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EVIDENCE BASED OUTCOMES OF *RASĀYANA* THERAPIES FOR MILD COGNITIVE IMPAIRMENT IN THE ELDERLY: A NARRATIVE REVIEW

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ABSTRACT
Mild cognitive impairment (MCI) is a prevalent age-related health concern that signifies a transitional phase between normal cognitive aging and early dementia, with Ayurveda correlating it to Jarajanya Smrthibramsa linked to aging and aggravated Vāta Doṣa. Its prevalence increases with age, affecting up to 25.2% of individuals aged 80-84. While early detection and interventions are essential, FDA-approved pharmacological treatments remain lacking. Ayurvedic modalities such as Rasāyana therapies can provide a viable strategy for managing MCI. In this narrative review, studies investigating the effects of Rasāyana on MCI were evaluated. A broad search strategy was employed using several online databases, covering articles from January 2000 to July 2024, resulting in the assessment of 23 articles. Evidence-based studies in Rasāyana therapy have examined improvements in nutritional quality, cerebral metabolism, and microcirculation, all of which support neuroprotection and cognitive function. This review underscores the direct and indirect roles of Ayurveda Rasāyana in the management and prevention of MCI.

KEYWORDS : *Mild Cognitive Impairment, Jarajanya Smrthibramsa, Rasāyana*

INTRODUCTION
Mild cognitive impairment is a prevalent age-related condition that signifies an intermediate stage between age-related cognitive changes and early dementia,[1] with Ayurveda correlating it to Jarajanya Smrthibramsa. As the elderly population increases, enhancing quality of life becomes increasingly important. Despite extensive clinical trials, the Food and Drug Administration (FDA) has not approved any pharmacological treatments for managing Mild Cognitive Impairment (MCI) or for preventing its progression to dementia. Rasāyana can be offered as a therapeutic option for MCI, as Rasāyana therapy provides rejuvenating and neuroprotective effects. Scientific evidence supports that a healthy lifestyle and proper nutrition can significantly slow the progression of MCI.[2]

MATERIALS AND METHODS
A comprehensive literature review was conducted according to the topic through contemporary online databases like Google Scholar, PubMed and ResearchGate. The articles published from January 2000 to July 2024 were checked in screening stages by online databases. The search strategy employed keywords and medical subject headings (MeSH) terms to ensure comprehensive coverage and Boolean operators were used to refine search strategy effectively. Search terms included ‘mild Cognitive impairment’ and ("*Rasāyana*," or "Nutrition,"or "cognitive functions"). The data extraction process included the interpretation of the research and findings of the outcomes summarized using a narrative approach. The schematic representation of the literature survey process illustrated in PRISMA flowchart is shown in Figure 1.

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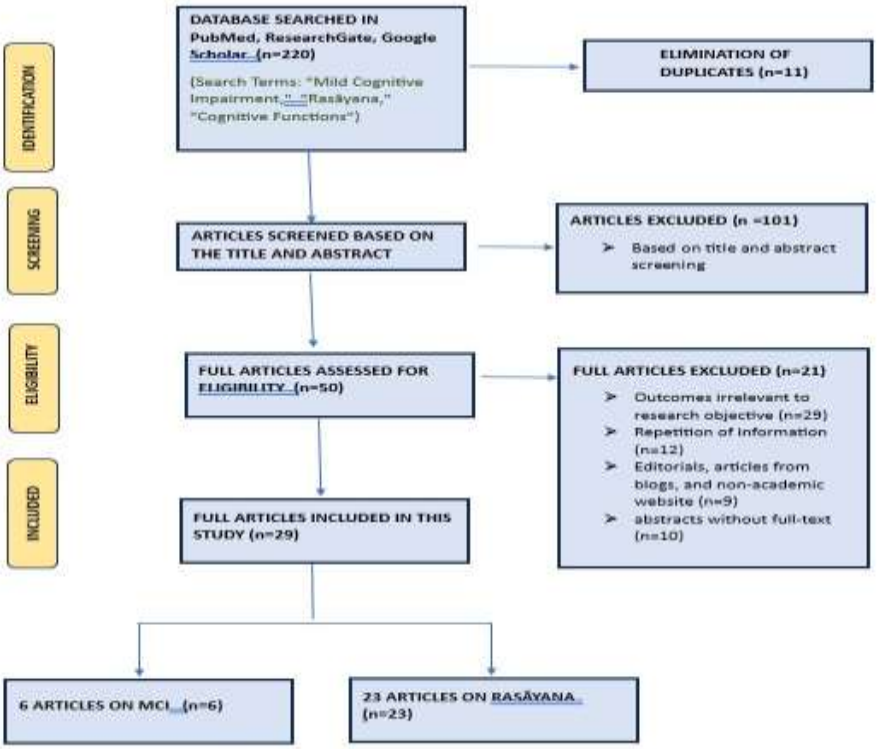


