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A Detailed Drug Review on *Seethamsa Rasam* with Reference to Classical Siddha Texts and Contemporary Evidence

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Abstract

Seethamsa Rasam (SR) is a classical herbo-mineral formulation referenced in authoritative Siddha text *Anuboga Vaidhya Navaneetham*. Traditionally indicated for fever *(Suram)*, inflammatory disorders, pain, and *Vatha-Pitha* derangements, SR plays a significant role in Siddha therapeutics. This review evaluates *Seethamsa Rasam* by analyzing its classical background, ingredient profile, preparation method, pharmacological basis and therapeutic actions. Siddha pharmacodynamics attribute SR with *Kaippu, Kaarppu,* and *Thuvarppugunam,* conferring analgesic, antipyretic and anti-inflammatory effects.Primarily indicated for the management of *PithaNoigal* (hyper-reactive Pitta disorders), pyrexia of unknown origin (PUO), intermittent fevers, dyspepsia, and systemic burning sensations, this preparation strategically integrates purified mineral lattices with a potent polyherbal matrix. This comprehensive review evaluates the classical textual lineage, standardized manufacturing methodologies, therapeutic mechanisms, and contemporary biomedical evidence of SR, integrating traditional knowledge with modern scientific interpretations. It highlights SR as a potent formulation that warrants further pharmacological and clinical validation.

Keywords: Seethamsa Rasam, Siddha medicine, Herbo-mineral formulation, Review.

1. Introduction

Siddha medicine is one of the oldest traditional systems of medicine originating in southern India, with root believed to trace back thousands of years. Siddha is a holistic health system addressing physical, psychological, social and spiritual well-being[1]. Herbal remedies, minerals, and animal products are used in treatment. The internal medicines are classified into 32 types in this system, one among them is *mathirai* which has half-life of one year. *Mathirai*is prepared by grinding raw materials with some leaf extract or decoction and made into small sized pills[2]. *Seethamsa Rasam*, a herbo mineral formulation, is used for many years in Siddha system of medicine has been indicated for *Seedhasuram* (Fever), *Soolai* (Throbbing pain), *Vaadhapaandu* (Anaemia), *Kaamalai* (Jaundice), *Suvasakaasam* (Bronchial asthma), *Udharanoigal* (Blood related disorders), *Katti* (Tumour), *Magodharam* (Acitis) and *Yaanaikaalvaatham* (Filariasis)[3]. Pathologically elevated *Azhal* (or *Pitha*) accelerates cellular metabolism, resulting in hyperthermia, inflammatory cascades, and visceral burning sensations. Seethamsa Rasam is formulated as a potent antipyretic and refrigerant compound. It functions by neutralising metabolic endotoxins, mitigating respiratory congestion, and down-regulating systemic inflammatory markers to restore humoral equilibrium.

2. Materials and Methods

Table 1. Ingredients of *Seethamsa Rasam*

S. No	The vernacular name of the ingredients	Botanical name/Chemical name	Quantity
1.	Purified *Thaalagam*	Yellow arsenic trisulphide	35gm
2.	Purified *Manosilai*	Red orpiment	35gm
3.	Purified *Nervaalam*	*Croton tiglium*	35gm
4.	Purified *Chukku*	*Zingiber officinale*	70gm
5.	Purified *Milagu*	*Piper nigrum*	70gm
6.	Purified *Thipilli*	*Piper longum*	70gm

Figure 1: *Thaalagam*

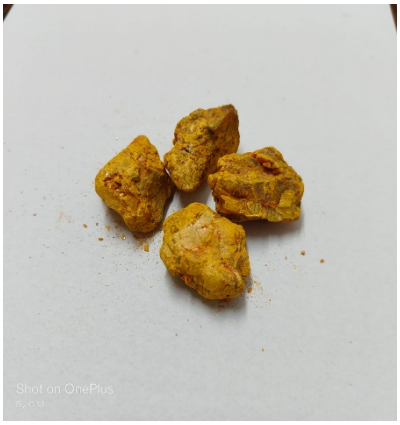

Figure 2: *Manosilai*

Figure 3: *Nervaalam*

Figure 4: *Chukku*

Figure 5: *Milagu*

Figure 6: *Thipilli*

2.1. Standard Operating Procedures: Purification and Processing

2.1.1. Purification of *Thalagam*(Yellow arsenic trisulphide): Yellow arsenic trisulphide is placed in between lime stone and palm toddy is poured to it. This process is repeated for 10 times[2,5].

