



Phytochemical and Therapeutic Potential of Herbal Cognitive Enhancer

Abhishek Bharti^{1*}, Kalpna Kashyap², Rutika³, Akhil Moudgil⁴,
Kundan Singh Bora¹ and Dinesh Kumar¹

¹University Institute of Pharmaceutical Sciences, Chandigarh University,
Mohali - 140413, Punjab, India; abhbharti.1998@gmail.com

²Government Pharmacy College, Kangra - 176047, Himachal Pradesh, India

³School of Pharmacy, Career Point University, Hamirpur - 176041, Himachal Pradesh, India

⁴Gautam College of Pharmacy, Hamirpur - 177001, Himachal Pradesh, India

Abstract

Memory is the most significant factor in distinguishing one person from another, as it is necessary to recognise one's own self. The brain can encode, store, and retrieve information using three different types of memory. Individuals who lack these basic forms of memory are unable to create personal relationships, acquire new knowledge, and perform basic everyday duties. Memory refers to a person's ability to encode, store, retain, and recall knowledge and past events in his or her brain. Memory gives a person the ability to learn from and adapt to previous experiences, as well as the ability to recall previously taught facts, skills, and habits. Today, poor memory, weak recall, and low retention are all typical issues. Memory deteriorates primarily because of stress and exhaustion. Memory loss, often known as age-related memory impairment, is frequent in those over the age of 40. This could be linked to the loss of hormones and proteins (growth factors) that repair brain cells as people get older. Herbs were employed to improve memory power in India throughout ancient times. Indian and Chinese cultures developed many traditional medicines from herbs to treat diminishing cognition, reverse memory loss, and improve learning power. Nootropic herbs are known for their brain-acting herbs and smart medications, which are derived from their isolated ingredients and aid to improve blood circulation in the brain. The focus of this review is on natural agents and herbs that work as memory enhancers. By using one of the herbs at a time, one can improve his or her memory.

Keywords: Acetylcholine, Alzheimer's Disease, Herbs, Memory, Nootropics

1. Introduction

Memory is a typical learning ability that indicates long-term changes in the nervous system caused by short encounters. Short-term memory and long-term memory are the two types of memory. There are a variety of drugs available in the market for maintaining memory or enhancing memory but some of them have huge side effects also especially in the case of synthetic drugs¹. *Bacopa monniera*, also called *Bacopa monnieri*, *Herpestis monniera*, and *Brahmi*, has been used in Ayurvedic medicine for millennia² in the case of study about memory the brain is the most important, the forebrain, midbrain,

and hindbrain are the three fundamental sections of the human brain. It includes the hypothalamus, thalamus, cerebellum, cerebral cortex, hippocampus, midbrain, and several other glands, with the Hippocampus being important for memory. Memory is a very significant aspect for recalling situations, information, and experiences, but because of certain conditions like stress, negative emotions cause various illnesses such as amnesia, memory loss, high blood pressure, anxiety, and several serious life treatments in that individuals can record events, information, and stimuli over a time. Thus, over recent decades, herbs and natural cures are very useful in the promotion of intelligence such as *Medhya* herbs related

*Author for correspondence

to our cortical brain centre's development of the Indian medicines *Ayurveda* "The herbs acting on the brain" and its isolated components called intelligent medications, the nervous systems and nootropic herbs. *Ayurveda* says that the three powers of intellect are the trinity of intelligence - to learn, retain and remember and the power of acquisition is to know, analyse and understand something new. The retention power is the second mind power that retains what has been taken or comprehended as short-term recollection, and the third intelligence triad indicates that knowledge is obtained in time after which long-term memory^{3,4}. The power of retention is also the power of recollection.

1.1 Various Therapies Can Be Used to Improve Cognition, Including

- Increasing blood flow to the brain.
- Precursors for neurotransmitters (chemical messengers in the brain) are provided.
- Providing the brain with useful energy.
- Neuron function is being improved.
- Defending brain cells and others from free radical and oxidative harm⁵ (Figure 1).