Figure 1: Detailed procedure of literature survey

MCI AND *SMRTHIBRAMSA*

Definition and Classification of MCI

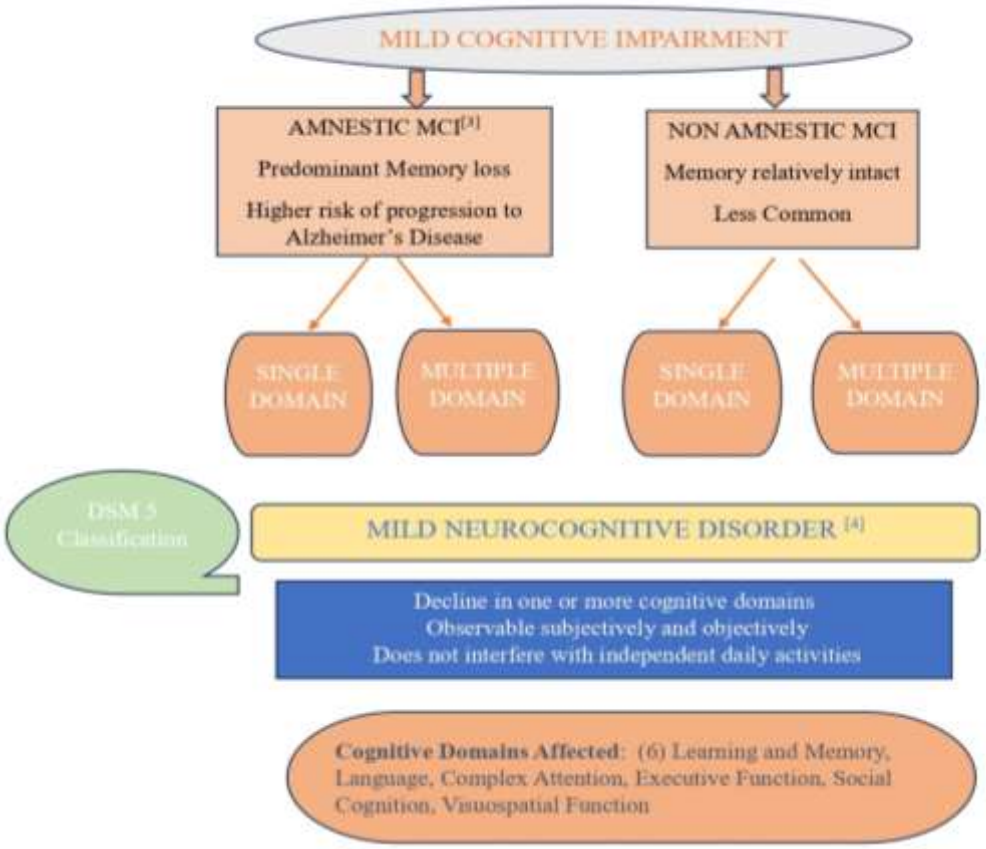


Figure 2: Definition and classification of MCI

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Prevalence of MCI and Modifiable Risk factors

The global Prevalence of Mild Cognitive Impairment ranges between 3% - 42% with India reporting about 4.3%.[5] The 2018 update by the American Academy of Neurology (AAN) highlighted that mild cognitive impairment (MCI) is common among the elderly with its occurrence increases with age.