Figure 7: *Thaalagam* is placed in between lime stone

Figure 8: After palm toddy is poured

2.1.2.Purification of *Manosilai* (Red orpiment):

Red orpiment is purified by boiling with lemon juice [2-4].

Figure 9: *Manosilai* after purification

2.1.3.Purification of *Nervaalam* (*Croton tiglium*)[6,7]

Figure 10: *Croton tiglium* tied with a cloth to hung within the pot

Figure 11: *Croton tiglium* is immersed in cow dung extract and heated

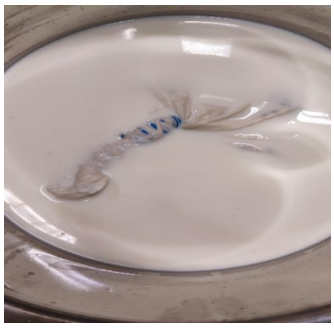

Figure 12: *Croton tiglium* is immersed into milk and heated

Figure 13: *Croton tiglium* is fried with ghee

2.1.4. Preparation of *Thaalagakattu:* Purified Yellow arsenic trisulphide is placed in a vessel filled with a litre of neem oil and burnt in low flame until the oil is reduced to half[3].

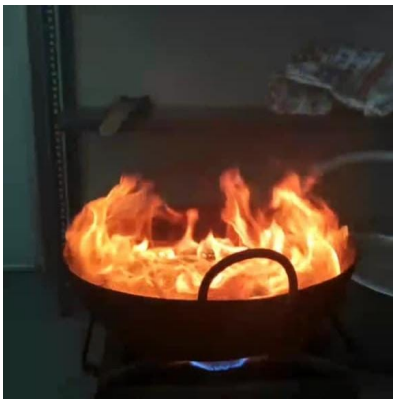

Figure 14: Purified *Thaalagam* is burnt with neem oil

Figure 15: *Thaalagakattu*

2.1.5. Preparation of *Vepampattai* decoction:
1part of bark of *Azadirachta indica (Vepampattai)* is added to 4part of water and prepared as decoction.

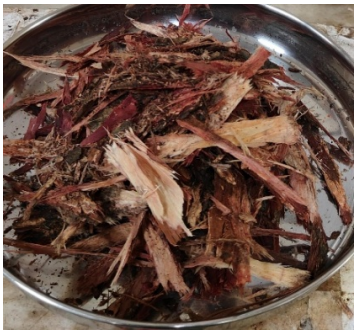

Figure16: *Vepampattai*

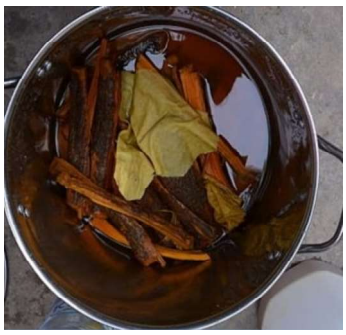

Figure 17: *Vepampattai* decoction

2.1.6. Preparation of *Seethamsa Rasam:*

Purified raw materials are powdered separately and mixed and grinded with *Vepampattai* decoction for 12 hours. It is made into *kundrimani* sized (130 mg) pills and dried under shade[3].

Figure 18: Powdered raw materials

Figure19: Grounded with *Vepampattai* decoction

Figure 20: *Seethamsa Rasam*

3. Literature review

3.1. *Thaalagam*(Yellow arsenic trisulphide)

3.1.1. Classical Literature Review of*Thaalagam* (2)

Based on color, appearance, and properties, yellow arsenic trisulphide is categorized into four types:

i. *Sivappuaridhaaram* (red orpiment) - This is effective in the treatment of fever with chills, pricking pain, itching, *vatha* disease and leprosy.
ii. *Madal aridhaaram*- It is effective in the treatment of asthma, *kapha*, constipation and cough. It heals non-healing chronic ulcers and eczema.
iii. *Pon aridhaaram* (gold orpiment) - This is effective in the treatment of asthma, high chronic fever, poisonous insect bite, tuberculosis (emaciating diseases), fatigue and skin diseases.
iv. *Karattuthaalagam*- Cough, tuberculosis (Emaciating diseases), *kapha vatha* diseases, eight types of ulcers

Actions: Expectorant**,** Antipyrectic**,** Emetic**,** Convalescent**,** tonic.