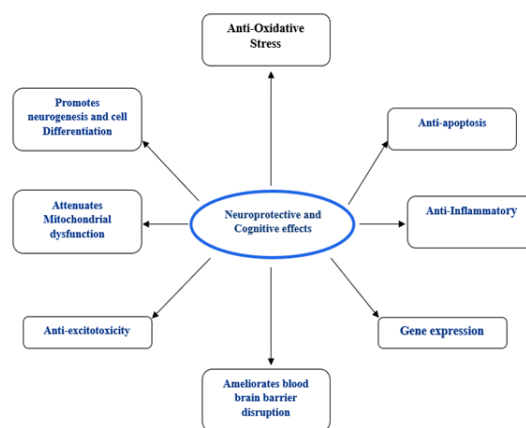


Figure 1. Mechanism of neuroprotective and cognitive enhancement effect^{6,7}.

1.2 Scientific Documentation of Herbs

Various plants used, such as for Alzheimer's Disease (AD) and other memory-associated problems in traditional medicine are used to recover cognitive impairments, as plant alkaloids have significant advantages over side effects and medication interactions. The cognitive capacity of several herbs, such as *Bacopa monniera* (Bramhi), *Ginkgo biloba*, *Shankhpushpi* etc. can be increased^{8,9} (Table 1).

Table 1. Plants used as memory enhancers

S. No.	Source	Family	Active constituent responsible	Part Used	Activity
1.	<i>Nardostachys grandiflora</i>	(Valerianaceae)	jatamansone, jatamansinol jatamansin	Rhizome, Roots	There is an essential oil in the hairy roots. The roots are regarded as tonic, stimulative, antimicrobial, and laxative. The roots of the brain are remarkable. memory enhancement was due to cholinergic transmission in the brain being facilitated ^{10,11} .
2.	<i>Bacopa monniera</i>	(Scrophulariaceae)	Bacosides A-B triterpenoid, saponins	leaves	Bacosides also aid in neural healing by increasing kinase activity, neuronal synthesis, restoring synapse function, and transferring nerve impulses ^{12,13} .
3.	<i>Withania somnifera</i>	(Solanaceae)	Ashwagandholine, AG Sitoindosides VII-X and withaferin	roots	The effects of a complete alkaloid extract of <i>Withania somnifera</i> roots on the central nervous system have been studied (ashwagandholine, AG) ¹⁴ . The effects of several kinds of <i>Withania somnifera</i> on brain cholinergic, glutamatergic, and Male Wistar rats' GABAergic receptors were investigated. Influence the expression of the serotonergic receptor 5-HT _{3A} , as well as the levels of ACh and 5-HT ¹⁵⁻¹⁷ .

4.	<i>Salvia rosmarinus</i>	(Lamiaceae)	Rosmarinic acid	Flower, roots	Moderate inhibition of acetylcholinesterase was caused by essential rosemary oil ¹⁸ .
5.	<i>Rhodiola rosea</i>	(Crassulaceae)	p-tyrosol, rhodioniside, rhodioline, and rosidin		First, it activates central nervous system neurotransmitters such as adrenaline, dopamine, serotonin, and nicotine cholinergic actions. Second, improved neurotransmitter effects on the brain via enhancing the blood-brain barrier's permeability for DA and 5-HT precursors ¹⁹⁻²⁶ .
6.	<i>Centella asiatica (vacha)</i>	(Umbelliferae)	rosavin, salidroside	Root, Leaves, flower	Asiatica can have longer-lasting positive effects on the mouse brain, as well as improve endogenous antioxidant enzymes in a rat brain by mediating action on the cholinergic and neuronal systems ^{8,27-30} .
7.	<i>Acorus calamus</i>	(Acoraceae)	beta-asarone alpha-asarone, saponins, lectins, sesquiterpenoids, lignans, and steroids ⁵	rhizomes	Anti-depressant, neuroprotective, stimulant digestive, nootropic, stimulant nervous, relaxing muscle ^{4,28-36} .
8.	Evolvulus alsinoides L. (shankhpuspi)	(Convolvulaceae)	scopoletin, umbelliferone, scopolin and 2-methyl-1,2,3,4-butanetetrol ⁶	Whole plant	Potentiating, reassuring and anxious qualities of memory ^{4,12} .
9.	<i>Caesalpinia crista linn.</i>	(Caesalpinaceae)	sitosterol and hepatsane, $\alpha, \beta, \gamma, \delta, \epsilon$ -caesalpin, and F-caesalpin.	Seeds	In part, suppression of AChE activity within the brain mediates effects ^{8,14} .
10.	<i>Vitex negundo</i>	(Verbenaceae)	Casticin, isoorientin, chrysophenol D, luteolin, p-hydroxybenzoic acid, D-fructose	Leaves, flowers	Its parts extract or a leaf extract is commonly used as nerve tonic ³⁷⁻³⁹ .
11.	<i>Cyperus rotundus</i>	(Cyperaceae)	Cineole Pinene isociprol	rhizome	anti-AChE activity
12.	<i>Celastrus paniculatus</i>	(Celastraceae)	Paniculatine celapanine, celapanigine, celapagine, celastrine,	seed	The seed oil improved learning and memory processes by lowering noradrenaline, dopamine, and 5-hydroxytryptamine levels in the rat brain; nevertheless, the oil was not neurotoxic.

