# *Original Research Article*

**EVALUATION OF ANTIASTHMATIC ACTIVITY**

**OF ERAIPPU NOI CHOORANAM (ENC)**

---


## Abstract

### Background

Eraippu Noi Chooranam is a modified Siddha Poly Herbal formulation indicated for respiratory diseases in the text Siddha research pharmacopoeia. The indicated traditional claim enforced to evaluate its efficacy in the management of Bronchial asthma.

### Aim:

The aim of study is to evaluate the anti asthmatic activity of ENC *in Bronchial asthma*.

### Materials and Methods:

In the present study, aqueous extract of *ENC* was evaluated for its antiasthmatic activity using histamine and acetylcholine-induced bronchospasm, in guinea pig at different dose levels.

### Result:

The test drug ENC at all the three doses of 100,200,300 mg/kg p.o significantly ( $p<0.01$) increased the latent period of convulsions following exposure to histamine aerosol when compared to control. The percentage of protection by the standard drug was 82.8 % whereas the protection offered by ENC at 100,200and 300 mg/kg was found to be 61.5%,71.1 % and 80% respectively. High dose of ENC offered highest protection which was comparable to standard.

### Conclusion:

It can be concluded that aqueous extract of *ENC* may be used in the management of asthma.



**Keywords :** Bronchial asthma, Siddha medicine, Poly Herbal formulation, Eraippu Noi Chooranam, Bronchospasm

## INTRODUCTION

Every human race has its own traditional system of medicines [1]. Our country has the oldest, richest and most diverse traditional medicine cultures in the world. In India several thousands of plant species are being used by thousands of ethnic communities. Siddha medicine is an integrated part of Indian system which is very potent and unique in its own right, by providing healing of the body, mind and soul. Siddha system propounded by the Siddhars is an all inclusive versatile system[2]

Asthma is a heterogeneous disease of the airways characterized by chronic inflammation associated with bronchial and smooth muscle hyper responsiveness. It is characterized by narrowing of airways, frequent wheezing, dyspnea, chest tightness, morning awakeness, and night coughing.[3] Asthma depends on the various factors such as allergens, respiratory infection, dust, cold air, exercise, emotions, occupational stimuli, certain drugs/chemicals, histamine, and heredity. These trigger factors accelerate the activation of immunoglobulin-E (IgE) mediated mast cell, release of interleukins (IL-4 and IL-5) and other inflammatory factors including eosinophils, neutrophils, β-cells, cytokines, and chemokines which lead to inflammation or obstruction in throat, bronchial hyperresponsiveness, and mucosal hypersecretions.[4]

Mast cells play a critical role in the pathogenesis of allergic asthma. Histamine is a central mediator released from mast cells through allergic reactions. Histamine plays a role in airway obstruction via smooth muscle contraction, bronchial secretion, and airway mucosal edema. It has been elucidated that four types of histamine receptors such as H1, H2, H3, and H4 exist in the airway and pulmonary tissue [5-8].The bronchoconstriction of smooth muscle mediated via H1 receptors is one of the most well-known biological actions of histamine in the respiratory system. It was reported long before that histamine evoked a contraction of human bronchi, and bronchoconstriction was recognized first as one of the biological actions of histamine[9].

Despite the availability of a wide range of antiasthmatic drugs, the relief offered by them is mainly symptomatic and show a poor or absent response even to high doses with more or less side effects. Hence, an ideal approach in the development of new drug toward safe and effective remedies is only from herbal sources to treat bronchial asthma. In this regard, a safe and effective herbal drug will be the choice of the individual to overcome the situation.

Though Siddha drugs are considered to be safe and effective, it is the utmost duty of the physicians to validate the formulation before trying out in humans. Eraippu Noi Chooranam is a modified Siddha Poly Herbal formulation mentioned in the text Siddha research pharmacopoeia. It is indicated for asthma, chronic bronchitis and flatulence[10]. It is a poly herbal drug and all the ingredients included are very effective in curing kapha diseases. The indicated traditional claim enforced to evaluate its efficacy in the management of Bronchial asthma.

## 2. Aim and objectives

The aim of this study is to evaluate the anti asthmatic property of the drug Eraippu Noi Chooranam by Histamin induced Bronchospasm.

