennywort, or Indian pennywort. *C. asiatica* is particularly renowned for its long use as a memory booster or brain tonic and for having the ability to rejuvenate neurons and brain cells. This rejuvenating herb has CNS effects such as nerve tonic, tranquilizer, and sedative effects along with diuretic, anti-convulsive, and spermatogenic effects. It is believed to improve memory, intelligence, and longevity (Shinomol *et al*., 2011).

It consists of a diverse range of phytochemicals, such as flavonoids, glycosides, triterpenoids (asiatic acid, asiaticoside, madecassoside, and madecassic acid), alkaloids, tannins, volatile fatty acids, and essential oils (Siddiqui *et al*., 2007). *C. asiatica* possesses anti-oxidative, neuroprotective, neuron regenerative, anti-inflammatory, anti-anxiety, and anti-depressive properties via modulation of the GABAergic system (Jana *et al*., 2010).

Administration of aqueous extract of *C. asiatica* decreased AChE activity, improved learning and memory, reduced amyloid-

β plaque accumulation in the hippocampus (Dhanasekaran *et al*., 2009), decreased oxidative stress, showed improvement in biochemical, mitochondrial and behavioral dysfunctions induced by D-galactose in animals, and prevented radiation-induced behavioral abnormalities in clinical treatment (Shobi & Goel, 2001). In the passive avoidance test, *C. asiatica* leaf extract improved the learning ability and memory retention power in adult rats, by modulation of several neurotransmitter levels in the rat brain, including serotonin, noradrenaline, and dopamine, indicating a possible therapeutic role in ameliorating AD-associated cognitive decline (Rao *et al*., 2007).

C. asiatica extracts showed improved dendritic arborization (length and branching) of neurons in the amygdala, one of the regions primarily linked to memory processing and learning (Mohandas Rao *et al*., 2009). Chronic administration of *C. asiatica* extract helped alleviate colchicine-induced (Kumar *et al*., 2009) and streptozotocin (STZ)-induced memory impairment and the associated oxidative damage. *C. asiatica* also inhibited scopolamine-induced memory impairment by inhibiting AChE activity (Orhan *et al*., 2013). In a clinical trial, the efficacy of 70% ethanolic extract of *C. asiatica* on generalized anxiety disorder was evaluated. About 33 volunteers received a fixed dose of 500 mg per capsule, taken twice daily for 60 days. The results demonstrated a significant reduction in anxiety-related disorders, stress, and its correlated depression (Jana *et al*., 2010).

Bacopa monnieri

The herb *B. monnieri*, also referred to as Brahmi or water hyssop is a well-known Indian medicinal herb that has traditionally been utilized for the past 3000 years as a memory booster. Bacopa has an extensive record of being used to treat a variety of ailments, including memory loss, lack of concentration, insomnia, learning disabilities, asthma, mental disorders, stroke, epilepsy, anxiety, sedatives, etc (Srivastava *et al*., 2019).

The primary nootropic bioactive components present in this herb are saponins (such as bacosides A, B and C, bacopasides I–XII, bacopasaponins A, B, C, and D, hersaponin, monnierin, and D-mannitol), flavonoids (luteolin and apigenin), alkaloids (like brahmine, nicotine, and herpestine), steroids (β-sitosterol and stigmasterol), and polyphenols. These constituents have positive effects on memory as well as cognitive performance. Furthermore, the bacosides are non-polar, making them accessible to the BBB. *B. monnieri* displays a range of pharmacological actions, including anti-inflammatory, anticonvulsant, antidepressant, neuroprotective, analgesic, antimicrobial, antiulcerogenic, antioxidant, and anxiolytic activity (Aguiar & Borowski, 2013). In a previous study, bacoside A treatment increased AChE activity within the cortical region of older rats, signifying its potential to strengthen the cholinergic system (Chaudhary & Bist, 2017).