1.3 Mechanistic Approaches for Cognitive Enhancement

A 200 mg/kg ethanolic extract of *Nardostachys grandiflora* (*jatamansi*) enhanced learning and memory in young mice while also correcting amnesia caused by diazepam (1 mg/kg i.p.) and scopolamine (0.4 mg/kg i.p.). Because the scopolamine-induced amnesia was reversed, the memory improvement was most likely due to increased cholinergic transmission in the brain. As a result, *N. jatamansi* may be an effective memory-restoring agent in the treatment of Alzheimer's disease in the elderly^{10,11}. Children and adolescents have been proven to benefit from *Bacopa* extracts in terms of cognitive and behavioural performance. It is also known as a memory booster and a brain tonic. BM was tested for its influence on serotonergic receptor 5-HT_{3A} expression, as well as ACh and 5-HT levels, during a hippocampal-dependent learning task. A standardised 80 mg/kg p.o. BM extract (555 per cent bacosides) was also shown to greatly reduce the memory impairment caused by 1-(m-chlorophenyl)-biguanide (5-HT_{3A} agonist). BM substantially raised levels of 5-HT (39%), ACh (20%), glutamate (20%), and -aminobutyric acid (GABA) (20%) in the hippocampus when compared to the control. BM lowered dopamine levels considerably but only minimally (16%). This finding is noteworthy because it adds to the growing body of data that BM components interact with the serotonergic system¹³. *Withania somnifera* (*Ashwagandha*) root extract's positive impact is related to its GABA mimic action. *Ashwagandha*, its components, and the metabolites of its constituents promote nerve growth after 7 days of administration. In a remarkable study, mice were given continuous oral therapy with anoside IV, which decreased axonal, dendritic, and synaptic losses, as well as memory impairments caused by amyloid peptide A β ¹⁷. In the scopolamine-induced dementia model of Alzheimer's disease, the memory-improving effect of rosemary extract (200 mg/kg, PO) has also been related to a direct influence on ACHE activity⁴⁰. While rosemary extracts reduced butyrylcholinesterase (BuChE) mRNA expression in the cortex, they enhanced it in the hippocampus. These impacts on enzyme expression, however, might be mediated indirectly through other methods⁴⁰. A meta-analysis of five trials revealed that *R. rosea*. considerably enhanced GSH levels. First, it activates central nervous system neurotransmitters such as adrenaline, dopamine, serotonin, and nicotine cholinergic actions. Second, improved neurotransmitter effects on the

brain via enhancing the blood brain barrier's permeability for DA and 5-HT precursors¹⁹⁻²⁶. *C. asiatica* is used in Ayurvedic medicine for its cognitive characteristics as a brain tonic, in the treatment of mental diseases, and as a memory enhancer^{6,7,12}. *C. asiatica* has been demonstrated to increase neuronal morphology, learning performance, and memory retention in animal models^{32,33}. Asiatic acid has been shown to boost learning and memory in both passive and active avoidance tests³⁴. *C. asiatica* has been demonstrated to increase cognitive function via a variety of mechanisms, including inhibition of acetylcholinesterase activity, reduction of phospholipase A₂ (PLA₂) activity, protection against β -amyloid formation, and protection against brain damage^{35,36}. The ethanolic extract of *Acorus calamus* was studied for its ability to improve learning and memory (doses of 25, 50 and 100 mg/kg, oral and intraperitoneal routes) (Table 1).

