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# NATURAL NOOTROPICS AND COGNITIVE ENHANCEMENT: A CRITICAL REVIEW OF HERBAL NEUROPROTECTIVE AGENTS

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**Abstract**

*Natural nootropics, derived from plant-based sources, have long been used to enhance cognitive function, dating back to ancient civilizations including those of India, China, and Mesopotamia. Coined by Corneliu Giurgea in the 1970s, the term "nootropic" refers to compounds that positively affect the mind, particularly in areas such as memory, attention, motivation, and learning. Unlike synthetic agents, natural nootropics offer neuroprotection with minimal toxicity and side effects. They exert their effects through multiple mechanisms, including enhancement of cerebral blood flow, antioxidative activity, neurochemical modulation, and neuroprotection. Prominent natural nootropics include Withania somnifera (Ashwagandha), Ginkgo biloba, Bacopa monnieri (Brahmi), and Magnolia officinalis, each exhibiting unique phytochemical profiles and cognitive benefits. These herbs have demonstrated efficacy in improving memory, reducing neuroinflammation, and mitigating cognitive decline. Traditional knowledge, supported by modern pharmacological insights, underscores the therapeutic potential of these botanicals in managing neurodegenerative conditions and cognitive disorders. Despite their advantages, careful consideration of dosage, harvesting methods, and contraindications is essential to ensure efficacy and safety. This review critically examines the historical relevance, pharmacological mechanisms, active constituents, and clinical applications of key natural nootropic agents, advocating for their integration into evidence-based cognitive health strategies.*

**Keywords:** *Ashwagandha, Cognitive enhancers, Herbs, Nootropics*

## INTRODUCTION

The flora considered to enhance and facilitate cognitive function are classified as natural nootropics, and they constituted a significant component of the pharmacological range accessible to ancient societies and civilizations (1). In the early 1970s, a Belgian pharmacologist of Romanian descent Corneliu Giurgea brought the term nootropics to life after studying 2-oxo-1-pyrrolidine derivatives, later coined racetams (2). The origin of the word "nootropic" can be traced back to a Greek term – noos or mind, and tropein or toward. Therefore, in Greek, the meaning of the word nootropic is "acting upon the mind". Psychotropic drugs acting upon the integrative functioning of the cerebral cortex telencephalic area through direct and selective action have also been nootropics in the past (3). The characteristics associated with nootropic drugs are the following: "Magnification or enhancement of learning acquisition, augmentation of retained behaviors against damaging agents, facilitation of interhemispheric information flow, and suppression of brain injury potential (4). Nootropics herbs identify compounds that augment cognitive performance via enhancement of memory, creativity, motivation, attention and mental functions, leading to increased alertness (1). Memory can be defined as the capacity of an individual to encode, store, and access information, events, and experiences. Memory deficits, low retention rate and delayed recall are attributable to the frenzied pace of modern society and competition (5). Since time immemorial, people have relied on illness avoidance strategies using plants and plant-based substances. Activities performed for the sharpening or enhancement of cognition, that is, those autonomic and highly developed functions which distinguish human beings from other life forms on the planet earth, is a notable segment which ancient cultures and civilizations attended to in the form of ancient medicine. It is a well-known fact that such

cultures and communities understand that improvement of cognition aids human beings in their thriving or optimum functioning and is directly connected with bringing forth better results in most of the domains or fields of life. A textbook of Ayurvedic medicine, which is believed to be from 6000 B.C.E, mentions the use of "Medhya Rasayanas", which refers to a class of herbs believed to possess the properties of enhancing memory and intelligence. Ashwagandha *(Withania somnifera (L.) Dunal)*, Brahmi *(Bacopa monnieri (L.) Pennell*

