A Review on the Role of *Naladadi Ghrita* (A Polyherbal Medicated Ghee) in the Management of *Jarajanya Medhakshaya* (Age Related Deterioration of Intellect)

Mridula.M.K, P.Y.Ansary, Sara Money Oommen, V.V.Shincymol, Sethu.R

**INTRODUCTION**

India has experienced a dramatic demographic transition in the past 50 years with a tripling of the population over the age of 60 years and is expected to reach 158.7 million in 2025. An analysis of morbidity patterns by age indicates that the elderly experiences a greater burden of ailments compared to other age groups and mental health conditions play a significant role in their morbidity and premature mortality. Ageing being a risk factor for neurodegenerative disorders contributes to the...
development of dementia in a large number of people\(^5\). Among all neuropsychiatric conditions, dementia is a leading contributor of disability in the elderly and these shifts in the paradigm may affect the prevalence of dementia in India\(^6\). A study on the prevalence of cognitive impairment and dementia in community-dwelling Indians from Singapore reported that among elderly Indians the overall prevalence of any cognitive impairment is 24.6% including 1.2% of dementia\(^7\). Memory loss in elderly will raise concern over cognitive abilities or to general cognitive decline, and not just memory even though some degree of cognitive slowing is a part of normal aging\(^8\). They can’t transform information quickly to make a decision which shows impairment in speed of processing, working memory, and executive cognitive function\(^9\). But the safety and long-term therapeutic benefits of currently available interventions remain uncertain and due to these unsatisfactory pharmacological therapies, many people with dementia and cognitive impairment turn to complementary medicine. Present era witnessed a tremendous urge to explore medicinal plants globally for improving cognitive function owing to their less adverse effects. Also, CNS acting drugs are highly dose dependant and always tends to result with addiction accompanied with withdrawal symptoms.

Concept of ageing (jara) including changes in body and mental functions is beautifully described in classics of Ayurveda. Age(vaya) is divided into childhood (balyam), middle age(madhyam), and old age (vidhha) and Acarya Charaka mentioned that cognitive functions like power of understanding (grahana), power of retention(dharana), power of memorizing (smarana), speech (vachana), and functions of sense organs get affected in old age\(^10\). Sarangadhara samhita clearly emphasizes that intellect (medha) and wisdom (buddhi) start to deteriorate between the fourth and ninth decades of life\(^11\). Being a holistic science Ayurveda gives equal importance to body and mind in health and disease. Ayurvedic principles pointed out the coexistence of body(sartra), sense organs (indiya), mind (sattva) and soul(atama) as ayu and the main motive of Ayurveda is the protection of ayu\(^12\). ‘Medha’ means intellect or retention and ayurvedic classics used this word synonymously with buddhi, smriti and dhi to denote grahana sakthi (grasping power) and dharana Shakti (retention power)\(^13\). It provides the power to obtain the knowledge of existing object. Medha can be particularized as an individual’s specific intellectual ability to retain a large amount of knowledge (cognition) and for a long time\(^14\). Medha affects the happiness or misery of the ‘ayu.

So, protecting medha is essential for fulfilment of motive of ayurveda. Among major disabilities faced by elderly, deterioration of memory and learning has considerable impact on their health. Ayurveda recognises this condition as medhakshaya (deterioration of medha). Acharyas has given much emphasis on drugs which will promote medha (medhya dravyas). Though medhya karma is related to manas, its specific concern with nervous system is undoubted which is considered as a prabhavajanya\(^15\). They can be utilized for the prevention and treatment of medhakshaya. Several medicinal plants mentioned as rasayana drugs in ayurveda are primarily claimed as medhya since they have the ability of mental upliftment\(^16\).

