

PHCOG REV.: Review Article Natural Memory Boosters

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ABSTRACT

Memory is perhaps the most vital of the aspects that differentiates human beings from other animals. Since ages, drugs and natural remedies have been prescribed to enhance memories in people. The Indian System of Medicine Ayurveda has a treasury of such memory enhancing drugs, which are today popular all over the world due to their proven effective qualities. The herbs acting on the brain are called as Nootropic herbs and their isolated constituents referred to as smart drugs. Memory enhancer herbs enhance the memory and increase blood circulation in the brain. This Review focuses on Herbs and other natural agents as memory boosters.

KEYWORDS: Memory, herbs, enhancers

INTRODUCTION

Memory is the ability of an individual to record sensory stimuli, events, information, etc., retain them over short or long periods of time and recall the same at a later date when needed. Memory is perhaps the most vital of the aspects that differentiates human beings from other animals. Poor Memory, lower retention and slow recall and are common problems in today's stressful and competitive world. Age, stress, emotions are conditions that may led to memory loss, amnesia, anxiety, high blood pressure, dementia, to more ominous threat like schizophrenia and Alzheimer's diseases and in that case the person is not able to make full use of his or her potentials.

The herbs that promote the intelligence are called Medhya (1) herbs. This action is related to our mind and mind resides in brain and nervous system - especially the higher cortical centers of brain. According to Ayurveda the intelligence is a triad of three powers of the mind - the acquisition, the retention and the recollection.

The Power of Acquisition: It is the capacity to grasp some topic or something new. It is the capacity to understand or analyze.

The Power of Retention: It is the capacity to retain what has been grasped or understood. This capacity also deals with short-term memory.

The Power of Recollection: This is the capacity to retrieve the information after some time. It can be compared to long-term memory.

Since ages, drugs and natural remedies have been prescribed to enhance memories in people. The Indian System of Medicine Ayurveda has a treasury of such memory enhancing drugs, which are today popular all over the world due to their proven effective qualities. The herbs acting on the brain are called as Nootropic herbs (Nootropic is derived from Greek and means acting on the mind) and their isolated constituents referred to as smart drugs. Memory enhancer herbs enhance the memory and increase blood circulation in the brain.

Several treatments, including mental exercises, nutrition, and drug therapy, are being evaluated for their use in maintaining

memory function over time. Mental exercises have been shown to improve memory in the elderly while good nutrition and drug therapy improve general health and increase blood flow to the brain (2, 3).

The following is a list of the most effective herbs used in memory enhancement all over the world:

Ginkgo biloba

Ginkgo biloba is also known as maidenhair tree, kew tree, ginkyo, yinhsing. The memory herb improves brain circulation, increase the supply of oxygen and nutrients. It helps the body to eliminate free radicals thereby improving memory (4), alertness, clarity, depression and apathy in some people.

This process is simple in allowing for increased blood flow to reach the brain, thus allowing for more oxygen hence allowing the cells to function at a faster pace. The active compounds for memory enhancement are present in the leaves. The concentrations of these active compounds in the leaves vary with the seasons, with the highest amount present in autumn. These constituents include terpenoids (eg, bilobalide [Figure 1]) and ginkgolides A, B, C, J, and M [Figure 2]), flavonoids (eg, kaempferol, quercetin, isorhamnetin [Figure 3], and polymeric flavonoids proanthocyanidins), steroids (eg, sitosterol and stigmasterol), and organic acids (ascorbic, benzoic, shikimic, and vanillic) (5). The flavonoids and terpenoids are believed to be responsible for the herb's pharmacologic actions, which include increasing blood flow, decreasing blood viscosity, antagonizing platelet-activating factor receptors, increasing tolerance to anoxia, inhibiting monoamine oxidase, protecting against infections, and preventing membrane damage by free radicals. The flavonoids are associated with the antioxidant and free radical scavenging properties of the herb, while the terpenoids are associated with the anti-infective properties and the antiplatelet-activating factor, which helps prevent membrane damage to vessels and decreases blood viscosity. Because *Ginkgo biloba* is believed to regulate the tone and elasticity of blood vessels, it could increase blood flow to the