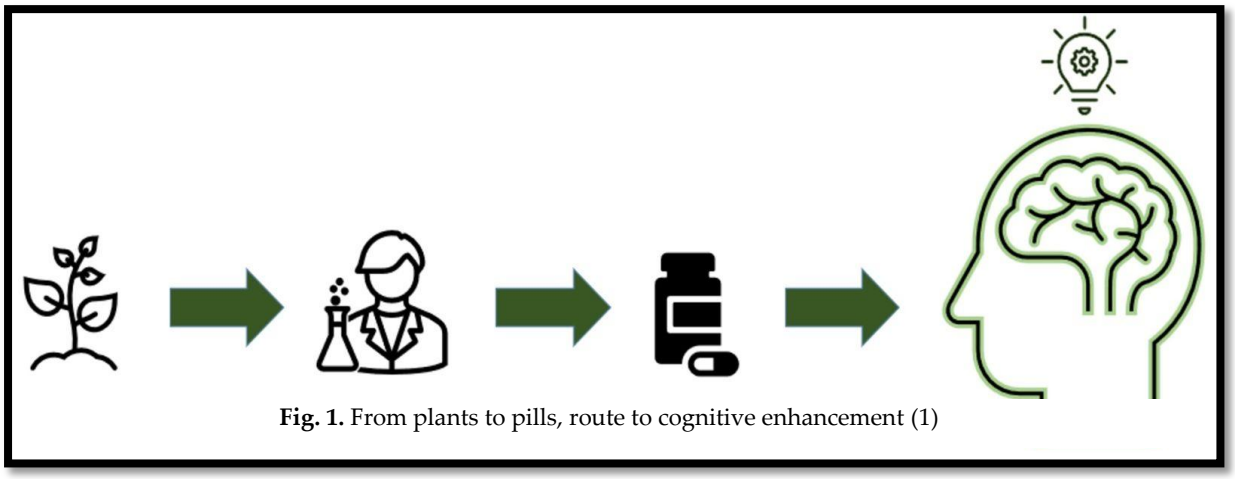

**Fig. 1.** From plants to pills, route to cognitive enhancement (1)

*(Bm)*, and Jyotiṣmatīr *(Celastrus paniculatus Willd)* are among the plants that fall under the Medhya Rasayanas. Additionally, the goal of employing plant-based materials such as Reishi mushroom *(Ganoderma lucidum (Curtis) P. Karst.)*, lion's mane mushroom *(Hericium erinaceus (Bull.) Pers.)*, and Polygala tenuifolia Willd. RAPO was to improve cognitive function. and attention to the early stages of cognitive function decline in TCM is attested in recovered manuscripts from almost five millennia ago. Natural nootropics were extolled in ancient medical writings from Arabia, Egypt and Sumeria, just to name a few. Nootropics are classified as substances which improve an individual's brain functioning and cognitive processes. There is a broad classification of compounds that make this category, which is quite loosely defined, such as B12, which is a vitamin in foods and protective for brain metabolism, thus enhancing cognitive performance. Nootropics improve cognitive function, however they are not always cognitive enhancers. A nootropic is a neuroprotective or extremely nontoxic cognitive enhancer (6).

Nootropics work through a variety of methods, including the following:

1. Improving blood flow to the brain.
2. Supplying the building blocks for neurotransmitters, which are the brain's chemical messengers.
3. Enhancing neuronal performance.
4. Preventing brain cell oxidative and free radical damage.
5. Giving the brain energy that can be used, etc.

## MECHANISMS OF ACTION

Nootropics improve the supply of glucose and oxygen to the brain, have antihypoxic qualities, and lessen neurotoxic damage without directly affecting neurotransmitter production or their interaction as receptor ligands. They have also been shown to improve neuronal protein and nucleic acid synthesis and promote phospholipid metabolism in neurohormonal membranes. It has been shown that several nootropics increase erythrocyte pliability, have anti-aggregation properties, and aid in the removal of free oxygen radicals. This enhances the blood's rheological properties, leading to improved cerebral blood flow. While these substances are metabolically active, most nootropics require multiple doses over a prolonged period to achieve results, particularly in penetrating the blood-brain barrier to optimize brain metabolism. Stabilized alterations demand extended usage (7).

## METHODOLOGY

The methodological framework for a review article from a systematic literature search across various databases (PubMed, Scopus, and Google Scholar). The criteria for inclusion would specifically target empirical studies that investigate the effects of herbal neuroprotective agents on cognitive functions. The

process of data extraction would involve a detailed examination of active constituents, mechanisms of action, and respective clinical outcomes. A rigorous critical analysis concerning the efficacy, safety, and possible adverse effects associated with these agents would be conducted, integrating findings to present a comprehensive perspective on natural nootropics.

