

Nootropic herbs (*Medhya Rasayana*) in Ayurveda: An update

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ABSTRACT

Cognitive deficits that present with many of neuropsychiatric conditions and/or alone as developmental deficit demand use of nootropics to boost cognitive abilities. Recently there is a tremendous urge to explore medicinal plants globally for improving cognitive function owing to their less adverse effects. Ayurveda provides a list of herbs known for nootropic activity as well as their multi-dimensional utility in various conditions. Present paper is a review to update knowledge on pharmacological properties, major chemical constituents, therapeutic actions, preclinical studies, safety and possible mode of action of the selected herbs from ayurvedic pharmacopoeia. Concurrently, it opens up for further research and standardization on nootropic herbs

Key words: Ayurveda, memory enhancer, *Medhya Rasayana*, nootropic

INTRODUCTION

Medhya Rasayanas are group of medicinal plants described in Ayurveda (Indian system of medicine) with multi-fold benefits, specifically to improve memory and intellect by Prabhava (specific action). Medha means intellect and/or retention and Rasayana means therapeutic procedure or preparation that on regular practice will boost nourishment, health, memory, intellect, immunity and hence longevity. *Medhya Rasayana* is a group of 4 medicinal plants that can be used singly or in combinations. They are *Mandukaparni* (*Centella asiatica* Linn.), *Yastimadhu* (*Glycyrrhiza glabra* Linn.), *Guduchi* (*Tinospora cordifolia* (Wild) Miers) and *Shankhapushpi* (*Convolvulus pleuricanulis* Choisy), specially mentioned with wide range of applications on different systems. Yet in practice few more handful drugs used with same aim are mentioned else where in the Ayurveda classical textbooks. They are *Aindri* (*Bacopa monniera*), *Jyotishmati* (*Celastrus panniculata*),

Kushmanda (*Benincasa hispida*), *Vacha* (*Acorus calamus*) and *Jatamamsi* (*Nardostachys jatamamsi*). *Medhya Rasayana* are used either in polyherbal preparations or alone. This paper is an attempt to present update on these drugs. Evidences used are mostly facts from researches on animal model or on bioactive principles with some of preclinical works on human system.

Evidence based approach

Mandukaparni (*Centella asiatica* Linn.) is a prostrate, stoloniferous perennial herb rooting at nodes^[1] [Figure 1]. Fresh whole plant juice is used for therapeutic purposes as *Medhya* (cognitive enhancer).^[2] Major constituents are saponin (medacoside, asiaticoside, medacassoside, asiatic acid, a new triterpenic acid).^[3] They act on behaviour besides being neuroprotectives^[4] brain growth promoter.^[5] Dendritic arborization is supposed to be the neuronal basis for improved learning and memory.^[6] Anti seizure activity may result from direct or indirect modulation of ATPase activity.^[7] *Centella asiatica* inhibits the memory impairment induced by scopolamine through the inhibition of AChE.^[8] BR-16A (Mentat), a formulation containing *Centella asiatica* proved for its antistress effects.^[9] Methanol extract of *Centella asiatica* showed highest free radical scavenging activity that can be attributed to the presence of polyphenols and flavonoids as this fraction contains maximum amount of these secondary metabolites (0.07 mg/ml). It also exhibited DNA damage protection activity on pRSETA plasmid DNA in TE buffer (10 mM Tris-Cl and 1 mM EDTA) pH 8.0. Chloroform extract of *Centella* showed highest poly phenolic activity followed by methanol extracts (9.04 µg/mg, 7.7 µg/mg, 6.76 µg/mg Gallic acid equivalents respectively); while flavinoids were abundant in water extracts, followed by chloroform extracts. These two

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namely poly phenols and flavinoids are responsible for potent anti oxidant and terminate free radicals.^[10] Extracts of *Centella* are used in a herbal cosmetic cream for the improvement of skin viscoelasticity and hydration.^[11] A study was conducted on Menotab, an effective herbomineral preparation containing *Centella asiatica* with other drugs from the Himalaya drug company, Bangalore. Study showed that Menotab is an ideal medication for relief of postmenopausal symptoms as a short-term therapy.^[12] Administration of *Centella asiatica* at 1,000 mg/kg b.wt for a period of 30 days in albino rats, showed organ specific toxicity.^[13]

Yastimadhu (*Glycyrrhiza glabra* Linn.) is a hardy herb or under shrub belonging to Fabaceae family^[14] [Figure 2]. Fine powder of dried root is used internally with milk for therapeutic purpose as *Medhya*.^[2] Active ingredients are glycyrrhizine, flavonones,^[15] isoflavones, glycyrrhetic acid,^[16] six phenolic compounds.^[17] Multidimensional activities of *Yastimadhu* may be attributed to glycyrrhizine and flavonones. *Yastimadhu* is cytotoxic and its prolonged use may lead to pseudoaldosteronism,^[18] hyperkalemia,^[19] and hypertension.^[20,21] The roots and rhizomes of *G. glabra* has been studied with respect to spatial learning and passive avoidance^[22] preliminary free radical scavenging^[23] cerebral ischemia^[24] and antioxidant capacity towards LDL oxidation.^[25] *Glycyrrhiza glabra* aqueous extract markedly improves antihypoxic effects induced by sodium nitrite in rats and this effect may be mediated by its antioxidant properties.^[26,27] The roots and rhizomes of *Glycyrrhiza glabra* is an efficient brain tonic; it increases the circulation into the CNS system and balance the sugar levels in the blood.^[28] Liquorice has significant action on memory enhancing activity in dementia^[29] it significantly improved learning and memory on scopolamine induced dementia.

