

## MAST CELL STABILIZATION AND BRONCHOSPASM INHIBITION BY ARITHRATHI CHOORANAM, A TRADITIONAL SIDDHA MEDICINE: EVIDENCE FROM PRECLINICAL STUDIES

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## Abstract

**Background:** Allergic disorders, including asthma, pose a significant health burden worldwide, with increasing prevalence due to environmental and genetic factors. Conventional treatments often have limitations in efficacy and safety, necessitating the exploration of alternative therapies. The Siddha system of medicine offers promising herbal formulations, such as Arithrathi Chooranam, traditionally used for respiratory ailments. This study evaluates its antihistaminic and antianaphylactic potential.

**Methods:** The study assessed mast cell stabilizing and bronchospasm inhibitory effects of Arithrathi Chooranam in animal models. Wistar rats were sensitized using horse serum and Bordetella pertussis antigen, followed by treatment with the formulation (200 mg/kg and 400 mg/kg orally). The percentage of degranulated mast cells was measured. In guinea pigs, histamine-induced bronchospasm was evaluated by determining the preconvulsive dyspnea (PCD) latency after exposure to histamine aerosol. Statistical analyses were conducted using one-way ANOVA.

**Results:** Arithrathi Chooranam demonstrated significant mast cell stabilization, reducing degranulated mast cells ( $P < 0.001$ ). In histamine-induced bronchospasm, treatment prolonged PCD latency ( $P < 0.001$ ), indicating an antihistaminic effect. These findings suggest its potential role in modulating allergic responses and preventing airway hyperresponsiveness.

**Conclusion:** Arithrathi Chooranam exhibits significant antianaphylactic and antihistaminic properties, supporting its traditional use for allergic and respiratory disorders. Further research is warranted to elucidate its molecular mechanisms and clinical applicability.

## Introduction

Allergy is one of the common diseases that affect mankind with diverse manifestations. The prevalence of allergy and asthma has risen 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 for an increase in the prevalence of upper and lower respiratory tract allergic diseases. Some of the postulated reasons are increasing environmental pollution [3] and increased predisposition of individuals producing excessive IgE 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 has 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 present study, the effects of Siddha formulation of arithrathi chooranam were studied on the active anaphylaxis and mast cell stabilization in rats, and histamine-induced bronchospasm in guinea pigs.

## Materials and Methods

Inbred Wistar rats (175–200 g) and guinea pigs (400–600g) of either sex housed in standard conditions (temperature  $22 \pm 2^\circ \text{C}$ , relative humidity  $60 \pm 5\%$  and 12 h light/dark cycle) were used. They were fed with standard pellet diet and water ad libitum. The Institutional Animal Ethics Committee approved the experimental protocol. Approval number: **IAEC/KMCP/230/2015-16**. Histamine and horse serum were procured from Sigma Chemicals and toluidine blue from Loba-Chemie, Mumbai. Elisa kit for IgE was supplied by Orion diagnostics, Espoo, Finland. All other chemicals and reagents were procured from HiMedia 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 negative control and received vehicle (water).

**Group II** : (sensitized control group)

**Group III** : Served as the treatment control, which was treated with arithrathi chooranam at a dose of 200mg/kg body weight, in oral route.

**Group IV** : Served as the treatment control, which was treated with arithrathi chooranam at a dose of 400 mg/kg body weight, in oral route.

In group I 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 mesentery 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<sub>2</sub> 2.2, NaHCO<sub>3</sub> 6.0, glucose 5.55 mM/L of distilled water) at 37°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/cm<sup>2</sup>) in an aerosol chamber (24 × 14 × 24 cm) made of perplexx 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 arithrathi chooranam at a dose of 200 mg/kg body weight, in oral route.

**Group III** : served as the treatment control, which was treated with arithrathi 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/cm<sup>2</sup>) 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 arithrathi chooranam Antigen challenge resulted in significant degranulation of the mesenteric mast cells. Pretreatment of sensitized animals with arithrathi 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 challenged with horse serum. [ Table – 1]

**Table No:1**

GROUPS	MAST CELLS	
	INTACT	DISRUPTED
NORMAL CONTROL	83.45±3.40	13.90±0.80
SENSITIZED RATS	12.76±0.92	88.40±2.60
arithrathi chooranam 200mg/kg	66.42±2.85*a	35.40±1.45*a
arithrathi chooranam 400mg/kg	64.30±2.65*a	34.95±1.55*a

effect of arithrathi chooranam on mast cell stabilization in sensitized rats • Values are expressed as Mean±S.E.M

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

#### **Effect on histamine-induced bronchospasm**

Arithrathi 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 2**

GROUPS	PRE-CONVULSION DYSPNEA (PCD)(SEC)		
	DAY 0	DAY 1	DAY 5
GP 1	175.35±7.30	260.20±9.2	213.30±9.6
GP 2 (arithrathi chooranam 200mg/kg)	182.10±6.40	222.15±6.5	414.30±13.2*a
GP3 (arithrathi chooranam 400mg/kg)	185.40±6.35	226.30±8.2	408.22±12.6*a

Effect of arithrathi chooranam on histamine induced bronchospasm in guinea pigs.

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, arithrathi chooranam prolonged the latent period of PCD in guinea pigs following histamine aerosol. This may be suggestive of an antihistaminic activity following treatment with arithrathi chooranam.

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

This antianaphylactic and antihistaminic 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 arithrathi chooranam treated animals. All the above findings lend credence to the beneficial use of arithrathi 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 antiasthmatic and antiallergic activity of arithrathi chooranam.

### Conclusions

The current research provides compelling experimental evidence supporting the antiasthmatic and antiallergic properties of a traditional herbal formulation known as arithrathi chooranam, tested in an animal model of asthma. Key findings from the study indicate that arithrathi chooranam demonstrates antihistaminic activity by extending the time it takes for histamine to induce airway constriction in guinea pigs. Additionally, it exhibits a stabilizing effect on mast cells, offering protection against mast cell degranulation in sensitized animals when exposed to an antigen challenge. The observed antianaphylactic and antihistaminic effects of arithrathi chooranam may be linked to its ability to stabilize mast cell membranes, reduce IgE antibody production, and inhibit the release of inflammatory mediators. These findings lend scientific credibility to the traditional use of arithrathi chooranam in managing asthma and related allergic conditions. However, further research is necessary to clarify the exact mechanisms of action and to assess its efficacy in various experimental models. Overall, this study underscores the potential therapeutic benefits of arithrathi chooranam in treating asthma and associated allergic disorders.

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