## HERBAL APPROACH

Regular drugs can improve cognitive performance by lowering inflammation, oxidative stress, and neurotoxicity. They also support the maintenance of amino acid levels, suppress neuronal death, and control the cholinergic system. Natural medications are less expensive, have fewer adverse effects, and are more readily absorbed by the brain than conventional medications. Some of nootropics detail is shown in Table I.

Wild gathering alone is insufficient for nootropic plant extracts because cultivation and timing are crucial for maximum output. Tree bark can be gathered all year round in tropical climates, although it is often taken in the early spring in temperate countries.

**Table I.** List of plant-derived nootropics: common names, uses, and constituents (1)

| S. No. | Botanical Name | Genus Family | Common Name | Parts used | Active Constituents |
|---|---|---|---|---|---|
| 1 | *Acorus calamus L.* | *Acorus* Acoracea | Sweet flag | Rhizomes | Alpha- and Beta-Asarone, Methyl isougenol |
| 2 | *Bacopa monnieri* | Bacopa Plantaginaceae | Brahmi | Whole plant | Bacosides A and B |
| 3 | *Celastrus paniculatus* | *Celastrus* Celastracea | Jyotishmati | Seeds | Alkaloids: Celastrine, Paniculatin, Calpagone, Calapanigine |
| 4 | *Ginkgo biloba L.* | *Ginkgo* Ginkoaceae | Ginkgo | Leaves | Flavanoids, Terpenoids, Kaempferol, Quercetin, Terepene lactonesGinkolides, Bilobalide |
| 5 | *Huperzia serrata* | *Huperzia* Lycopodiaceae | Club moss | Moss | Huperzine A and B |
| 6 | *Magnolia officinalis* | *Magnolia* Magnoliaceae | Houpu Magnolia | Bark | Magnolol, Honokiol |
| 7 | *Withania somnifera* | *Withania* Solanacea | Ashwagandha | Roots | Withanolides, Sitiindosites-VII, VIII, IX, X, Withaferin |

It is ideal to gather rhizomes and roots in the spring or fall when they are dormant, flowers before they blossom, and fruits and seeds once they have ripened. To preserve their active ingredients, harvested portions are air-dried before being turned into teas, extracts, pills, or capsules (8).

Herbal medications have advantages such as minimal side effects, efficacy for specific health conditions, and cost-effectiveness (9). However, limitations include inadequate handling of severe cases, potential risks of self-treatment without proper dosage instructions, and the possibility of unsafe or allergic reactions. Treatment with herbal drugs usually requires more time and patience (10).

## SPECIFIC NOOTROPIC HERB, SHRUB AND TREE SPECIES

The rising demand for nootropic plant formulations has made wild harvesting insufficient. Proper timing of harvest is crucial, as active compounds vary by developmental stage. In temperate zones, bark is collected in early spring, while in tropical areas, harvesting is possible year-round. Roots, rhizomes, and similar parts are best collected during dormancy (spring or fall); stems and leaves during blooming; buds before flowering; and fruits/seeds when fully ripe. After harvesting, plant parts are typically air-dried and processed into teas, powders, tablets, or capsules. Active compounds are extracted through methods like distillation, pressing, or solvent extraction. Ongoing research focuses on phytochemicals—bioactive compounds with cognitive benefits—many of which are rooted in traditional medicine and show promise as natural nootropics or "smart drugs (1).

## *ASHWAGANDHA (Withania somnifera (L.) Dunal)*

*Withania somnifera*, better known as Ashwaghandha or Indian Ginseng, within the *Solanaceae family*, is one of the most popular components in the traditional Indian medicine practices. The herbaceous plant ashwagandha, which belongs to the Solanaceae family, can grow up to 2.5 meters but usually only reaches 100 cm. It has smooth roots 1–2 cm thick and 30–40 cm long. Its milky-yellow-green flowers appear near leaf axils and shoot tips, and it bears red berries enclosed in a calyx. Despite its medicinal value, ashwagandha cultivation is limited due to low-yielding varieties that struggle in diverse climates. Native to North Africa, it is now found in China, Pakistan, Iraq, and northern India, with southern Indian farmers increasingly cultivating it. It also grows in dry, rocky areas, savannas, and semi-deserts. Withaferin A is the main active compound in ashwagandha, primarily found in its roots. The plant also contains withanolides, alkaloids like ashwagandhine and withanodinins, and steroidal compounds based on an ergostane skeleton, resembling ginsenosides in ginseng as illustrated in Fig. 2.