In the rat hippocampus, alcoholic extract of Brahmi increased the protein kinase C (PKC) activity, resulting in improved learning and memory. This enhanced cognition in rats resulted from bacosides A and B. Also, studies suggest that *B. monnieri* extracts prevent β-amyloid-induced cell death in neurons by suppressing cellular AChE activity (Goswami *et al*., 2011). In a study, *B. monnieri* extracts significantly increased the reduced Brain-Derived Neurotrophic Factor (BDNF) levels in rats that were exposed to chronic stress (Kumar & Mondal, 2016). Rat models of AD were administered an alcoholic extract of Brahmi and their escape latency time in the Morris water maze test was improved. It also reduced neuronal loss and mitigated reduction in cholinergic neuron densities (Uabundit *et al*., 2010). In another experiment, *B. monnieri* standardized extract reversed the cognitive deficits and oxidative stress triggered by colchicine by increasing the antioxidant levels and attenuating protein carbonyl content in the hippocampal and cortical regions (Saini *et al*., 2012). Evidence suggested that alcoholic extract of *B. monnieri* effectively mitigates cognitive dysfunction due to olfactory bulbectomy in mice. Its neuroprotective effects are attributed to enhancing synaptic plasticity-related signalling, promoting BDNF transcription, and preserving cholinergic function. Additionally, *B. monnieri* treatment inhibits AChE activity, further supporting its role in improving memory and cognitive function (Le *et al*., 2013).

Preliminary clinical investigations have further indicated that *B. monnieri* treatment significantly improved neurocognitive functioning in humans, enhancing language learning, memory retention, and information processing when taken over a longer period; however, lower doses (300 mg) (Nathan *et al*., 2001) had no acute impact on cognitive performance (Neale *et al*., 2013). Brahmi helps calm and relax the brain cells and return them to their normal operating state in adults. Additionally, the effects of Brahmi on memory have been the focus of most clinical research. In a placebo-controlled, randomized experiment, 300 mg of *B. monnieri* extract was administered to a group of healthy individuals for 12 weeks. After completion of the test duration, the rate of learning and memory consolidation was significantly improved as compared to the placebo group (Stough *et al*., 2001).

Panax ginseng

P. ginseng commonly called ginseng, is a plant widely used in traditional Chinese and Japanese medicine. The word 'ginseng' in Korean means 'the root of life'. For a long time, it has been used in Asian countries in the treatment of a variety of conditions, including cognitive impairment and neurodegenerative disorders (Rajabian *et al*., 2019). It is generally used as a memory tonic to enhance learning and memory, particularly in old people.

A wide range of biologically active compounds found in *P. ginseng* are ginsenosides, ginseng saponins, triterpenoids (dammarane), proteins, peptides, alkaloids, polyacetylenes, polysaccharides, essential oils, vitamins (B_1, B_2, B_{12}, C), flavonoids, and fatty acids (Shin *et al*., 2015). Ginsenosides stimulate choline uptake, crucial for learning and memory and they have also demonstrated anti-Alzheimer's activity. Over 200 ginsenosides and non-saponin components of ginseng have been isolated and identified. Rb1 and Rg1 are the two most potent ginsenosides of the 30 primary ginsenosides found in Panax species. In healthy rats and mice, Rg1 enhances learning and memory. In rat hippocampus, ginsenosides have been shown to attenuate kainic acid (KA)-induced neurotoxicity, thus protecting hippocampal CA1 and CA3 cells (Lee *et al*., 2002). Another study provided evidence of the anti-neuroinflammatory actions of ginsenoside Rb1. In an AD model, ginsenoside Rb1 helped reverse alterations in neuroinflammation markers in the rat hippocampus (Wang *et al*., 2011). In a scopolamine-induced

memory deficit mice model, ginsenoside Rh3 increased the latency time in the passive avoidance test, inhibited AChE activity in a dose-dependent manner, and reversed the expression of BDNF in the hippocampus (Kim *et al*., 2013). In the passive avoidance test, subchronic administration of ginseng (10 or 20 mg/kg, p.o. for 14 days) prolonged latency time, indicating improved memory retention. Additionally, treatment elevated the levels of the phosphorylated extracellular signal-regulated kinase (pERK) and phosphorylated protein kinase B (pAkt) in the hippocampus, suggesting their role in enhancing cognitive function (Lee *et al*., 2013).