Table 1 : Prevalence of MCI and Modifiable Risk factors

Age Group (Years)	Prevalence of MCI (%)[6]	Modifiable Risk Factors [7]
60-64	6.7%	-Metabolic conditions (e.g., diabetes) -Mental health concerns (e.g., depression) -Vascular issues (e.g., hypertension) -Lifestyle choices (e.g., poor nutrition, physical inactivity) -Social factors (e.g., isolation)
65-69	8.4%	
70-74	10.1%	
75-79	14.8%	
80-84	25.2%	

Smṛtibhraṃśa

MCI may be considered *Smṛtibhraṃśa* which is related to ageing. Though MCI is not mentioned as a separate disease in Āyurvedic classics, references about it get scattered. In *Ayurveda*, cognition involves *Jnaanotpatti*, [8] which includes *Medha* (grasping and retention), *Buddhi* (reasoning), and *Smṛti* (memory). These processes integrate *Indriyaartha*,[9] *Indriya*,[10] *Buddhi*, *Manas* (mind), and *Atma* (soul).

Medha declines after the fourth decade, signalling potential declines in *Smṛti* and *Buddhi*. Jarāvasthā (old age) and *Smṛtibhraṃśa* , dominated by aggravated *Vāta Doṣa* is influenced by *Hīna Satva (weak mental strength)*, *Rajas* predominant *Prakṛti (* a temperament dominated by activity and restlessness), stress, and a diet high in *Tamas* and *Rajas Guṇa (* qualities that cause dullness and agitation) , leading to diminished *Dhṛti* (cognitive resolve).Impaired manas(mental functions) and *Indriya(sensory organs)* result in incorrect or absent knowledge, with *Manovibhrama* (sensory deficits). An imbalance in *Doṣā* also vitiate corresponding *Manasadoṣas*; *Vāta* exacerbates *Rajas (*restlessness), and *Kapha* exacerbates Tamas(dullness). This results in *Agniduṣti (*disturbances in digestion), *Āmotpatti (*production of waste), *Doṣaduṣti* , and *Srotovaiguṇya (* impaired microcirculatory channels) , leading to *Apatarpaṇa* (nutritional deficiencies)and *Dhātu Vaiguṇya (*tissue impairment). These changes cause *Indriya Vaiṣamya* and *Manovaiṣamya (*sensory and mental imbalances), particularly affecting *Smṛti*.[11]

***Rasāyana* for MCI**

Rasāyana [12] is the therapy that destroys age related diseases. *Rasāyana* refers to therapeutic formulations or procedures when utilised consistently comprises will improve nutrition, general health, cognitive function, intellectual capacity, immune function, and longevity.[13] Early-stage cognitive disorders often lead to energy-protein malnutrition risks and micronutrients deficiencies primarily due to the aging process and the specific ways cognitive disorders can alter eating habits and energy balance.[14]

Rasāyana can be used as a preventive as well as early-stage management strategy. *Rasāyana* treatment improves nutrition by directly increasing the *Rasa dhathu* (vital fluids), optimizing *Agni* (metabolism) and supporting the function of *Srotas* (microvasculature)[15] *Prabhavajanya Karma* of these drugs also effect into multidimensional action on mental health. In classic textbooks, there are various drugs mentioned that affects *Dhi, Dhriti, and Smruti*. Thus, they could be

- *Medhya Rasāyana* (cognitive enhancers),
- *Vayasthapana* (anti-aging)
- *Naimittika* (disease-specific)

a. Medhya Rasāyana

Medhya Rasāyana is a subtype of *Kamya Rasāyana* intended to improve concentration, intellect, and memory. They enhance cognitive functions such as *Dhi (comprehension), Dhriti (retention),* and *Smriti*, and have a neuro nutrient effect by promoting cerebral metabolism. Medhya Rasāyana drugs are recognised for their ability to promote mental performance by boosting the functions of "*Buddhi*" and "*Manas*" while correcting imbalance in "*Rajas*" and "*Tamas*". Specific *Rasāyana* is said to promote and nourish respective *Dhatus* or tissues.[17]



