Kushmanda Ghrita: An Effective Management for Apasmara

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Abstract: Apasmara is a disease which has a lot of importance since ancient time because it affects all the aspects of life of an individual either an adult or it may be a child. It is a disease due to vitiation of three sharirik doshas and two manshik doshas. The clinical features of Apasmara can be correlated with epilepsy in modern medicine. The disease epilepsy is featured about disturbed normal pattern of neural activity causes strange sensation, occasional convulsion, muscles spasm and loss of consciousness. The treatment modalities of Apasmara are of many kinds in which Use of medhya rasayana is a unique method of treatment described in Ayurveda for Apasmara. Kushmanda Ghrita is a unique Ayurvedic formulation recommended in the management of various psychological disorders mentioned in Astanga Hridaya and also in Bhaishajya Ratnavali. In this article an attempt has been done to rationalize the use of Kushmanda Ghrita in the management of Apasmara (Epilepsy).

Keywords: Apasmara, Epilepsy, Kushmanda Ghrita, Medhya Rasayana.

1. Introduction

Apasmara (epilepsy) is defined by Acharya Charaka as Apagama (deterioration) of Smriti (retention) associated with BibhatsaChesta (seizers) due to derangement of Dhi and Sattva¹. The vitiated Dosha related to the condition are Vatadi three sharirik doshas and two manshik doshas (traja &tama). The main features of Apasmara are impairment in memory or awareness. Even though most of the times, it is considered as Manasrogas (psychic disorders), it is not a Mana-sroga. Apasmara is one of the diseases, which affects both Sharira and Manas.

Kushmanda Ghrita: As a potent antiepileptic

KushmandaGhrita has been described in Astanga Hridaya, in the context of ‘ApasmaraPratishedha’ i. e., Dhi - vak - Swa-rapradam (it improves intellect, word and voice) ². It is also mentioned in Bhaishajya Ratnavali³. There are 2 drugs used in the preparation of Kushmanda Ghrita in addition to go - ghrita. It contains Kushmanda swarasa, Yashtimadhu kalka and Go ghrita. Kushmanda has been repeatedly mentioned for its ‘chetovikaranasam’ (Psychological disorder) due to its medhya (noortropic) effect. Yashtimadhu is included in main Medhya rasayanas (noortropic drugs) by Acharya Charaka and it is commonly used for treatment of mental illness⁴. Ghrita is generally used in the psychic disorder and seem to improve the faculties of mind. Ghrita is considered as the best “snehadrayya” because of its speciality i. e. Sanskarṣayaamuvartanam (the continuance of refinement) means Ghrita carries the properties of drug without leaving its own inherent properties⁵.

<table>
<thead>
<tr>
<th>S. no.</th>
<th>Latin name</th>
<th>Family</th>
<th>Part used</th>
<th>Form</th>
<th>Ratio</th>
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<tr>
<td>Kushmanda</td>
<td>Benincasa hispida</td>
<td>Cucurbitaceae</td>
<td>Phala</td>
<td>swarasa</td>
<td>18 lit.</td>
<td>Medhya, anticonvulsant</td>
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<tr>
<td>Yashthimadhu</td>
<td>Glycyrrhiza glabra</td>
<td>Leguminosae</td>
<td>Mula</td>
<td>Kalka</td>
<td>250 gm</td>
<td>Medhya, anticonvulsant</td>
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<tr>
<td>Go - Ghrita</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 kg</td>
<td>Medhya</td>
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Kushmanda: Benincasa hispida

It belongs to the Cucurbitaceae family and also known as Kushmanda, winter - melon, asguard, Chinese water - melon, white guard or petha. It is described in Samhitas and Nighantas under Shakavarga, valliphala and koshatakikula. It is mentioned as a Rasayana, brihana, balya and Dhatupushitikar. In ancient time kushmanda is used instead of animal in yajna for sacrifice. It is a famous vegetable group in Asian communities for nutritional values, medicinal values and divine values.