## 3. Materials and Methods

### 3.1 Collection and Identification of plant materials

The herbal ingredients were authenticated by the Assistant Professor of Medicinal botany, National Institute of Siddha, Chennai. The raw drugs were purified as per the methods mentioned in the literature.

### 3.2 Preparation of the drug Eraippu Noi Chooranam[11]:

**Ingredients:**

Kuppaimeni leaves choornam (*Acalypha indica*) - 224 gms

Chiru Cherupadai leaves choornam (*Mollugo lotoides*) - 224 gms

Potrilai kaiyan leaves choornam (*Eclipta prostrata*) - 224 gms

Vembu leaves choornam (*Azadiracta indica*) - 224 gms

Milagu fried chooranam (*Piper nigrum*) - 112 gms

Arisi thippili chooranam (*Piper longum*) - 112 gms

Amukkara chooranam (*Withania somnifera*) - 112 gms

Kadukkai thol chooranam (*Terminalia chebula*) - 112 gms

Cane sugar powder -392 gms

### 3.3. Purification of raw drugs[12,13]:

The raw drugs are purified as per the methods mentioned in the Siddha literatures.

### 3.4 Preparation of trial drug:

All the ingredients were powdered separately and mixed together as per the mentioned composition and bottled up.

## 4. Physicochemical Analysis[14]

Preliminary Physicochemical analysis of the test drug was carried out in the aqueous extract of ENC which revealed that it was of standard quality. Phytochemical analysis revealed the presence of phytosterols, flavanoides, aminoacids, carbohydrates, terpenoids, phenolic compounds and tannin.

## 5.Toxicity Study of ENC[15]

Single dose acute toxicity study revealed that Eraippu Noi Chooranam was safe and did not produce any toxic effect at the dose of 2000 mg/kg.

Repeated dose administration of ENC in sub acute toxicity study reported that there were no treatment related histopathological abnormalities in any of the organs noticed and hence NOAEL of ENC was greater than 900 mg/kg/b.w in rats

### 6.Histamine induced bronchospasm[16]

The guinea pigs (400-600 g) of either sex were purchased from Sree Venkateshwara Enterprises Pvt. Ltd, Bangalore and housed in standard laboratory condition in Polypropylene cages, in a well ventilated room under an environmental temperature of 22±3°C and relative humidity of 30-70%, with a 12-h light/dark artificial light cycle. They were provided with standard pellet diet from 'Sai Durga Animal Feed, Bangalore and water *adlibitum.* In addition to pellet diet guinea pigs were supplemented with Lucerne.

### Experimental design

Group 1: Control -Aerosol Of 0.1% Histamine Hydrochloride

Group 2: Standard Chlorpheniramine Maleate 2 Mg/Kg, P.O +

Aerosol Of 0.1% Histamine Hydrochloride

Group 3: Eraippunoi Chooranam 100mg/Kg +

Aerosol Of 0.1% Histamine Hydrochloride

Group 4: Eraippunoi Chooranam 200mg/Kg +

Aerosol Of 0.1% Histamine Hydrochloride

Group 5: Eraippunoi Chooranam 300mg/Kg +

Aerosol Of 0.1% Histamine Hydrochloride

### Procedure

The animals were kept in a closed chamber (30×30×15cm) and were then exposed to an aerosol of 0.1% Histamine hydrochloride. The time of aerosol exposure to the onset of dyspnoea leading to the appearance of convulsions termed as pre-convulsion time (PCT) was noted. As soon as symptoms similar to that of convulsion occurs , animals were removed from the chamber and kept in fresh air to recover. This value of PCT was taken as basal value. Later, all groups were treated with their respective drugs once daily for a period of 7 days. After 7 days, respective drug treatment were given and two hours after the treatment , animals were exposed to an aerosol of 0.1% Histamine hydrochloride and PCT was measured by nebulizer pump (Aero space nebulizer). The protection percentage rendered by the treatment was calculated by the following formula,

Percentage protection = {1- T1/T2}× 100

Where, T1 = PCD time in second before treatment; T2 = PCD time in second after treatment

