Review Article

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AN OVERVIEW OF SIDDHA POLYHERBAL FORMULATION: MILAGU LEGIYAM

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ABSTRACT

Milagu Legiyam is a polyherbal Siddha formulation mentioned in the Siddha literature "Aathmaratchamirtham". It indicates silethumam 96. In the Siddha system of medicine, the clinical presentation of acute pharyngotonsillitis is described under "virana silethumam". Vitiation of kabam is responsible for the virana silethumam. According to modern medicine, this occurs due to the viruses and beta-hemolytic group A streptococci. Nowadays, this is a common illness in children that often leads patients to consult paediatricians. The hot potency of the ingredients of Milagu Legiyam plays the leading role in the management of virana silethumam. Hence, this review highlights the fields of research conducted on the ingredients of Milagu Legiyam. The data was collected from the scientific databases and various textbooks. This review revealed the presence of antimicrobial, antiviral, antioxidant, anti-inflammatory, analgesic, antipyretic, anthelmintic and anticancer activities.

Keywords: Milagu legiyam, silethumam, tonsillitis, Siddha, antimicrobial, streptococcal infection

INTRODUCTION

Siddha is one of the traditional systems of medicine in India. Siddha formulations are derived from herbs, metals, minerals and animal origin. Siddha medicine comprises 32 internal and 32 external medications. Legiyam is the semisolid preparation of herbal drugs prepared in decoction or extracts of different herbs by adding sweetening agents like jaggery. It retains its effectiveness for six months[1]. Milagu Legiyam is a polyherbal Siddha formulation mentioned in the Siddha literature "Aathmaratchamirtham". It indicates silethumam 96 (Kabam)[2]. In the Siddha system of medicine, the clinical presentation of acute pharyngotonsillitis is described under "virana silethumam". This occurs due to the vitiation of kabam. The ushna viryam (hot potency) of the ingredients present in Milagu Legiyam pacifies the kabam and treats acute pharyngotonsillitis. Nowadays, this is a common illness in children that often leads patients to consult paediatricians[3]. There are about 7,455,494 cases of tonsillitis in India per year, and about 200,000 tonsillectomies are performed in India per year[4]. Viruses account for over 50% of all cases of pharyngotonsillitis[5]. Beta-hemolytic group A streptococci (e.g., *Streptococcus pyogenes*) are responsible for 15–30% of all pharyngotonsillitis[6].

The antibiotic more commonly prescribed by paediatricians for treating bacterial pharyngotonsillitis is phenoxymethylpenicillin[7]. The poor immune system of children is responsible for recurrent pharyngotonsillitis. The repeated inflammation of the tonsil gland causes the enlargement, which is irreversible after medications. This is the main reason for tonsillectomy in school-going children and adolescents[8]. 35% of cases fail in the treatment of penicillin[9]. So, this is the right time to explore the cure for pharyngotonsillitis in traditional medicine. Hence, this review highlights various research fields in Siddha, including literary, fundamental, drug, pharmaceutical and clinical research.

Review of Milagu Legiyam: The ingredients of Milagu Legiyam are mentioned in Table 1[10].

Table 1: Ingredients of Milagu Legiyam

Tamil name	Botanical name	Quantity
Milagu	*Piper nigrum*	100 palam (3500 grams)
Akirakaram	*Anacyclus pyrethrum*	1 palam (35 grams)
Seeragam	*Cuminum Cyminum*	1 palam 35 grams)
Kirambu	*Syzygium aromaticum*	1 palam (35 grams)
Vaividangam	*Embelia ribes*	1 palam (35 grams)
Elam	*Elettaria cardamomum*	1 palam (35 grams)
Paththiri	*Myristica fragrans*	1 palam(35 grams)
Narukkumoolam	*Piper longum*	1 palam(35 grams)
Kostam	*Costus speciosus* J. Konig	1 palam(35 grams)
Athimadhuram	*Glycyrrhiza glabra*	1 palam(35 grams)
Karkandu		10 palam (350 grams)

Method of preparation: All the drugs mentioned above should be powdered separately except pepper and mixed. Pepper is crushed and added to 1 thooni (21.5 L) of water and made as decoction (1:8). Ten palam (350 gm) of rock candy is added to the filtered decoction and heated till it attains string consistency.