Figure 3: Medhya Rasayana

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Mandukaparni (*Centella asiatica Linn.*) is restrained by blocking AChE, a neuroprotective brain growth promoter, and scopolamine-stimulated memory deterioration. *Yastimadhu* (*Glycirrhiza glabra Linn*.) improves memory, learning, and CNS circulation in dementia caused by scopolamine. *Tinospora cordifolia (Wild) Miers*, often known as *Guduchi* have properties that improve memory and learning, serve as an antioxidant, reduce stress, and improve both normal and cognitively impaired animals' cognitive function in behavioural tests. *Bhrama* (Vertigo), behavioral issues, mental deficiencies, and low IQ levels are all treated with it. *Convolvulus leuricaulis Chois*, or *Shankhapushpi* effective against C*hittod Vega* (anxiety disorders), reduces the stress caused by social isolation, improves overall motor function, and increases the antinociception created by stress.[19]

Table 2. Studies showing the effects of drugs in *Medhya Rasāyana*

***Medhya* Plant/Herb**	**Study Authors and Year**	**Study Participant/Type/ Intervention Type/Groups Assigned**	**Significant Findings**
Mandukaparni (Centella asiatica Linn.)	Effect of *Centella asiatica* on cognition and oxidative stress in an intracerebroventricular streptozotocin model of Alzheimer's disease in rats-[20] Veerendra Kumar MH, Gupta YK-2003	Male Wistar rats/Aqueous extract of C. asiatica (100, 200, and 300 mg/kg/day for 21 days)	C. asiatica at 200 and 300 mg/kg improved cognitive behavior in passive avoidance and elevated plus-maze tests. It reduced MDA levels, indicating less oxidative stress, and increased glutathione and catalase levels. It also protected against cognitive deficits caused by i.c.v. STZ.
	Centella asiatica (L.) Leaf Extract Treatment during the Growth Spurt Period Enhances Hippocampal CA3 Neuronal Dendritic Arborization in Rats-[21] Mohandas Rao KG, Muddanna Rao S, Gurumadhva Rao S.-2006	Neonatal rat pups (7 days old)/CeA fresh leaf extract (2, 4, or 6 ml/kg/day for 2, 4, or 6 weeks)	CeA extract at 4 and 6 ml/kg/day for 4 to 6 weeks significantly increased dendritic length and branching points in hippocampal CA3 neurons. This enhanced dendritic arborization in both apical and basal dendrites, highlighting CeA extract's potential to stimulate neuronal dendritic growth, beneficial for stress, neurodegenerative, and memory disorders.
	Neuroprotective evaluation of standardized extracts of *Centella asiatica* in monosodium glutamate-treated rats-[22] Ramanathan M et al-2007	Female Sprague Dawley rats/CA extract (100 and 200 mg/kg)	CA treatment improved catalase, SOD, and lipid peroxide levels in the hippocampus and striatum of MSG-treated rats, without altering glutathione levels. It protected general behaviour, locomotor activity, and the CA1 region of the hippocampus from MSG-induced neurodegeneration, attributed to its antioxidant effects. CA shows potential for treating conditions like epilepsy, stroke, and other glutamate excitotoxicity-related degenerative diseases.
Yasthimadhu (Glycirrhiza glabra Linn.)	Anxiolytic activity of *Glycyrrhiza glabra Linn*-[23] Ambawade SD, Kasture VS, Kasture SB.-2001	Mice/Hydroalcoholic extract (doses ranging from 10 to 300 mg/kg, i.p.)	Lower doses of Glycyrrhiza glabra extract effectively alleviated anxiety in animal models (elevated plus maze, foot shock-induced aggression, amphetamine-induced stereotypy). It increased open arm occupancy, delayed aggression onset, and reduced stereotypic behaviors, demonstrating anxiolytic activity.
	Memory-enhancing activity of *Glycyrrhiza Glabra* in mice-[24] Dhingra D, Parle M, Kulkarni SK.-2004	Mice/Aqueous extract (75, 150, and 300 mg/kg, p.o. for 7 days)	150 mg/kg of Glycyrrhiza glabra extract improved learning and memory in mice. It reversed amnesia induced by diazepam and scopolamine, possibly due to its anti-inflammatory, antioxidant properties, and facilitation of cholinergic transmission. Glycyrrhiza glabra shows promise as a memory-enhancing agent.
	The memory-strengthening activity of *Glycyrrhiza*	Mice/Aqueous extract (75, 150, and 300 mg/kg, p.o. for 7 days)	150 mg/kg Glycyrrhiza glabra improved memory in mice, reversing amnesia induced by diazepam, scopolamine, and ethanol, possibly due to anti-