1.4 Herbal Drugs for Cognition Enhancement

1.1.1 *Nardostachys grandiflora* (Valerianaceae)

Nardostachys jatamansi is a Himalayan flowering plant. It contains Spikenard, a very fragrant essential, amber-coloured oil. The hairy roots contain essential oil. The roots are said to be tonic, stimulant, antibacterial, and laxative. Acacin, ursol, octacosanol, kanshone A, nardosinonediol, nardosinone, aristolene-9 β -ol, oleanolic acid, and beta-sitosterol are active substances that improve brain tone. The plant grows to a height of 10–50 cm and has pink and bell-shaped blooms⁴¹. The plant may weigh between 4 and 20 pounds. It is situated at an elevation of 3,000–5,000 m (9,800–16,400 ft) above sea level. Crush and distil rhizomes to get a very scented, amber-coloured essential oil with a thick density (underground stems)^{41,42}.

1.1.2 *Bacopa monniera* (Scrophulariaceae)

Bacosides A and B⁴³⁻⁴⁷ are the active ingredients responsible for cognitive benefits of *Bacopa monniera*, is also known as neural tonic and memory enhancer. Most of the research is focused on the mechanism behind these qualities, which is employed mostly for therapeutic means, to improve cognitive function. *Brahmi's* potential to improve nerve impulse transmission is due to the triterpenoid saponins and its bacosides. Increase kinase activity, neuronal synthesis and restore the synaptic activity and transmission of nerve pulses⁴⁸ also helps the

bacosides to heal damage on neurons. An investigation into senior individuals in 2012 showed that the *Bacopa monnieri* eliminates ACHE, which in turn improves attentiveness, memory processing and workplace memory^{49,50}. In the same way, the children's research shows significant advantages from a 12-week *Brahmi* treatment with improved repetition of sentences, logical memory and paired associated learning tasks⁵⁰.

1.1.3 *Withania somnifera* (Solanaceae)

African somnifera, usually called the *Ashwagandha*, is an annual evergreen bunch, or night shade family, in India, the Middle East and portions of Africa⁴⁹. The Indian ginseng, poisonous gooseberry, or wind cherry²⁹ is an annual evergreen bunch. Several additional types are morphologically similar³¹ in the genus *Withania*. *Withania somnifera* roots have been tested for their effects on the central nervous system (ashwagandholine, AG) as a total alkaloid extract⁵¹⁻⁵³. Effects in brain cholinergic, glutamatergic, and GABAergic receptors in male Wistar rats were examined using the sitoindoside VII-X and withaferin obtained in an acoustic methanol extract from *Withania somnifera*-produced varieties¹⁵. The compounds were observed in lateral septum and globus pallidus to have slightly higher acetylcholinesterase activity (AChE) and lower AChE activity in a diagonal vertical band. These changes were accompanied in several cortic regions, including the denticulate, frontal, piriform, pari- and retro-spinal cortex, by elevated M1-muscarinic-cholic receptor binding in lateral and medial septum, as well as frontal cortices. Then the data reveal substances activate processes in the cholinergic signal transduction cascade of the cortical and basal forebrain selectively. The increase in pharmaco-induced capability of cortical muscarinic acetylcholine-receptors may partially explain the effects of *Withania somnifera* extracts on animals and humans on both cognition and memory⁵³.

1.1.4 *Salvia rosmarinus* (Solanaceae)

The *Salvia rosemary*, generally referred to as rosemary, is a shrub native to the Mediterranean region that has aromatic and evergreen, needle-like leaves with flowers in white, pink, violet or blue⁵⁴. By 2017 *Rosmarinus officinalis*, now a synonym was known by his scientific name. She is a part of the *Lamiaceae* wise family, which contains many other herbs. The term "rosemary" comes from the Latin *ros marinus*^{55,56}. It is generally known as rosemary and is a shrub that is native to the Mediterranean region with

aromatic, evergreen, needle-like leaves and white, pink, purple or blue blooms⁵⁴. By 2017 *Rosmarinus officinalis*, now a synonym was known for his scientific name. In stimulating the neurological system under sympathetic control, the key effect of rosemary essential oil results in better memorisation and concentration⁵⁷. Essential Rosemary oil has caused mild acetylcholinesterase inhibition³. The olfactive effects on cognitive performance and mood of volunteers of essential oils of lavender and rosemary. Rosemary reported significant performance improvements in the overall memory quality and in secondary memory factors, but also impaired the memory speed component compared with the control. It is a part of the *Lamiaceae* wise family, which contains many other herbs. The word 'romary' comes from the Latin *ros marinus*⁵⁸.