brain and improve the tolerance of the brain to hypoxia (6).
Huperzine A

Another herb that is purported to improve memory is *Huperzine A*, which is also known as HupA, Huperzine-A, and selagine and is an alkaloid chemically isolated and purified from Chinese club moss, *Huperzia serrata*, or *Lycopodium serratum*. Huperzine A is a reversible inhibitor of acetylcholinesterase (AChE) and crosses the blood-brain barrier. It can inhibit AChE activity in the brain for up to three hours. It has been used for treating Alzheimer's disease, enhancing memory and learning (7), reversing age-related memory impairment, increasing alertness and energy, protecting against neurotoxic agents, and treating myasthenia gravis (8).

Periwinkle (Vinca major/minor)

It enhances the ability of the brain to utilize oxygen and glucose and thus stimulates brain function. It is the aerial part of the garden periwinkle that is used for memory enhancement, not the Madagascar species. The main chemical constituent responsible for the activity is Vincamine and the chemically modified derivative Vinpocetine.

Vincamine (Figure 4), an alkaloid obtained from *Vinca minor* is thought to increase cerebral circulation and the brain's use of oxygen. Aethroma, Centracetam, and Dipervina are products that contain vincamine.

Vinpocetine- a chemically modified derivative of vincamine, vinpocetine (Figure 5), also known as cavinton, ethyl apovincamate is thought to have some effect on memory. The mechanism of action of this compound is unclear. Some studies indicate that vinpocetine may enhance cerebral blood flow without affecting peripheral blood flow. It is believed that its actions upon the brain are due to indirect or direct cholinergic activity, augmented norepinephrine effects on cortical cyclic adenosine monophosphate, increased turnover of brain catecholamines, and inhibition of adenosine reuptake. It has been used orally for enhancing memory (9); improving cerebral blood flow (9), oxygen, and glucose use by the brain; and protecting against age-related cognitive impairment. It has also been used in the treatment of Alzheimer's disease, cerebrovascular disease, organic psychosyndromes, intractable tumoral calcinosis in hemodialysis patients, menopausal symptoms, and seizure disorders, as well as in the prevention of poststroke morbidity and mortality (8).

Bacopa monnieri (Brahmi)

Bacopa monnieri is a nervine tonic famous for its memory and attention enhancement functions. It is a well known memory booster Indian herb commonly given to infants to boost memory power intelligence, and mental health. It is also called Brahmi, a name derived from Brahma, the creator god of the Hindu pantheon of deities. It is celebrated for its diversity of usage. It is said that the use of *Bacopa monnieri* for memory enhancement (12) goes back 3000 years or more in India, when it was cited for its medicinal properties, especially the memory-enhancing capacity, in the Vedic texts "Athar-Ved Samhita" (3:1) of 800 B.C. (10) and in Ayurveda.

Acorus calamus - A semi-aquatic, medicinal herb, *Acorus calamus* (also called Sweet Flag) is a valuable medicinal plant found almost through out India. It is traditionally employed in nervous disorders. It increases the overall memory of the person and strengthens the nervous system. The rhizomes of *Acorus calamus* are used in loss of memory given in combination with other drugs like *Centella asiatica*, *Bacopa moneira* and *Rauwolfia serpentina* as a memory booster. *Acorus calamus* well known for its memory enhancing (12) activity enhanced learning performance, of the descendents of drug-administered animals, and the animals themselves.

Celastrus paniculata (Jyotishmati)

Celastrus paniculata belonging to the genus of woody, climbing shrubs is distributed almost all over the India. In folk medicine the seeds are boiled and taken for blood purification. The seeds constitute the drug; they are bitter, and have an unpleasant odor and are traditionally used for sharpening the memory. Recent preclinical studies of the seed extract on male rats showed an improvement in learning and memory (11-12) in both the shuttle-box and step-through paradigms.

Centella asiatica (Gotu Kola)

Centella asiatica, commonly known as Mandookaparni is a widely available Indian herb has been used for centuries in Indian systems of medicine. In India for the last 3,000 years of Ayurvedic medicine, it has been used for the purposes like boosting memory, wound healing, a mild diuretic, increasing concentration, alertness, as well as anti-anxiety and anti-stress.

