Brahmi: Nature's Gift to Memory Enhancement in Pharmaceutical Sciences

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Abstract

For *Bacopa monnieri*, the ancient medical system used the terms Brahmi and water hyssop. As a brain tonic in the past, it was used to improve memory and learning help treat epileptic or anxiety issues. In addition, the plant has been utilized to treat heart problems, digestive issues, and bronchoconstriction-related respiratory issues. Bacosides A and B are present in Brahmi, and the primary alkaloid is Brahmin. Nicotine is also present. In addition to D-mannitol, the Brahmi plant has other vital ingredients including potassium salts, hersaponin, and Bacoside A and B. We focus our discussion in this study on the chemical structure, pharmacological characteristics, and scientific studies that substantiate the claims made in Ayurveda that are not just limited to its traditional applications. Older persons who have Alzheimer's disease (AD) suffer from a neurological illness. The significant rise in its incidence has forced the creation of more modern medications. Because of their biosafety profile and potential benefit for treating cognitive impairment, Ayurvedic herbal medicines are being studied more and more. In this post, we provide a critical analysis of one such Medhya Rasayana (nootropic medication) that is made with *Bacopa monnieri* extract (EBm). Brahmi is a good brain tonic and it can be taken at any age.

Key words: Brahmi, cognition, saponins, food systems, herbal flavor, nootropic medications, therapeutic benefits, active ingredient

INTRODUCTION

hese substances are referred to as "Brahmi" or "Brahmin-supporting" substances. The mythological creator of the Hindu pantheon is known as Brahma, and the brain is the seat of all creative activities in the body. The Charak Samhita[1] has the earliest explicit mention of Brahmi with regard to memory enhancement, in which Brahmi is recommended as mostly a remedy as a mental disease (imbecility) that leads to madness. According to Charak, a mixture of worry, a poor intellect, and a lack of concentration is the etiology of the mental disease. Brahmi is said to be effective in treating memory loss and intellectual decline in the Susruta Samhita, another reliable Ayurvedic work. It has been utilized and is classified as a "Medhya Rasayan" medication for approximately 3000 years by Ayurveda physicians in India to heal or enhance memory and intelligence (Medhya). In traditional medicine, plants have been employed; study suggests that some of the natural substances present in these formulations may have nootropic effects.[2] They are used

in a variety of formulations to treat a number of disorders. Brahmi contains medicinal substances called bacosides that improve memory, treat associated conditions, and boost nerve impulse transmission efficiency, hence enhancing cognition and memory. Because they have fewer side effects than more modern synthetic drugs, herbal medicines are growing in popularity. The oldest known medical practice known to humans is the use of herbs as medicine, and it has been practiced historically throughout all societies. Due to all these activities, chitosan is widely used in biomedical applications and drug delivery. Metoprolol succinate (MS), a medication in the BCS-I class, decreases heart rate, contraction force, and cardiac output by blocking cardiac beta 1-adrenergic receptors.

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DESCRIPTION OF PLA

Bacopa monnieri, a psychoactive medicinal plant, grows widely in hotter regions of Asia, Australia, America, and India. It is a slender, sensitive herb with a slight aroma that is found in abundance in damp soil. [7] Mandukaparni, Brahmi, and Gotu Kola are the names given to the herb in Ayurveda, Unani medicine, and Western herbal medicine, respectively. It has many branches and small, rectangular, moderately thick leaves that are positioned opposite one another on the stem, giving it the appearance of a creeping perennial. Little flowers have five to four petals and are pale purple or white. Wetland areas, shallow water, damp, and muddy shorelines are all ideal for its natural growth. It is a common aquarium plant because of its capacity to grow in water plant as like as shown in Figure 1.

Benefits of Brahmi and various treatments of illness are shown in Figure 2.

ACCOUNTS ON BRAHMI

Classification

Brahmi is the Ayurvedic plant which is used as the brain tonic.^[8] It belongs to the kingdom plantae and the order of Brahmi is Lamiales^[9] while it belongs to family Plantaginaceae and the genus of Brahmi is Bacopa.