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	glabra in exteroceptive and interoceptive behavioral models-[25]Parle M, Dhingra D, Kulkarni SK-2004		inflammatory, antioxidant effects, and enhanced cholinergic transmission.
Guduchi(Tinospora cordifolia (Wild) Miers.)	Effect of *Tinospora cordifolia* on Learning and Memory in normal and memory deficit rats-[26] Agarwal A et al-2002	Rats/Alcoholic and aqueous extracts of Tc (administered orally for 15 days)	Tc extracts (alcoholic 200 mg/kg, aqueous 100 mg/kg) improved learning and memory in rats. They mitigated cyclosporine-induced memory deficits and protected against hippocampal neurodegeneration.
	Rubia cordifolia, Fagonia cretica Linn. and *Tinospora cordifolia* exerts neuroprotection by modulating the antioxidant system in rat hippocampal slices subjected to oxygen-glucose deprivation-[27] Avinash KR, Manohar GM, Saibal KB.-2004	Rat hippocampal slices subjected to OGD/RC, FC, TC (OGD + drug-treated groups)	RC, FC, and TC protect rat hippocampal slices from oxygen-glucose deprivation (OGD) by enhancing antioxidant enzymes, scavenging free radicals, and modulating gene expression to reduce oxidative stress and neuronal injury.
Shankhapuspi (Convolvulus pleuricaulis Chois.)	Evaluation of comparative and combined depressive effect of *Brahmi*, *Shankhpushpi*, and *Jatamansi* in mice-[28] Indurwade NH, Biyani KR.-2000	Mice (66 mice of either sex)/ *Brahmi, Jatamansi, Shankhpushi,* and their combination	Combined Brahmi, Jatamansi, and Shankhpushpi extracts show potent depressive activity in mice, with Jatamansi exhibiting the strongest effect individually.
	A clinical study on the role of *Jaladhara* and *Shankhapushpi (Convolvulus pleuricaulis*) in the management of Chittodvega (anxiety disorder)-[29] Parsania S. Jamnagar: Dept. of Kayachikitsa, IPGT and RA, Gujarat Ayurveda University;-2001	36 patients with Anxiety disorders/Group-J: *Jaladhara* for 30 minutes daily in the morning for 6 weeks, with a 1-week gap after 3 weeks. Group-SR: *Sankhapuspi Rasāyana* (3 gms orally three times a day) for 6 weeks.	*Jaladhara* provided better relief in panic attacks and phobic disorders- *Sankhapuspi Rasāyana* was more effective in generalized anxiety disorder- Both therapies showed encouraging results and may be considered as first-line treatments for *Chittodvega* (Anxiety disorders).
	Effect of *Convulvulus pluricaulis Choisy.* on learning behaviour and memory enhancement activity in rodents-[30] Nahata A, Patil UK, Dixit VK-2008	Rodents (rats)/Ethanolic extract, ethyl acetate, and aqueous fractions of CP (100 and 200 mg/kg p.o.)	Significant improvement in learning and memory in rats- Reversed scopolamine-induced amnesia- Potent memory-enhancing effects in step-down and shuttle-box avoidance paradigms- Further studies are needed to identify the exact mechanism of action.