Further findings have revealed the role of different ratios of protopanaxadiol (PD) and protopanaxatriol (PT) saponins in improving scopolamine-mediated learning dysfunction in mice. Ginseng saponin having a low PD to PT ratio enhanced spatial working memory in normal mice, but high PD to PT ratios showed no such effects. A double-blind, placebo-controlled trial was conducted to evaluate the cognition-enhancing effect of *P. ginseng*. Ninety patients with MCI received 3 g of *P. ginseng* powder for six months. The treatment group showed greater cognitive improvement than the placebo group (Park *et al*., 2019). In another 12-week trial, sixty-one AD patients were divided into three groups. Fifteen subjects received a low dose of *P. ginseng* (4.5 g/day), another 15 were given a high dose (9 g/day), and the remaining 31 were taken as control. Patients in the high-dose group showed remarkable improvement in cognitive functioning at the end of 12 weeks of *P. ginseng* therapy, indicating the clinical efficacy of ginseng in treating AD (Heo *et al*., 2008).

Rosmarinus officinalis

R. officinalis, commonly called rosemary, is among the most popular perennial culinary herbs grown globally. This potent plant comes from the Mediterranean region (Ribeiro-Santos *et al*., 2015). It has traditionally been used to enhance liver function, reduce thirst, cure cognitive deficiencies as well as improve memory, and slow age-related memory loss in people (Singhal *et al*., 2012).

In ancient Greece and Rome, rosemary was considered a memory enhancer and a brain stimulant. Fresh and dried rosemary leaves are used for their distinct aroma in cooking and herbal teas. Rosemary extracts, known for their antioxidant properties, are commonly used to preserve perishable foods. Oils of *R. officinalis* are utilized in perfumes, foods, and pharmaceuticals (Amaral *et al*., 2019).

Several fractions of biologically active substances are present in rosemary leaf extracts, such as essential oil, significant amounts of phenolic diterpenes (carnosic acid, carnosol), phenolic acids (rosmarinic acid, chlorogenic acid), pentacyclic triterpenes (betulic, ursolic, and oleanolic acid), and flavonoids (derivatives of luteolin and apigenin) (Herrero *et al*., 2010). Rosemary extracts have a variety of bioactivities, including antidiabetic, antibacterial, anticancer, hepatoprotective, anti-inflammatory, antinociceptive, antioxidant, and antithrombotic properties. These bioactivities are associated with the constituents of phenolic compounds, primarily rosmarinic acid, carnosic acid, and caffeic acid (Bao *et al*., 2020).

R. officinalis has neuroprotective properties against several neurological disorders such as dementia and AD. The essential oil from the plant contains terpenes and rosemarinic acid, which has been shown to have anti-AChE and anti-BChE (butyrylcholinesterase) activity, raising total choline levels in the brain. This may lessen not only AD but also anxiety, memory loss, and depression (Ozarowski *et al*., 2013).

In an experiment on scopolamine-induced rats, the administration of rosemary extracts (200 mg/kg, p.o.) resulted in improved long-term memory, likely due to its inhibitory effect on AChE activity in the hippocampus and frontal cortex (Ozarowski *et al*., 2013). In a rat model of sciatic nerve chronic constriction injury (CCI)-induced neuropathic pain, treatment with ethanolic extract of *R. officinalis* and rosmarinic acid resulted in a decrease in neuroinflammatory markers, suggesting its potential as an anti-inflammatory agent and in treating neuropathic pain (Rahbardar et al., 2017). A double-blind, placebo-controlled study including twenty-eight elderly people was conducted with different doses of *R. officinalis*, with the lowest dose of 750 mg and the highest dose of 6000 mg. This study highlighted the dose-dependent impact of rosemary on memory speed, showing improved performance at the lowest dose but a negative effect at the highest dose compared to a placebo (Pengelly *et al*., 2012). Students in Greece still burn the plant while studying, as it is believed to enhance mental alertness and stimulate blood flow to the brain.

Glycyrrhiza glabra

G. glabra, commonly called licorice, sweet wood, or mulaithi, is a widely distributed herb, known worldwide for its various curative properties. In the Ayurvedic medical system, this plant is referred to as 'Medhya dravya'. Licorice, an extract from the root of *G. glabra*, is traditionally used as a brain tonic and revitalizer to enhance memory and intellect. Licorice exhibits antioxidant activity, which helps mitigate brain damage by neutralizing free radicals and improving neural function and memory (Kim *et al*., 2012).

