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Anti Pyretic Activity of Linga Mathirai (Mercuric Sulphide Preparation) in Experimental Animals

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Abstract: ***The present pharmacological investigation was undertaken to study the anti-pyretic activity of Linga mathirai Siddha sastric Herbo mineral formulations in albino rats against yeast induced pyrexia. Five groups of six animals were used for the experiment. The yeast induced pyrexia method was standardized first by injecting 12.5% yeast suspension (s. c) followed by recording the rectal temperature at every hour of intervals. Then the evaluation of anti-pyretic activity of Siddha sastric Herbo mineral formulations was carried out by using this standard procedure. Both the samples including vehicle significantly attenuated the raise in temperature after three hours of yeast injection. The data generated during all stages of study showed that the test drug Linga mathirai (5.85 mg/kg per day) exert highly significant (P<0.001) decrease in temperature after 1 hr of administration except which was non-significant after 1 hr. The test drug Linga mathirai with high dose (58.5 mg/kg) was found to be significant (P<0.05) even after 3 hrs in comparison to standard drug (Paracetamol). The results of present study show the importance of mercury in intensifying the therapeutic efficacy of a formulation***

Keywords: Siddha sastric medicine, Linga mathirai, Pyrexia, Brewer's yeast, Paracetamol, Anti-pyretic activity

1. Introduction

Siddha system of medicine is one of the ancient traditional system of the world. Siddha medicine is practiced principally by the people of Tamil Nadu and practiced in the nations where Tamil peoples live. It is accredited that the system have been established by the Siddhars to seek eternity [1]. The human body (Seven constituents-Udalthathukkal) is made up of five elements of presented in the universe (Earth, Water, Fire, Wind & Space) and they are ruled by the three forces (Humors) called Mukkuttram namely Vali (Vatham–Wind), Azhal (Pittham-Fire), Ayam (Kabam-Water). Siddha science quotes nature and man as essentially one. Nature is man and man is nature. Man is said to be the microcosm and universe is the macrocosm because what exists in the world exists in man. A universe originally consisted of atoms which contributed to the five basic elements, viz., earth, water, fire, air and space which corresponds to the five senses of the human body and they are the fundamentals of all corporeal things in the world [2].

The fundamental subjects of Siddha methodology are Vadham (Alchemy), Vaithiyam (Medicine), Yogam (Yoga) and Gnanam or Thathuvam (Philosophy). In Siddha medicine, the general mode of treatment lies in the normalization of the vitiated vital force i. e., Valli, Azhal, and Iyyam. Pharmacodynamics in Siddha is based on the fundamental "Pancha Bootham" and "Mukkuttram" which govern's the physico-chemical and biological phenomenon. Siddha, accepting the law of uniformity of nature and statesthat drugs and living bodies are similar in composition and such drugs influence the body by altering the proportion of factors in composition. Diagnostic tools used by the Siddhars is done with the help of a simple discriminating approach called "EnvagaiThervu" [3]. by thismethod, the disease is recognized by observing and analyzing the eight features of the patients like pulse, touch, tongue, colour, speech, eye, feces and urine (8 Weapons of a Siddha Physician). The changes in the body caused by the deranged vital humors are well demonstrated by these eight features of the body.

a) Medicines in Siddha

"Maruppathuudalnoimarunthenalaagum
Maruppathuulanoimarunthenasaalum
Maruppathininoivaraathirukka
Maruppathusaavaiyummarunthenalaamae"
-*ThirumoolarThirumanthiram*

The verse in the Tamil literary classic defines the principles regarding medicine [4]. Medicine is a drug or a substance which cures a disease physically and mentally, and protects the body and soul from diseases. The above definition is well correlated with the concept of health defined by WHO. Medicine can be classified as 32 types of Internal and 32 types of External. The shelf life of each internal and external medicine has been ascertained by the Siddhars. Most of the higher order medicines (Prepared using metallic ingredients) such as Parpam, Kattu, Urukku, kalanguhas 100 years, Chunnamhas 500 years, and Karpam, Satthuand Gurukuligai has more than 500 years of shelf period[4]. `

b) Metallic drugs

Alchemyis defined as a branch of medicine that deals with the splitting of a metal into separate particles and making them into a compound by adding another matter to it. Commonly, it indicates an attempt to convert a base metal into gold. It is considered to be one of the mind blowing inventions of Siddha medicine. The process of making

metallic drugs involves melting, sublimation, amalgamation, calcination, etc.