Names of Brahmi in different languages

The Latin name for Brahmi is *Bacopa monnieri*, and it is known by a variety of names in different states and languages. In English, it is also known as Herb of grace, Indian pennywort. In Hindi language, Brahmi is the same name, also in west Bengal or in Bengali, Brahmi known as Birami. Indeed in Telugu language, the name of Brahmi is Sambarenu. Many other names of Brahmi in different languages like in Kannad, the name is Jala Brahmi; in Tamil, the name is Neera Brahmi; in Sinhala language, the name is Lunuvila; and in Chinese, the name is Jia-ma-chi-xian.

GENERAL INFORMATION OF BRAHMI

- Botanical Classification: Brahmi is a member of the Plantaginaceae family. Its scientific name is Bacopa monnieri.
- b. Habitat: The plant is commonly found in damp and marshy areas, including near ponds, streams, and other water bodies.^[10]
- c. Cultivation: Brahmi can be cultivated in both soil and water. It is often grown in pots or containers with waterlogged soil or directly in water gardens.



Figure 1: Medical plant known as Brahmi

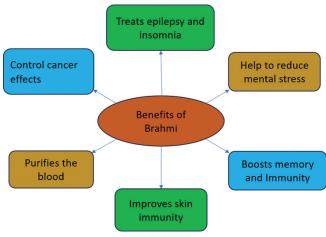


Figure 2: Benefits of Brahmi

- d. Propagation: It can be propagated through seeds or stem cuttings. The cuttings are often placed in water until they develop roots before being transplanted into soil.^[11]
- e. Medicinal Uses: Apart from cognitive benefits, Brahmi is sometimes used in traditional medicine for its potential to alleviate stress, improve hair health, and support skin health.
- f. Culinary Uses: In some regions, Brahmi leaves are used in culinary preparations, such as salads or chutneys. They have a slightly bitter taste.
- g. Side effects of Brahmi: It should take cautiously if you have a history of stomach ulcers, lung disorders, or thyroid issues.
- h. Is it safe to consume Brahmi every day?
- i. According to licensed Ayurvedic physicians, consuming2-3 g of Brahmi powder daily with meals is safe.
- j. Adults can consume 25 to 50 cc of the cooked water-based decoction of Brahmi powder each day.
- k. Can Brahmi be taken with milk?
 - Brahmi with milk that works wonderfully to boost the brain's functionality.
 - For children, small doses of Brahmi powder mixed with ghee, honey, and some water are great to boost brain power and immunity.

GEOGRAPHICAL SOURCE OF BRAHMI

This plant is common in crop fields and other waste locations across India up to an altitude of 600 m, as well as in Pakistan, Sri Lanka, and Madagascar. It is also found in swampy areas of India.

Growing conditions for Brahmi

Brahmi likes to grow in a moist soil, in a warm position. It tolerates full sun and grows well in a part of sun.^[12] It can be grown in the edge of pond.

LOCATIONS

Brahmi is mostly found in various parts of India like south Indian places such as Kerala, Tamil Nadu, Karnataka and northern parts such as Punjab, Haryana and also at the foothills of Himachal Pradesh and also other parts of India such as Uttar Pradesh, Bihar, Uttaranchal, and eastern India like Bengal.

CHEMICAL CONSTITUENTS

According to the current theories, the primary nootropic components of *Bacopa monnieri* are bacosides, which are classified as dammarane kinds of triterpenoid saponins and have aglycone units containing jujubogenin or pseudojujubogenin moieties. 38 bacosides comprise a family of 12 known analogs. Bacopasides I–XII, 39 new saponins, have just been discovered. 40–42 The alkaloids d-mannitol, apigenin, hersaponin, monnierasides I–III, cucurbitacins, and plantainoside B are in the list of substances that have been identified. 43–50 The substance known as bacoside A, which

is composed of bacoside A3, bacopaside II, bacopasaponin C, and a jujubogenin isomer of bacopasaponin C, is the one that has drawn the most attention. 48 The quantities of bacosides may differ depending on the portion of the plant from which they are isolated in these assays because whole plant extract was used. Rastogi *et al.* discovered this bacoside profile in one *Bacopa monnieri* sample: bacoside I (5.37%), bacoside A3 (5.59%), bacoside II (6.9%), bacoside C isomer (7.08%), and bacoside C (4.18%). 66 There is now work being done to fully analyze *Bacopa monnieri*.

