



## MANAGEMENT OF COGNITIVE DECLINE DURING AGEING: EVIDENCES FROM AYURVEDA

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**KEYWORDS:** Ayurveda, *Medhya rasayana*, Cognitive decline, Nervous system.

### ABSTRACT

Deterioration in the levels of vital capacity, memory and intellectual abilities are commonly observed in geriatric age group. The prevalence of age related cognitive decline is becoming an important public health concern as there is premature ageing due various environmental and lifestyle changes. According to the surveillance studies 15% people are suffering from moderate to severe cognitive decline/dementia after the age of 65 years. If left unchecked, symptoms most of the times progress into more serious conditions, such as dementia and depression, or even Alzheimer's disease. Dementia accounts for one of the major disability in older people. Alzheimer's disease is now recognized as the most common disorder of dementia. Cognitive decline in advanced age make the person handicap for his daily activities of living and pose burden on his family and society. *Rasayana* in Ayurveda are the drugs which are known to specifically improve the body tissues and possess adaptogenic activity and therefore delay premature ageing process. Some of the *Rasayana* are specific to brain tissue known as *Medhyarasayana*. Present article reviews the evidences regarding the efficacy of Ayurveda *Medhya rasayana* drugs on prevention and management of cognitive decline in advanced age.

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### INTRODUCTION

Ayurveda is traditional system of medicine which emphasizes prevention of diseases and rejuvenation of our body systems. Among the eight divisions of Ayurveda seventh division is '*Rasayana Chikitsa*' which provides longevity, memory, intelligence, freedom from disorders, youthful age, excellence of luster, complexion and voice, oratory, optimum strength of physique and sense organs, respectability and brilliance.<sup>[1]</sup>

The *Medhya Rasayana* provides immunity against diseases, strength, complexion, voice and specifically acts upon neurodegenerative disorders which effect quality of life.<sup>[2]</sup>

Ageing is multi-factorial natural phenomenon which reflects at cellular, organ and organism levels. Such type of degenerative changes lead to dementia and other neurodegenerative disorders. Number of people over 60 years has grown rapidly to 10% of the world population.<sup>[3]</sup> Increasing number of individuals in advanced age group is the increase in number of patients suffering from age-related disorders. According to the surveillance studies 15% people are suffering from moderate to severe dementia after the age of 65 years. Alzheimer's disease is now recognized as the most common disorder of dementia.<sup>[4,5]</sup> Dementia is a chronic disorder which is characterized by memory loss, difficulty in learning and retaining new information like

depressive symptoms. There is no any specific treatment is available in modern science to prevent or delay this process of ageing which is a burning problem in all over the world among elderly individuals.

In Ayurveda literature, *Jara* (aging) at the appropriate age is termed as "*KalajaJara*".<sup>[6]</sup> Deterioration of *Medha* (intellect) and *Buddhi* (wisdom) is clearly emphasized in *Sharangdhar Samhita* in the forth and ninth decade of life.<sup>[7]</sup> *Grahana* (power of understanding), *Dharana* (power of retention), *Smarana* (power of memorizing), *Vachana* (speech) and functions of sense organs qualitatively are affected in old age according to *Charaka Smahita*.<sup>[8]</sup>

Aging is a natural process of physical, psychological and social change in multidimensional aspects. This process is inevitable and it can only be delayed. *Rasayanas* are organ and tissue specific. Those specific to brain tissue are called *Medhya Rasayana*.

### Aims and Objectives

1. To search and re-evaluate effect of *Medhya Rasayana* in various texts and literature with references.
2. To understand the anti-anxiety, memory enhancer, nervine tonic, anti-oxidant effect of four herbs which are included in *Medhya Rasayana*.

## Material and Methods

*Medhyarasayana* drugs are reviewed and re-evaluated for their activity in various Ayurvedic texts and literature. Further, the activity of *Medhyarasayana* drugs on CNS were searched from various clinical and experimental studies published in various papers.