1.1.5 *Rhodiola rosea* (Crassulaceae)

A perennial plant of flora in the *Crassulaceae* family is *Rhodiola rosea*⁵⁹. It grows natively in European (e.g., UK), Asia and North America's Wild-Arctic regions⁶⁰. While traditional medicine uses *Rhodiola rosea*, there is no quality clinical proof of its efficacy in the treatment of any diseases^{62,63}. Effects of *Rhodiola rosea* are, firstly, stimulating neurotransmitters such as epinephrine, dopamine, serotonin, and cholinergic nicotine in the central nervous system; secondly, strengthening blood barriers to precursors of DA and 5-HT in the brain, and secondly, enhancing neurotransmitters¹⁰⁻¹³. The release from the ascendant routes of the brain stem of norepinephrine, serotonin and dopamine activates the brain cortex and limbic system. The cognitive processes, attention, memory and learning of the cortex were therefore strengthened, as well as the functions of the prefrontal and frontal cortex. In addition, other neuronal systems such as the cholinergic system use the acetylcholine neurotransmitter (Ach) and contribute to the memory function via pathways up from the limbic system's memory storage on various cerebral cortical areas (memory retrieval).

Blocking agents Ach inhibit and disrupt memory activation in these upward paths. This blockage was reversed by *Rhodiola rosea*^{42,43}.

1.1.6 *Centella asiatica* (Umbelliferae)

Another *Centella asiatica* (L) Urban's (*Umbelliferae*/*Apiaceae* family) name is *Vacha*/*Mandukparni*. It is used in India as a tonic to enhance memory, immune

boost, antisstress, anti-epileptic and anxiety for spices or cultivation as a vegetable and herbal composition. *Centella asiatica* works as an antioxidant to remedy neurotoxicity generated by lead acetate, amnesia, and thoughts. *C. asiatica* can create longer-lasting effects on the mouse brain during early postnatal developmental stages by modulating the cholinergic system and neuronal architecture and improving the endogenous antioxidant enzymes in the rat brain^{8,27}.

1.1.7 *Acorus calamus* (Acoraceae)

Acorus calamus is a scientific name for *Vacha* (the Hindi name) grown in the Himalayas up to 6000 feet above sea level which is used as a brain tonic in Indian and in Chinese herbal traditions. Stain, roots, and leaves are employed by herbal professionals for efficient supplements. Sweet medication (*Acorus calamus*) from the *Acoracean* family is known in traditional medicine. In spices and in medicinal products the sweet flags use fragrant leaves and rhizomes as a flavour. It is propagated largely by vegetative and demand ways because of different plant uses. *Acorus calamus in vitro* preserves germplasm to the advantage of the medicinal industry. *Vacha* is effective in treating nerve disorders as assists in attention, thinking and detoxifying of brain tissue. It works as an intellect promoter, antidepressant, neuroprotective, digestive stimulant, nootropic, stimulant nervous, and muscle relaxant. *Vacha* plant is an efficient herb that aids students, musicians, mediators, and researchers in their work in mental focus and concentration^{2,31}.

1.1.8 *Evolvulus alsinoides* L. (Convolvulaceae)

Its name is common (*Shankhpushpi*). In the Himalayas *Evolvulus alsinoides*, known as *Shankhpushpi* in *Ayurveda* for its therapeutic values of nervous weakness, memory increase and epilepsy, is found in 6000 feet of *Convolvulaceae* family, known to be used in common language. It is used to stimulate memory, reassuring characteristics, and calming effects by inculcating the complete plant of '*Shankhpushpi*'. The *Evolvulus alsinoides* extracts as ethyl acetate, aqueous and ethanolic have shown antibacterial and anthelmintic effects, as well as an increased memory retention and learning process in rats^{2,12}.