This is a perennial herb that has been reported to address many health problems, such as hyperdipsia, fever, sexual debility, epilepsy, respiratory disorders, paralysis, stomach ulcers, hemorrhagic diseases, skin diseases, jaundice, and rheumatism (Damle, 2014). Furthermore, in ancient times, it was used for its diverse therapeutic properties, including as a laxative, memory stimulant, antiviral, anti-ulcer, anti-inflammatory, anti-arthritic, and antibiotic. Its actions as a monoamine oxidase (MAO) inhibitor, antitussive, hypolipidemic, anticancer, anti-mycotic, estrogenic, anti-caries, antioxidant, anticholinergic, and diuretic agent contributed to its wide range of applications (Zadeh *et al*., 2013).

G. glabra contains a wide range of phytochemicals with significant therapeutic potential including triterpenes (glycyrrhizin or glycyrrhizic acid, glycyrrhetinic acid, monoglucuronide), flavonoids (liquiritin, liquiritigenin, isoliquiritin, rhamnoliquirilin, etc.), isoflavonoids (dehydroglyasperin C), tannins, saponin, glycosides, etc (Batiha et al., 2020). The main constituent is glycyrrhizin, a saponin compound with antioxidant, antiviral, and anti-inflammatory activity (Wang *et al*., 2015; Frattaruolo *et al*., 2019).

Different plant parts are utilized to treat a variety of health disorders such as stems for tuberculosis, roots for diabetes, Graves' disease and flatulence, and leaves for wounds (Halder

et al., 2021). The rhizomes and roots of *G. glabra* are the most crucial medicinal parts, often used alone or in combination with other herbs to treat various digestive system disorders (e.g., flatulence, hyperdipsia, colic, and stomach ulcers), respiratory system disorders such as tonsillitis, coughs, asthma, and sore throat, sexual debility, fever, paralysis, epilepsy, rheumatism, psoriasis, haemorrhagic diseases, leucorrhoea, jaundice, malaria, and prostate cancer (Batiha et al., 2020).

The effects of *G. glabra* root extract on learning and memory were investigated in mice by conducting neurobehavioral studies such as an Elevated Plus maze and a Morris water maze. Orally administered 150 mg/kg dose of *G. glabra* aqueous root extract for 7 days alleviated memory and learning impairment. Furthermore, this extract significantly reversed the scopolamine-induced and diazepam-induced amnesia (Dhingra *et al*., 2004). Liquiritigenin (LIQ), a bioactive compound from licorice roots effectively inhibited the apoptosis in glutamate-treated hippocampal neuronal cells in mice by preventing lipid peroxidation, Ca^{2+} influx, and intracellular ROS production, thus exhibiting a strong neuroprotective effect (Yang *et al*., 2013).

Licorice exhibits a wide range of pharmacological properties, making it valuable for various clinical applications. Oral preparations containing glycyrrhizin are effective in managing gynecological issues (e.g., premenstrual syndrome (PMS), and menopause), acute intermittent porphyria, inflammatory or allergic conditions, viral infections (e.g., the common cold, viral hepatitis, and HIV/AIDS), Addison's disease, and metabolic syndrome (syndrome X). Isoflavan compounds derived from licorice have been found to influence the serotonergic system by blocking radioactive serotonin reuptake, leading to antidepressant effects in both pre- and postmenopausal women (Ofir *et al*., 2003). Topical formulations with glycyrrhetinic acid are beneficial for skin conditions like herpes, eczema, dermatitis, melasma, and psoriasis showcasing the wide-ranging therapeutic potential of licorice (Murray, 2020). Deglycyrrhizinated licorice (DGL) is primarily used for treating ulcerative conditions of the gastrointestinal tract, such as canker sores, inflammatory bowel disease, and peptic ulcers. A study assessing the antiulcer effects of DGL in gastric ulcer treatment involved thirty-three patients who received 760 mg of DGL three times daily for one month. Findings revealed a significant reduction in ulcer size, with a 78% improvement in the DGL group compared to 34% in the placebo group (Turpie *et al*., 1969).

Convolvulus pluricaulis

C. pluricaulis, also called shankhpushpi, has been used as a brain or nervine tonic in improving memory and intellect. This perennial herb is referred to as Majjadhatu rasayana (rejuvenating nervous tissue) and Medhya rasayana (promoting intellect). In the Ayurvedic system of medicine, it was utilized for its memory-enhancing, psychostimulant, and tranquilizing properties (Mishra & Sethiya, 2010).