Siddhars formulated the drugs in such a way that it is easily absorbable by the body in the form of nano particles. They have explained synergist (Mithru) and antagonist (Sathru) substances and converted the raw metals considered as poisonous materials into good medicines by removing their toxicity by a special process of purification. The higher order medicines prepared from metals are used without loss of potency for many years whereas herbal formulations could be used for a period of one year. One of the advantages of metallic drug is that they exert their potency even in very small doses and they are potent enough to treat chronic disorders [5].

c) Role of Mathirai in medicine

Mathirai, otherwise called as Kuligai (Pill) is one among the internal medicines and is prepared by triturating the raw ingredients with either herbal juice or decoction or water or breast milk and made into pills and dried [4]. Mathirai, a common dosage form of medicine has been frequently prescribed in the clinical practices having advantages such as accurate dose, convenient to use, economical, more stable, easy to consume, portable and has the ability to mask unpleasant taste. Most of the mathirai form of drugs was prepared using herbal ingredients having shelf life period of one year. Mathirai containing metallic ingredients, the shelf period is for many years and exerts their potency in very small dose.

2. Review of Literature

Siddha system uses raw materials from ThathuVargam (Mineral kingdom), JeevaVargam (Animal kingdom) and MooligaiVargam (Plant kingdom) for the preparation of medicines. For the preparation of our test drug Linga Mathirai, ingredients added from Thathuand Jeeva Vargam. Thathuvargamis classified into 11 Ulogangal (Metals), 64 Padanagal (Arsenic and Mercurial Compounds –Toxicants), 25 Karasarangal (Salts) and 120 Uparasangal (Secondary minerals) [4].

2.1 Lingam

Chemical name: Mercuric sulphide (HgS)
Common name: Cinnabar, Vermilion
Cinnabar is a toxic mercury sulphide mineral with a chemical composition of HgS. It is the only important natural ore of mercury. The word „Cinnabar" has been taken from the Persian noted as "dragon's blood". It is found in the regions of Spain, Serbia, China, California and Arkansas in the United States of America.

a) Synonyms

Tamil: Inkuligam, Raasam, Kadaivanni, Karpam, Kalikkam, Kaanjanam, Kaaranam, Sandagam, Samarasam, Saaniyam, Chendooram, Maniraagam, Milecham, Vanni.

Sanskrit: Hingula, Hingulam, Ingulam, Mleccham, Raktam, Barbara, Cuurnapaaradam, Rasodphaabam, Rannjnam, Kapasiirsakam, Rasagarbha, Raktakaayah, Daradam, and Citraangam

Hindi: Hingul
Urudu&Farsi: Singaraf
Telugu: Ingiliikam
Kannada: Laglika
Malayalam: Caayilyam

2.2 Synthetic Method of preparation (4)

Purified Mercury-280 g
Sulphur-70 g
Potassium nitrate-70 g
Mercury is thoroughly mixed and triturated with sulphur. Potassium nitrate is then added; placed in a conical flask and burnt for 18 hrs. After cooling, the red sulphide of mercury is collected out

2.3 Physical Properties

Crystallization: Trigonal, trapezohedral, hexagonal
Habit: Small as earthy or granual encrustations
Color: Bright red to brownish red, sometimes lead grey
Streak: Scarlet Red
Diaphaneity: Transparent to opaque
Cleavage: Perfect, Prismatic
Fracture: Sub concoidal to uneven
Elasticity: Imperfectly sectile Mohs
Hardness: 2 –2.5
Specific gravity: 8 –8.2
System: Trigonal
Melting Point: 580^{o}C

2.4. Lingam in siddha

a) Purification methods for Lingam (4)

Alanguim bark (A. salvifolium) –1400 g is powdered and added with vinegar 5.2 L and placed in dews in the night. Next day it is rubbed and kindled well.35 g of Cinnabar is tied well in a cloth and put into the above liquid. The pot is covered with another pot and sealed with mud pasted cloth, dried and exposed in dew for one day. It is heated with low intensity fire (flame) until the liquid is dehydrated for 24 hrs. Then the Cinnabar is taken out and cleaned well. Theprocedure is separated using the vinegar soaked individually with the whole plant of Vitislanata (Puli karanai) and Indian Sarasaparilla root.