3.1.2. Modern Scientific Evidence of *Thaalagam* (5)

Geological name - Orpiment
Chemical name - Arsenic disulphide
Associated Minerals - Usually forms with regular. In fact the two minerals are almost always together. Other minerals are stibnite, pyrite, sphalerite, calcite, antimony ores, barite and gypsum.
Colour - Lemon-yellow
Streak - same coloration but palor
Cleavage - highly perfect
Hardness - 1.5-2
Specific Gravity - 3.5
Density - 3.49-3.56, Average = 3.52
Melting point - 300°C
Boiling point - 707°C
Transparency - Crystals are translucent to transparent
Fracture - bladed (flaky)
Lustre- Resinous to pearly

Induction of Apoptosis (Programmed Cell Death): When absorbed by malignant cells, As_2S_3 alters intracellular signalling to trigger destruction without causing widespread tissue necrosis. (32)

Generation of Reactive Oxygen Species (ROS)

The compound induces high levels of oxidative stress within target cells.It stimulates the accumulation of free radicals (ROS), which overwhelms the cell's antioxidant defenses.High ROS levels damage cellular structures, cause DNA fragmentation, and activate stress-responsive kinase pathways (like JNK) to halt rapid cell division.(33)

3.2. *Manosilai* (Red orpiment)

3.2.1. Classical Literature Review of *Manosilai*(2)

Manosilai (Bisulphuret of arsenic) is of two types:

1. Piravisarakku
2. Vaippusarakku.

Vaippusarakku is obtained by adding 5 parts of arsenic trioxide and 3 parts of sulphur. It has got body strengthening and rejuvanating properties. It's potency is old. This is effective in the treatment of skin leprosy, fever with chills, asthma, eye diseases, urinary tract infections, kapha diseases, cervical adenitis etc. It is also effective in the treatment of *Ajakalligai* (a type of boil occurring in children).

3.2.2. Modern scientific evidence of *Manosilai*(5)

Geological name - Realgar
Chemical name - Arsenic sulphide
Molecular Weight - 213.97

Physical state at room temperature - Solid
Colour - Orange red to Aurora red
Streak - varying from Orange red to Aurora red
Fracture - small conchoidal
Cleavage - Fair
Hardness - 1.5 – 2
Lustre - Resinous
Solubility - Practically insoluble in water
Major products of combustion - Sulphur dioxide gas and Arsenic trioxide
Flammability - Ignites at high temperatures
Boiling point - 565^0 C
Density - 3.5

PML-RARα Oncoprotein Degradation: In Acute Promyelocytic Leukemia (APL), the disease is driven by the abnormal fusion gene *PML-RARα*, which blocks white blood cell differentiation.[34]

Cell Cycle Arrest (S and G_2/M Phases): Instead of allowing uncontrolled tumor cell replication, red orpiment halts cell progression during active division. [35]

3.3 *Nervaalam (Croton tiglium)* [7]

3.3.1. Classical Literature Review of *Nervaalam*

Part used - Seed
Taste - Bitter (Nauseating)
Potency - Hot
Division - Pungent
Actions - Purgative, Rubefacient

It removes various ano-rectal disorders and *vatha*diseases. It removes the poisons by expelling stools and removes diseases.It also cures *muppini, kudaichal*, abdominal disorders.

3.3.2. Modern Scientific Evidence of *Nervaalam:*

i. Gastrointestinal and Laxative Mechanisms

Protein Kinase C (PKC) Activation: Studies published in journals like *Phytomedicine* reveal that the phorbol esters found in *Croton tiglium* seeds act as powerful PKC activators.

