

## A comprehensive review on natural Nootropics that boost brain and mental health

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### Abstract

Memory is a key aspect of human cognition, ensuring resilience and endurance. It includes holding data in the psyche. The hippocampus, a fundamental cerebrum district, can be impacted by factors like acetylcholine levels, influencing memory and mental capabilities. Allopathic drugs are commonly used for memory-related issues, but this review examines their adverse reactions and side effects. Home grown medication is acquiring notoriety around the world because of its regular beginning and less secondary effects. The audit provides an overview of herbal plants known for their memory-enhancing properties, including their names, types, families, parts used, and active constituents. Bioavailability is a challenge for phytoconstituents, but nano-technology can enhance their interaction with phospholipid molecules, improving their effectiveness. The review also explores recent advancements in novel drug delivery systems and nanoformulations for herbal products.

**Key words :** Cognition, Cognitive impairment, Natural medications, Nootropics, Phytoconstituents and Novel drug delivery system.

The human psyche is the most jumbled organ in the body. One of its most basic focuses is the capacity to hold data<sup>2</sup>. In any case, when we examine comprehension, it isn't just the upkeep of data, nearby it we besides consider several connected terms like-understanding, data, thought, focus, individual satisfaction and so forth<sup>19</sup>. Ayurveda makes reference to three pieces of intellectual abilities, *i.e.*, Dhi (communication of procurement/ learning), Dhuti (pattern of maintenance) and

Smriti (pattern of review)<sup>5</sup>. Material memory or Famous memory (the vital opportunity immediately the tremendous extents of data that individuals experience dependably)<sup>19</sup>.

### *Cognition inside the brain :*

Right when we are inspecting about taking care of memory inside the brain, we want to know the instrument by which various kinds of information are taken care of inside

our frontal cortexes. There is a region in our frontal cortex, named 'Hippocampus', arranged in the normal transient bend of the brain. This hippocampus is the point of convergence of this large number of memory and mental capacities. Immediately, our neurotransmitters handle anything we see, hear or do; then, at that point, the hippocampus closes whether or not the information we made sense of is essential to store; if hippocampus decides to store the information, it holds inside our brains and we can hold it, anyway, the information gets eradicated from our frontal cortex normally<sup>21</sup>. Acetylcholine (ACh) is the principal neurotransmitter related with memory and mental capacities isolated from a couple of neurodegenerative pathogenicities<sup>18</sup>.

#### *Cognitive impairment :*

Unfortunate memory, low maintenance power, trouble to review, absence of focus, frail breaking down capacity these are a lot of normal issues of the cutting-edge world<sup>8</sup>. Mental impairment is not a separate illness, but a symptom of an underlying condition. It includes memory difficulties, learning problems, vision issues, speech impairments, and trouble recognizing people and places. Other signs include feeling overwhelmed, confusion, mood changes, and behavioral and speech changes. Urgent medical interventions may be necessary depending on the cause, such as infections, head injury, or dementia. Dementia is a significant mental decline disorder that is irreversible<sup>3</sup>.

#### *Epidemiology :*

Neurocognitive issues, especially

major mental shortage<sup>1</sup>, have serious implications for individuals and families, clinical consideration structures, and the economy. From 1990 to 2016, the amount of people encountering dementia has emphatically expanded by and large<sup>10</sup>, and in 2019, 57.4 million individuals had dementia, expected to increment to 83.2 million by 2030, and 152.8 million<sup>15</sup> by 2050. The World Prosperity Affiliation revealed that the expense of dementia overall was \$1.3 trillion out of 2019 and is supposed to ascend to \$1.7 trillion by 2030. Dementia pervasiveness altogether increments with age, multiplying at regular intervals after 65. It is more predominant in ladies because of their more extended life expectancy<sup>11</sup>.

#### *Etiology :*

Cognitive deficits can arise from a variety of factors, including birth defects, cerebral injury, psychological disorders, and neurological issues. It is more common among the elderly, but can also develop during childhood or adolescence due to various conditions. Aging, neurological conditions, certain medications, and head injuries can all contribute to cognitive deficits at any age<sup>3</sup>.

#### *Pathophysiology :*

Senile plaques, brought about by A $\beta$  amassing, and NFTs, made out of tau protein clusters, alongside irritation and oxidative pressure, bring about neuronal degeneration, apoptosis, and mental impedance. Cholinergic brokenness and harm to acetylcholinergic nerves<sup>1</sup>.