Lime juice, cow's milk and the Indian Acalyphajuice are mixed in equal proportion and allowed to fuse cinnabar so as to get in a consolidated potency state. . The crude form of red sulphide of mercury is soaked for 1 day in mother's milk and lemon juice respectively it becomes purified.

b) Therapeutic properties:

"BaedhisuramSanniPeruviranaNeerodu
ThagaadhakadiKaasamKarappanPunnoadha
UruvavilingaSangadamaVurukattiyumpoam
KuruvilingasangamathaiKol"
"AadhiRathavuruKaadhalaJothilinga
MadhilrathagunaMutrudalilTheethupuri
KuttamKirandhiKodunsoolaiVaathamudhal
UttanguNoikolaiYottum"

Lingamcures diarrhoea, pyrexia, delirium, urticaria, diuresis, TB, scabies, unknown insect bites, syphilis leprosy, eczema, skin diseases, throbbing pain, &vatha diseases [6].

Medicinal preparations using Lingam as ingredient

Name of the Medicines

1) Linga Parpam[6]: for the treatment of dropsy, fever, ulcers, venereal diseases, perversion, bearing down pain, Rheumatism, itching, delirium.
2) Linga Chendooram[6]: for the treatment of vatha and kapha diseases, venereal diseases (Gonorrhea)
3) Linga Kattu[6]: for the treatment of Heart attack, Diarrhoea, Abdominal distension, Delirium, Syncope
4) SandarasaParpam [6]: for the treatment of Diarrhoea, cholera,
5) Linga Parpam[6]: for the treatment of Gunma Vayu, Delirium due to Vatha, cough Hemylegia, Throbbing pain, TB, Pyrexia
6) Padigalingachendooram: for the treatment ofDysentry, Menorrhagia, cholera, Diarrhoea associated with fever
7) Sathisambeerakuzhambu[6]: for the treatment of Loss of Appetite, Diarrhoea, Fever, Syncope, Vomiting, Thirst due to pitta, Discolouration of the body, Nausea
8) Linga Pugai: for the treatment of Ext. as fumes Deep wounds and foul smelling ulcers
9) AyakanthaChendooram [7]: for the treatment of acute and chronic Edema
10) Linga Chendooram[8]: for the treatment of Heart attack, Vayu, Dizziness, Throbbing pain, PithaAnemia, Abdominal pain.
11) KaadikaraChendooram[9]: for the treatment of Hemiplegia, Cholera
12) ShayaKulandaga Chendooram[10]: for the treatment of Diabetes, Cough, Kapha diseases
13) KasthuriKaruppu[11]: for the treatment of Cold, Fever, Cough, Asthma
14) PattuKaruppu[11]: for the treatment of Throbbing pain in uterus, Apoplexy. Heat sensation in uterus
15) Linga Padangam[12]: for the treatment of Nausea, Diarrhoea, Edema, Jaundice, Anemia
16) KumattiKulambu[13]: for the treatment of Ulcer, Ascites, Anemia
17) Nandhi Mai [14]: for the treatment of 18 types of chronic throbbing pain, 8 types of ulcer, 18 types of Eczema, 8 types of fistula
18) PanchaSoothaMelugu[15]: for the treatment of 13 types of Apoplexy All types of fever, 8 types of ulcer, Heart diseases, Hemiplegia
19) MagaVeeraMezhugu[16]-for the treatment of venereal diseases.
20) AnandhaBairavam[17]-for the treatment of Kapha related diseases.

