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ANTI-INFLAMMATORY AND ANTI-PYRETIC ACTIVITY ON SIDDHA FORMULATION *ELATHI KULIGAI* IN WISTER RATS

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ABSTRACT

Siddha system of medicine is one among the ancient Indian system of medicine. The word Siddha denotes one who has achieved some extraordinary powers (*siddhi*). In our system first preference is given for plant-based medicine. Herbal remedies and treatment aim to clean the body and fight against toxins and diseases. Bronchitis is inflammation of the bronchial airway. Bronchitis, is a major health issue in many developing and developed countries. Bronchitis, both acute and chronic is prevalent throughout the world and is one of the top five reasons for childhood physician visits in countries. Bronchitis occurs most commonly in children younger than 2 years with another peak seen in children aged 9-15 years. Doctor may prescribe a cough suppressant. In most cases, you should simply do all the things you usually would do for a cold: It produces dizziness, headache, vomiting, drowsiness, and skin rashes. Doctor may prescribe a 5-10 days course of broad-spectrum antibiotics, which fight a range of bacteria, may cause an overweight in children. So, the Anti-inflammatory and anti-pyretic activity of *Elathi kuligai* was carried out in Carrageenan-induced paw edema and Brewer's yeast induced pyrexia in Wister rats. The study result concluded that the drug *Elathi kuligai* has got significant Anti- inflammatory and anti-pyretic activity.

KEY WORDS

Elathi kuligai, Siddha drug, Anti-inflammatory and Anti-pyretic activity and Bronchitis.

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INTRODUCTION

This system is first described by lord Siva, so he is called first siddhar. In our county one medicinal system is made by 18 sidhhar. So the system is called siddha medicinal system. The word Siddha denotes one who has achieved some extraordinary powers (*siddhi*). The system is described about 4448 type of disease, medicinal remedies, and prevention and rejunuvative therapies. Main concept of in our medicinal system is "food as a medicine medicine as a food". In Siddha system, so many types of

medicinal preparations are available. Siddha medicines are made from plants, metals, minerals and animal products.

Bronchitis is characterized by the development of cough or small sensation in the back of the throat with or without production of sputum, mucous that is expectorant or coughed up from the Respiratory tract. Bronchitis refers to non-specific bronchial inflammation and is associated with a number of childhood conditions, acute bronchitis is a syndrome, usually viral in origin, and with cough as prominent feature[1]. Bronchitis is a major health issue in many developing and developed countries. Bronchitis, both acute and chronic is prevalent throughout the world and is one of the top five reasons for childhood physician visits in countries. Bronchitis occurs most commonly in children younger than 2 years with another peak seen in children aged 9-15 years[2]. In children, bronchitis caused by viral (90%) and bacterial (10%) infection. Non-infectious inflammation of the bronchi caused by physical and chemical irritants such as inhale dust, pollen grain organic substance[3].

The clinical features of bronchitis correlates with the symptoms of *kabasuram* dry or productive cough with expectoration wheeze, malaise, fever, constipation, URTI like nasopharyngitis, rhinitis sore throat described in the Siddha text[4]. In Siddha literature *kabasuram* is one of the twenty types of *"sura noi"* that occurs in children. This respiratory disease was described by various Siddhars in detail about the general etiology, signs and symptoms and prognosis on the basis of three *Thosha* and *Envagai thervugal*. The medicine was chooses for treatment and management of the *kabasuram* was *elathi kuligai* ½ to 1 tablet(185-370mg) internally, twice a day after food with milk described in *Sarabenthirar vaithiya muraikal surarogam*[1]. The Physico Chemical Analysis shows that it contains iron, chloride, starch, reducing sugar, steroid and alkaloids. PH of the trial drug is 4.2, moisture content is 0.309%, and total ash value is 3.37%. Acute and sub-acute toxicological studies shows that, it has no significant toxic effect.

MATERIALS AND METHODS

Sop of *Elathi Kuligai*

Elathi Kuligai[5] is a Herbal Siddha formulation comprising of sixteen different types of herbs like Elam (*Elettaria cardamomum*), Ilavangam (*Syzygium* aromaticum), Chukku (*Zingiber officinale*), Vellilolthiram *(Sypmlocos racemosa*) Santhanam *(Santalum album*), Kadugurogini (*Picrorhiza scrophullariiflora*), Elupaipoo *(Madhuca langifolia*), Nannari Root (*Hemidesmus indicus*), Vettiver *(Vettiveria zizanoides)* Athimathuram*(Glycyrrhiza glabra*), Koraikilangu*(Cyperus rotundus),* Koththamalli vithai (*Coriandrum sativum*) Thiratchai *(Vitis vinifera*), Paerichai (*Phoenix dactilifera*) sarkkarai and Sugarcane juice *(Saccharum officinarum*)[6,7]. The raw drugs were identified and authenticated by the Botany department in siddha central research institute Arumbakkam, Chennai. The purified raw drugs are made into fine powder, then it is grinded in *Kalvam* (stone martar) with sugarcane juice, after that makes it as 370 mg pills and dry. The trial drug *Elathi kuligai* is stored in clean dry air tight container and it is dispensed to the patients in packets.