This mechanism stimulates aggressive smooth muscle contractions in thegut, explainingits fast-acting cathartic and purgative effects.[8,9]

Gut Microbiota Regulation: A study using 16S rDNA high-throughput sequencing found that processed *Croton tiglium* seed powder effectively ameliorated loperamide-induced constipation in animal models. [10]

i. ii. Oncology and Cellular Apoptosis

Anti-Proliferative Activity: Research on *Croton tiglium* essential oil (CTEO) shows that it significantly inhibits the proliferation and migration of lung cancer cells (A549).[11]

Mitochondrial Pathway Disruption: The essential oil operates by disrupting the cancer cell cycle, downregulating key replication proteins (cyclin A, cyclin B, and CDK1), and reducing mitochondrial membrane potential to trigger caspase-dependent apoptosis (programmed cell death).[11]

Cytotoxic Diterpenoids: Newly isolated tigliane diterpenoids and sesquiterpenes from the plant's leaves have demonstrated direct cytotoxic effects against various cancer cell lines, making them active targets for future drug design. [9,12-14]

ii. iii. Dermatological Applications & Dermal Remodeling

Deep Chemical Peels: In dermatology, *Croton tiglium* oil is widely used in standardized phenol-croton oil chemical peels. Scientific evaluation confirms that its phorbol esters induce controlled, intense neutrophilic inflammation that stimulates fibroblasts. This promotes profound dermal remodelling and new collagen deposition (specifically type III), repairing aged or scarred skin.[15]

Antidermatophytic and Antiviral Effects: Chromatographic and *in vitro* assays demonstrate that ethanolic extracts from the stems and seeds exhibit robust antifungal activity against common skin pathogens (such as *Trichophyton rubrum* and

Candida albicans), substantiating its traditional use against ringworm and warts. [16,17]

iv. Neuroinflammation and Anti-Inflammatory Effects

Microglia Inhibition: Laboratory evaluations of *Croton tiglium* extracts (CTE) reveal that they can inhibit excessive pro-inflammatory activity in brain cells (microglia and astrocytes). By reducing the secretion of damaging pro-inflammatory cytokines, isolated elements of the plant are being studied for potential neuroprotective pathways against degenerative diseases. [8]

3.4. *Chukku (Zingiber officinale)*

Actions: Stimulant, Stomachic, Carminative

Table 2: Pharmacological Studies on Ginger (*Zingiber officinale*)

S.No	Title	Author	Methodology	Results
1	Analgesic, anti inflammatory and hypoglycaemic effects of ethanol extract of *Zingiber officinale* (roscoe) rhizomes (zingiberaceae) in mice and rats (18)	John a. O. Ojewole	Hot plate method, Acetic acid test, Hind paw oedema, Inducing diabetes by streptozotocin ip.	Ethanolic extract of *Zingiber officinale* possess analgesic, anti inflammatory and hypoglycaemic property.
2	Antiulcer activity of steamed ginger extract against ethanol/Hcl-induced gastric mucosal injury in rats [19]	Jun-kyu shin et al	Ulcer induced by EtOH/hcl treatment.	Steamed ginger extract has therapeutic activity against gastritis.
3	Comparison of phytochemicals, antioxidant and anti-inflammatory properties of sun-, oven- and freeze-dried ginger extracts [20]	Iswaibahmustafa et al	Frap assay, Radical scavenging assay, Murine macrophage cell line for antiinflammatory activity.	The sun-dried ginger extract had enhanced bioactivities. All dried ginger showed significant antioxidant and antiinflammatory property compared to fresh ginger.
4	Gastroprotective effect of ginger rhizome (*Zingiber officinale*) extract: role of gallic acid and cinnamic acid in H+, K+ATPase/h. Pylori inhibition and anti-oxidative mechanism [21]	Siddaraju m. Nanjundaiah et al	H+, K+-ATPase assessment, Agar diffusion assay, Radical scavenging assay.	Ginger protects the gastric mucosa from stress induced mucosal lesion and inhibits gastric acid secretion, inhibits growth of h. pylori.
5	Biochemical analysis, phytochemical and pharmacological actions on Siddha paediatric drug – chukkupodi[22]	S. Vadivelan et al	Complete chemical analysis.	Biochemical analysis showed the presence of ferrous iron in chukkupodi and various chemical components like tannins, alkaloids, saponins.

3.5. *Milagu (Piper nigrum)* [7]

Actions: Acrid, Carminative, Antiperiodic, Anti-vatha, Antidote, Resolvent, Rubefacient, Stimulant.