2.5 Lingam in Ayurveda[18]:

a) Hingulais of two types

- Khanija (Available in mines)
- Krtrima (Made up of mercury and sulphur)

b) Natural cinnabar is 3 types

- Carmaara (Greenish red)
- Sukatunda (Yellowish red)
- Hamsapaada (blood red-considered as best)

Some say that Carmaarais in black color, Sukatundais yelow in color, Hamsapaadais red in color. Rasavaagbhata mentioned only two varieties of cinnabar

- Sukatunda, which is also known by name carmaara, inferior in qualities
- Hamsapaada, looks like coral with whitish striations.

2.6 VENGAARAM

Chemical name: Sodium biborate
Common name: Borax

Vengaaram is a Kaarasaram group occurs in the regions of arid and obtained abundantly in Borax Lake and Searl's Lake in California. It is also found in Kashmir, Tibet & Nepal [19]. Much greater deposits were later found in the South western U. S. They are translucent when fresh. When Borax loses water, it alters into a new mineral called Tincalonite, which contains the same elements as in Borax but has half of water content and crystallizes in a different crystal system.

Synonyms

Tamil: Porikaram, Karam, Urukkinam, Urukkumithiran Danganam, Thoomathaiyadakki
Sanskrit: Tankana, Tanka, Draavaka, Lohadraavii, Sowbaagyaa
Hindi: Suhaaga, Tankan Khaar, Tinkaal
Telugu: Veligaaramu
Malayalam: Ponkaaram
English: Borax
Synthetic preparation
Ingredients.

Group A

1) Fuller's earth-1.3 L
2) Water-10.4 L

Group B

Alum-3500 g
Potassium nitrate-219 g
Milk spurge burnt ash-1.3 L
Abrusprecatorius leaf juice-1.3 L
Castor oil-650 L

Fuller's earth is dissolved in H2O and filtered. Group B drugs are added to the above filtrate and isolated. It becomes black. Then, the other three drugs are added to it and heated as Kamalakkini for 96 minutes. Then, it is placed on a earthen pot with wider mouth and insolated the end the product is collected [19].

3. Materials and methods

3.1. Preparation of test drug Linga mathirai

3.2. Procurement and collection of raw materials

Minerals such as Lingam (Cinnabar) andVengaaram (Borax, Sodium biborate) were procured from RNR Country drug store, Chennai, Tamilnadu, India

Herbs such as Erukku (Calotropisgigantea) and Kuppaimeniilai (Leaves of Achalypaindica) were collected from Herbal garden at Velumailu Siddha Medical College and Research Centre, Chennai, Tamil Nadu, India

Raw drug-Lingam

The raw *Lingam* purchased from country drug store to be subjected for purification processes (Sample R)

Raw drug-Vengaaram

The raw *Vengaaram* purchased from country drug store subjected for purification process

3.3 Purification and detoxification of Lingam by Surukku process

This is the common routine method employed for the purification of Lingam which is cited in the text of Gunapadam (Siddha Materia Medica) [20].

a) Materials

A single piece of Lingam (Cinnabar, Red Sulphide of Mercury –Natural) – 57.83g
Cow's milk – 150 mL
Lemon juice – 150 mL

b) Method

- Cow's milk, Lemon juice and Acalypha indica juice were mixed well in a glass jar.
- A single piece of Lingam weighed 57.83 g was placed on a mud plate and heated over hot plate mounted on it.
- The juices in the glass jar were instilled over the Lingam drop by drop for 3 h continuously.
- After 3 h, the Lingam was allowed to cool and washed out with water and dried.
- This purified Lingam was coded as sampleS.

Purification of Lingam by Surukku process

3.4 Quality assessment of purified Lingam sample

This was done by comparing the macroscopic features, contents of Mercury and Sulphur through Inductive coupled plasma optical emission spectroscopic study among a raw sample and purified samples. Inductive coupled plasma optical emission spectroscopic study was performed at Sophisticated Analytical Instrumentation Facilities, Indian Institute of Technology-Madras, Chennai, Tamil Nadu, India. The best purified Lingam was utilized for the preparation of LM[21].

3.5. Physical parameters analyses

a) Macroscopic features

The raw and purified Lingam coded as sample R, and A was observed for Cleavage, Colour, Crystal form, Fracture, Hardness, Lustre, Magnetism, Reaction to HCl, Streak, Luminescence and Loss of weight. Colour was examined under visible light and the form of crystal was examined by the observation of geometric shape such as trigonal, cubic, hexagonal, etc.

