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ANTIHISTAMINIC AND ANTIANAPHYLACTIC ACTIVITY OF SIDDHA FORMULATION OF *LAVANKATHI CHOORANAM* IN WISTAR RATS AND GUINEA PIGS

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ABSTRACT

Bronchial asthma (*Iya Iraippu Noi*) is a very common disease in the society, due to increasing exposure to air pollution and western life style. It is common in both sexes. The prevalence of bronchial asthma has increased significantly since the 1970s. According to the study in 2025, will expecting more than 300 million people will affect asthma.

In the present study, Anti Histaminic and Anti anaphylactic of *Lavankathi Chooranam* (LC) is investigated in animal models. Antihistaminic activity was studied in guinea pigs using histamine-induced bronchospasm, where pre convulsive dyspnea was used as an end point following exposure to histamine aerosol. It was evaluated for antihistamine and bronchodilator activities and it administrated at the doses of 200 and 400 mg/kg body weight. A dose response curve for histamine is lower, when compared with histamine induced contraction ($p<0.05$) at moderate dose level. The LC at moderate dose level significantly prolonged the latent period of convulsions as compared to control following the exposure of histamine aerosol. The result of study showed that *Lavankathi Chooranam* (LC) significantly protected the Guinea pigs against histamine-induced bronchospasm. Significant increase in between pre and post treatment period (**$P<0.01$). End of the study reveals that the *Lavankathi Chooranam* (LC) is more effective in the treatment of Bronchial asthma.

KEYWORDS: *Lavankathi Chooranam* (LC), Asthma, Antihistaminic activity, Antianaphylactic, Bronchodilator activity

INTRODUCTION

Allergy is one of the common diseases that affect mankind with diverse manifestations. The prevalence of allergy and asthma has been raised in the recent years despite an improvement in the general health of the population.[1] Allergic diseases are responsible for significant morbidity and have severe economic impact.[2] Various epidemiological studies have identified the causes upper and lower respiratory tract allergic diseases. Some of the postulated reasons are increasing environmental pollution [3] and increased pre disposition of individuals producing excessive Ig_E through a major change in the gene pool, changing lifestyles, and an increasing awareness of the disorders.[4]

Intensive research during the last several decades is highlighted the role of lymphocytes, immunoglobulins, mast cells, and various autacoids in the etiopathogenesis of allergic conditions. In spite of the voluminous literature on the subject, the treatment of allergic diseases continues to be far from satisfactory. The available treatment options for upper and lower respiratory tract allergic diseases have major limitations owing to low efficacy, associated adverse events, and compliance issues.[5]

AYUSH, an Indian system of medicine, has described several drugs from indigenous plant sources for use in the treatment of bronchial asthma and allergic disorders. In the this study, the effects of Siddha formulation of *Lavankathi Chooranam* were studied on the active anaphylaxis and mast cell stabilization in rats, and histamine-induced bronchospasm in guinea pigs.

Since the disease occurs due to the derangement of three life factor Siddhars have classified the disease accordingly .They classified as *Vatham* disease 80, *Pitham* disease 40, *Kapham* disease 21. *Iya Iraippu Noi* is one among the *kapha* disease.

As per *Yugi*, *Iya Iraippu* is a disease condition contributed by the following sign and symptoms such as sever cough with or without expectoration, Expiration is like a hiss of a serpent, frequent hemming, sense of heat in both nostrils, Hoarseness of voice, indigestion, flatulence which may be co-related to the disease condition “Bronchial Asthma” in modern science.

MATERIALS AND METHODS

Animals

Inbred Wistar rats (175–200 g) and guinea pigs (400–600g) of either sex housed in standard conditions (temperature 22 ± 2° C, relative humidity 60 ± 5% and 12 h light/dark cycle) were used. They were feed with standard pellet diet and water ad libitum. The

Institutional Animal Ethics Committee approved the experimental protocol. Histamine and horse serum were procured from Sigma Chemicals and toluidine blue from Loba-Chemie, Mumbai. Elisa kit for Ig_E was supplied by Orion diagnostics, Espoc, Finland. All other chemicals and reagents were procured from Hi-Media Laboratories limited, Mumbai.

Mast cell stabilizing activity

Treatment protocol

Twenty-four rats were divided into four groups of six animals in each group.

- **Group - I** : Served as control and received vehicle (water).
- **Group - II** : (Sensitized control group)
- **Group – III :** Served as the treatment control, which was treated with *Lavankathi Chooranam* at a dose of 200mg/kg body weight, in oral route.
- **Group - IV** : Served as the treatment control, which was treated with *Lavankathi Chooranam* at a dose of 400 mg/kg body weight, in oral route.