In pharmacological and clinical trials, *Centella asiatica* (11-12) has been found to improve the power of concentration and general ability and behavior of mentally retarded children. The clinical trials demonstrated that the extract increases the intelligence quotient in mentally retarded children.

Withania somnifera

Withania somnifera (Ashwagandha) has been used for thousands of years as a popular remedy for many conditions. *Withania somnifera* is one of the best known and most researched Ayurvedic herbs and holds a place in the Ayurvedic traditions similar to Ginseng in Chinese therapies. For that reason, *Withania somnifera* has been often referred to as the "Indian Ginseng". *Withania somnifera* is used in several indigenous drug preparations for maintaining health as well as treatment of several disease conditions. Studies have shown that ashwaganda stimulate growth of axons and dendrites in human neuroblastoma cells and in rat neurons (13-14) and enhance cognition and improve memory effects (15-16).

Withania somnifera extract (50, 100 and 200 mg/kg; orally) improved retention of a passive avoidance task in a step-down paradigm in mice. It also reversed the scopolamine-induced disruption of acquisition and retention and attenuated the amnesia produced by acute treatment with electro convulsive shock (ECS), immediately after training.

Glycyrrhiza glabra (Mulethi)

Mulethi is none other than licorice, the herb already known worldwide for its various curative properties. 'Charaka' - An

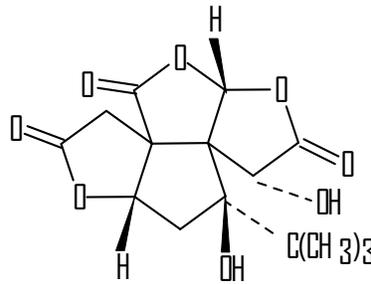
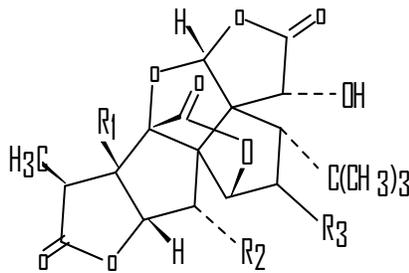
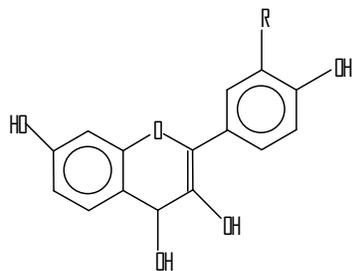


Figure 1: Bilobalide Structure of *Ginkgo biloba*



Compound	R ₁	R ₂	R ₃
Ginkgolide A	OH	H	H
Ginkgolide B	OH	OH	H
Ginkgolide C	OH	OH	OH
Ginkgolide J	O	OH	OH
Ginkgolide M	OH	H	OH

Figure 2: Ginkgolide Structure of *Ginkgo biloba*



Compound	R
Quercetin	OH
Kaempferol	H
Isorhamnetin	OCH ₃

Figure 3: Flavonoid Structure of *Ginkgo biloba*

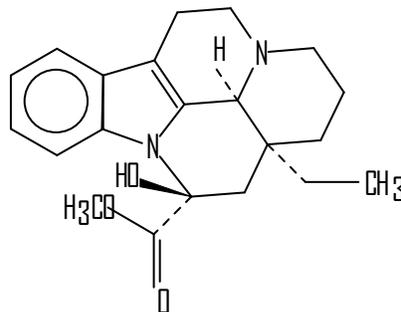


Figure 4: Vincamine Structure

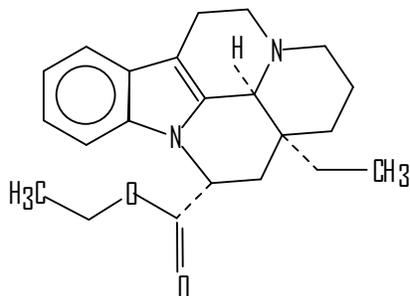


Figure 5: Vinpocetine Structure

Authority on Ayurveda (1500 B.C.) has termed this valuable herb as 'Medhya dravya' i.e. which improves memory and intellect. Mulethi (17) is an efficient brain tonic and a revitalizer for the brain. Like most of the other herbs mentioned here, Mulethi also rejuvenates the brain. In times of stress, mulethi can stimulate mental functions so as to feel a calming and relaxing effect. Mulethi increases the circulation into the central nervous system and balances the sugar levels in the blood. Mulethi is frequently provided to students who are preparing for important examinations, as it helps to remember small facts and bits of information.