Fracture denotes the areas where the sample is broken (irregular or concoidal).

Hardness was observed by scratching the samples using Mohs Hardness kit and Mohs scale was recorded.

Lustre, was observed by the appearance of sample in metallic and non-metallic states.

Magnetism was done to analyse the presence of electromagnetic force using magnet.

Reaction to HCl was done to know the presence of Calcium carbonate in the sample confirmed by the formation of effervescence.

Streak was evaluated by determining the colour of the sample on grinding the sample into powder on a porcelain streak plate.
Luminescence was done by using UV lamp to analyse the fluorescence property.

Loss of weight in percentage was estimated in the purified samples to determine the reduction of metallic concentration by the formula [(Weight of the sample before purification-

Weight of the sample after purification) / Weight of the sample before purification] x 100.

b) Estimation of Mercury and Sulphur

The concentrations of Mercury and Sulphur were observed between Sample R, E and S by Perkin Elmer Optima 5300 DV Inductive coupled plasma optical emission spectrometer (ICP-OES). The study was performed at Sophisticated Analytical Instrumentation Facilities, Indian Institute of Technology-Madras, Chennai, Tamil Nadu, India.

3.6 Purification and detoxification of Vengaaram

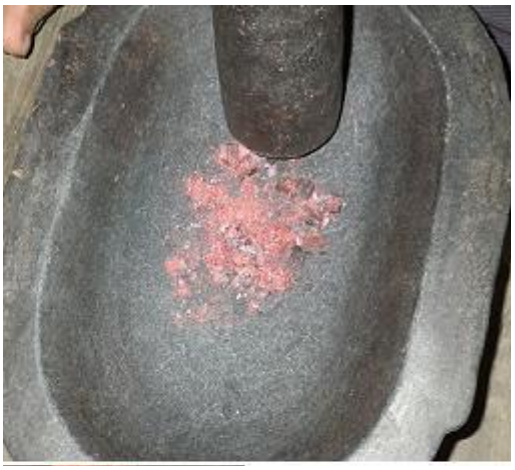
Aadequate quantity of Vengaaram (Borax, Sodium biborate) was coarsely powdered in the black stone mortar and roasted over the mud plate until water material evaporated out. The fried Vengaaram became puffing out [22].

Purification process of Vengaram

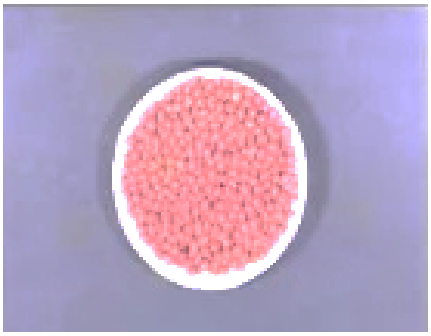
3.7. Preparation process of Linga Mathirai

The method adopted for the process was referred from the literature *AnuboghaVaidhyaNavaneetham*[23].

1) Equal parts of purified Lingam 65 g and purified Vengaaram 65 g were grounded to fine powder separately in the kalvam (Black stone mortar) and mixed well and again grounded till loss of refinement



2) This mixture was triturated for 3 h in Mulaippal (Human breast milk) – 250 mL and made into paste consistency (non-sticky nature)
3) The paste was rolled into pills of black pepper size approximately 5 mm diameter manually with hands under aseptic condition



4) The rolled pills were stored in air tight sterile dark glass container and utilized for further studies.

3.8. Physicochemical characterization of Linga mathirai-sample LM

3.8.1. Physico-Chemical Parameters of Linga Mathirai

a) Physical Parameters

The colour, odour and taste were analyzed.3 g of LM was analyzed for the estimation of Total Ash value, Acid Insoluble and Water soluble ash value.5 g of LM was analyzed for the estimation of Alcohol and Water soluble extractive values.2 g of LM was analyzed for the estimation of Moisture content by loss on drying at 105˚C and total solid content. The average diameter of the pill and disintegration time was analyzed for LM. The above parameters were analyzed following the protocol mentioned in Pharmacopoeial Laboratory for Indian Medicine (PLIM) [24].

b) Weight variation test

The weight variation test was carried out by weighing the 20 tablets individually using analytical balance, then calculating the average weight and comparing the individual tablet weights to the average [25].