Pharmacodynamic ⁶:

Rasa: Guru, Snigdha
Guna: Unripe Fruit - Snigdha, Guru, Pakwaphala - Laghu, Kshara
Vipaka: Unripe Fruit - Katu, Ripe Fruit - Madhura
Virya: Unripe Fruit - Sheeta, Ripe Fruit - Alpasheeta
Dosha - Karma: Vata - Pitta Shamaka, Ripe Fruit - Sarvadoshahara
Prabhava: Medhya

Classical indication: Medhya, Vrishhya, Bastishodhak, Shonitastapana, Brihana, Rasayana, Nidrajanana, Krimighan, Balya, Dahaprashmana, Trishnanigrahana, Kshayahara.

Therapeutic evaluation: It is mentioned as Medhya, Rasayana, Brihana, Balya and Dhatupushitikar. It is medhya due to prabhava. The mature fruits are said to increase digestive fire (Deepanam), diuretic (Vastishodhanam)⁷, appetizer. Due to its Madhura vipaka and Shitaviyra it acts as a Medhya dravya. Medhya Rasayana are known to have specific effect on mental performance by promoting Buddhi smiriti and Manas by correcting the disturbance of Rajas and tamas Dosha. They act at level of Rasa, act by stimulating and im-
proving the function of Agni, improve circulation of Rasa by opening and cleaning the microchannel and thus improving Medha function.

Chemical constituents: It contain vitamin. B - 12, a building block, which as direct impact on the energy level, brain functioning and cell metabolism. In various phytochemical studies showed that the major constituents of benincasa hispida fruits are voltileoils, flavonoids, glycosides, saccharides, proteins, carotenes, vitamins, minerals, b - sitosterin and ursinic acid.

Experimental studies: Anticonvulsant activity8: Anticonvulsant activity evaluated using chemo - convulsive agents such as pentylenetetrazole, strychnine and picrotoxin and maximal electro seizure (MES) model in mice at dose levels ranging from 0.2 - 1g/kg, IP. The extract at 0.2 - 0.6g/kg significantly inhibit the hind limb extension induced by MES and at 0.4 and 0.6 g/kg, the extract significantly increase the latency of convulsions and death induced by pentylenetetrazole and strychnine, However, even at 1 gm/kg the extract failed to protect the convulsion induced by picrotoxin. The fruit B. hispida possess potential anti - convulsant activity.

1) Antiepileptic activity9: Screening of antiepileptic activity of both swarasa and aqueous extract on albino rats using MES induced method shows, swarasa at the dose of 0.9ml/200 gm of rats show significant protection against shock induced convulsions. Aqueous extract at dose 100mg/200 gm of rats show lesser protection compare to swarasa.

2) Antipyretic activity10: Study results indicate that the ethanolic extract of kushmanda possesses potent antipyretic effect and pharmacological justifies its folkloric use for fever and pain conditions

3) Anti - angiogenic effect11: study showed the seed extract of kushmanda decrease Bgf - Induced endothelial cell proliferation and tube formation in a dose dependent manner. It showed no cytotoxicity and showed potent inhibitory effect on Bgf - induced angiogenesis in vivo. Seed extract of Kushmanda supports its anti - angiogenic property through inhibition of endothelial cell proliferation.

4) Gastroprotective/Anti - oxidant12: effect - Study resulted were comparable with the omeprazole treated group. Study showed decrease in ulcer index in animal treated with fruit extract of kushmanda contains active principle - Terpenes, flavonoide, glycoside and sterols which have antioxidant effect, probably helping to inhibit gastric mucosal damage by scavenging free radicals and repressing production of superoxide dismutase.

5) Bronchodilator effect13: effect of methanolic extract of kushmanda against histamine and acetylcholine induced bronchospasm in guinea pigs. The extract of kushmanda showed excellent protection against histamine - induced bronchospasm probably through an antihistamine activity.

6) Anti nociceptive and anti - pyretic activity14: In an experimental study the ethanol extract of kushmanda seed was used to study anti - nociceptive and anti - pyretic effects, yeast (15%) was used to induce pyrexia in rats. The extract was non - lethal to the rats up to the dose of 5000 mg/kg b. d. At doses of 250 and 500 mg/kg b. w, the extract significantly shows improvement.

7) Anti - Diarrheal activity15: study showed the methanol extract of fruit showed significant inhibitory activity against castor oil - induced diarrhea and inhibition PGE2 induced enteric pooling in rats. Result establish its efficacy as an anti - diarrheal agent.