b. Vayasthapana Gana

Acharya Charaka identified ten drugs and listed them under *Vayasthapana Gana*. *Vayasthapana* dravyas are known to counteract the degenerative changes, promote longitivity with sustained health. A study on *Vayasthapana* [31] drugs indicated an 80% potential for Deepana action, 70% for Rasāyana action, 50% for both Balya and Medhya actions, 40% for Hridya action, and 20% for both Vrushya and Brumhana actions. These

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properties make Vayasthapana Dashakashaya particularly effective in slowing the aging process and reducing its negative impacts. The bulk of the ingredients in *Vayasthapana Dashakashaya* have pharmacodynamic qualities such as *Madhura rasa*, *Laghu Guna*, *Madhura Vipaka*, *Sheeta Veerya*, and *Tridoshaghna* characteristics. Through these properties the drugs have the above said actions.

Table 3 : Vayasthapana gana [C.Sutra 4/18]

Sl No	Name of Drug	Botanical name
1	*Amṛtā*	*Tinospora cordifolia Miers*
2	*Abhayā*	*Terminalia chebula Linn*
3	*Dhātrī*	*Emblica officinalis Gaertn*
4	*Rasna*	*Pluche alanceolata*
5	*Sveta Aparajita*	*Clitoria ternetia Linn.*
6	*Jivanti*	*Leptadenia reticulate W&A*
7	*Shatavari*	*Asparagus racemosus Willd*
8	*Mandukparni*	*Centella asiatica Linn.*
9	*Sthira*	*Desmodium gangeticum D.C*
10	*Punarnava*	*Boerhaavia diffusa Linn.*

c. Naimittika* (Disease-specific) *Rasāyana

Since *Smruti Bramsha* is the main feature of *Apasmara*, the line of treatment advocated for *Apasmara* can be applied for MCI. Formulations like *Mahapaishachika Ghritam*.[32] *Acharya Vagbhata* mentioned as *Bhudhi Medha Smrutikaram* and in *Brahmi Ghritam* [33] mentioned as "*Smruti Medhakrut*" can be symptomatically used against MCI.

Table 4: Evidence Based studies showing the effect of Naimittika Rasāyana (Compound Formulation) in Cognition

Medhya Formulation	Study, Authors and Year	Study Participants/Type/ Intervention Type/Groups Assigned	Significant Findings
Brahmi Ghrita	Beneficial effect of Brahmi Ghrita on learning and memory in normal rat[34], Kapil Deo Yadav, K. R. C. Reddy, and Vikas Kumar, 2014	24 normal rats, experimental study/ Group 1: Control, Group 2: BG 400 mg/kg, Group 3: BG 800 mg/kg, Group 4: Piracetam 500 mg/kg	BG and piracetam treated rats showed a significant decrease in transfer latency (improved learning) and increased step-through latency (improved memory) in a dose-dependent manner. BG enhances learning and memory similarly to piracetam.
	Critical review on effect of brahmi ghrita in psychiatric disorders[35], Prabhakar Manu , Suhas Kumar shetty , Savitha H.P, 2017	Multiple clinical and experimental studies/ Brahmi Ghrita (various dosages and conditions)	Brahmi Ghrita showed improved learning and memory, anticonvulsant action, CNS depressant activity, anti-amnestic actions, and effects on depression and ADHD in children. It was noted for its ability to cross the Blood Brain Barrier (BBB) and act on the brain.
	A Review on the Neuroprotective action of Brahmi ghrita [36] – A Polyherbal Ayurvedic formulation, Santhosh Chandrasenan, Amritha MS, 2021	Review of Ayurvedic classics and clinical practices/ BG1: Brahmi Ghrita with Brāhmī, Vacā, Kuṣṭha, Śaṅkhapuṣpī in equal parts; BG2: Brahmi Ghrita with 16 times Brahmi swarasa	Ghee-based polyherbal formulations are indicated for various neuropsychiatric disorders. BG1 and BG2 are traditional formulations with BG2 containing a higher concentration of Brahmi. BG2 lacks scientific evaluation, which is needed given its unique composition and clinical use.
Mahapaishachika Ghruta	Cognitive effect of mahapaishachik ghrita in diazepam Induced amnesia in adult mice [37], Dipali S Kashid, Sarita M Kapgate, 2020	Adult Swiss albino mice, experimental study/ Group 1: Normal control, Group 2: Disease control (Diazepam), Group 3: Standard control (Rivastigmine 2.4 mg/kg), Group 4: MG 5.2 gm/kg, Group 5: MG 10.4 gm/kg	Higher doses of MG showed reduced transfer latency (TL) and significant amelioration of Diazepam-induced amnesia compared to controls. MG demonstrated nootropic effects and prevented Diazepam-induced memory impairment.