The percentage of weight variation among pills was calculated by using the following formula.

% of wt. variation = Individual wt. – Average wt. x 100
Average wt.

Weight Variation limits of Tablets (IP)

Average weight of tablets Maximum percentage of weight difference allowed
80 mg or less ±10.0
Between 80 mg and 250 mg ±7.5
250 mg and more ±5.0
Suspected tablet: Not more than six tablets are outside the percentage limit and no tablet differs by more than two times the percentage limit according to the table. Rejected tablets: One tablet differs by more than two times the percentage limit according to the table. More than six tablets are outside the percentage limit

3.9 Pharmacological study

3.9.1. Anti-pyretic activity

a) Effect of Lingamathirai on Brewer's yeast induced pyrexia in rats
Pyrexia or fever is caused as a secondary impact of infection, malignancy or other diseased states. It is the body's natural function to create an environment where infectious agents or damaged tissues cannot survive. Normally, the infected or damaged tissue initiates the enhanced formation of pro inflammatory mediators (cytokines, such as interleukin 1β, α, β, And TNF-α), which increase the synthesis of prostaglandin (PgE2) near hypothalamic area and there by trigger the hypothalamus to elevate the body temperature[26].

b) Procedure
Before yeast injection the basal rectal temperature of rats was recorded, Baseline body temperature was measured by inserting the digital rectal tele thermometer in to the anal cavity of the rat for about 2 mins. The steady temperature readings obtained were recorded as the pre temperature. After recording animals were given subcutaneous injection of 10 ml/ kg of 15 % w/v yeast suspended in 0.5 % w/v carboxymethyl cellulose solution for elevation of body temperature of rats. Rats were then returned to their home cages.18hrs after yeast injection, rats with elevated body temperature was selected for grouping and the LM and standard drug was suspended in CMC and administered by gastric tube[27].

c) Dosage schedule:
The required dose for mice/rat will be calculated by using the standard dose calculation procedure from recommended clinical dose.

d) Preparation of the Tet drug:
100mg of Linga mathirai was suspended in 10ml of Injikudineer and each rat was given 2ml orally. This 1 ml contain 10 mg of the drug

e) Conversion formula:
human dose is 65mg, BD
Total clinical dose (a) x conversion factor (b) 0.018 = (c) per 200 gm of rat
65 mg x 0.018 = 1.17mg (c) /kg
1.17x1000/200 = 5.85 mg/kg

Table 1

S. no	Groups	Dose/kg. weight	Dose/gmt. weight	Volume of administration
1	Vehicle control	--	--	0.5 ml
2	Therapeutic dose	5.85	1.17	0.5 ml
3	Average dose	29.25	5.85	0.5 ml
4	High dose	58.5	11.7	0.5 ml

4. Results

4.1. Physical properties

The results of table 2 show the similarities and differences in the physical observations among the raw and purified samples. It was observed that Sample S differs in its lustre (decreased adamantine), hardness (increased – Penny) and change in colour (Blackish red) on compared with Sample R. After purification, sample S loss its 10.34 g% weight and qualitatively indicated that the concentrations of mercury and sulphur was reduced better on compared with Sample R

Table 2: Physical properties

Physical parameters of *Lingam* before and after purification processes Parameters	Sample R*	Sample S*
Cleavage	Perfect	Perfect
Colour	Brownish red	Blackish red colour
Crystal form	Trigonal	Trigonal
Fracture	Brittle	Brittle
Hardness	Finger nail 2.5	Penny 3
Luster	Adamantine	Adamantine but decreased on compared to Sample A
Reaction to HCl	No effervescence	No effervescence
Streak	Bright red	Bright red
Luminescence	Non fluorescent	Non fluorescent
Loss of weight	-	10.34 g %

Sample R-Raw drug lingam Sample S-Purified Lingam

4.2. Mercury and Sulphur contents

The concentrations of mercury and Sulphur estimated using ICP-OES in different samples were shown in the table 3.83.20 % of mercury was reduced in sample S and 33.60 % of mercury was reduced in sample E on compared with sample R.66.33 % of sulphur was reduced in sample S and 11.06 % of sulphur was reduced in sample E on compared with sample R.