In group11 to group - IV were sensitized by injecting 0.5 ml of horse serum subcutaneously along with 0.5 ml of triple antigen containing 20,000 million Bordetella pertussis organisms (Serum Institute of India Ltd.,Pune), Once a day for 14 days.

On day 14, the rats were sacrificed 2 h after the treatment and the intestinal mesentry was taken out for the study on mast cells. Mesenteries along with intestinal pieces were excised and kept in Ringer Locke solution (NaCl 154, KCl 5.6, $CaCl_2$ 2.2, $NaHCO_3$ 6.0, glucose 5.55 mM/L of distilled water) at 37^{o}C. The mesenteric pieces were challenged with 5% horse serum for 10 min after which the mast cells were stained with 1.0% toluidine blue and examined microscopically for the number of intact and degranulated mast cells.[6]

Histamine-induced bronchospasm in guinea pigs

Bronchospasm was induced in guinea pigs by exposing them to 1% histamine aerosol under constant pressure (1 kg/cm2) in an aerosol chamber (24 × 14 × 24 cm) made of perplex Glass,of the three groups of six animals each.

- **Group - I** : Served as control.
- **Group - II** : Served as the treatment control, which was treated with *Lavankathi Chooranam* at a dose of 200 mg/kg body weight, in oral route.
- **Group - III** : Served as the treatment control, which was treated with *Lavankathi Chooranam* at a dose of 400 mg/kg body weight, in oral route.

The animals were exposed to 1% histamine aerosol under constant pressure (1 kg/cm2) in an aerosol chamber on day 0 without any treatment. The end point, preconvulsive dyspnea

(PCD) was determined from the time of aerosol exposure to the onset of dyspnea leading to the appearance of convulsions.[7] As soon as PCD commenced, the animals were removed from the chamber and exposed to fresh air. This PCD was taken as day 0 value. On days 1 and 5, 2 h after the administration of the drug, the time for the onset of PCD was recorded as on day 0.

Statistical analysis

The results of various studies were expressed as mean ± SEM and analyzed statistically using one-way ANOVA, followed by Newmann keul's multiple range tests. $P<0.05$ was considered statistically significant. The analysis was performed using Graphpad Prism software package (Version 4.0).

RESULTS

Mast cell stabilizing potential of *Lavankathi Chooranam* is Antigen challenge resulted in significant degranulation of the mesentric mast cells. Pretreatment of sensitized animals with *Lavankathi Chooranam* at a dose of 200mg/kg and 400mg/kg, p.o., for 2 weeks resulted in a significant reduction in the number of disrupted mast cells ($P <0.001$) when it was challenged with horse serum.

Effect on histamine-induced bronchospasm

Lavankathi Chooranam at a dose of 200mg/kg and 400mg/kg p.o., significantly prolonged the latent period of PCD ($P <0.001$) as compared to control, following exposure to histamine aerosols on day 5 [Table no. 2].

TABLE NO:1 EFFECT OF *LAVANKATHI CHOORANAM* ON MAST CELL STABILIZATION IN SENSITIZED RATS

GROUPS	MAST CELLS	
	INTACT	DISRUPTED
Normal control	83.50±3.46	13.90±0.83
Sensitized rats	12.80±0.92	86.34±2.63
Lavankathi Chooranam 200mg/kg	65.36±2.86*a	35.30±1.42*a
Lavankathi Chooranam 400mg/kg	63.28±2.75*a	35.86±1.52*a
Normal control	Intact	Disrupted