CLINICAL STUDIES

Numerous clinical studies have investigated Brahmi's effects on memory and cognitive function. [13-15] While results are promising, the quality of studies and variation in dosage and extract preparation methods make it challenging to draw definitive conclusions. [16] Some studies have reported improvements in memory, learning, attention, and information processing. The exploration of Brahmi's cognitive enhancing potential has prompted a multitude of clinical studies aimed at elucidating its effects on memory, learning, and overall cognitive function. [17] While the diverse methodologies and variations in extract preparations have led to some inconsistencies, a growing body of evidence underscores the promising role of Brahmi as a natural memory booster. [18-20]

Memory and Learning: Several randomized controlled trials have investigated Brahmi's impact on memory and learning. In a double-blind study conducted on healthy participants, Brahmi supplementation demonstrated significant improvements in memory retention and learning capacity. Similar findings were reported in a study involving older adults, where Brahmi supplementation was associated with enhanced memory performance, including the ability to recall newly learned information. Formulations and Uses of Brahmi are mentioned in Table 1.

Bacopaside II

Bacoside X

Bacoside A3

Bacopasaponin C

Table 1: Formulation and uses of Brahmi	
Formulations of Brahmi	Uses
Bio- Ayurveda, Brahmi Tablets.	For brain power and Mental clarity.
Baidyanathi, Ayurvedant Brahmi Churn	Improve Memory.
Baidyanath, Brahmi Bati (Tablets) (Budhiwardhak)	Useful in weakness, promotes memory and intelligence.
Himalaya, Brahmi Mind wellness	Supports Menal alterness and help to empower clarity of thoughts.
Magarjuna, Brahmi Thailam	Used for the treatment of headache, dizziness, antividant, stress.
Girueda, Brahmi tablets	Helps in increasing memory and concentration.
Actizeet, Brahmi organic Brahmi powder.	Promotes relaxation or improve sleep quality.
Dabur, Brahmi vati	It helps in improving memory retention and useful in treatment of arthritis and strengthening and immune system.

 Attention and Concentration: Attention span and concentration and critical cognitive domains, particularly in today's fast-paced world. Clinical trials exploring Brahmi's effects on attention have revealed encouraging outcomes. A study involving children with attention-deficit hyperactivity disorder found that Brahmi supplementation led to notable improvements in attention and behavior.

SAFETY CONSIDERATIONS

Brahmi is generally considered safe when taken in recommended doses.^[21] However, some individuals may experience mild side effects like gastrointestinal discomfort. Pregnant breastfeeding women, as well as individuals with any type of health issues, should consult a doctor or gynecologist before using Brahmi supplements.^[22]

- Adverse Reactions: Brahmi is generally well-tolerated when used within recommended dosages. However, a small percentage of individuals may experience mild side effects such as gastrointestinal discomfort, nausea, and stomach cramps. These effects are typically transient and subside once the body adapts to the supplement.
- Pregnancy and Breastfeeding: Special caution should be exercised by pregnant and breastfeeding women. While limited research is available on the effects of Brahmi during pregnancy and lactation, it is advisable to consult

a healthcare professional before incorporating Brahmi supplements. This cautions approach ensures the well-being of both the mother and the developing child.

MEMORY AND COGNITIVE FUNCTIONING OF BM

Research has been done to determine whether BM, which is referred to as a Medhya Rasayana in Ayurveda, can enhance memory and learning.[23] In their initial research, which was completed in 1959, Malhotra and Das employed the entire plant to encourage increased learning in rats. [24,25] By boosting all facets of the consolidation, acquisition, and retention of newly learned behavioral responses, a plant extract in alcohol was claimed to dramatically improve the learning capacity in rats. According to additional research by the same authors, the effect on cognition is due to the presence of the two active saponins bacosides A and B in the ethanol extract of BM. When utilized in learning activities with both positive and negative reinforcement, they discovered that the separated bacosides A and B enhanced memory in rats. The cerebral cortex, hippocampus, and hypothalamus of the brain, as well as the protein levels and protein kinase activity, were all affected by the bacosides, according to this study. This improved neurotransmission, sped up the recovery of damaged neurons, and helped the regeneration of neuronal synapse. The Morris water maze test revealed better memory in bacoside-treated mice, and experimentally induced anterograde amnesia was milder. Wistar rats used in passive avoidance and spatial learning (T-maze) tests were recently used to examine the effects of standardized BM extract on age-matched control rats. Evidence suggesting exposure to BM improved learning and memory in rats given BM extract included improvements in spatial learning capacity and higher memory retention.[26]