Several clinical and experimental studies have proved that these four drugs of *Medhya Rasayanas* having potential to delay the process of ageing specifically over brain tissue. The present paper presents a review of *Medhya rasayana* drugs from clinical and experimental evidences for their activity on CNS.

### *Centella asiatica* (Mandukaparni)

*Mandukaparni* (*Centella asiatica* Linn.) is a perennial herb which is one of *Medhya Rasayana* as described in *Charaka Samhita*.<sup>[9]</sup> Its fresh whole plant juice is used for therapeutic purposes as *Medhya* (cognitive enhancer).<sup>[10]</sup> *Medhya* properties of *Centella asiatica* are described in various Ayurvedic classics, some of which are listed below:

- *Medhya Rasayana*
- Drug of choice as *Rasayana* drug for *Manas Roga* (Psychological disorders)

Fresh whole plant juice contains Glycosides, tannin, flavonoids vitamins B & C, Ca, Mg, and Na all of which helps in improvement of brain health.

- Inhibition of memory impairment: *Centella asiatica* inhibits AChE which induces scopolamine resulting in inhibition of memory impairment. [11] It has been shown to improve the altered levels of neurotransmitters such as 5HT, acetylcholine, epinephrine, nor-epinephrine, GABA (gamma-aminobutyric acid) and glutamate. It has been shown to improve the mental ability and fatigability of subjects under stress. [12] The CeA (*Centella asiatica*) has not accelerated the learning process, but rather significantly facilitated the retention of learnt task as a good retention of memory for longer period which provides the further support for the earlier reports on cognitive enhancing ability of CeA. [13]
- **Neuroprotectives and brain growth promoter:** Constituents of *Centella asiatica* are saponin (medacoside, asiaticoside, medacassoside, asiatic acid, a new triterpenic acid. [14] which are neuroprotectives and brain growth promoter. [15,16] Asiatic acid, showed a strong inhibition of beta-amyloid- and free radical-induced cell death which can be used for treatment of Alzheimer's disease that protects neurons from beta-amyloid toxicity. [17] The 3 derivatives of Asiatic acid significantly attenuated decreases in the levels of glutathione, glutathione peroxidase and other enzymes and significant neuroprotective effects on cultured cortical cells by their potentiation of cellular oxidative defense mechanism. [18]
- **Anti-oxidant activity:** It is effective in reducing brain regional lipid peroxidation (LPO) and protein carbonyl (PCO) levels and in increasing anti-oxidant status [19]. There are some evidences which shows that water extracts of *Centella asiatica* contains flavinoids

which were abundant in water extracts, while chloroform extracts 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). These flavonoids and two poly phenols are responsible for potent anti-oxidant and eliminate free radicals. [20]

- **Antidepressant properties:** The antidepressant effects of *Centella asiatica* were observed In the study, imipramine and total triterpenes from CA reduced the immobility time and ameliorated the imbalance of amino acid levels confirming the antidepressant activity of CA. [21]
- **Anti-ageing:** *Centella asiatica* re-vitalize the brain and nervous system, increase attention span and concentration and combat aging. [22]
- **Behavioral effect** – The result of double blind trial of *Mandukaparni* on mentally retarded children showed a very significant increase in both general ability and behavioral pattern when the drug was administered even for a short period of 12 wks. It produced a significant improvement and behavioral change. [23]
- **Changes in Hippocampus** – Adult rats (2.5 months old) were fed with 2, 4 & 6 ml/kg of fresh leaf extract of *C. asiatica* for 2, 4 and 6 wks, respectively. After the treatment period, the rats were killed, brains were removed and hippocampal neurons were impregnated with silver nitrate (Golgi staining). The results showed a significant increase in the dendritic length (intersections) and dendritic branching points along the length of both apical and basal dendrites in rats treated with 6 ml/kg/d of *C. asiatica* for 6 wks while the rats treated with 2 & 4 ml/kg/d for 2 & 4 wks did not show any significant change in hippocampal CA3 neuronal dendritic arborization. [24]