Add the powdered raw drugs to the above mixture and stir well. Add 1padi (1400 ml) Ghee and stir well until it reaches the required consistency. Add ½ padi (700 ml) honey and blend well. Store it in a separate, dry, airtight container.

Indications: Silethumam 96, neer thodam, visham, vatham.

Milagu (*Piper nigrum*)

Parts used: Seeds
Family: Piperaceae
Chemical constituents: Piperine and other phytochemicals such as amides, piperidine, pyrrolidines, and trace amounts of safrole are present[11].
Pharmacological activity: Taqvi *et al*. noted the anti-hypertensive action of pepper due to the presence of piperine[12]. Zou L *et al*. reported the chloroform extract of black pepper has antimicrobial activity against *Escherichia coli* and *Staphylococcus aureus*[13]. Black pepper has been said to have a gastrointestinal activity to increase appetite, piles, anti-diarrheal, antispasmodic and anthelmintic[14]. Piperine is responsible for the antidepressant activity of black pepper[15]. Few studies have revealed the anticancer, cytotoxicity and antitumor potential of piperine[16-19]. Jeena *et al*. recorded that black pepper possesses great antioxidant activity[20].

Akkirakaram (*Anacyclus pyrethrum)*

Parts used: Root
Family: Asteraceae
Chemical constituents: Sarcosine, N-(trifluoroacetyl)-butyl ester, levulinic acid, malonic acid, palmitic acid, morphinan-6-One,4,5.alpha.-epoxy-3-hydroxy-17-methyl,2,4-undecadiene-8,10-diyne-N-tyramide, and isovaleric acid[21].
Pharmacological activity: Manouze *et al.* reported the antioxidant activity of *A.pyrethrum* through three studies: 2,2-diphenyl-1-picrylhydrazyl (DPPH), ferric-reducing antioxidant power (FRAP) and beta carotene bleaching (BCB)[22]. The aqueous root extract of *A. pyrethrum* administered on diabetic rats induced by alloxan and streptozotocin significantly lowers the blood glucose levels[23]. *A. pyrethrum* possesses neuropharmacological activities such as anesthetic[24], antidepressant[25], and anticonvulsant[26]. Analgesic activity of *Anacyclus pyrethrum* demonstrated by formaldehyde and acetic acid method. Anti-inflammatory activity of different parts of *A. pyrethrum* exhibited on carrageenan-induced paw oedema in rats[27].

Seeragam (*Cuminum Cyminum*)

Parts used: Seeds
Family: Apiaceae
Chemical constituents: b-pinene, p-cymene, g-terpinene, and cuminaldehyde[28].
Pharmacological activity: Cuminaldehyde and cuminol in Cumin seeds significantly reduce the blood glucose levels in streptozotocin-induced rats[29]. Cumin seeds have great antimicrobial activity[30]. At a concentration of 0.1 microl/ml, oil of *Cuminum cyminum* destructed Hela cells by 79% and showed antitumor activity[31,32]. The hypocholesterolemic effect of methanolic extract of Cuminum cyminum (MCC) was revealed in ovariectomized (OVX) rats[32]. Acetic-acid-induced writhing, hot plate, Carrageenan-induced paw oedema and Cotton-pellet granuloma methods were used to evaluate the analgesic and anti-inflammatory effects of *Cuminum cyminum* extracts. These studies significantly reduced the pain and inflammation[33-36].

Kirambu (*Syzygium aromaticum*)

Parts used: Dry flower buds
Family: Myrtaceae
Chemical constituents: Sesquiterpenes, monoterpenes, eugenol acetate, eugenol, carvacrol and β-caryophyllene[37]
Pharmacological activity: *Syzygium aromaticum* extract was the most active against multi-drug resistant and gram-negative uropathogens[38]. Clove has a potential antioxidant property tested by using 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid), oxygen radical absorbance capacity, ferric-reducing antioxidant power, xanthine oxidase, and 2-deoxyguanosine[39]. Eugenol and carvacrol could exert promising antifungal agents for treatment and prophylaxis for vaginal candida[40]. Eugenol was isolated from clove and tested against Herpes virus strains, which are effective[41]. Eugenol is responsible for the analgesic activity of cloves[42].