Descriptions about various rasayanas in the form of rejuvenative recipes, dietary regimen, special health promoting behaviour and drugs can be seen in authentic ayurveda text books. Properly administered rasayanas can provide longevity, memory, intelligence and freedom from diseases. They are classified on the basis of benefit, method of use, or material used and aushadha rasayanas(drugs) plays a major role in rasayana chikitsa. Some of the aushadha rasayanas are organ and tissue specific and those specific to brain tissue are called medhya rasayana. They will help to retard brain aging and helps in regeneration of neural tissues besides producing antistress, adaptogenic and memory enhancing effects\(^17\). Powder of Glycyrrhiza glabra Linn (yashtimadhu churna), juice of Centella asiatica (L.) Urb. (mandukaparni swarasa), paste of Convolvulus pleuricaulis Choisy (shankhpushpi kalka) and Juice of Tinospora cordifolia (Willd.) Hook.f. & Thomson (guduchi swarasa) are advised to use as medhya rasayana by acharyas\(^18\). Apart from these single drugs many polyherbal formulations are described in Ayurveda classics which will perform medhya karma. Naladadi ghrita is such a formulation described in rasayana prakarana of Ashtanga hridaya and widely used medicine in Kerala. It contains around 17 herbs and Convolvulus pleuricaulis Choisy (Shankha pushpi) is the major ingredient\(^19\). Gupta and Mamidi reported that Naladadi ghrita is effective in the management of ADHD in children. They have observed a significant improvement in ADHD rating scale in children\(^20\). This review is an attempt to analyse the role of Naladadi ghrita in the management of medhakshaya due to ageing.

**MATERIALS AND METHODS**

Organized collection of data from classical text books of Ayurveda and electronic databases (pubmed and google
scholar). Ayurvedic literature relating to the formulation and ingredients of Naladadi Ghrita is collected from samhithas and nighantus. Botanical sources were identified from Indian Medicinal plants, a compendium of 500 species. Pharmacological evaluations conducted with the part used and phytoconstituents of individual drugs were collected from the research articles available online mainly through PubMed search engine. Ingredients of Naladadi ghritam as per Indian Medicinal Plants Vol (1-5)21(Table 1)

Indications22
1. By regular intake of this ghrita, even mute or retarded persons will become talkative which indicates its action in areas of speech (Jado api Vagmi Bhavet)
2. Regular use of this also improves the ability to understand, capacity to retain memories, ability to analyze and draw logical conclusions (Srutadhari)
3. Enhance the intellect and make a person more creative. (Pratibhavan)
4. Regular use will improve general health. (Aroga)

Method of preparation. As per the general method, paste of drugs(kalka), ghee(ghrita) and liquids(kwatha/swarsa) will be taken in a ratio of ¼:1:4 and will cook until it attains paka lakshanas24. Here as per the textual reference, 1 athaka of ghee (approx.2.56 kg) will be mixed with 10.24 kg of sankhpushpi swarasa and milk each. Then 0.64 kg of kalka prepared with the remaining ingredients will be added to this mixture and will be cooked in mild fire till paka lakshana.

Dose -General dose for snehakalpana is 1 pala25. But there are various factors to be considered before deciding the dose of a drug. Acharya Caraka stated that the standard dose of a drug is suited for young person(madhyamavastha)26. Sarngadharana elaborated the same by mentioning the age specific doses for powder(churna), paste(kalka) and decoctions(kwatha)27. Apart from this strength of the patient and disease, digestive power, bowel, sex, power of drug etc are also the determining factor for dose28. So, the dose of Naladadi ghrita should decide considering all these factors since there is no specification of dose in the textual reference.

Pharmacological Properties (Rasapanchakas) of the drugs from various Nighantus29 (Table 2)
It is difficult to explain the effect of all medhya drugs since they show varied properties. Nagarjuna opined that the medhya dravyas acts by their achintya veerya (prabhava).