### *Convolvulus pluricaulis* (Shankhapushpi):

*Shankhapushpi* (*Convolvulus pleuricaulis* Chois) is a perennial herb [25]. It is recommended therapeutic form is fine paste of whole plant. [26] Its medicinal properties are as follows:

- *Medhya Rasayana*
- Drug of choice as *Rasayana* drug for loss of *Medha* (Intellect) in fourth decade according to *Sharangdhar Samhita*.
- *Satwavajaya Chikitsa Chittodvega* (anxiety disorders) [27]

The active constituents in *Convolvulus pleuricaulis* include Glycosides coumarins, flavonoids, and alkaloids like microphylllic acid, shankhapushpin, kaempferol-kaempferol-3-glucoside, 3,4 dihydroxycinnamic acid, sitosterols. There are various evidences available to prove its activity over nervous system.

- **Antioxidant property:** above active principles of *Convolvulus pleuricaulis* free radical scavenging and antioxidant property. [28] The *C. pluricaulis* extract possesses significant anticonvulsant activity when tested *in vitro*. [29] Some of the studies shown that when scopolamine is induced, the *C. pluricaulis*

extract may exert its potent enhancing activity through anti-AChE and antioxidant action.<sup>[30]</sup> An ethanolic extract of CP possesses significant antioxidant activity when tested in vitro.<sup>[31]</sup>

- **Memory enhancer:** Dose dependent increase in AGhE activity in CA1 with AS and CA3 area with *Convolvulus Pluricaulis* treatment over hippocampal regions associated with the learning and memory functions.<sup>[32]</sup> It was also found that convolvine potentiates the effects of arecoline, a muscarinic memory enhancer that ameliorates cognitive deficits in Alzheimer's disease.<sup>[33]</sup>
- **Anxiolytic effect:** Some evidences shows that the flower extract of plant exerted anxiolytic effect in mice on EPM.<sup>[34]</sup> Ethanolic extract of *C. Pluricaulis* exerted a negative inotropic action on amphibian and mammalian myocardium. It has shown spasmolytic activity on smooth muscles.<sup>[35]</sup>

### *Tinospora Cardifolia (Guduchi)*

*Tinospora Cardifolia* (Family: Menispermaceae) commonly known as Guduchi is an Indian medicinal plant has been used in various ailments throughout the centuries. There are certain references in Ayurveda which describes its *Rasayana* properties as follows:<sup>[36]</sup>

- *Medhya Rasayana*
- *Rasayana* for *Meda Dhatu*
- Drug of choice as *Rasayana* drug for *Amavata* (Rheumatoid Arthritis), *Manasroga* (Psychological disorders).
- *Tridosahara*

*Tinospora Cardifolia* also containing some properties which supports it as *Rasayana* drug. Few of them are listed below:

- **Antioxidant activity:** Leaf extract of *Tinospora cardifolia* had appreciable anti-oxidant and hydroxyl radical scavenging activities.<sup>[37]</sup> An extract of *Tinospora cardifolia* reduced the toxicity induced by free radicals and inhibited lipid peroxidation in vitro. It also partially reduced lipid peroxides in serum liver as well as alkaline phosphatase and glutamine pyruvate transaminase.<sup>[38,39]</sup> Prophylactic benefits of *Tinospora cordifolia* have been shown in middle cerebral artery occlusion model of stroke in rats. The benefits have been ascribed to its potential for preventing oxidative stress injury and regulation of cytokine levels and growth factors in the blood of angiogenesis-induced animals.
- **Immunomodulatory effect**<sup>[40,41]</sup>: *Tinospora cardifolia* is a potential immunomodulator.<sup>[42-44]</sup> A novel polysaccharide from the medicinal plant. *Tinospora cordifolia* has Immune stimulating properties.<sup>[45]</sup> *Tinospora cardifolia* extract has effect