8) Antioxidant/Alzheimer's disease16: Result revealed chronic treatment of kushmanda pulp extract markedly decrease lipid per oxidation level, significantly increase superoxide dismutase. CAT and reduced glutathione level in different part of the brain. Study showed the antioxidant property of kushmanda may be beneficial in the management of colchicines - induced rat model of Alzheimer's disease.

9) Anorectic/potential Anti - obesity benefits17: Study investigated the anorectic effect of the methanol extract of kushmanda in swiss albino mice. Result reveals, for the first time a possible anorectic activity of Kushmanda probably through CNS mediation, with no effect on gastric emptying.

Toxicology:
1) In a study of acute toxicity in rats, the aqueous and ethanolic extract of Benincasa hispida Were found to be safe and no mortality was observed at a dose as high as 5 g/kg bd.18
2) The chloroform extract was tested for its acute toxicity in albino rats (0.25 g/kg, 0.5 g/kg, 0.75 g/kg and 1 g/kg). The parameters which were observed were hyperactivity, sedation, loss of righting reflex, respiratory rate and convulsions. No toxic effects and mortality were recorded.19
3) In acute toxicity in rats, the aqueous and ethanolic extract of kushmanda was found to be safe and no mortality was observed at a dose as high as 5 gm/kg body wt.

Madhuyasthi: (Glycyrrhiza glabra) It is a small perennial herb, commonly known as licorice, sweet wood, or Mulathli. It is widely distributed worldwide and it consist of more than 30 species. The name Glycyrrhiza glabra was obtained from the Grecian words glukys, which mean sweet and rhiza, which means root, while the glabra species name refers to the smooth husks and it is from the latino word glaber that implies bare or slick.

Pharmacodynamic20:
Guna: Guru, Snigdha
Rasa: Madhura
Vipaka: Madhura
Virya: Sheeta
Dosha - Karma: Vata - Pitta Shamaka
Prabhava: Medhya

Classical indication - dahashamaka, Keshya, Vednasthanana, ShothaharaNadibalya, Medhya, Chhardinigrahana, Trishnaniagrahana, Vatanuloma, Mridurechana, Shonitasthapan, Kaphanisarakara, Kanthya, Mootrala, Kundughna, Jwarashamaka, Rasayana, Balya, Chakshushya.

Therapeutic evaluation:
It has Madhura Rasa, ShitaVirya, MadhuraVipaka and vata - pitta shamaka property. Yasthimadhu is Medhya by it’s

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Prabhava (special effect). Medhya Rasayanas strengthen the body and maintain normal body function. Medhya Rasayanas help to maintain Vata, Pitta, and Kapha - Doshas normal functions. Madhura, Shita qualities, Vatapitta shamaka and Rasayana effects of Yashimadhu bring about soothing effect, and probably this helps in bringing about Stairya and Dhriti to establish stability of mind and for enhancing memory.

Chemical constituents: the root of G. glabra Linn. contains the active principles, glycyrrhizin, glycoside, isoliquiritin, liquiritin, steroid estrogen, hispaglabridin B, isoliquiritigenin, and paratocarpin B. Experiments showed that G. glabra Linn. increases the blood circulation to the central nervous system and balances the sugar levels in the blood. The isoflavones glabridin and hispaplaglabridins A and B of G. glabra Linn. have significant antioxidant activity. The antioxidants protect susceptible brain cells from the oxidative stress, resulting in reduced brain damage and improved neuronal function, thereby enhancing the memory. Studies have proven that a chemical extract from the root of Yashimadhu named Glabridin reduces the brain cholinesterase activity and appeared to be a promising drug for memory improvement.