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Amalaki Rasāyana & Rasa sindoor	Ayurvedic formulations amalaki Rasāyana and rasa sindoor improve age-associated memory deficits in mice by modulating dendritic spine densities[38], Bhupender Verma, Priyanka Sinha, Subramaniam Ganesh, 2022	Two-month-old mice, experimental study/Group 1: Amalaki Aasayana (AR, 1025 mg/kg per day), Group 2: Rasa Sindoor (RS, 41 mg/kg per day), Group 3: Regular chow control, Group 4: Blank jelly control	AR and RS significantly improved episodic, working, and reference-spatiotemporal memory. There was an increase in dendritic spine density in hippocampal neurons, but no significant effect on gliosis or corpora amylacea. AR and RS can prevent or delay age-associated cognitive decline.
Chyawanprasha	Beneficial effect of chyawanprash on cognitive function in aged mice[39], Nitin Bansal, Milind Parle, 2010	Young and aged mice, experimental study/Group 1-8: Young mice, Group 9-17: Aged mice, Chyawanprash (1% and 2% w/w of diet) for 15 days	Chyawanprash significantly improved memory in aged mice, decreased acetylcholinesterase activity, reduced brain TBARS, and increased GSH levels. This indicates enhanced cholinergic transmission and antioxidant effects, suggesting it as a useful memory enhancer.

DISCUSSION

The significant prevalence of Mild Cognitive Impairment (MCI) highlights the critical need for effective interventions to prevent or slow down its progression. The evidence from the findings strongly suggests that *Rasāyana* interventions have a significant impact on managing MCI. Numerous studies, whether directly or indirectly, have demonstrated the benefits of *Rasāyana* on MCI. Rasāyana formulations contain diverse phytochemicals that can work synergistically to influence neuronal metabolism within the central nervous system, particularly enhancing cognitive function in situations of neuronal damage or degeneration. Rasāyana may help to correct specific nutritional deficiencies that impact cognitive health, making it a valuable approach in countering cognitive decline. While the precise mechanisms by which Ayurveda Rasāyana improve cognitive functions are not fully understood, it is hypothesized that these interventions exert their effects, in part, through their well-documented antioxidant properties.

To successfully manage MCI, a mono therapeutic drug strategy may not be optimal. A pragmatic approach involves targeting the underlying MCI pathophysiology using a network-based, multi-therapeutic approach may be feasible and potentially more effective . While each individual strategies has been shown to reverse cognitive decline and increase neuroplasticity,their combined use could produce additive or synergistic effects.

CONCLUSION

MCI management and prevention have to be given due importance as MCI may progress to a more serious and irreversible condition like Alzheimer's disease. *Ayurveda* has the potential to address neurodegeneration and its effects on cognition. Treatments like *Rasāyana* have been found effective in improving cognitive abilities among the elderly with MCI, enhancing their overall quality of life. Considering the growing body of evidence suggesting potential benefits and the generally safe nature of *Rasāyana* administration, further studies are warranted to substantiate their efficacy, understand their mechanisms of action, and develop standardized protocols for their integration into clinical settings.

Conflict of interest:- Nil.

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