Immunomodulatory effect in HIV positive patients.<sup>[46]</sup>

- **Antidepressant activity:** An ethanolic extract of the roots of *Tinospora cordifolia* normalized stress induced biochemical changes in norepinephrine Antistress activity<sup>[47]</sup>. It has shown to increase Monoamine oxidase (MAO-A and MAO-B) activities, the elevated levels of which have increased levels of brain monoamines leading to significant antidepressant activity.<sup>[48,49]</sup>
- **Enhance cognitive power:** Both alcoholic and aqueous extract of Tc have enhanced the cognition in normal rats as seen in behavioural test-Hebb William maze and the passive avoidance task. The probable mechanism of cognitive enhancement by Tc could be by immunostimulation and increasing the synthesis of acetylcholine which is an important neurotransmitter in learning and memory process.<sup>[50]</sup> Antistress activity in brain: Normalization of stress-induced biochemical changes in norepinephrine (NE), dopamine (DA), and 5-hydroxytryptamine (5-HT) in experimental rat models and improved levels of 5-hydroxyindoleacetic acid (5-HIAA) (a metabolite of 5-HT) in mice with ethanolic roots extracts.<sup>[51]</sup>

### *Glycyrhiza glabra (Yastimadhu)*

*Yastimadhu (Glycyrhiza glabra* Linn.) is a hardy herb or under shrub.<sup>[52]</sup> Whole plant is known to possess therapeutic benefits. *Glycyrhiza* is indicated to be used in powdered form for its better action in Charaka Samhita.

- *Medhya Rasayana*
- Drug of choice as *Rasayana* drug for *Manasroga* (Psychological disorders).

This herb contains several types of alkaloids, flavanoids, and coumarins as active chemicals that bring about its biological effects.<sup>[53]</sup> The plant has been found to be effective in reducing different types of stress including psychological, chemical and traumatic.

- **Antioxidant properties:** The aqueous extract improves hypoxic effects induced by sodium nitrite in rats and this effect may be mediated by its antioxidant properties.<sup>[54]</sup> Studies show that *Glycyrhiza glabra* has Antioxidant properties<sup>[55]</sup> and antioxidant capacity towards LDL oxidation.<sup>[56]</sup>
- **Anxiolytic effect:** *Glycyrhiza glabra* possesses anxiolytic activity<sup>[57]</sup>
- **Memory enhancing activity:** Liquorice (*Glycyrhiza glabra*) has significant action on memory enhancing activity in dementia and improved learning and memory on scopolamine induced dementia.<sup>[58]</sup>

### Summary

Sr. No.	Sanskrit Name	Botanical Name	Activities
1.	<i>Mandukaparni</i>	<i>Centella asiatica</i>	Inhibition of memory impairment
			Neuroprotective and brain growth promoter
			Anti-oxidant activity

			Antidepressant properties
			Anti ageing
			Behavioral effect
			Change in hippocampus
2.	<i>Shankhapushpi</i>	<i>Convolvulus pluricaulis</i>	Anti-oxidant activity
			Memory enhancer
			Anxiolytic effect
3.	<i>Guduchi</i>	<i>Tinosporacardifolia</i>	Anti-oxidant activity
			Immunomodulatory effect
			Antidepressant properties
			Enhance cognitive power
4.	<i>Yastimadhu</i>	<i>Glycirrhzaglabra</i>	Antioxidant properties
			Anxiolytic effect
			Memory enhancing activity

## CONCLUSION

The present review reveals that the Medhya drugs mentioned in Ayurveda classics possess antioxidant, antidepressant, neuroprotective, anxiolytic, memory enhancing activities. These drugs can be used safely and effectively in prevention and checking the progress of senile dementia.

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**Cite this article as:**

Rashmi Pareek, Nisha Ojha, Satyendra Kumar Tiwari. Management of Cognitive Decline During Ageing: Evidences from Ayurveda. AYUSHDHARA, 2016;3(1):513-518.

**Source of support: Nil, Conflict of interest: None Declared**