Table-1. Nootropic Treatment (Ai Et Al., 2023)

Category	Classification	Representative Drugs	Adverse Reactions	Indications
Drugs acting on the cholinergic system	Cholinesterase inhibitors (ChEI)	Tacrine, Donepezil, Rivastigmine, Galantamine, Huperzine	Incorporate queasiness, heaving, loose bowels etc.	Mild and moderate Alzheimer disease (AD).
Drugs acting on the non-cholinergic system	NMDAR antagonists	Memantine	Confusion, constipation, dizziness etc.	Moderate to severe AD.
	Cerebral vasodilator drugs (Calcium antagonist)	Nimodipine, Nicardipine, Flunarizine HCl, Flunarizine, Nitrendipine	Discombobulation, migraine, tingling of the skin, and so on.	Adjunctive therapy Vascular dementia (VD).
	Brain metabolic activator	Oxiracetam, Piracetam, Aniracetam	Dry mouth, loss of appetite, vomiting, insomnia.	Mild to moderate VD, AD.
	Ergot alkaloids	Hydergine, Nicergoline	Sickness, heaving, absence of hunger.	Mild to moderate VD, AD.
	Antioxidants, anti-inflammatory drugs	L-ascorbic acid, Vitamin E, Monoamine Oxidase Inhibitors, Idebenone, Melatonin, Edaravone, Aspirin, Indomethacin, Tenidap	Hypersensitive responses, rash, queasiness, loss of craving.	Deferred beginning of Alzheimer's illness; mild to moderate VD, AD
	Neurotrophic drugs	Nerve Growth Factor, Estrogen, Ganglioside, Pyridoxine dihydrochloride, Ginkgo leaf preparation	In a few cases, headache, rash, drug fever, diarrhea, loss of appetite.	Aids in improving Alzheimer's symptoms

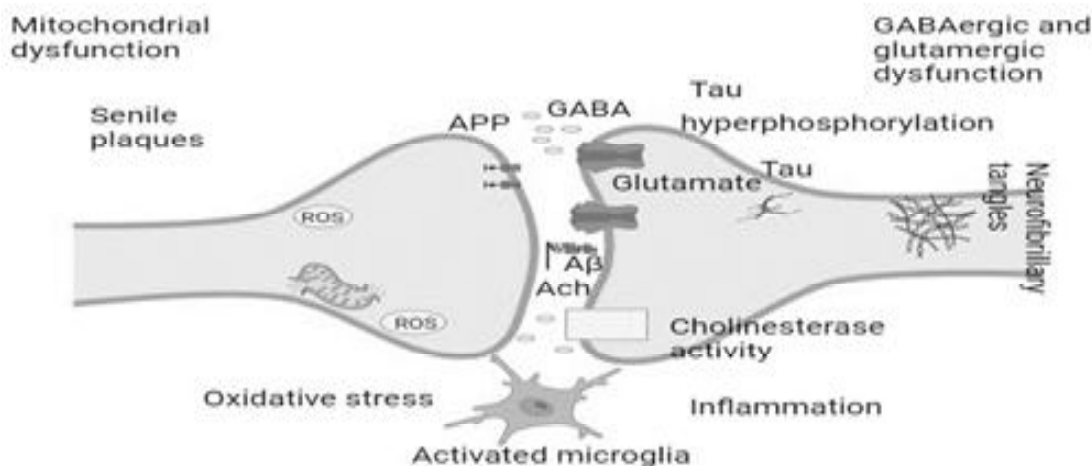


Fig. 1. Pathophysiology of Neurodegeneration

#### *Nootropics :*

Nootropics, also known as “smart drugs,” are a diverse group of compounds that enhance mental abilities, such as memory and learning. They inhibit the metabolism of neuronal cells in the central nervous system. The term “nootropic” was coined in 1972/1973 by Cornelius E. Giurgea and comes from two Greek words: *nōos* that implies thinking, and *tropein* that means to guide<sup>12</sup>.

#### *Herbal approach :*

Regular medication may improve cognitive function by reducing neurotoxicity, oxidative stress, and inflammation. It also regulates the cholinergic system, inhibits neuronal apoptosis, and maintains amino acid levels. Compared to existing drugs, natural medicines are cost-effective, have fewer side effects, and easily penetrate the blood-brain barrier<sup>1</sup>.