Experimental studies
1) **Antimicrobial Activity**[^21]: Hydro - methanolic root extract of mulethi exhibit potent anti-bacterial activity due to the presence of secondary metabolites such as alkaloids, flavonoids, saponins.
2) **Anticonvulsant activity**[^22]: the ethanolic extract of roots and rhizomes of Glycyrrhiza glabra various dose of extract (10, 30, 100 and 500mg/kg) delayed the onset of convulsions caused by pentylenetrazone and lithium pilocarpine.
3) **Hepatoprotective activity**[^23]: Glycyrrhizin a triterpene glycoside from root of Glycyrrhiza glabra, has positive effects on inhibition of hepatic apoptosis and necrosis by suppression of TNF-a and caspase -3, an important cytokine, which is a key mediator of hepatic apoptosis and necrosis in LPS/D-GaAIN - induce liver failure and down regulation of matrix metalloproteinase - 9 in Lipopolysaccharide/D - galactosamine - induced liver injury.
4) **Antifungal Activity**[^24]: It is due to its active compound like as glabridin which also demonstrates the resistance modifying activity against drug resistance mutants Candida albicans and Aspergillusniger.
5) **Anti - Malarial Activity**[^25]: The in vitro and in vivo antimalarial activity of 18 - b - glycirrhetic acid an active constituent of mulethi was found.
6) **Anti - Cancer Activity**[^26]: the polyphenol molecule extract of madhuyasthi shows cytotoxic effect on breast and prostate cancer cells.
7) **Immunomodulatory effect**[^27]: it possesses immunomodulatory effect at 100micro gm/ml concentration. It increases fabrication of T lymphocytes and macrophages from human granulocytes, it keeps the ascent for complexes related to autoimmune system.
8) **Antihyperlipidemic and anti hyperglycemic effect**[^28]: in a study oral dose of 100mg/kg of hyperglycemic acid possesses a suitable the anti - hyperglycemic effect in streptozotocin induced diabetic rats that is comparable with glibenclamide.
9) **Antioxidant activity**[^29]: studies reported that flavonoids have 100 times strong antioxidant activity when compared with antioxidant activity of vitamin E. This is due to free radical scavenging, metal ion chelating, hydrogen donating activity.
10) **Memory enhancing effects**[^30]: The dose of 150mg/kg of the aqueous extract of liquorice significantly improved learning and memory of mice.

Toxicology
1) 100mg/day glycyrrhizin which approximates to 60 to 70 gm of liquorice is safe but more than this can reduce blood potassium levels resulting in abnormal heart rhythms, high blood pressure, edema, lethargy, heart failure and hypokalaemic myopathies manifesting flaccid paralysis[^31].
2) The United States Food and Drug Administration believes that foods containing liquorice and its derivatives is safe if not consumed excessively. Other jurisdiction has suggested about 100 mg to 200 mg of glycyrrhizin / day, the equivalent of about 70 gm to 150 gm of liquorice is safe[^32].

**GO - GHrita** - In Ayurvedic Literature Chaturvidha Sneha are described by nearly all Acharyas. These are ghrita, taila, Vasa and Majja. Here ghrita indicates ghee, Taila is oil, Vasa is fat of the body and Majja means bone marrow. In all of these Ghrita is most important because it has more medicinal benefits due to its Samskaranavartiguna, so it is used in many medicinal preparation. In sneha - paka Kalpana ghrita is the main basic ingredient. Go - ghrita is an oily liquid or semi solid, granular, and white or light yellow in appearance.

**Pharmacodynamic**[^33]:
Rasa: Madhura
Guna: Snigdha, mridu, guru, yogvahi
Virya: Sheeta
Vipaka: Madhura
Dosha shamakata: Tridoshashamaka

**Classical indication**: Agnidipana, balya, cakshushya, dipana, hridya, medhyaRasayana, snehana, ojovardhaka, vayaasapana, virya

**Therauptic evaluation - Go - ghrita** used as the base of formulation in Kushmanda Ghrita. Properties of Ghrita are Madhura Rasa, Guru, Snigdha Guna, Mridu, Sheeta Virya, Madhura vipakaand act as Tridoshahara, Agnideepana, Ayushya, Balya, Dipana, Hridya, Medhya, Oja - vardhaka, Rasayana. Ghrita proven for itself possessing Medhya property.