Table 3: Pharmacological Studies on Black Pepper (*Piper nigrum*) and Piperine

Sno	Title	Author	Method	Results
1	Analgesic and anti-inflammatory activities of *Piper nigrum* L. [23]	Farhana Tasleem et al	Analgesy meter, Hot plate method, Acetic acid induced writhing test, Carrageenan induced paw inflammation.	Potent analgesic and anti-inflammatory activity.
2	Evaluation of Antimicrobial Activity and Cytotoxicity Effects of Extracts of *Piper nigrum* L. and Piperine [24]	Fabrine Silva Alves et al	Disc diffusion method, MTT assay.	Inhibition against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Salmonella* spp. Piperine exhibited inhibition against tumor cell lines.
3	In vitro and In vivo evaluation of hepatic protection and anti-ulcer activities of piperine gastro retentive microspheres [25]	Bindu Madhavi Boddupalli et al	Paracetamol induced method, Ethanol induced ulcers.	Piperine can show better hepatoprotective and anti-ulcer activity when used as gastro retentive microsphere rather than conventional microsphere.
4	In Vitro Study of Wound Healing Potential in Black Pepper (*Piper nigrum* L.) [26]	Chin Mee Wong et al	Oris pro cell migration assay.	Piperine showed cell migration activity with no direct cytotoxicity.
5	*Piper nigrum* and *Ferula foetida* shows Significant Antisecretory and Anti-Ulcer Activity in Rats [27]	Vuyyala Balakrishna et al	Cysteamine induced duodenal ulcers, pylorus ligation method, cold restraint stress induced ulcer.	*Piper nigrum* and *Ferula asafetida* has significant antiulcer activity.

3.6. *Thippili (Piper longum)*

Action: Stimulant, Carminative

Table 3: Pharmacological Studies on *Piper longum*

S.No	Title	Author	Method	Result
1	Analgesic activity of *Piper longum*Linn.root[28]	G. Vedhanayaki et al.	Tail flick method.	Analgesic activity is present due to the alkaloids present in it.
2	Anti-inflammatory activity of two varieties of Pippali (*Piper longum* Linn.) [29]	Mamta Kumari et al.	Carrageenan-induced paw edema, Formaldehyde-induced paw edema.	Chotti variety of *Piper longum* has better anti-inflammatory effect than badi variety.
3	Effect of *Piper longum*, *Zingiber officinale* and *Ferula* species on gastric ulceration and secretion in rats [30]	A. K Agrawal et al.	Cold restraint stress, Aspirin induced gastric ulcers, Pyloric ligation.	The results demonstrated the anti-ulcerogenic activity of pippili, sringvera and hingu.
4	Anti-inflammatory and anti-microbial activity of silver nanoparticles synthesized using *Piper longum*[31]	Obuli Ganesh Kishore.S et al.	Albumin denaturation assay, Agar well diffusion method.	*Piper longum* has better anti-inflammatory and anti-fungal activity.

4. Discussion

The comprehensive literature review of *Seethamsa Rasam* (SR) highlights its significance as an important herbo-mineral formulation within the classical Siddha text Anuboga Vaidhya Navaneetham. It provides a valuable therapeutic option for managing hyper-reactive *Pitha* conditions (*Pitha Noigal*), fever (*Suram*), and localized inflammatory pain. Modern in-vitro profiling confirms that *Seethamsa Rasam* possesses broad-spectrum antimicrobial activity against enteric and respiratory pathogens. The *Azadirachta indica* matrix contributes key tetranortriterpenoids (such as nimbin and azadirachtin), which possess documented cyclooxygenase (COX) inhibiting properties. This down-regulates prostaglandin E_2 (PGE_2) synthesis, mimicking conventional antipyretic pharmacodynamics.

5. Conclusion

Seethamsa Rasam represents a highly sophisticated herbo-mineral complex capable of treating metabolic hyperthermia, chronic pyrexia, and inflammatory *Pitha* disorders. Empirical scientific evaluations validate that its traditional manufacturing processes safely modify potentially toxic mineral compounds into therapeutic, bio-available matrices. This formulation highlights the therapeutic value of integrating traditional Siddha pharmacology with modern translational research.

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