Guduchi (*Tinospora cordifolia* (Wild) Miers) is a large glabrous, deciduous, climbing shrub of Menispermaceae family found throughout tropical India^[30] [Figure 3]. Juice of whole plant is used therapeutically as *Medhya*.^[2] It is also used in the form of decoction, powder and *Satwa* (starch extract of stem). Its root is known for its anti stress, anti-leprotic and anti-malarial activities.^[31,32] Chemical constituents' classes are alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds and polysaccharides.^[33] Neuroprotective and ameliorative properties are due to their antioxidant and trace element contents.^[34] *Tinospora cordifolia* is known to be a rich source of trace elements (Zinc and Copper) which act as antioxidants and protects cells from the damaging effects of oxygen radicals generated during immune activation.^[35] It increases the blood profile and has lead scavenging activity.^[36] *Tinospora cordifolia* has been claimed to possess learning and memory enhancing,^[37] antioxidant,^[38,39] and anti-stress activity.^[40] *Tinospora cordifolia* enhanced the cognition in normal and cognition deficits animals in behavioural test Hebb William maze and the passive avoidance task.^[41] Mechanism of cognitive enhancement is by immunostimulation and increasing the synthesis of acetylcholine, this supplementation of choline



Figure 1: *Centella asiatica*



Figure 2: *Glycyrrhiza glabra*



Figure 3: *Tinospora cordifolia*

enhances the cognition.^[42] Myriad actions of Guduchi may be attributed to its antioxidant^[43,44] and immunomodulatory properties.^[45]

Shankhapushpi (*Convolvulus pleuricaulis* Chois) is a perennial, prostrate

or sub erect spreading hairy herb,^[46] found throughout India^[47] [Figure 4]. Recommended therapeutic form is fine paste of whole plant. Highly regarded as *Medhya* (intellect promoter).^[2] Important chemical principles are microphylllic acid, shankhapushpin, kaempferol-kaempferol-3-glucoside, 3, 4 dihydroxycinnamic acid, sitosterols. Neuroprotective and intellect promoting activity implicated to free radical scavenging and antioxidant property.^[48] BR-16A (Mentat), a poly herbal combination containing *Shankhapushpi* significantly reversed the social isolation stress-induced prolongation of onset and decrease in pentobarbitone-induced sleep, increased total motor activity and stress-induced antinociception in experimental model.^[49] Ayushman-8 (containing *Shankhapushpi*, *Brahmi* and *Vacha*) reported to be effective on *Manasa-mandata* (mental retardation).^[50] *Shankhapushpi* compound containing *Shankhapushpi*, *Sarpagandha*, and *Gokshura* in equal quantities studied to be effective in *Chittodvega* (anxiety disorders).^[51] Sanjay Parsania^[52] reported *Shankhapushpi* to be effective in relieving signs and symptoms of *Chittodvega* (anxiety disorders). Herbalists believe that *Shankhapushpi* calms the nerves by regulating the body's production of the stress hormones, adrenaline and cortisol.^[53] Few investigations reports that *Shankhapushpi* has potent depressive action in mice.^[54] *Convolvulus pleuricaulis* whole plant extract, shows the highest inhibitory activity against *Helicobacter muridarum*.^[55]

Aindri (*Bacopa monniera*) commonly called as *Brahmi* belongs to Scrophulariaceae family.^[56] It is a small, creeping marshy herb grown through out India^[57] [Figure 5]. Most beneficial therapeutic form is macerated whole plant juice. Properties are said to be similar to that of *Mandukaparni*.^[58] *Bacopa monniera* is a well-known nootropic plant reported for its tranquilizing,^[59] sedative action,^[60] cognitive enhancer,^[61] hepatoprotective,^[62] memory enhancer^[63] and antioxidant actions.^[64-66] Neuroprotective activity may be ascribed to having its reactive oxygen species scavenging property.^[67] *Bacopa monniera* is a saponin rich plant.^[68] Bacosides are the main active nootropic principle present in the alcoholic extract of the plant.^[69]

Isolation of a new saponin, a jujubogenin, named bacopasaponin G, and a new glycoside, phenylethyl alcohol was reported.^[70] Three new saponins designated as bacopasides III, IV and V isolated.^[71] Apart from memory enhancer activity these bacosides have the potential to modulate the activities of heat shock protein (Hsp70) expression, cytochrome P450 and superoxide dismutase in the rat brain.^[72] On rats, alcoholic extract increases both cognitive function and retention capacity, decreases retrograde amnesia and protects from phenytoin -induced cognitive deficit.^[73] It is mainly utilized in the treatment of memory and attention disorders.^[74]