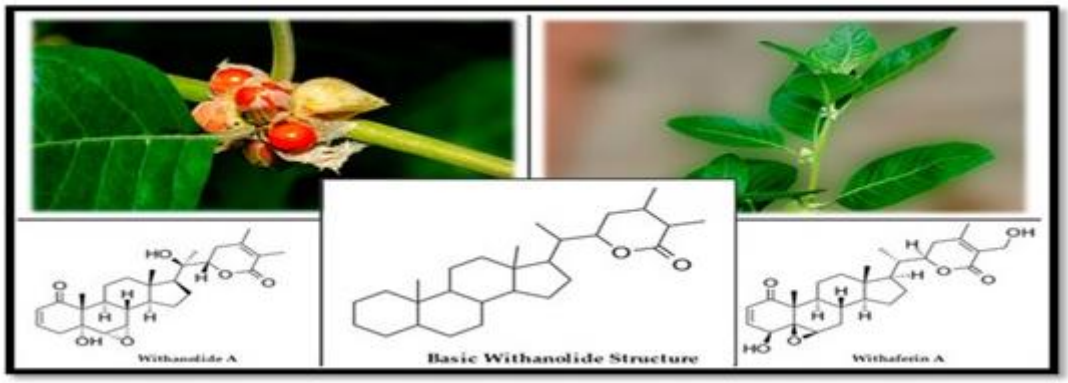


**Fig. 2.** *Withanka somnifera's* main bioactive compounds, with anolides and their chemical structures

The roots of Withania somnifera (ashwagandha) are the most commonly used parts, while the leaves are sometimes dried and made into tea. The fruit is occasionally used as an emetic. Traditionally, ashwagandha is known as an adaptogen and is used to treat insomnia and various neurological disorders. It has also been recommended as a natural remedy for traumatic brain injuries, brain tumors, and neurodegenerative diseases. Ashwagandha is generally safe, but best taken in the evening due to its sedative effects. High doses may cause gastrointestinal distress and vomiting, so it's recommended to start with a low dose and increase gradually. It is not advised during pregnancy or in cases of hyperthyroidism(1, 11).

## *GINKGO (Ginkgo biloba L.)*

Ginkgo is regarded as a living fossil and is thought to be 250–270 million years old. Trees of this species were cultivated by monks by the 10$^{th}$ century in China, as it was believed to enhance one's mental alertness. Its resilience was highlighted when one tree survived the Hiroshima bombing, marking it as a symbol of hope for Japanese people. A deciduous tree growing up to 40 m bearing fan-shaped lobed leaves that turn gold in autumn, it has ginkgo leaves. It also bears dioecious flowers and has foul-smelling yellow drupes due to butyric acid in the seed coat. The lifespan of the ginkgo tree is more than a millennium. Antimicrobial and astringent properties come from rich ginkgotoxin, ginkgolic acid, flavonoids, phenolic compounds and ginkgo seeds and leaves as shown in Figure 3. They also possess triterpene lactones.


**Fig. 3.** *Ginkgo biloba* L. main bioactive compounds, Ginkgolide's and their chemical structures

Used traditionally for enhancing cognitive abilities ginkgo also enhances cerebral blood flow, antioxidant activity, and neurotransmitter modulation. Improved long-term motivation and memory have also been observed with ginkgo extracts. In some cases, it results in headaches and reactions on the skin along with palpitations and gastrointestinal issues. Those with bleeding disorders, seizures, or on NSAIDs and anticoagulants should avoid before surgery due to ginkgolide-linked recoil seizures and blood-thinning properties(1, 12).

## *BACOPA MONNIERI*

One of the most significant herbs in Ayurveda is brahmi. Bacopa monnieri, or Brahmi, has medhya rasayana powers for 3000 years of practice, aiding in boosting the memory and mental clarity in scholars.