#### *Nootropic natural plants :*

Utilizing nootropic botanical extracts is increasingly widespread, requiring more than just gathering wild plants. Timing is crucial for optimal collection as the plant's active components vary throughout its development. Tree rind is typically harvested early in the spring in calm zones, while in jungles, it can be collected year-round. Rhizomes and roots are best harvested in spring or sometimes fall when they are dormant. Stems and leaves are typically harvested before or during flowering, and flowers are gathered before they fully mature. Seeds and fruits are always collected when fully ripe. The plant parts reaped at the most reasonable time are air-dried and afterward exposed to additional handling by different techniques. Plant parts can be dried and used as tea, extracted for active substances, or incorporated into food, tablets, or capsules<sup>13</sup>.

Table-2. List of Nootropic natural plants having Cognition enhancing Properties (Halder *Et Al.*, 2021).

S. No.	Botanical Name	Genus Family	Common Name	Parts Used	Active Constituents
1.	<i>Acorus calamus</i> L.	<i>Acorus</i> Acoraceae	Sweet flag	Rhizomes	Alpha- and Beta-Asarone, Methyl isougenol
2.	<i>Bacopa monnieri</i> L. Pennell	<i>Bacopa</i> Plantaginaceae	Brahmi	Whole plant	Bacosides A and B
3.	<i>Celastrus paniculatus</i> Willd	<i>Celastrus</i> Celastraceae	Jyotishmati	Seeds	Alkaloids: Celastrine, Paniculatin, Calpagone, Calapanigine
4.	<i>Ginkgo biloba</i> L.	<i>Ginkgo</i> Ginkgoaceae	Ginkgo	Leaves	Flavanoids, Terpenoids, Kaempferol, Quercetin, Terepene lactones- Ginkgolides, Bilobalide
5.	<i>Huperzia serrata</i> (Thunb. ex Murray) Trevis	<i>Huperzia</i> Lycopodiaceae	Club moss	Moss	Huperzine A and B
6.	<i>Magnolia officinalis</i> Rehder & wilson	<i>Magnolia</i> Magnoliaceae	Houpu Magnolia	Bark	Magnolol, Honokiol
7.	<i>Withania somnifera</i> (L.) Dunal	<i>Withania</i> Solanaceae	Ashwaga- ndha	Roots	Withanolides, Sitiindosites- VII, VIII, IX, X, Withaferin

Herbal medications have advantages such as minimal side effects, efficacy for specific health conditions, and cost-effectiveness. 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<sup>4</sup>.

#### *Novel drug delivery system :*

Novel drug delivery system (NDDS) is an articulation chiefly connected with the plan of new drug structures which have upgraded attributes, for example, more modest molecule size, higher porousness boundaries,

and specific site focusing on. NDDSs can be utilized to upgrade the exhibition of biotherapeutic specialists when contrasted and their impact in the traditional measurement structures<sup>6</sup>. In the beyond couple of many years, impressive consideration has been focused on the advancement of a NDDS for home grown drugs. Novel home grown drug transporters fix specific sickness by focusing on only the impacted zone inside a patient's body and shipping the medication to that locale<sup>20</sup>. Recent advancements in NDDS are Phytosome, Liposome, Nanoparticles, Emulsions, Microsphere, Ethosome, Solid lipid nanoparticles, Niosomes, Proniosomes, Transdermal drug delivery system, Liquid crystals Dendrimers, Hydrogels<sup>17</sup>.

Table-3. Nano formulations of herbal products for cognition enhancer and alzheimer Disease (Gaikwad *Et Al.*, 2021), (Ovais *Et Al.*, 2018), (Moradi *Et Al.*, 2020)

S.No.	Trade Name/Component	Plant
1.	Vitablue Phytosome™	<i>Vaccinium angustifolium</i>
2.	Virtiva®	<i>Ginkgo biloba</i>
3.	Curcumin-Nanoparticles	<i>Curcuma longa</i>
4.	Bacoside-Nanoparticles	<i>Bacopa monnieri</i>
5.	Ginsenoside-Nanoparticles	Ginseng
6.	Thymoquinone	<i>Nigella sativa</i>

Novel drug delivery systems have several advantages: improved solubility, increased bioavailability, reduced toxicity, enhanced pharmacological effects, and protected from degradation<sup>4</sup>.

Home-grown medications play a vital role in improving memory. Medicinal plants from various traditional medicine systems, such as Indian Ayurveda, Traditional Chinese medicine, Korean medicine, African medicine, and American medicine, have been found to enhance memory and cognition in animal models. These plants contain phytochemicals that improve comprehension, intelligence, attention, and focus by regulating the neurotransmitter ACh in the brain. However, the limited bioavailability of herbal drugs can be overcome by using phytochemical-based nanocarriers, which are safe, eco-friendly, cost-effective, and capable of improving the delivery and effectiveness of these medications in the central nervous system.

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