Convolvulus pluricaulis (Shankpushpi)

This beautiful white flowered plant really enhances the mind ability to recollect and remember the things in a very effective manner. It relieves mental stress, controls blood pressure and also improves mind's ability. People in India are using this herb for centuries for their children to improve their memory especially during exams. Shankpushpi has gained popularity worldwide due to its natural memory (17-20) enhancing properties.

Tinospora cordifolia (Giloy)

This multipurpose herb is useful in many illnesses. It improves body's defense mechanisms. It repairs the damaged cells. It gives new life to dying brain cells and rejuvenates the whole body. It is best anti-cancer, immunomodulator and memory (18-20) enhancing herb.

Avena sativa (Oats)

It is useful for rebuilding nervous tissue (21) and brain tissue. They also decrease oxidation of cells and are useful for stroke, blows to the head and severe anorexia where cell death may have occurred. Avoid rolled oats, as these are a processed grain that has lost most of its nutrient content.

Turnera diffusa (Damiana)

It is a great herb for the nervous system (21-22) helping in conditions such as nervous debility, anxiety, poor concentration and fluttering of the mind. It acts to regulate brain activity by being calming when you need to be calm and stimulating when you need to be alert. Damiana also acts as a male and female sexual tonic and an anti-depressant.

Hypericum perforatum (St John's wort)

It facilitates nervous regeneration (21-22) especially of the myelin sheath that surrounds nerves. It is an excellent tonic for brain damage, post-stroke and multiple sclerosis.

Rosmarinus officinalis (Rosemary):

It has been used since antiquity to improve and strengthen the memory. Even today it is burned in the homes of students in Greece who are about to take exams. Rosemary was a symbol of fidelity between lovers, due to its ability to improve the memory. It's a warming herb that stimulates circulation of blood (23) to the head, improving concentration and memory (24).

Salvia officinalis (Common sage)

Common sage (*Salvia officinalis*) is perhaps one of our best known herbs, both in the kitchen and medicinally. It was regarded as a fertility drug by the Egyptians, and throughout the centuries sage has been used for wounds, insect and snake bites, sores, ulcers, sore throats, coughs, fevers, digestive problems, vaginal infections, diarrhoea and as a memory enhancer (25). Sage (*Salvia*) has a longstanding reputation in British herbal encyclopaedias as an agent that enhances memory. On going research on the herb is showing promise for the treatment of mild to moderate Alzheimer's disease. Scientists have found that sage inhibits the action of an enzyme called acetylcholinesterase (AChE). This enzyme breaks down a chemical called acetylcholine which is typically found deficient in Alzheimer's patients. Preliminary data showed that sage appeared to have a significant effect on the behaviour and attention (26), and when combined with lemon balm there was a marked improvement in memory and mood.

Ginseng

For thousands of years, Chinese medicine has used the herb ginseng (27) as a memory (28) tonic with the belief that ginseng can improve learning and memory, especially in aging humans. It improves mental sharpness (31-33), performance (29-30) and attention span to improve memory. It improves both motor co-ordination and increases to physical and mental stress (29-30). Experiments done on rats have shown that ginsenosides (34), the saponins of ginseng, can partially prevent scopolamine-induced memory deficits in rats. Ginsenosides are thought to increase choline uptake in the central cholinergic nervous system, which plays important roles in learning and memory.

Crataegus laevigata (Hawthorn)

Hawthorn is often used in combination with ginkgo biloba as a memory enhancer. It improves head circulation, which in turn improves memory (35-36). It also helps in removing atherosclerotic plaques strengthens capillaries and provides antioxidant protection to tissue against free radicals. Improve heart output and strength and increases oxygen supply to

brain (37) carry important nutrients for neurotransmitter development.