The diverse phytochemicals responsible for the pharmacological actions of the plant include flavonoids (kampferol), alkaloids (convolamine and shankhpushpine), phytosterol, volatile oils, proteins, fatty acids, amino acids, gums, scopoletin, mucilages, and β-sitosterol. These bioactive compounds display nootropic, neuroprotective, antioxidant, antimicrobial, antistress, antidepressant, anxiolytic, anticonvulsant, antiamnesic, antiulcer, anticatatonic, antibacterial, hepatoprotective, immunomodulatory, sedative and cardiovascular activities of this plant which are well documented (Kizhakke et al., 2019).

Rats received oral doses of 100 and 200 mg/kg of *C. pluricaulis* ethanolic extract, which significantly improved memory and learning ability in passive avoidance paradigms, Cook and Weidley's Pole Climbing Apparatus, and active avoidance tests. In addition, it reversed amnesia induced by scopolamine in rats suggesting better retention and recovery (Nahata *et al*., 2008). Similarly, treatment of *C. pluricaulis* in mice showed increased AChE activity in a dose-dependent manner in the CA1 and CA3 areas of the hippocampus (responsible for learning and memory functions). Although, memory retention was higher in young mice as compared to old ones (Sharma *et al*., 2010). Studies have also shown that ethanolic extract of *C. pluricaulis* alleviated neuronal injury in the hippocampus by mitigating the effects of oxidative damage and kainic acid-induced excitotoxicity in mice, thus displaying antioxidant potential (Parihar & Hemnani, 2003). A three-month administration of aqueous extract (150 mg/kg) of *C. pluricaulis* inhibited aluminium-induced neurotoxicity by decreasing ROS levels and AChE activity and sustaining the function of Nerve Growth Factor-Tyrosine kinase A receptor (NGF-TrkA) and ChAT (Bihaqi *et al*., 2009).

ACh, a key component of the cholinergic system, is essential for memory function in both humans and rodents. Cholinergic and muscarinic agonists have been shown to enhance memory by inhibiting β-amyloid formation via the glycogen synthase kinase-3 (GSK-3) enzyme pathway (Forlenza *et al*., 2000). *C. pluricaulis* is believed to enhance memory by modulating ACh levels in the brain (either by stimulating its synthesis or inhibiting AChE activity), or by functioning as a muscarinic agonist to reduce β-amyloid formation (Malik *et al*., 2011).

A clinical study involving ten healthy subjects (16–60 years) over a 30-day trial examined the combined effects of Shankhpushpi syrup (10 ml twice daily) and Rajat Bhasma (100 mg once daily) on memory, using the PGI memory scale. Results showed statistically significant improvements in multiple cognitive domains, including remote and recent memory, attention, recall, and retention. Although some aspects of memory showed improvement, the study's small sample size limits its reliability, requiring further research with a larger sample size to confirm the results (Devi & Kashyap, 2019). Another clinical trial involving thirty individuals aged 16 to 25 years explored the impact of Shankhpushpi tablets, formulated by processing its powdered form with its fresh juice through Bhavana (levigation), over a duration of two months. Using Weschler's memory scale, results showed significant improvements in auditory and visual memory, particularly long-term recall (Amin *et al*., 2014). Another randomized, placebo-controlled trial on "Dr. Brain" syrup (10 ml twice daily) containing *C. pluricaulis* evaluated its effects on thirty patients over six weeks. Compared to a placebo, the syrup not only improved memory, but also significantly reduced anxiety and depression without adverse effects. This effect of "Dr. Brain" syrup may be attributed to its ability to regulate neurotransmitter levels, including serotonin, noradrenaline, and dopamine (Patel *et al*., 2016).

These findings indicate that both formulations have the potential to enhance cognitive function and support mental well-being. However, the lack of multicentric studies on *C. pluricaulis* highlights the need for broader clinical trials to gain a deeper understanding of its effectiveness.