Preparation of stock solution

The suspension of Siddha drug *Elathi kuligai* in 2% (W/V) CMC (Chemistry Manufacturing and Controls) was prepared for oral administration by gastric intubation in rats.

Chemicals, Reagents and Animals

All chemicals and reagents were obtained from sigma chemicals Ltd, USA. All other reagents used in the study were of analytical grade were obtained from Qualigen fine chemicals Pvt.Ltd. Wistar rats of either sex weighing about 220-250 gm were obtained from the animal house of king institute of preventive medicine, Guindy, Alanthur Road, SIDCO Industrial estate, chennai-600 032, Tamil Nadu. The animals were acclimated to standard laboratory condition (temperature between 22± 2° C and humidity 60-70%) and illumination cycle changed on 12 hr light/ dark cycle. The animals were housed in polypropylene cages and were housed in groups of three animals of similar sex,

feed with Standard pellet feed was provided. Potable water passed through *ad libitum* in rat feeding bottles with stainless steel sipper tubes. . The present study was approved by the Institutional Animal Ethical Committee (IAEC), C.L. Baid Metha College of Pharmacy, Thoraipakkam, Chennai-97. The approval number: IAEC/XL/05/CLBMCP/2013.

Evaluation of the Anti-Inflammatory Activity

Aim

To evaluate the anti-inflammatory activity of *Elathi kuligai* on Carrageenan-induced paw edema in rats.

Principle

Carrageenan-induced paw edema in rats as an in vivo model of inflammation has been frequently used to assess the anti-edematous effect of natural products. Carrageenan induced paw edema is a useful model in assessing the contribution of mediators involved in vascular changes associated with acute inflammation. Edema formation in the carrageenan-induced paw edema model is a biphasic response. After carrageenan injection, there is a release of histamine, serotonin, and bradykinin affecting vascular permeability. The edema induced by carrageenan, is characterized by the presence of prostaglandins and other compounds of slow reaction. Injection of carrageenan into the rat paw induced the liberation of bradykinin, and then further induced the biosynthesis of prostaglandin and other autacoids. However, in the carrageenan-induced rat paw edema model, the production of prostanoids has been through the serum expression of COX-2 by a positive feedback mechanism.

Procedure

Acute inflammation was induced in all groups by injecting 0.1 ml of 1% w/v carrageenan into the sub plantar region of the right hind paw of rats. *Elathi kuligai* was administered one hour prior to the carrageenan injection and paw volume was measure before and after injection of carrageenan at a fixed interval of 0, 30, 60, 120 and 180 mins. Standard Diclofenac sodium (50 mg/kg) p.o were used as standard drug and administered as CMC suspension by oral route. The change in hind paw volume was measured using plethysmometer and expressed as mean paw volume of the rats. The change in paw volume was measured as the difference between the final and initial paw volume.

Animal Grouping

Group I- Negative control – injected with 0.1 ml of 1% w/v carrageenan into the sub plantar region of the hind paw of rats.

Group II- carrageenan + 200 mg/kg of *Test drug*

Group III- carrageenan + 400 mg/kg of *Test drug*

Group IV- carrageenan + Standard drug Diclofenac sodium (50 mg/kg) p.o.

Evaluation of the Anti-Pyretic Activity

Aim

To evaluate the antipyretic activities of the *Elathi kuligai* by using Brewer's yeast induced pyrexia in Wister rats.

Principle

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 thereby trigger the hypothalamus to elevate the body temperature.

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 *Elathi kuligai* and standard drug was suspended in CMC and administered by gastric tube.

Animal Grouping

Group I- Negative control – injected with 10 ml/ kg of 15 % w/v yeast given subcutaneous injection.

Group II- Yeast +200 mg/kg of *Test drug*, p.o.

Group III- Yeast +400 mg/kg of *Test drug*, p.o.

Group IV- Yeast + Standard Paracetamol (150 mg/kg) p.o.

Rectal temperature was recorded by digital rectal thermometer at 0, 1, 2 3hrs after drug administration.

Statistical Analysis

The statistical analysis was carried by one way ANOVA (Analysis of variance) followed by Dunnet's"t" test and Results are expressed as mean ± standard error.

RESULTS AND OBSERVATION

Anti-inflammatory activity

Observation of results predicts that carrageenan induced group shows increased displacement value ranges from 0.325 to 1.512.

Treatment with *Test drug* at the dose of 200mg/kg shown displacement value ranges from 0.343 to 1.22 ml.