Zingiber officinale (Ginger)

It improves memory (35) and blood circulation to all parts of the body and brain. It also helps to increase the supply of nutrients to the brain.

Rhodiola Rosea

Rhodiola rosea is a perennial plant that grows in the arctic areas of Europe and Russia. It has long been used in the traditional medicines of Russia and Scandinavia and has been extensively researched in Russia and China for the last several decades. Studies have shown that *Rhodiola rosea* stimulate the body (38), decrease fatigue (39) and decrease stress (40-43).

The clinical investigations revealed that it significantly decreases the percent of errors made in a proof-reading test (44-45). It has more intellectual capacity increase than siberian ginseng (46).

Memory vitamins - B Vitamins and Coenzymes

The B vitamins can be considered memory vitamins. These include thiamin, riboflavin, niacin, nicotinamide, and NADH - nicotinamide adenine dinucleotide. Additional memory vitamins include Pantothenic acid and Pantothenic acid, Pyridoxine and Pyridoxal Phosphate, and vitamin B12. Deficiencies in B vitamins can lead to fatigue and poor mental functioning.

- B1 vitamins have many roles to play in ensuring optimal brain function. Vitamin B1 provides cognitive benefits, including faster reaction times, clear-headedness, and increased concentration (47-48) and improves mood and energy (49).
- Niacin, or B3, is particularly good for memory enhancement as it improves alertness.
- B5 (pantothenic acid) is essential for the brain to make acetylcholine.
- B6 (pyridoxine) is also essential for the manufacture of neurotransmitters, especially serotonin, the mood enhancer. A study involving elderly males showed pyridoxine to help improve long-term memory (50).
- B12 has been shown to accelerate learning in rats and is very important for the health of brain cells. Methylcobalamin is a coenzyme form of vitamin B12 (cyanocobalamin). Studies have shown Methylcobalamin to:
 - Protect brain cells against glutamate toxicity (51).
 - Decrease amount of time people sleep while improving the quality of sleep so that the individuals awake feeling more refreshed (52).
 - Potentially help regenerate nerves (53).
 - Help regenerate damaged brain axons (53).

In summary, B vitamins work together in many ways to help the brain make and use neurotransmitters. It is important that B vitamins should be taken in a complex ie. all together.

Other Natural agents:

- **Phosphatidylserine (PS)** is a phospholipid that is bound to an amino acid (serine), a very prevalent molecule in

the brain. Known as the memory molecule, phosphatidylserine (PS) is another smart nutrient that can genuinely boost your brain power. While the body can make its own PS we rely on receiving some directly from diet, which makes PS a semi-essential nutrient. Human bodies require folic acid and B12 to produce phosphatidylserine and our ability to produce it decreases as we age.

- **Carnitine** is a vitamin-like compound that transforms fatty acids into energy for muscular activity. It's concentrated in the brain, sperm and the skeletal muscles. A special form of carnitine, L-acetylcarnitine (LAC) is used to improve memory, cognitive ability and Alzheimer's disease. Studies have shown that acetyl-L-carnitine facilitates regeneration of nerves (54), reduce the formation of a cell-clogging pigment called lipofuscin (55), work synergistically with CoQ10 and alpha lipoic acid creating an anti-aging effect which helps to maintain mitochondria function (54-55), provide significant improvements in cognitive function for people with mild cognitive impairment after 45 days of use (55), provide significant improvement in memory, mood, and response to stress for elderly people after 90 days of use and the effects lasted at least 30 days after the trial had ended (56).
- **Phosphatidylcholine (lecithin)** is a type of B vitamin that is found in garlic, soy, lettuce, whole grains and cauliflower. Lecithin may be useful to enhance healing of nervous and brain tissue and has been shown to increase levels of acetylcholine in the brain, making it useful for memory loss in Alzheimer's and bipolar depression.
- **N-Acetyl Tyrosine** is an acetylated derivative of the essential amino acid L-Tyrosine. Acetylation helps to improve the metabolic effect of L-Tyrosine. L-Tyrosine is the precursor of several neurotransmitters in the brain including epinephrine, norepinephrine, and dopamine. Studies have shown that Tyrosine act as an antidepressant (61), improve learning and alertness (57) and reduce mental and physical fatigue (57).
- **Trimethylglycine** is also known as betaine and its functions are similar to folic acid and vitamin B12 (58-59). Trimethylglycine was originally discovered in the 1950's to be beneficial to the heart, but soon after some users indicated improvements to their energy, alertness, and mood.
- Other popular herbal memory vitamin includes Vitamin E. Low levels of Vitamin E may increase the risk of neurological diseases including the dreaded Parkinson's. People who are not taking these vitamins in required quantities are known to suffer from memory loss, dementia, and forgetfulness.