As Go - Ghrita is a good medium for absorption, transport and delivery of drug. Physico - Chemically Ghrita is lipid in nature. Because of this property it rapidly cross the blood brain barrier, which in turn enhance drug feasibility to the brain. It may facilitate drug non obstructed quick entry into the targeted cell and enhance memory. Go - Ghrita is oil that can bond with lipid - soluble nutrients and herbs to penetrate the lipid - based cell walls of the body. Thus, it increases the potency of certain herbs by carrying the active components.
to the interior of the cells. It are also used as a carrier of nutrients to be absorbed across the cell membrane. The potency and efficiency of a drug is usually dependent on its

Experimental studies
1) Cardioprotective activity[34] - The American Heart Association recommends limiting the consumption of saturated fats to less than 7% of energy to reduce the risk of cardiovascular disease. Previous results from laboratory indicates that 5 and 10% ghee supplemented diets fed for 2 weeks to 2 months did not have any significant effect on serum total cholesterol and triglyceride levels in Sprague - Dawley rats, how ever a 10% ghee supplemented diet fed for 2 months increased total cholesterol and triglyceride levels.
2) Anti cancerous activity[35] - As per a study published in the journal nutrition shows that cow ghee contains various fatty acids which enhance the anti tumor effect of CLA. This was a study conducted on mice implanted with breast cancer cells, one group of mice were fed a diet with a high level of corn oil and second group received standard food in addition to CLA and one final group received CLA combined with ghee, As per findings the group which consumed ghee had far fewer areas where cancer had taken hold (metastases) the ghee also brought down the amount of CLA to a level that was necessary to have an effect.
3) Anti Alzheimers activity[36] - Cow ghee is also a great source of butyric acid a short chain fatty acid that is good for our gut. Butyric acid antiviral anti cancer properties and also aids in prevention and treatment of Alzheimers.
4) Anticarcinogenic activity[37] - In a recent issue of Indian journal of medical research, scientist from the National dairy research institute (NDRI) have reported that cow ghee enhances the availability of those enzymes that contribute to detoxification of cancer causing substances, Ghee also reduces availability of those enzymes that are known to activated carcinogens.
5) Anticonvulsant activity[38] - Ghee contains vitamin a, d, e and k. Vitamin in which a and e are anti - oxidant and are useful in preventing oxidative damage to the body &brain. He concluded that most of the components have anticonvulsant activity through one or other mechanism[37].

Mode of Action of Kushmanda Ghrita on Aspamara:
In drug Kushmanda Ghrita all the content like Kushmanda Swarasa, Madhuyasthi Kalka and Go - Ghrita are mainly vata - pitta shamsaka and therapeutics properties like Bhirnana, Virshya, Medhya and Vaka Visadhikara. The study drug “Kushmanda Ghrita” possesses Madhura rasa, guru snigdh aguna, sheeta vyra and madhura vipaka nourishes the body and tranquilizes the mind leading to Dhhee, Dhriti And Smriti. Madhura Rasa promotes ojas and nourishes five senses, Mind and Medha. Kushmanda Ghrita having Medhya property produces good quality of Sadhaka Pitta responsible for comprehension and data analysis. It uplifts the Sattva Guna and Counteracts the aggeravated Rajas and Tamas guna. It acts on Agni especially the Bhutagni responsible for nutrition to brain cells by improving the process of transformation and assimilation. It promotes Clearance of Srotas i. e. microcirculatory channel in body leading to better bioavail-
ability of nutrition and tissue perfusion. Thus Medhya Rasayana may help in promotion of nutritional status of nervous system to improve function of Medha.

2. Discussion
Aspamara is a disease mainly due to Smriti - Naasha (loss of memory). In drug Kushmanda Ghrita all the contents are Medhya in their property. Medhya Rasayana are known to have specific effect on mental performance by promoting Buddh, Smriti And Manas by correcting the disturbance of Raja and Tama. They act at level of Rasa, act by stimulating and improving the function of Agni, improve circulation of Rasa by opening and cleaning the microchannel and thus improving medha function.

3. Conclusion
Kushmanda Ghrita act as a memory booster by its “prabhava” effect. As per its rasa, virya, vipaka Kushmanda Ghrita act as a medhya and balya also. Kushmanda Ghrita by attaining prakritik Avalambaka and Tarpaka kapha, normal functioning of Prana Vayu and Sadhaka pitta, elevation of ojas, upliftment of Sattva guna, re - establishment of Dhriti and Smriti, correcting the disturbed Raja and Tama by eliminating Srotorodha helps in relieving the sign of Aspamara like Smriti naash (loss of memory), vibithascheta (Abnormal movements) etc. After reviewing these facts it may concluded that kushmanda ghrita is a potent antiepileptic drug.

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