1.1.9 *Caesalpinia crista* Linn. (Caesalpinaceae)

Caesalpinia crista (in Hindi) is commonly referred to as *kat-takaranja* and the *Caesalpinaceae* family found in

India and Sri Lanka are called *sagargotas* (in Marathi). Plant seeds consist of the protein enzymes starch, saponin, bonducin, sucrose, two phytosterols, sitosterol and hepatsanic, and are made up of palmitic acid, stearic acid, lignoceric acid, oleic acid, linolenic acid, and the kernel seed of *Furano caesalpine*, β -*caesalpine*, *cesalpine*, *maesalpine* and *F. caesalpine*. Enhances the learning and memory activity, impairments of scopolamine and these actions are partly mediated by an inhibition of AChE activity in the brain. Ethanolic extracts from *Caesalpinia crista's* dried-seed kernel Lin. It operates as a non-diabetic, antiproliferative, adaptogenic, anti-filarial, utero-contractile, anticancer and antioxidant activity.

1.1.10 *Vitex negundo* Linn. (Verbenaceae)

Vitex negundo, often known as *Bana* or *Sambhalu*, is a huge aromatic shrub with quadrangular, thickly white, tomentose branchlets. It's popular in traditional medicine, especially in South and Southeast Asia. Casticin, isoorientin, chrysophenol D, luteolin, p-hydroxybenzoic acid, and D-fructose are the main components of the leaf juice. The oil's primary ingredients are sabinene, linalool, terpinen-4-ol, -caryophyllene, -guaiene, and globulol, which account for 61.8 percent of the oil. Aside from its nerve tonic qualities, it is also beneficial in asthma, lung disorders, spleen enlargement, tonsillitis, sciatica, and rheumatism. To keep pests at bay, dried leaves are mixed in with grains³⁷⁻³⁹.

1.1.11 *Cyperus rotundus* (Cyperaceae)

Sedge, also known as *C. rotundus*, is a member of the *Cyperaceae* family. *Cyperus* rhizome is high in essential oils, including pinene, a trace of cineole, terpenes, and isociprol, a novel alcohol. Several chemical components of *C. rotundus* rhizome ethanol extract have been identified, and some of these compounds show anti-AChE action⁶⁵. According to research, the severity of dementia in Alzheimer's disease is determined by the loss of neurons in the Meynert nucleus, which is accompanied by a considerable drop in the number of acetylcholine transferase enzymes in the cortex and amygdala, resulting in impaired learning⁶⁶. The bulk of the nucleus basalis of Meynert NBM cells are cholinergic and are found in the frontal base of the brain⁶⁷. Because cholinergic ramifications are delivered from the Meynert nucleus to the cortex and septum, electrical injury of the NBM causes cholinergic cell death in the nucleus and decreases acetylcholine levels in the cortex⁶⁸.

1.1.12 *Celastrus paniculatus* (Celastraceae)

C. paniculatus (Celastraceae) is an Indian medicinal plant that has long been employed in the ancient Ayurvedic medical system. *C. paniculatus* is a stimulant, nervine tonic, rejuvenator, sedative, tranquillizer, and diuretic⁶⁹. Plant seed and seed oil are said to be quite good for stimulating the mind and sharpening the memory. According to one study, oral treatment of the seed oil decreased levels of noradrenaline, dopamine, and 5-HT in the rat brain, improving learning and memory functions; additionally, the oil was not neurotoxic. Rats were also given seed oil, which restored a scopolamine-induced performance impairment⁷⁰. An aqueous seed extract had an antioxidant impact on the central nervous system, which may explain the rumoured memory benefits, as this extract improved cognition *in vivo*⁷¹. At a dose of 200 mg/kg, the aqueous extract of *C. paniculatus* improved learning and memory tasks in both the shuttle-box and step-through paradigms. When the animal is given 200 mg/kg body weight of *Celastrus* seed oil, there is a little increase in AChE activity in the hippocampus⁷².

2. Conclusion

One of the most complex organs ever produced is the human brain. The brain's power to keep memories is one of the most interesting elements. Memory is one of the differences between humans and animals. But for numerous reasons, memory might become defective and the person cannot fully utilise his potential. Some herbs help strengthen your memory better. There has been research on memory improvement and finds that herbs have been utilised as memory boosters. This article described how herbs are usually used as memory boosters and how they help memory improvement through biochemical measures.

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