Table 3

Estimation of Mercury and Sulphur content in *Lingam* before and after purification process Element	Wave length (nm)	Sample R*	Sample S*
Mercury	254.652	152.250 mg/L (150.422 ppm)	26.247 mg/L (25.75 ppm)
Sulphur	186.731	448.024 mg/L (450.538 ppm)	148.04 mg/L (150.195 ppm)

4.3. Physical Parameters

The concise results of physical parameters of LM were shown in the **Table 4**.

Physical Parameters of *LingaMathirai* Parameter	Result
Total Ash %	36.1 ± 1.15 (n = 3)
Acid Insoluble ash %	4.53 ± 0.52 (n = 3)
Water soluble ash %	35.76 ± 1.47 (n = 3)
Alcohol soluble extract %	1.10 ± 0.16 (n = 3)
Water soluble extract %	12.126 ± 2.08 (n = 3)
Moisture content %	11.67 ± 1.26 (n = 3)
Solid content %	84.33 ± 1.26 (n = 3)
Weight (mg)	71.45 ± 11.19 (n = 20)

4.4. Anti-pyretic activity

4.4.1. Effect of Linga mathirai on brewer's yeast induced pyrexia in rats

GPS	Only Yeast	Yeast + PARACETAMOL (250mg)	YEAST + LM 5.85 mg/Kg	YEAST + LM 29.25mg/Kg	YEAST + LM 58.5 mg/Kg
Initial Rectal Temperature 0 hr	58.543± 18.618	57.8333± 19.631	58.521± 18.9275	59.833± 20.308	57.3333± 18.462
Rectal Temperature After induction with Yeast 18hr	77.867± 25.0261	85.133± 28.431	78.633± 25.2823	79.667± 25.6461	84.533± 29.463
Temperature After Treated with Test and Standard 1sthr	83.8767± 26.9434	88.105± 28.3479	81.783± 27.299	82.683± 26.6027	88.517± 28.706
2ndhr	86.9833± 26.996	87.8167± 27.1763	77.3667± 24.8392	75.9833± 25.4682	83.9833± 27.1018
3rdhr	79.2333± 25.3779	77.8833± 25.06	75.2333± 24.1443	73.5± 23.6678	78.17± 26.216
4thhr	80.8± 26.881	76.35± 23.448	72.3167± 22.24	71.7667± 22.295	71.4667± 22.185
5thhr	79.35± 26.4619	71.05± 23.805	67.6333± 22.7313	67.2167± 22.6276	66.8167± 22.5417
6thhr	79.233± 26.355	61.745± 20.888	64.198± 21.534	62.625± 21.151	60.109± 20.378