This plant can be found in South Asia and in southern parts of USA. Bacopa monnieri is cane-like herb having succulent shaped elongated leaves along with purple or white flowers flourishin in warm and marshy areas. Succinct areas Where this plant is found, it is used as herbal medicine around the world. The pharmaceutical industry uses plant extracts as standardized products. Bacosides A & B, as well as some alkaloids and flavonoids (apigenin & lutelin) are included in the CDRI-08 extract as illustrated in Figure 4. These are important active chemicals, which support neuron protection, better communication, and stronger synapsis formation. Training in memory, attention, learning, and even ADHD. Supports cognition in mild Alzheimer's disease. Bacopa monnieri enhances retentive logical ability and language comprehension. Its chronic effect on language comprehension also retentive logical skills is being evaluated further. Though there are no notable side effects of taking Bacopa monnieri, some users have stated dry mouth, drowsiness, or even fatigue as a secondary issue, along with irritation of the GI tract. However, such cases are when an excessive dose is taken, so it is wise to avoid taking too much of it. Though Brahmi enhances the ability of conducting sedative action or CNS depressants, it is wise to avoid it during pregnancy or having a disorder related to the thyriod glands. For non-pregnant women with normal level of thyroid, it is safe. To avoid drowsiness, stop using it two weeks before surgery (13, 14).


**Fig. 4**. *Bacopa monnieri* main bioreactive compounds, bacoside's and their chemical structures

## *MAGNOLIA OFFICINALIS*

In Traditional Chinese Medicine, Magnolia bark (houpu) is well-known for stress and cognition treatment, having historical applications in simple formulas like Banxia Houpu Tang. Uses of the herb can be traced back centuries. It is harvested from Magnolia Officinalis or M. Obovata. The trees grow in mountain ranges of China and can reach heights of 20 meters. The thick, dark bark of the tree is its therapeutic element. Includes the two neolignans magnolol and honokiol, both having neuroprotective and anti-anxiety active functions. Also includes essential oils, tannins, and flavonoids, shown in Fig. 5.

Provides better memory retention, cognition, focus, reduced anxiety levels, better sleep, and protection of the brain cells. Its antioxidant properties aid in the overall health of the brain. At higher doses, may result in sedation and allergic skin and respiratory reactions, as well as gastrointestinal problems. Do not use with sedatives or SSRIs/MAOIs as these may lead to respiratory depression or serotonin syndrome (15, 16).


**Fig. 5**. *Mangolia officinalis* main bioreactive compounds and their chemical structures

## *ACORUS CALAMUS L.*

This plant has long been claimed to be beneficial for health, used in Ayurveda and TCM, originating from America and known as sweet flag or Vacha. In Ayurveda, Acorus calamus is prized as a medhya rasayana for enhancement of cognition. As for other regions, the plant is semi aquatic and extends vertically in Asia, Europe and North America, where the wetlands lie. With its rhizome being used medicinally, it comes with sword-like leaves alongside yellow and green flowers, in addition to being aromatic. Also rich in eugenol and sesquiterpenoids, β-asarone and $\alpha$-asarone are compounds that make this plant unique seen in Figure 6. The love-hate relationship extends towards β-asarone, as it is also linked to cognitive effects, which in this case, concerns toxicity, especially in Asian variants, helping to improve and increase memory chains in Alzheimer's patients, along with decreasing muscular tension and having calming effects, also providing anticonvulsant effects. Calamus is used for several respiratory ailmants and when applied with aromatherapy, the plant helps reduce stress. Some might find themselves at the risk of getting their calamus regiones inflamed, feeling sick, or even throwing up. With limits being on the rise, the use of β-asarone can lead to carcinogenic and hepatotoxic thrusts, which also add to 'side effects of regulatory limits attached. Not for those with liver issues or pregnancy, as these two conditions can be harmful when using the plant. As a result of the effects targeting the CNS, the use of sedatives or anticonvulsants renders it unsafe, leading to grounds for concern (17-19).