PATENT CONCERNING BRAHMI

Along with the current investigations on the development and use of pure BM and CA preparations in vitro and in vivo, other innovative studies have resulted in brand-new patents. Although there are many patents relating to Brahmi, only a few noteworthy ones are discussed in the following section due to restrictions. Improvements to Brahmi extract formulations as well as bacoside and other active chemical enrichment are discussed in some patents. For instance, Kahol et al. described an enhanced method for producing BM extracts in a patent. This provides a thorough overview of the drying and processing of freshly collected herbs as well as the extraction and enhancement of bacosides. To create jujubogenin and pseudojujubogenin glycosides, this invention contained directions on how to enrich BM with up to 100% of the total saponin content of Bacopa. The invention also provides guidelines for enriching new formulations and unique saponin components from BM to > 95% purity. It also goes through how to calculate the total Bacopa saponin fraction for therapeutic purposes using an HPLC-based approach. Another recent patent, number, refers to the "Becoming®" herbal compound, which is made from BM and augmented with bacosides and other active ingredients. It is a potent and improved synergistic herbal compound. This composition has been shown to improve learning, memory, cognition, and ADHD or ADD. Most patents are actually for enhanced or novel herbal remedies that can be used either alone or in conjunction with other plant products to treat a wide range of human problems. Two of these patents are related to a natural remedy for the treatment of cardiovascular and neurological conditions. This formulation includes Dioscorea bulbifera (DB), Hippophae rhamnoides (HR), and BM extracts. While the terpenoidal glycosides make up the majority of the DB's tuberous portion, HR preparations also include several vitamins, amino acids, and 5-hydroxytryptamine and have been used as medicines. It has been claimed that the preparation can assist postpone the onset of hypertension in humans by slowing down the atherosclerotic alterations.^[27,28]

PHARMACOLOGICAL PROPERTIES

Assisting to repair the brain: All medical practitioners use an activity on the brain known as "brain repair," or "BM," which standards for brain maintenance. BM is one of the best-known plants for regenerating nerve and brain cells. Traumatic and acquired brain injury are the two forms. Vehicle accidents, sports injuries, head trauma, physical assaults, etc. can all cause traumatic brain injury. Potential causes of acquired brain injury include poisoning or exposure to harmful substances, infection, strangulation, tumors, strokes, and neurological diseases. Brain damage during pregnancy and delivery can result from a variety of conditions, including oxygen deprivation, infant jaundice, physical stress from labor and delivery, and infections in the mother's body. The infant's subsequent brain injury can range widely in severity and result in a variety of disabilities and psychological issues. For a very long time, scientists believed that brain damage was irreversible. Yet, research shows that it is possible for brain cells to repair, leading to brain restoration. The significant nootropic properties of BM have expedited the repair of injured neurons. Raising cognitive standards and raising IQ reducing mitochondrial peroxidation. Nootropics are "smart drugs" that fundamentally help the brain's natural processes. They accomplish this by increasing blood oxygen levels, enhancing glucose absorption, and promoting the growth of neurons. Studies have shown that BM has a significant antioxidant that is helpful in reducing the effects of lead poisoning since lead serves no biological role in humans but impairs the development of the central nervous system. Nonetheless, Brahmi is a helpful plant for increasing brain activity.