Acorus calamus

A. calamus, commonly referred to as "sweet flag" or "calamus" is a semi-aquatic, perennial herb distributed in India, Central Asia, Northern America, Southern Russia, Eastern Europe, and Siberia. In Ayurveda, this plant has been utilized in many herbal traditions as a brain tonic in strengthening the nervous system and enhancing overall memory and intellect (Mukherjee *et al*., 2007a). This indigenous herb is used to cure several diseases like neurosis, chronic diarrhea, hysteria, insomnia, melancholia, cough, gout, hemorrhoids, skin diseases, tumors, epilepsy, intermittent fevers, digestive problems (such as gas, bloating, etc.), bronchitis, depression, memory ailments, and other mental disorders (Sharma *et al*., 2014).

Roots and rhizomes of this plant have been used in the Chinese and Indian medicinal systems for their therapeutic role and possess a wide range of pharmacological activities, such as anticholinergic, antioxidant, antimicrobial, antifungal, analgesic, antidiabetic, CNS depressant, antispasmodic, anti-inflammatory, and cardiovascular, insecticidal agent, anti-aging, and anthelmintic properties (Parki *et al*., 2017). *A. calamus* contains several phytoconstituents such as alkaloids, iso asarone, essential oils, saponins, lectins, flavonoids, sesquiterpene, isoeugenol, monoterpene, mucilages, phenylpropanoid, phenols, quinones, caryophyllene, safrole, acorin, etc (Joshi, 2016).

The major phytoconstituents found in the essential oil are α-asarone and β-asarone. α-asarone exhibits numerous therapeutic actions such as neuroprotective, anticonvulsive, anti-apoptotic, antidepressant, anti-amyloidogenic, anxiolytic, antioxidative, and cognition-enhancing effects. In lipopolysaccharide (LPS) treated mice hippocampus, α-asarone has been reported to ameliorate memory deficits by reducing the induced over-expression of pro-inflammatory cytokines, attenuating the apoptosis of CA1 neurons and microglial activation, thus enhancing overall cognitive functions (Shin *et al*., 2014). α-asarone (300 µg/ml) displayed neuroprotective action by inhibiting N-methyl-D-aspartate (NMDA) receptor-induced excitotoxic neuronal death in rat cortical cells (Cho *et al*., 2002). Methanolic extract of *A. calamus* and α-asarone produced an anti-stressor effect by increasing the antioxidative capacity of discrete regions of the rat brain against the white noise stress (100dBA/4h/d) exposure (Manikandan *et al*., 2005).

β-asarone exhibits neuroprotective properties and is believed to have the ability to cross the BBB. Also, β-asarone is effective against neuronal apoptosis, cerebral ischemia, ischemia–reperfusion-induced autophagy, reperfusion-induced injury, experimental AD models, epilepsy, and oxygen-glucose deprivation. Findings also show that in LPS-activated microglial cells, β-asarone helps reduce neuroinflammation by suppressing the excessive release of pro-inflammatory cytokines through the Nuclear Factor-kappa beta (NF-κB) signalling pathway (Lim *et al*., 2014). Studies have reported the role of β-asarone in memory improvement which could be attributed to its inhibitory effect on AChE, thus affecting cholinergic activity in the CNS. (Mukherjee *et al*., 2007b). As *A. calamus* exhibits potent anti-neuroinflammatory properties, it holds promise as an effective remedy to combat cognitive decline.

Phyllanthus emblica

P. emblica or *Emblica officinalis*, commonly called Indian gooseberry or Amla is well known for its medicinal and pharmaceutical properties. *P. emblica* is one of the most common medicinal herbs widely distributed in central and southern India, Southeast Asia, southern China, Pakistan, Bangladesh, Ceylon, Malaysia, and Srilanka (Variya *et al*., 2016). In the Ayurvedic system of medicine, amla has been used to treat several ailments such as CNS and neurological disorders, diabetes, cancer, hyperlipidemia, inflammation, ophthalmic diseases, osteoporosis, hypertension, parasitic diseases, infectious and non-infectious diseases, and lifestyle diseases. The medicinal properties of *P. emblica* extend to all its parts, but its fruits are predominantly utilized in treating ailments (Kumar *et al*., 2012; Yadav *et al*., 2017).