Vaividangam (*Embelia ribes*)

Parts used: Seeds
Family: Myrsinaceae.
Chemical constituents: Vilangin, embelin, christembine (alkaloid), phenolic acids such as caffeic acid, vanillic acid, chlorogenic acid, cinnamic acid, and o-coumaric acid[43]. Embelinol, embeliaribyl ester and embeliol are also present[44].
Pharmacological activity: The aqueous extract isolated from the fruit of the *E. ribes* significantly lowers the blood glucose levels in type 2 diabetes rats[45]. The methanolic and aqueous extracts of *Embelia ribes* showed antibacterial activity against *Salmonella typhi*, *Staphylococcus aureus, Streptococcus pyogenes, Shigella flexneri, S. sonnei*, *Pseudomonas aeruginosa, E. coli* and *Klebsiella*[46-48]. The *Embelia ribes* showed a potent anthelmintic property compared to other plants like *Gynandropsis gynandra, Impatiens balsamina, Celastrus paniculatus* and *Mucuna pruriens*[49]. The embelin component and its salts showed analgesic activity, while the 2:5 isobutyl amine embelin showed significant analgesic properties[50]. The antioxidant activity of *Embelia ribes* was revealed through DPPH radical and hydroxyl radical-induced deoxyribose degradation[51].

Elam (*Elettaria cardamomum)*

Parts used: Unripe fruit
Family: Zingiberaceae
Chemical constituents: 8-cineole, α-terpinyl acetate, α-terpineol, sabinene, nerol, linalyl acetate, linalool, limonene, 4-terpineol, α-pinene, β-pinene, myrcene, octanal, p-cymene, geranyl acetate, β-caryophyllene, β-selinene, γ-cadinene, trans linalool oxide, α-tocopherol, γ-tocopherol, δ-tocopherol, oleic acid, palmitic acid, linoleic acid[52].
Pharmacological activity: The aqueous extract of *E. cardamomum* seeds using the enzyme-linked immunosorbent assay revealed significantly enhanced and suppressed T helper (Th)1 and (Th)2 cytokines released by splenocytes and exerted proinflammatory and anti-inflammatory roles. It also possesses the anticancer activity[53]. Cardamom oil has potent antioxidant activity through an increase in the levels of glutathione[54]. The anti-inflammatory and analgesic activity was demonstrated using the carrageenan-induced rat paw oedema and p-benzoquinone-induced writhing method. Studies reveal that antispasmodic action is produced through muscarinic receptor blockage[55]. Crude extract from fruit showed diuretic and sedative activity[56].

Paththiri (*Myristica fragrans*)

Parts used: Outer shell of seed
Family: Myristicaceae
Chemical constituents: Myristicin, elemicin, safrole, terpenes, alpha-pinene, beta-pinene, myristic acid, and trimyristin[57,38]
Pharmacological activity: The methanolic extract of *M. fragrans* had antibacterial properties and inhibitory solid activity against *Streptococcus mutans*, an oral pathogen causing dental caries[59]. Dihydroguaiaretic acid from mace has also shown actions against *Helicobacter pylori*[60]. The petroleum ether extract showed activities similar to non-steroidal anti-inflammatory drugs[61]. Mace lignan isolated from *M. fragrans* had a hepatoprotective effect on cisplatin-induced hepatotoxicity in mice[62]. The methanolic extract of nutmeg seed showed good antioxidant activity by methods of 2,2-diphenyl-1- picrylhydrazyl (DPPH) and ferric reducing antioxidant power (FRAP) due to high content of tannins, flavonoids, and terpenoids[63].