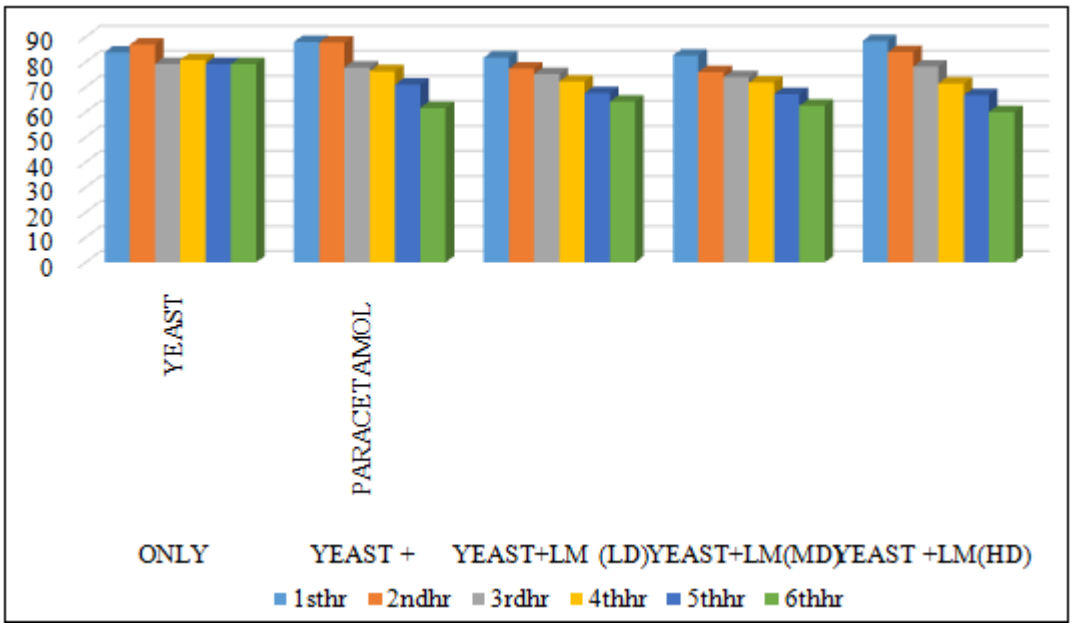


Figure 1: Temperature After Treated with Test and Standard

5. Discussion

Siddhars have converted potentially toxic heavy metals and its salts such as elemental mercury and its compounds, arsenic, copper sulphate, etc., into good medicines by removing their toxicity by a special process of *Suddhi* purification [28].

Lingam commonly known as Cinnabar is an insoluble form of Mercuric sulphide utilized extensively in the preparation of medicinal formulations in Siddha, Ayurveda, Unani and Chinese Medicine. Many preparations used *Lingam* as one of the ingredients to treat *Vatha*diseases [29].

The antidote for the *Lingam* toxicity is also mentioned in the literature as the aqueous decoction made with 4 g *Myristicafragrans* (Nut meg), 4 g *Piper cubeba* (Cubeb), 4 g Root bark of *Gossypium arboretum (*Red Cotton) with 35 g rock candy. In Ayurveda, it is cited that *Lingam* which has not undergone *Suddhi*is likely to cause mental disorders, blindness, weakness, fatigue, giddiness, delusion and urinary disorders[30].

The Pharmacopoeia of China (2010) illustrate that Cinnabar shall be administered at the doses of 0.1-0.5 g/day up to 10 days [31]. Chronic administration of cinnabar at its effective dosage causes anxiolytic effects due to decrease in brain Serotonin level [32].

In the study, Cinnabar was detoxified by the purification processes and that purified samples were analyzed for physicochemical properties. Lingam purified by making it into consolidate state (Surukku method) has been considered as a better detoxified form. Raman Spectrum study on the purified Lingam (Surukku method) infers that the sample is free from Sulphide functional groups. The concentration of Mercury and Sulphur is very much reduced in this purified sample. This purified sample was utilized for the preparation of test drug *Linga mathirai*.

Linga mathirai was prepared by following the procedure mentioned in the literature [33]. For the preparation of test drug, purified and detoxified form of Lingam and Vengaaram were used. Human breast milk has the property of detoxification by removing the impurities and it is frequently used in many preparations for blending the compounds. During the repeated trituration of the Lingam and Vengaaram with human breast milk, they were further detoxified and the particles were coated with lipid substances. The quality of the test drug LM were confirmed by classical methods i. e. non stickiness, no cracks, and uniformly rolling over the plane surface. The moisture content was very low in LM prevents the degradation of efficacy and loading of microbial contaminants.

Anti-pyretic activity of test drug Linga mathirai carried out by using yeast-induced method. The drug Linga mathirai showed potent antipyretic activity.

6. Conclusion

The test drug showed highly significant result at an interval of one hour after dose administrationand showed a significant result to reduce rectal temperature up to 3 h, which was compared to standard control drug, as onset of therapeutic action and duration of therapeutic action of Siddha formulation are believed to be more. The results of the present study shows the importance of Siddha mineral formulations for intensifying the therapeutic efficacy of a formulation as encouraging results were obtained in groups treated with Linga mathirai best results obtained in. It is self-explaining about the importance of the concept of Siddha sastric mineral formulations.

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