They may act at level of rasa, agni, and srotas. They may stimulate and improve the function of agni30. Researches reported the role of digestion and metabolism in control of brain function. Since brain consumes an immense amount of energy relative to the rest of the body, the mechanisms that are involved in the transfer of energy from foods to neurons are likely to be fundamental to the control of brain function. Several gut hormones have been found to influence emotions and cognitive processes31,32. Some dietary components have been identified as having effects on cognitive abilities33,34. At level of Srotas, they may improve the circulation of rasa by opening and cleaning the micro channel and then ultimately improve the function of Medha.

As per Ayurveda principles, action of a dravya is decided by its rasapanchaka which are ultimately different combination of panchamahabhootas. They possess characteristics of satva, raja and tama. Since medha is attributed to predominance of satva guna, akashya tajasa and apya dravyas having satva guna predominance will improve medha. Analysis of rasapanchaka of Naladadi ghrita revealed madhura, tikta and katu rasa predominance in the ingredients. They are either madhura or katu in vipaka. Tikta rasa has a direct action on the promotion of medha. It performs their function by its laghu guna, deepana-pachana and srotosodhaka karma. Bitter substances are reported to possess potent effects to stimulate the secretion of gastrointestinal hormones and modulate gut motility35. Studies reported humans have bitter taste receptors (25 T2Rs) that are expressed in the oral cavity, gastrointestinal and neuroendocrine cells36. Madhura rasa also by promoting the formation of oja nourishes indriyas,manas and medha. Katu rasa possess deepana and pachana property. It dilates channels (srotosodhana). Seeta veerya and mahura vipaka promotes kapha and enhances dharana karma. Ushna veerya and tikta rasa promotes pitta and enhances grahana and smaranara (ie grasping power and memory)37. Sankhpushpi (Convolvulus pleuricaulis Choisy) is the main ingredient of Naladadi ghrita. Acharyas explained the medhya karma of this plant in various classics and it is said to be superior to other medhya dravyas. Hypotensive and tranquilizing effects of the plant is evident from various pharmacological studies. And some clinical studies have shown its beneficial effects in anxiety neurosis38. Nahata A etal reported a significant improvement in learning and memory in rats after treatment with ethanolic extract of Convolvulus pleuricaulis Choisy(CP)39. A study
by Jai Malik reported neuroprotective activity of CP extract against 3-NP-induced neurotoxicity and can be further explored for its efficacy against Huntington’s disease. Phytochemical evaluation of the plant revealed the presence of Kampferol, a natural flavonol which possess a wide range of pharmacological activities including neuroprotective and anxiolytic activity. 

_Nalada_ (Nardostachys jatamansi DC) is an ingredient of various Ayurveda formulations and acharyas explained its _medhya karma_. This plant has been claimed to possess antidepressant, sedative, antiparkinsonian and memory enhancing activities. Studies reported significant improvement in learning and memory in young mice after treatment with ethanol extract of the plant. They also reported reversal in aging-induced amnesia of mice. Administration of powdered roots daily for one month showed statistically significantly improvement in latency to falling asleep, duration and undisturbed restful sleep in Indian patients with primary insomnia of up to 5 years duration. Rucker G et al reported that one active sesquiterpene in this plant named valeronone exhibits activities typical for tranquilizers.

_Madhuka_ (Glycyrrhiza glabra Linn) is an important ingredient in many ayurvedic formulations. Parle M et al reported a significant improvement in learning and memory in mice after pre-treatment with aqueous extract for 7-days. Also a reversal in scopolamine-induced amnesia, decrease in brain AChE activity, and production of antidepressant-like effect were reported. Various studies reported significant enhancement in spatial memory retention and learning by pretreatment with its aqueous extract. Glycyrhrizin, a saponin present in this plant is residing in its volatile oil. Furthermore, its curative power is immense and appropriate medicines, its curative power is immense and adequate.