Treatment with *Test drug* at the dose of 400mg/kg shown displacement value ranges from 0.383to 1.173 ml.

Treatment with standard drug Diclofenac at the dose of drug at 50mg/kg shown displacement value ranges from 0.351 to 0.968 ml (Table No.1).

Anti-pyretic activity

Observation of results (Table No.2 and 3) predicts that yeast induce animals shows increased body temperature Treatment with *Test drug* at the dose of 200mg/kg shown significant decrease in body temperature from 40.83 to 38.65 ºC.

Treatment with *Test drug* at the dose of 400mg/kg shown significant decrease in body temperature from 40.31 to 38.22 ºC.

Treatment with standard drug at the dose of 150mg/kg shown significant decrease in body temperature from 40.73 to 37.6 ºC.

DISCUSSION

The ingredients of trial formulation have been already proved to possess anti-inflammatory (all drugs) and antipyretic activities. Vettiver *(Vettiveria zizanioids)*, Chukku (*Zingiber officinale*), Koraikizhangu *(Cyperus rotundus).* Certain ingredients also prove the presence of antimicrobial activity. Chukku (*Zingiber officinale*), Koraikizhangu, *(Cyperus rotundus),* Santhanam *(Santalum album*), Elam *(Elettaria cardamomum*), *Athimathuram (Glycyrrhiza glabra*), *Athimathuram (Glycyrrhiza glabra*), *Paerichu* (*Phoenix dactilifera*) being a strong Anti-tussive and Bronchodilators used in cough, asthma and respiratory tract infections by siddhars for numerous years. *Vettiver (Vettiveria zizanoides), Korai kizhangu (Cyperus rotundus),* and *Santhanam* have diaphoretic properties supporting the clinical trial. Also, *Vettiver (Vettiveria zizanoides),* and *Paerichu* (*Phoenix dactilifera*) possess febrifuge actions. *Kadugurogini* (*Picrorhiza scrophullariiflora*), cures lung diseases said by Ancient Siddhar's also found to have anti-asthmatic activity. *Elupai Poo (Maduca langifolia*), *Paerichai* (*Phoenix dactilifera*), *Thiratchai (Vitis vinifera*) is good expectorants. All together these herbs help to improve the pulmonary functional capacity[5-7].

Table No.1: Evaluation of the Anti-Inflammatory Activity

S.No	Paw volume (ml) was measured on days /Mean Displacement Value(ml)(mean ±SEM)					
1	Groups and Drugs	0 min	30 min	60 min	120 min	180 min
2	Carrageenan, 0.1 ml	0.325± 0.01408	0.905± 0.01586	1.165± 0.01746	1.285± 0.004282	1.512± 0.006009
3	Carrageenan + Low dose of Test Drug (200 mg/kg,)	0.3433± 0.006667	0.8033± 0.01202	0.8783± 0.02496	0.925± 0.02262	1.222± 0.02937
4	Carrageenan + Low dose of Test Drug (400 mg/kg,)	0.3833± 0.0152	0.7233± 0.01333	0.8217± 0.01641	0.865± 0.01285	1.173± 0.0206
5	Diclofenac sodium (50 mg/kg)	0.3517± 0.01797	0.5317± 0.01352	0.7367± 0.0152	0.815± 0.006191	0.9683± 0.02701

Table No.2: Baseline Body temperature

S.No	Group	Body temperature ºC (mean ±SEM)
1	Group I	37.25 ±0.1258
2	Group II	37.29±0.04264
3	Group III	37.18 ±0.0431
4	Group IV	37.15 ±0.05358

Table No.3: Final Body temperature after 18 hrs

S.No	Group	Body temperature ° C (mean ±SEM)			
		0 hour	1st hour	2nd hour	3rd hour
1	Group I	40.83± 0.01887	42.24± 1.655	40.4 ± 0.02366	39.87± 0.06872
2	Group II	40.83± 0.01939	39.8± 0.04505	39.26 ± 0.06794	38.65 ± 0.03715
3	Group III	40.31± 0.06146	39.36± 0.05955	38.84 ± 0.03146	38.22 ± 0.08333
4	Group IV	40.73± 0.1059	38.83±0.008028	38.63 ± 0.0147	37.63 ± 0.1174

CONCLUSION

The results of the present study demonstrate that the drug *Elathi Kuligai* has significant anti-inflammatory both the dose level significantly reduced the paw edema induced by Carrageenan, and anti-pyretic study was concluded that test drug *Elathi kuligai* at both the dose level significantly reduced the pyrexia induced by Brewer's yeast. It has been concluded that the potent Anti-inflammatory and anti-pyretic activity of *Elathi Kuigai* in rats and this results contribute towards the validation of the traditional use of *Elathi Kuligai* in the treatment of bronchitis in children.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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