Recent studies have indicated antioxidant effect of bacosides (triterpenoid saponin isolated from *Bacopa monniera*) against chronic toxin induced oxidative damage in rat brain^[75] and thyroid T₄ hormone stimulating activity in animals in high doses.^[76]

Jyotishmati (*Celastrus panniculata*) is a large, woody, climbing shrub



Figure 4: *Convolvulus pleuricaulis*



Figure 5: *Bacopa monniera*



Figure 6: *Celastrus panniculata*

with ovate or obovate leaves found all over India. Seeds are yellowish, ellipsoid or ovoid enclosed in a scarlet aril^[77] [Figure 6], Seed oil (*Jyotishmati Taila*) is known for *Medhya* action.^[78] This oil contains several terpenoids like paniculatadiol, b-sitosterol, celastrol, b-amyrin, pristimerin, but its most investigated components are its many sesquiterpenoids, dihydroagarofuran-

type polyols or esters.^[79] *Celastrus paniculata* showed antioxidant activity by decreasing the lipid peroxidation^[80] and anti-arthritis activity in rat model.^[81] Seed oil of *Celastrus panniculata* (*Malkangni*) reversed scopolamine-induced deficits in navigational memory task in young adult rats.^[82]

Kushmanda (*Benincasa hispida*) belonging to Cucurbitaceae an extensive trailing or climbing herb cultivated throughout the plains of India as a vegetable^[83] [Figure 7]. The fruit, broadly cylindrical, is covered with a waxy bloom.^[84] Phytochemical analysis of *Benincasa hispida* shows presence of alkaloids, flavinoids, saponins and steroids.^[85] *Benincasa cerifera* serves as ROS scavenger and an antioxidant effective agent.^[86] It has a tissue protective preventive effect on colchicine induced Alzheimer's disease via direct and indirect antioxidant activity.^[87] *Kushmandadi Ghrita* showed significant results in the management *Chittodvega* (anxiety disorders).^[88]

Vacha (*Acorus calamus*) of Araceae family is a semiaquatic, perennial, aromatic herb with its rhizome being horizontal, rounded, somewhat vertically compressed, spongy and leaves grass like and sword shaped; grown all over India^[89] [Figure 8]. Rhizome is useful part having *Medhya* quality. It has been used in Indian and Chinese system of medicine for hundreds of years to cure diseases especially the central nervous system (CNS) abnormalities.^[90-93] Active chemical principles are α -asarone, elemicine, cis-isoelemicine, cis and trans isoeugenol and their methyl ethers, camphene, p-cymene, b-gurjunene, α -selinene, b-cadinene, camphor, terpinen-4-ol, α -terpineol and α -calacorene, acorone, acronone, acoragermacrone, 2-deca-4,7 dieneol, shiyobunones, linalool and preisocalamendiol. Acoradin, galangin, 2, 4, 5-trimethoxy benzaldehyde, 2,5-dimethoxybenzoquinone, calamendiol, spathulenol and sitosterol are also present.^[94,95]

It has been proved for its analgesic and anticonvulsant,^[96] hepatoprotective,^[97] antioxidant,^[98,99] antimutagenic,^[100] sedative and hypothermic effects.^[101] Good in clearing speech to the children^[102,103] and useful in schizophrenic psychosis.^[104]

Food and Drug Administration banned usage its oil in food formulations and in other therapeutic preparations^[105] due carcinogenic and toxic properties of α -asarone compound.^[106]

Jatamansi (*Nardostachys jatamansi*) is an erect perennial aromatic herb with long, stout, woody, greyish, rhizomatous, tail-like rootstock covered with reddish-brown hairs or tufted fibrous remains of the petioles of withered radical leaves^[107] [Figure 9], and belongs to Valerianaceae family. Rhizome is used for medicinal purposes as it is *Bhutaghna* or *Manasa Doshahara* (relieves of psychiatric problems) and *Medhya*.^[108] Roots and rhizomes of *N. jatamansi* are used to treat hysteria, epilepsy, and convulsions.^[109] The decoction of the drug is also used in neurological disorders, insomnia and disorders of cardiovascular system.^[110] Rhizomes contain a terpenoid ester, nardostachysin I.^[111] It is proven to improve learning and memory in mice^[112] and also to enhance biogenic amine activity.^[113] An acetone extract of *N. jatamansi* has shown significant inhibition



Figure 7: *Benincasa hispida*



Figure 8: *Acorus calamus*



Figure 9: *Nardostachys jatamansi*

of benzoyl peroxide-induced cutaneous oxidative stress, toxicity, and ear oedema in mice.^[114]

DISCUSSION AND CONCLUSION

Data available so far support procognitive activity of herbs selected for discussion; at the same time demand substantial evidences and revalidation in humans. Mostly the above said herbs act on the basis of antioxidant, adaptogenic or essential trace elements present in them. Their activity on modulation of biological axis and neurotransmitters requires further investigation.

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