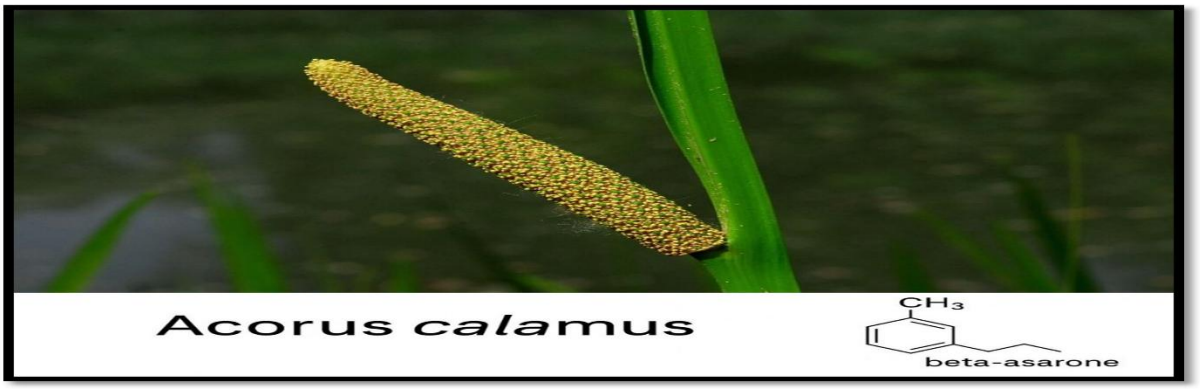


**Fig. 6**. *Acorus calamus* main bioreactive compounds and their chemical structures

## *CELASTRUS PANICULATUS L.*

This "jyotishmati" historically was used to improve mental clarity and neuropsychiatric issues over 2000 years ago and is referred to as "Intellect Tree" in Ayurveda. This plant is a woody climbing shrub that is 10 m tall and has orange red seeds, and green, white flowers. It can be found in Southeast Asian and Indian tropical woods. Active compounds include alkaloids (celastrine), teine sesquiterpenes (celapanin), triterpenoids (pristimerin), and fatty acids from the seed oil. These aid cognition and exert antioxidant properties as mentioned in Fig. 7.

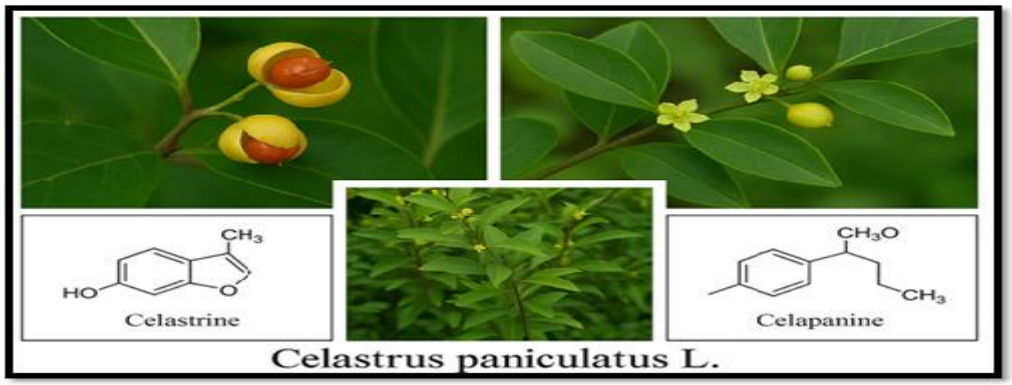


**Fig. 7.** *Celastrus paniculatus L.* main bioreactive compounds and their chemical structures

Enhances memory through protection of acetylcholine, reduction of oxidative stress, and preservation of neurons. Has anxiolytic and antidepressant properties. Infrequent skin allergy reactions, nausea, insomnia and restlessness are caused by high doses. Interaction with stimulants, sedatives and antidepressants should be used with caution. Avoid taking during pregnancy (20).

## *HUPERZIA SERRATA*

Traditional Chinese Medicine has utilized the Qian Ceng Ta for inflammation and cognitive issues. It raised interest scientifically in the 1980s for huperzine A – a strong memory-enhancing alkaloid. It is a spore-bearing clubmoss found in humid East Asian forests. The height ranges from 10 – 30cm and the entire plant is considered medicinal. It has needle-like leaves and slim stems. Key components include huperzine A, which is an AChE inhibitor. Huperzine B, lycodine alkaloids, and triterpene compounds that promote neuroprotection are also present in Fig. 8.