- iii. Anti-stress Exercise: Brahmi standard extract exhibits adaptogenic properties. Only plasma AST and changes in ulcer index were significantly reversed by pre-treatment with aBM extract at a modest dose, but alterations in the ulcer index, adrenal gland 1 2 weight, AST, and CK were also considerably reversed by pretreatment with a larger dose.
- iii. Anti-cancer properties: Brahmi pretreatment effectively decreased the rise in the ulcer index, adrenal gland weight, blood sugar, aspartate aminotransferase (AST), and creatinine kinase (CK) that was brought on by acute stress (AS) in cancer patients. Because their suppression can interfere with signaling pathways that are involved in tumor formation and growth, members of the receptor tyrosine kinase (RTK) family are desirable targets for cancer therapy. Because BM is a recognized hyperaccumulator of cadmium, chromium, lead, and mercury, it is used in phytoremedies.
- iv. Anti-Inflammatory: Through regulating the release of pro-inflammatory mediators, BM can reduce inflammation, i.e., it has strong anti-inflammatory properties, which may explain why traditional medicine has found it to be beneficial in treating a variety of inflammatory disorders. In addition, it dramatically reduced the activities of 5-lipoxygenase (5-LOX), 15-LOX, and cyclooxygenase-2 (COX-2). Triterpenoids and bacosides in it may be the cause of this activity.
- W. Heart and blood vessel activity: In an isolated rabbit heart, *Bacopa monnieri's* ethanolic extract demonstrated cardiac depressing effect on heart rate, coronary flow, and left ventricular contractility. It also showed that Brahmi has a protective impact on the pulmonary artery and the aorta.
- vi. Antidepressant: Brahmi methanolic extract may have antidepressant effects in rodents. In the depression models that are learned helplessness and forced swimming, the extract was discovered to have potent antidepressant effects when administered orally for 5 *days* at doses of 20 and 40 mg/kg, and its efficacy was comparable to that of imipramine.
- vii. Anticonvulsive: In Ayurvedic medicine, Brahmi is recommended as a treatment for epilepsy, and studies on animals revealed that it does contain anticonvulsant activity - but only when taken in large doses spread out over a long time.[29] Furthermore, it has been asserted that a Brahmi crude water extract lessens epilepsy in test animals. It naturally had a sedative effect and considerably prolonged the hypnotic effects of phenobarbital. GABAstimulating drugs recognized to have resources and human resources, analgesic, as well asnarcotic effects. It implies that the GABAergic system is involved in CNS mediation. For its impact on mice's locomotor activity, maximal electroshock seizures, and PA task, Brahmi was tested both by itself and in combination with phenytoin (PHT). Improvements were seen in memory retention and learning without altering PHT's anti-convulsive action more research involving Brahmi.

- viii. Anti-Asthamatic activity: The tracheal muscles of rabbits and guinea pigs were shown to be relaxed by BM extract when combined with (beta)-adrenoreceptor and prostaglandins.[30] The herb's historical use in treating a range of respiratory illnesses was substantiated by the finding that it also caused bronchial dilatation in rats under anesthesia. The bronchodilator qualities of the extract may be the cause of carbachol's antagonistic effects on inspiratory and expiratory pressures. The extract showed a two-fold effect on carbachol-induced bronchoconstriction. Low doses (25 and 37 mg/kg) considerably reduced inspiratory pressure while high doses (50 mg/kg) only suppressed expiratory pressure. This characteristic of the plant extract shows how various distinct pathways may be involved in the beginning of bronchodilation. Prostaglandin release, (beta)-adrenoreceptor activation, inhibition of calcium mobilization, and antagonistic interactions between muscarinic receptors are a few potential mechanisms. The same authors' most recent research indicates that the calcium antagonistic activity of BM is present in the ethanol extract. In addition, it has been found that the BM methanolic extract includes a sizable amount of a mast cell stabilizer, raising the possibility of using BM leaves to treat allergic diseases.
- ix. Anti-nociceptive activity: Bacopa monnieri aqueous extract (AEBM) has analgesic effectiveness throughout many pain pathways, i.e., by activating 5-HT receptors, 1-adrenergic, and 2-adrenergic receptors. The fact that the latency for the analgesic effect was not increased when AEBM and naloxone were administered together also shows that opioid receptors are involved in the analgesic activity.
- x. Anti-spasmodic activity: The voltage- and receptoroperated calcium channels in the cell membrane are less active when BM extract is present, which causes smooth muscles to become spasmolytic. The absence of any apparent effects of BM extract on the mobilization of intracellular calcium, however, suggests that this natural material has no effect on the contractions that caffeine or noradrenaline-induced.
- xi. Anxiolytic activity: In comparison to LZP, the higher doses of BM extract considerably increased the anxiolytic effects. The fact that BM does not cause amnesia and has a memory-promoting effect in both animals and people gives it a distinguishing advantage over lorazepam (LZP). Shanker and Singh confirmed these findings and said that BM extract had anxiolytic properties.
- xii. Cardiovascular activity: In an isolated rabbit heart, the left ventricular contractility, pulse rate, and coronary flow were all reduced by an ethanol extract of BM. It was demonstrated that BM has a protective effect on the pulmonary and aortic arteries.