Natural brain chemicals: (60-63)

- DMAE and Choline - The Building Blocks of Acetylcholine

The key brain chemical for memory is acetylcholine, deficiency of which is probably the single most common cause for declining memory. It is derived from the nutrient choline, the richest dietary sources of which are egg yolks and fish,

especially sardines. Vitamin B5 (pantothenic acid) is essential for the formation of acetylcholine in the body, as are vitamins B1, B12 and also vitamin C.

DMAE (again sardines are a rich source) is a precursor of choline that crosses much more easily from the blood into brain cells, accelerating the brain's production of acetylcholine. It reduces anxiety, stops the mind racing, improves concentration and promotes learning and acts as a mild brain stimulant.

- DHA

Docosahexaenoic acid (DHA) is a major omega-3 fatty acid of the brain that is necessary for good brain function. It is found mainly in oily fish. DHA is particularly important for mental performance and has an important role in the development of the brain during foetal development and infancy. It is therefore essential that pregnant women either have a regular dietary source of these Omega 3 fats or supplement them. DHA is highly concentrated in our brain and nervous system and not only improves learning and age-related memory but also greatly enhances mood. In one study, people with depression were given fish oils and experienced substantial improvement in their manic depression over a four month period. DHA is associated with both higher levels of acetylcholine and serotonin, a neurotransmitter that improves mood. DHA has also been found to improve dyslexia and dyspraxia.

- Pyroglutamate - The master of communication

A key brain chemical in enhancing memory and mental function is the amino acid pyroglutamate and its derivatives, which are highly concentrated in the human brain and spinal fluid. It improves learning, memory, concentration and the speed of reflexes. In fact, so powerful are its effects, that there are now many slight variations of this key brain chemical being marketed as drugs for learning and memory-related problems. Numerous studies using these 'smart drugs' have proven to enhance memory and mental function, not only in those with pronounced memory-decline but also people with so-called normal memory function. Pyroglutamate does three things that help memory and mental alertness. It not only increases the production of acetylcholine, it also increases the number of receptors for acetylcholine and improves communication between the left and right hemispheres of the brain. In other words, it improves the brain's talking, listening and cooperation.

Pyroglutamate is found in many foods, including fish, dairy products, fruit and vegetables.

- Glutamine - Amazing Brain Fuel

While acetylcholine is the major player as far as memory is concerned many neurotransmitters are also involved. Some stimulate mental processes, while others prevent information overload. You need a balance. For example, the stimulating neurotransmitter glutamate helps forge links between memories, but too much can literally overexcite neurons to death. This is how MSG (mono-sodium glutamate) turns up the volume on tastes, but too much can definitely be a bad thing. GABA, a close relative of glutamate, calms down the nervous system. The right balance of these neurotransmitters is important for learning. Supplementing glutamine, an amino

acid from which the brain can build and balance these neurotransmitters, can help promote memory. Glutamine can be used as fuel for the brain and has been shown to enhance mental performance and decrease addictive tendencies.

Other Considerations:

Aromatherapy is also very important to help to improve memory and brain function. The good scents that help in this regard are rosemary, bergamot, basil, and grapefruit. A useful trick for people wanting to memorize something is to smell one of these essential oils while memorizing and then sniff it again when trying recalling it. Nutrients contained in the Grape seed extract have shown to protect the brain by preventing neuronal toxicity.

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