Improves memory retention and learning by increasing production of acetylcholine. Its use is supported in mild cases of Alzheimer's. Provides neuroprotection via anti-inflammatory and antioxidant action. High doses may cause nausea, cramps, bradycardia, and other cholinergic symptoms. Allergic reactions, however rare, may occur. Avoid alongside other ACE inhibitors or anticholinergics. Should not be taken in pregnancy or for those with a tendency for seizures (21-24).


**Fig. 8.** *Huperzia serrata main* bioreactive compounds and their chemical structures

# DISCUSSION

*Acorus calamus L.* is found in Holarctic regions (North America, Europe, Northern Asia) and has a traditional Ayurvedic use for memory enhancement (25). A clinical trial reported that low-dose extracts improved cognitive function in elderly individuals with mild cognitive impairment (MCI). However, further studies are needed due to the potential carcinogenic and neurotoxic effects of beta-asarone observed in animals (26).

*Bacopa monnieri* has long been used in traditional medicine for cogn0itive enhancement and has shown potential in managing Alzheimer's and Parkinson's diseases. [26] Clinical trials since 2020 report improved memory, concentration, and neuroprotection through neurotransmitter modulation and reduced neuroinflammation. Findings also indicate reduced amyloid plaques and increased dopaminergic activity,

promoting neurogenesis and synaptic function, though more research is needed to confirm these therapeutic effects (27).

*Celastrus paniculatus* has demonstrated nootropic effects in animal studies, where seed extracts improved memory via restoration of BDNF levels and reduction of pro-inflammatory cytokines (IL-6, TNF-$\alpha$). It also inhibited acetylcholinesterase, enhancing cognitive performance compared to controls (28). In Alzheimer's patients, ginkgolides *(from Ginkgo biloba)* and huperzine A *(from Huperzia serrata)* have demonstrated therapeutic efficacy in enhancing memory, cognition, and neuropsychiatric symptoms. Ginkgo improves cerebral blood flow and reduces oxidative stress, while Huperzine A inhibits acetylcholinesterase, preserving acetylcholine for better learning and memory. Their combined use suggests a synergistic potential in reducing neurodegeneration(29).

*Magnolia officinalis* shows strong neuroprotective and nootropic effects by safeguarding neurons and brain microvascular endothelial cells. It enhances memory and learning by modulating neuronal function, reducing neurotoxicity, and suppressing neuroinflammation (30).

*Withania somnifera (Ashwagandha)* demonstrated cognitive benefits in a clinical trial using COMPASS tests. It improved memory, attention, and reaction time by reducing neuroinflammation, crossing the blood-brain barrier, and balancing neurotransmitters. These results support its use as a natural nootropic (31).

# CONCLUSION

In today's time, the use of nootropics has become a well-known therapy for memory retention and cognitive learning, particularly among students, academic professionals and scholars, as well as individuals looking for mental focus and acuity. Although the use of herbal medicines is steadily increasing in Pakistan and other developing countries due to affordability and cultural acceptability, this trend is often accompanied by challenges such as self-medication, lack of standardized dosages, and inadequate regulatory oversight. These issues raise concerns about safety, potential drug interactions, and inconsistent therapeutic outcomes. Even-though extensive research has been done on the drugs and herbs to prove their nootropic effects, further studies and more promising results are required to support their long-term safety. Despite the increasing use of herbal medicines across South Asia, there remains a significant lack of standardization in terms of formulation quality, dosage consistency, and safety profiles. Given the ethnopharmacological diversity and widespread traditional usage in the region, there is a pressing need for rigorous standardization of herbal formulations to ensure reproducibility and therapeutic efficacy. Moreover, well-designed clinical trials specific to South Asian populations are essential to validate the efficacy and safety of these formulations under real-world conditions, accounting for genetic, dietary, and cultural factors unique to this demographic.

## Conflict of interest:

The authors declare no conflict of interest.

## Authors' contribution:

TM: Writing of original draft, conceptualization, conducted experiment and data analysis; OUR: Supervision; HS Reviewed the original draft; RK: Conceived the Idea, overall management of the work; MK, MUM & SA: Helped in data analysis; RM, AS: Reviewed the final draft. All the authors reviewed the results and approved the final version of the manuscript.

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