MECHANISM OF ACTION

Brahmi is thought to enhance cognitive function through multiple mechanisms, including:

- Enhancing nerve impulse transmission.
- Promoting synaptic transmission and enhancing nerve growth factor,
- Modulating levels of neurotransmitters such as acetylcholine, serotonin, and dopamine.
- Reducing oxidative stress and inflammation in the brain.
 - Neurotransmitter Modulation: One of Brahmi's pivotal mechanisms of action revolves around the modulation of neurotransmitter levels. Neurotransmitters, such as acetylcholine, serotonin, and dopamine, play integral roles in memory, mood, and cognitive function. Bacosides, the primary bioactive compounds in Brahmi are believed to influence the synthesis, release, and receptor sensitivity of these neurotransmitters. This modulation contributes to the improvement of memory consolidation, attention, and overall cognitive performance.
 - Synaptic Transmission Enhancement: Brahmi's impact extends to the very core of neural communication synapses. The bacosides found in Brahmi are suggested to promote the growth and branching of dendrites, the intricate extensions of neurons that facilitate connections between brain cells. This dendritic growth leds to denser network of synaptic connections, enhancing the overall efficiency of communication between neuron. Consequently, this phenomenon is thought to bolster learning, information retention, and cognitive processing speed.
 - Nerve Growth Factors: Brahmi's influence on cognitive enhancement is intricately linked with its ability to stimulate the production of nerve growth factors, such as brain-derived neurotrophic factor. Nerve growth factors play a pivotal role in promoting the survival, growth, and differentiation of neurons. Through this mechanism, Brahmi fosters neurogenesis the birth of new neurons and encourages their integration into existing neural networks. This process is believed to contribute to improved cognitive functions, such as memory formation and learning.
 - Oxidative Stress Mitigation: Oxidative stress, resulting from an imbalance between antioxidants and harmful free radicals, is a critical factor in cognitive decline and neurodegenerative disorders. Brahmi's rich content of antioxidants, including a flavonoids and bacosides, confers it with potent neuroprotective abilities. By neutralizing free radicals and reducing oxidative stress, Brahmi helps safeguard neurons from damage, thereby preserving cognitive function and memory.

REMEMBRANCE AND KNOWLEDGE

Several laboratories have thoroughly investigated the neuro pharmacological effects of plant extracts and extracted bacosides, and there are a lot of articles available demonstrating their nootropic action. Rats treated with the Brahmi herb or its alcoholic extract showed better learning capacities, according to preliminary research. Later research showed that the presence of Bacosides A and B was what caused the ethanol extract to have a cognitive-enhancing effect. In addition to improving memory and learning in healthy rats, these active ingredients significantly mitigated the amnesic effects of scopolamine, electroshock, and immobilization stress. It' is yet unclear what causes these pharmacological effects. According to one theory, bacosides cause membrane dephosphorylation, which boosts the metabolism of proteins and RNA in particular brain regions. According to research, Brahmi increases protein kinase activity in the hippocampus, which may have contributed to its former nootropic effects. The neurotoxic colchicines, which reduced acetyl cholinesterase activity binding, lowered muscarinic cholinergic receptor activation, and caused the frontal cortex and hippocampus to lose acetylcholine, were similarly mitigated by Brahmi administration for 2 weeks. Chitosan is a biologically active molecule. It shows several biological activities such as antimicrobial, antifungal, antitumor, anticancer, anti-diabetic, wound healing, and antioxidant. DOSAGE: Bacopa monnieri was traditionally taken three times a day in amounts of 5-10 gm of nonstandardized powder, 8-16 ml of infusion, and 30 ml of syrup. The 1:2 fluid extract should be taken daily by adults in doses of 5 to 12 ml and by children between the ages of 6 and 12 in doses of 2.5 to 6 ml. Dosage for adults is 200-400 mg daily in divided doses for Brahmi extracts standardized to 20% Bacosides A and B, and for children is 100-200 mg daily in divided doses.

CONCLUSION

Bacopa monnieri, as a sedative, antipyretic, analgesic, memory-improving, anti-inflammatory, and antiepileptic agent, traditional Ayurvedic medicinal plant has been used for ages. Pre-clinical and clinical research conducted more recently confirmed the cognitive-improving effects of several Brahmi extracts, but the precise mechanism of action is still unknown due to the complicated pharmacology of this plant's many active ingredients. Brahmi may have similar protective and cognitive-improving properties to Ginkgo biloba, modulating the cholinergic system and contrasting oxidative stress.

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