P. emblica extract contains numerous phytoconstituents including alkaloids, vitamin C, fixed oils, minerals, tannins, polyphenols (e.g. gallic acid, ellagic acid, leutolin, etc.), phyllemblin, amino acids, phenolic glycosides, flavanol glycosides, flavone glycosides, vitamins, flavonoids, etc (Zhang *et al*., 2003). The amount of vitamin C is reported to be the highest (478.56 mg/100 ml) in Amla compared to other citrus fruits. Amla, being abundant in Vitamin C, contributes to enhanced memory and has a calming effect and anti-cholinesterase activity. The pharmaceutical properties of this herb include nootropic, antioxidant, antianxiety, antistress, anticancer, adaptogenic, immunomodulatory, anti-inflammatory, antimicrobial, and anti-diabetic activity (Krishnaveni & Mirunalini, 2010).

A study reported that oral administration of Anwalachurna, a traditional Ayurvedic formulation of *P. emblica* (at doses of 50, 100, and 200 mg/kg), led to a dose-dependent improvement in memory function in both young and aged rats. Additionally, it effectively counteracted amnesia induced by scopolamine (0.4 mg/kg, i.p.) and diazepam (1 mg/kg, i.p.) (Vasudevan & Parle, 2007). Another study revealed the antidepressant-like effects of an aqueous extract of *P. emblica* fruits (200 and 400 mg/kg). The extract significantly reduced immobility time in forced swim tests and tail suspension tests in mice by reducing the levels of monoamine oxidase-A (MAO-A) and GABA in the mice brain (Dhingra *et al*., 2012).

P. emblica is a potent medicinal herb with clinically validated therapeutic benefits. It is widely used alone or in polyherbal formulations for various health conditions. Commercially available products like Triphala, Pepticare, EuMil, and Brahma Rasayana serve as health tonics and remedies. Among them, Triphala is extensively studied and clinically proven for its immuno-stimulatory and cytoprotective properties. In a phase I clinical trial, healthy human subjects were administered three capsules of Triphala for two weeks. The results demonstrated the immunostimulatory effects of Triphala, showing a significant increase in cytotoxic T cells and natural killer cell activity (Phetkate *et al*., 2012).

Conclusion

Traditional medicinal systems have been using these herbal systems for the enhancement of cognition, a practice now increasingly supported by emerging scientific research. Herbal phytochemicals exhibit diverse therapeutic properties, including anti-inflammatory, antioxidant, and neuroprotective effects, which eventually establish them as memory-enhancing substances. These phytochemicals effectively target the CNS to enhance memory, intellect, learning, and attention. With the ability to cross the BBB, they hold promise as potential therapeutic agents for CNS disorders. Most studies have concentrated on improving cholinergic function by inhibiting excess AChE activity to maintain optimal ACh levels in the brain. Disruptions in this cholinergic system contribute to cognitive decline and memory impairment. Also, medicinal phytoconstituents contribute significantly to environmental sustainability by offering natural alternatives to synthetic drugs, reducing chemical waste, and minimizing pharmaceutical pollution. By integrating phytochemicals into modern medicine through eco-friendly extraction and formulation techniques, we can ensure a balance between human health benefits and environmental preservation, fostering a more sustainable approach to global healthcare.

Plant nootropics are generally well tolerated; however, they contain bioactive phytochemicals that may pose potential risks, making toxicological evaluation essential. Therefore, seeking medical advice before use is recommended. Although these findings are encouraging, rigorous clinical trials for validating the effects, establishing optimal dosages, and long-term safety are further warranted. Future research should also clarify the exact mechanisms through which these herbs exert their cognitive benefits. This could lead to the development of safe and novel treatment approaches for conditions such as dementia, and AD among various other models of cognitive impairment. The medicinal potential of these memory-boosting herbal systems can be fully realized by integrating traditional knowledge with modern-day scientific research, providing hope for better management and prevention of neurological and neurodegenerative disorders.

Acknowledgment

Work from our laboratory was supported by the Department of Zoology, University of Rajasthan, Jaipur, Rajasthan, India. The Council of Scientific and Industrial Research Human Resource Development Group (CSIR-HRDG), New Delhi, India provided financial support.

Author Contribution

This review was contributed by Sonika Kashyap and Renu Bist, all of whom were responsible for the study, concept, and design of this review article. Sonika Kashyap performed the acquisition, interpretation of literature, and drafting of the manuscript under the supervision of Renu Bist and also reviewed and revised the manuscript.

Conflict of Interest

Authors have no conflict of interest.

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