_Agaric (Agaricus arvensis)_ is also reported to possess sedative, and respiratory depressive activities of the rhizomes are also reported. Two bitter principles named acorin and acoretin are reported in this plant. Studies reported a significant free radical scavenging capacity of methanol and aqueous extracts of _Katuka rohini_ (Picrorhiza kurroa Royle ex Benth.) Studies reported a significant sedative effect in mice after treatment with sandal oil and alpha and beta santalols are responsible for sedative effect of sandalwood preparations. A clinical study reported significant subjective sedative effect by alpha santalol in healthy Thai volunteers. Invito antioxidant activity of _Terminalia chebula_ Retz is reported by various studies.

_Golechha_ M et al reported memory enhancing, and antioxidant activity of hydroalcoholic extract of _Emblica officinalis_ Gaertn. in scopolamine-induced cognitive impairment in mice. Antidepressant-like effect in mice was observed by treatment with aqueous fruit extract. Pretreatment of rats with hydroalcoholic extract improved cognitive deficit and ameliorated oxidative stress. Gallic acid, methyl gallate, corilagin, furosin and geraniin were identified as the chemical constituents responsible for nitric oxide scavenging activity.

Ginger powder and juice is reported to provide protection from oxidative stress, lowers lipid peroxidation and maintains activities of antioxidant enzymes, protection against behavioural dysfunction and Alzheimer-like symptoms in rats. Improvement in cognitive performance, memory impairment and antioxidant markers in cerebral ischemic rats were also reported. Studies reported that administration of methanol fruit extract of _Piper nigrum_ Linn improved memory and exhibited anxiolytic and antidepressant effects in spatial memory impairment in rat.

Enhanced learning and spatial memory in aged rats, significant increase in recognition memory, and protection of brain against neurotoxic insults by administration of _Curcuma longa_ Linn were reported. Curcumin supplemented-diet improved age-related cognitive functions in rats and significantly improved cognitive tasks, locomotor activity, oxidative defence in mice. Curcumin also protected against acute ethanol-induced memory deficit significantly reversed brain oxidative damage. Berberine, a major alkaloid of _Berberis arista_ Sims is reported to possess antidepressant activity.

Ghee is mentioned as best suited for those desirous of dhi (intelligence), smrithi (memory) and medha by acharyas. It is said to be beneficial for mental alertness and memory in adults as well in children. When processed with appropriate medicines, its curative power is immense and adequate.
can be used in several diseases\textsuperscript{98}. Acharya Vagbhata suggested daily intake of ghee before food for vayasthapan\textsuperscript{99}. Several ghee-based formulations are recommended by acharyas for the preservation and promotion of brain and neurological health especially in chapters dealing with Unmada and apasmara. These include Kalyana ghrita, Mahakalyana ghrita, Mahapaishaachika ghrita, Brahmi ghrita, and Lasunadi ghrita\textsuperscript{100}. Ingredients of Naladadi ghrita contain many lipophilic terpenoids, flavonoids etc. So, ghee medium will help to extract the maximum therapeutic properties of ingredients in to the formulation. Blood-brain barrier acts as a major obstacle to the delivery of drugs to the central nervous system. Membrane separating the central nervous system tissue and circulating blood is lipophilic. Thus, it selectively permits the passage of lipids and lipid-soluble drugs across it. Therefore, any drug given in the form of ghee will not only be processed and absorbed fast but also be able to reach some of the most hard-to-reach areas of the body like the CNS. This clarifies the better efficacy of various psychotropic drugs given in the form of ghee in CNS diseases\textsuperscript{101}. Acharya Vagbhata added Ksheera as an ingredient in Naladadi ghrita. Ksheera is the best jeevanceeya dravya and its daily use is will do rasayana karma. Goksheera is said to be having rasayana property. Also, balya, brimhana and kshayahara properties of the ksheera could make it to use in rasayana chikitsa.