- Values are expressed as Mean ± S.E.M

*a significantly different from sensitized control at $p<0.01$

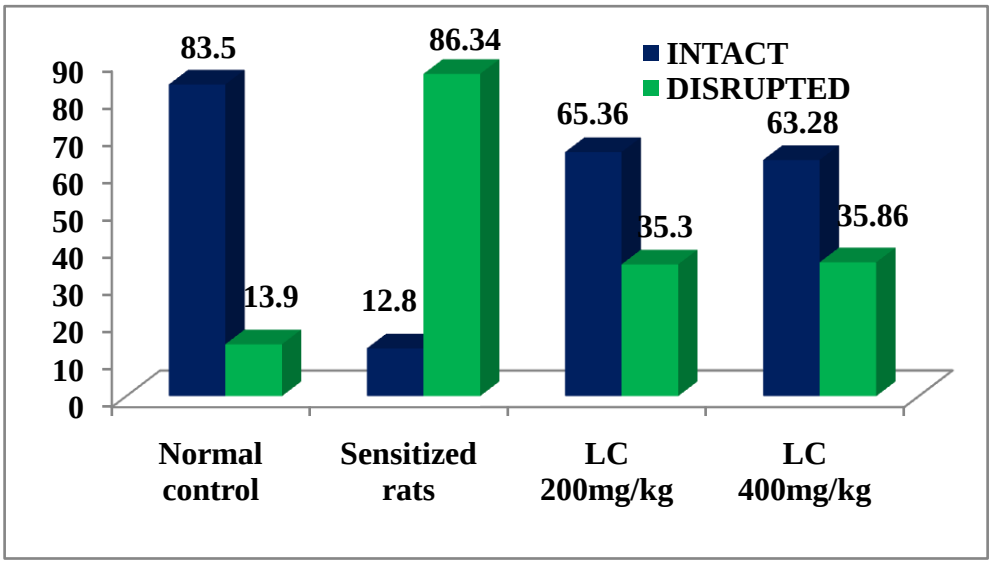


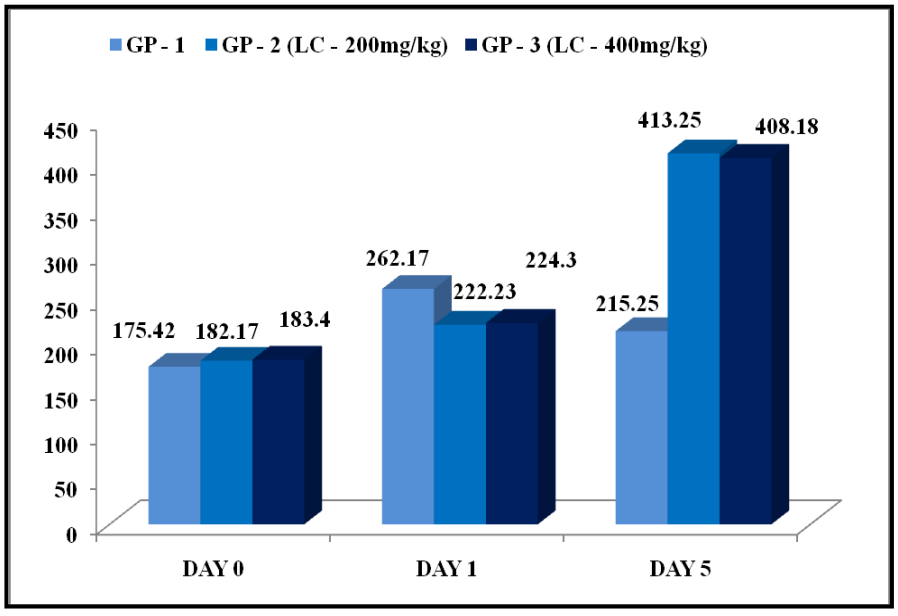
TABLE NO 2 :

EFFECT OF *LAVANKATHI CHOORANAM* ON HISTAMINE INDUCED BRONCHOSPASM IN GUINEA PIGS.

GROUPS	PRE-CONVULSION DYSPNEA (PCD)(SEC)		
	DAY 0	DAY 1	DAY 5
GP - 1	175.42±7.30	262.17±9.6	215.25±9.6
GP - 2 (LC - 200mg/kg)	182.17±6.40	222.23±6.5	413.25±13.1*a
GP - 3 (LC - 400mg/kg)	183.40±6.30	224.30±8.4	408.18±12.3*a

Values are expressed as Mean ±S.E.M

*a significantly different from control on day 5 at p<0.001



DISCUSSION

Experimental animal model of asthma is characterized by allergen-induced immediate airway constriction and late airway reactivity to a pharmacological vasoconstrictor such as histamine and leukotrienes. Histamine is a central mediator in the pathogenesis of allergic and inflammatory disorders. In the present study, *Lavankathi Chooranam* prolonged the latent period of PCD in guinea pigs following histamine aerosol. This may be suggestive of an antihistaminic activity following treatment with *Lavankathi Chooranam*.

Antigen challenge, in sensitized animals, results in the degranulation of mast cells, which is an important feature of anaphylaxis. In the present study, *Lavankathi Chooranam* show marked protection against the mast cell degranulation following antigen challenge in sensitized animals. Mast cell stabilizing activity of *Lavankathi Chooranam* may be attributed to the presence of active constituents which are known for their mast cell stabilizing potential against antigen–antibody reaction or due to the suppression of IgE antibody production, which is responsible for degranulation mast cells.[8]

This antihistaminic and antianaphylactic effect may be caused by the stabilization of the mast cell membrane, suppression of IgE, and inhibition of pathological effects induced by the release of inflammatory mediators in *Lavankathi Chooranam* treated animals. All the above findings lend credence to the beneficial use of *Lavankathi Chooranam* in the treatment of asthma and related conditions.

However, further studies with other experimental models, especially to explore the role of cytokines are warranted to substantiate the antihistaminic and antianaphylactic activity of *Lavankathi Chooranam.*

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