Narukku Moolam (*Piper longum*)

Parts used: Root
Family: Piperaceae
Chemical constituents: Cepharadione B, cepharadione A, cepharanone B, aristolactam A II, Norcepharadione B, 2-hydroxy1-methoxy-4H-dibenzo, quinoline-4, 5(6H)-dione, 10-amino-4-hydroxy-3-methoxyphenanthrene-1-carboxylic acid lactam [piperolactam A], 10-amino-4-hydroxy-2, 3-dimethoxyphenanthrene-1-carboxylic acid lactam [piperolactam B], pluriatilol, fargosin, sesamine, asarinine, guineensine, and pipercide[64].
Pharmacological activity: Khan and Siddiqui reported the extracts of *P. longum* L. have antimicrobial activity against *Staphylococcus albus, Salmonella typhi, P. aeruginosa, E. coli, Bacillus megaterium*, and *Aspergillus niger*[65]. *P. longum* extract in variable doses possesses significant action to reduce the rectal temperature of rats[66]. Sharma tested the antiviral activity of *P. longum* against ribosome-inactivating proteins (RIP) by inhibiting the proteins in viral infections[67]. The immunoregulatory potential of *P. longum* was also exhibited. Vedhanayaki *et al.* evaluated the analgesic activity of *P. longum* root using rat tail-flick method and acetic-acid writhing method[68]. Stöhr *et al.,* the Piper extracts and piperine possess inhibitory activities on prostaglandin and leukotrienes COX-1 inhibitory effect and thus exhibit anti-inflammatory activity[69].

Kostam (*Costus speciosus*)

Parts used: Root
Family: Costaceae
Chemical constituents: Diosgenin, gracillin, dioscin, pro sapogenins A and B of dioscin, eremanthin, costunolide, β-sitosterol, β-D-glucoside, β-carotene, α-tocopherol quinine, dihydrophytylplastoquinone, 5α-stigmast-9(11) en3β-ol, tetracosanyl octadecanoate, methyl hexadecanoate, methyl octadecanoate, cycloartenol, cycloartanol, and cycloalaudenol[70].
Pharmacological activity: Diosgenin, along with an important sesquiterpene, costunolide performs significantly high antioxidant, anticancer and antidiabetic activities[70,71]. The diuretic potential of *C. speciosus* has been done on Wistar albino rats using different plant extracts such as leaves and rhizomes[72]. Moderate level of antispasmodic activity exerted in the different extracts of *C. speciosus*[73]. Methanolic and aqueous extracts of the *C. speciosus* have shown anthelmintic activity against one of the most common and widely spread worms, *Pheretima posthuma. C. speciosus* showed antibacterial activity against bacteria such as *Staphylococcus aureus, Salmonella, Bacillus subtilis, Shigella, Klebsiella pneumoniae, Pseudomonas,* and *Escherichia coli*[74]. It also possesses anti-inflammatory activity[75],

Athimathuram (*Glycyrrhiza glabra*)

Parts used: Root
Family: Fabaceae
Chemical constituents: Glycyrrhizin,18β-glycyrrhetinic acid, glabrin A and B, and isoflavones[76].
Pharmacological activity: The compound glycyrrhizin is responsible for the antiviral activity against coronavirus and Human Immunodeficiency Virus[77,78]. Some studies revealed the anticancer activity in vitro human hepatic cell lines[79] (Huh7, HepG2, Sk-Hep-1) and human gastric cancer cell lines[80] (MKN-28, AGS, MKN-45). The glabridin exhibits the great antioxidant[81] and anti-inflammatory activity[82]. The antimicrobial activity of liquorice was revealed against *Staphylococcus aureus*[83], *Mycobacterium tuberculosis*[84] and *Pseudomonas aeruginosa*[85].

CONCLUSION

The present review on Milagu Legiyam showed that the ingredients present in this formulation had antimicrobial, antiviral, antioxidant, anti-inflammatory, analgesic, antipyretic, anthelmintic and anticancer activities. Hence, this medicine might be effective in acute pharyngotonsillitis even with co-morbid conditions. Further clinical studies are warranted to prove the efficacy of Milagu Legiyam in tonsillitis patients.

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