DISCUSSION

Review of individual drugs of Naladadi ghrita revealed their role in digestion and various brain functions. Madhura, katu and tikta rasa predominant drugs by their nourishing role in the indriyas and manas, deepana and pachana properties and srotosodhana action helps to maintain the normal functioning of doshas and anulomna gati of vata. Srotosodhana action helps to normalise manovahasrotas also. Since regular use of this ghrita enhances physical health, it can be utilised as a nervine tonic. Researchers identified a relationship between enteric nervous system and neurological disorders\textsuperscript{102}. Concept of gut-brain axis links emotional and cognitive centres of the brain with peripheral intestinal functions and importance of gut microbiota in influencing these interactions are evident from recent researches\textsuperscript{103}. Studies has revealed a linking between several pathophysiological conditions with an impaired gut microbiome, the effects of which extend beyond the gut and in particular to the brain. This microbiome-gut-brain axis considerably affects neural function and pathophysiology like susceptibility to autism, neurodegenerative diseases\textsuperscript{104}. Considering these factors, we can identify Naladadi ghrita as an ideal drug for various neurological conditions including Dementia, Parkinsons disease, Alzheimer’s disease etc. Ayurveda system of medicine uses a single drug and polyherbal formulations for the treatment of various ailments. Use of polyherbal formulations dated back to the time of acharya sarpagadha and is said to be achieve extra therapeutic effectiveness. Scientific studies have revealed that combination of plants will produce a greater result as compared to individual use of the plant and also the sum of their individual effect through a positive herb-herb interaction known as synergism\textsuperscript{105}. Hence combination of drugs of Naladadi ghrita also may produce an extra therapeutic effectiveness by synergism and can be utilised for the treatment of various CNS disorders including jarajanya medhakshaya.

CONCLUSION

Satisfactory effect and safety of Ayurvedic polyherbal formulations making them one of the highly selected drugs of choice for treatment and prevention of various ailments. Naladadi ghrita is such a formulation indicated in rasayana prakarnana of Ashtanga hridaya and literature review of its individual drugs revealed its action on memory, learning and other neuroprotective activities. Correct and rational use of this formulation will help to prevent and treat various central nervous system disorders including Jarajanya medhakshaya.

Acknowledgements: - Nil
Conflict of Interest – None

Source of Finance & Support - Nil

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Available from: https://irjay.com;
Doi: https://doi.org/10.47223/IRJAY.2022.5119
Table 1 Ingredients of *Naladadi ghritam* as per Indian Medicinal Plants Vol (1-5)\textsuperscript{21}

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Botanical name</th>
<th>Family</th>
<th>Part used</th>
</tr>
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<tbody>
<tr>
<td>Nalada</td>
<td><em>Nardostachys jatamansi</em> DC</td>
<td>Valerianaceae</td>
<td>rhizome</td>
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<tr>
<td>Katukurohini</td>
<td><em>Picrorhiza kurroa</em> Royle ex Benth</td>
<td>Scrophulariaceae</td>
<td>rhizomes</td>
</tr>
<tr>
<td>Payasya</td>
<td><em>Pueraria tuberosa</em> DC</td>
<td>Fabaceae</td>
<td>tuberous roots</td>
</tr>
<tr>
<td>Madhuka</td>
<td><em>Glycyrrhiza glabra</em> Linn</td>
<td>Fabaceae</td>
<td>roots</td>
</tr>
<tr>
<td>Chandana</td>
<td><em>Santalum album</em> Linn</td>
<td>Santalaceae</td>
<td>heartwood</td>
</tr>
<tr>
<td>Sariba</td>
<td><em>Picrorhiza kurroa</em> Royle ex Benth</td>
<td>Scrophulariaceae</td>
<td>roots, stem</td>
</tr>
<tr>
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<td><em>Acorus calamus</em> Linn</td>
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<td>Haritaki</td>
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<tr>
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<td><em>Terminalia bellerica</em> Roxb.</td>
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<td>fruits</td>
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<td><em>Trichosanthes cucumerina</em> Linn</td>
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Table 2 Pharmacological Properties (*Rasadi Gunas*) of the Drugs from various Nighantus\textsuperscript{29}

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<td>Sara</td>
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