## 7. RESULT

Release of inflammatory mediators such as histamine, acetylcholine, prostaglandins, tryptase and leukotrienes are initiated by getting exposed to irritants, allergens, cold air or exercise during the early stage of asthma, [17] . Some of these mediators directly results in acute bronchoconstriction. Medications such as spasmolytic drugs are used to give quick relief in such acute asthmatic attacks [18] . In the present study, histamine aerosol was used as spasmogen to cause bronchoconstriction in guinea pigs. CPM (Chlorophenarmine maleate ) (2mg/kg) was included as the reference standard against histamine induced bronchospasm.[19] The test drug ENC at all the three doses of 100,200,300 mg/kg p.o significantly ( $p<0.01$) increased the latent period of convulsions following exposure to histamine aerosol when compared to control. Effect of ENC against bronchoconstriction induced by histamine in the guinea pigs is shown in Table.1 and fig.1. The percentage of protection by the standard drug was 82.8 % whereas the protection offered by ENC at 100,200and 300 mg/kg was found to be 61.5%,71.1 % and 80% respectively. High dose of ENC offered highest protection which was comparable to standard and it was illustrated in Table.2 and fig .2

**Table.1 Effect of ENC on Histamine induced bronchospasm**

| GROUPS | PCD IN SECONDS | | % OF PROTECTION |
|---|---|---|---|
| | | | |
| CONTROL | 121.6± 3.17 | 131.2± 2.6 | 7.3 |
| CPM (2mg/kgbw) | 124.2± 2.52 | 720± 17.01** | 82.8 |
| ENC LD 100mg/kg | 123± 3.65 | 319.2± 12.82** | 61.5 |
| ENC MD 200mg/kg | 121.6± 3.70 | 421.4± 8.10** | 71.1 |
| ENC HD 300 mg/kg | 122.8± 4.04 | 614.8± 9.54** | 80 |

Values are expressed as mean ± SEM. N=5 ** $P<0.05$ when compared to control. Statistically analysed by one way ANOVA followed by Dunnett's test.

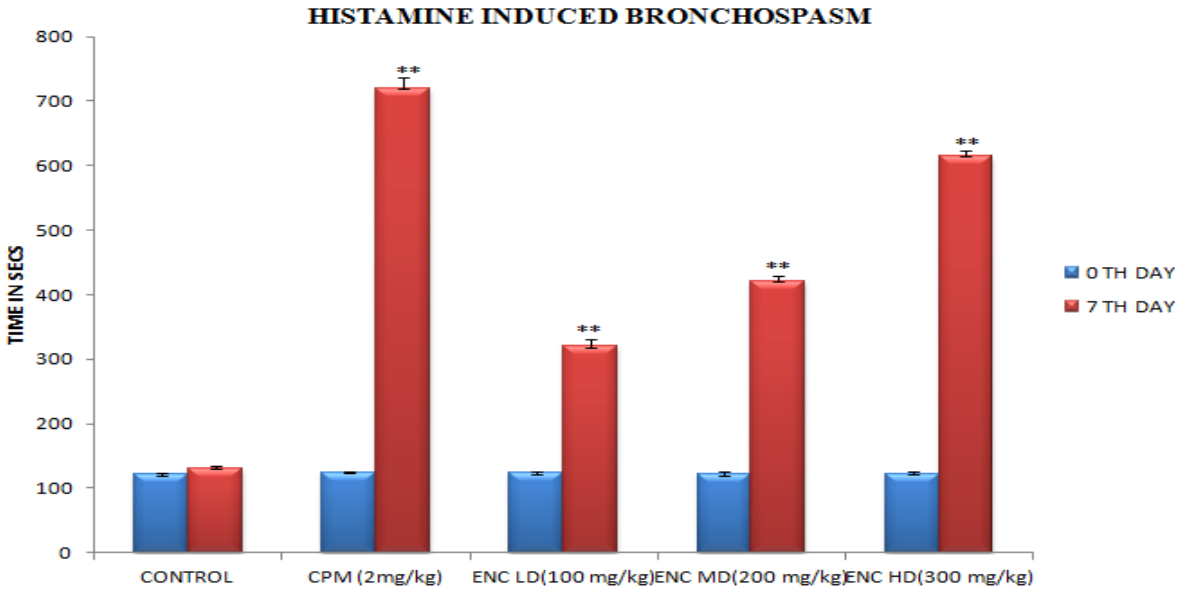


**Fig.1 Effect of ENC on Histamine induced bronchospasm**

**Table.2 Protection offered by ENC on Histamine induced Bronchospasm**

| GROUPS | % OF PROTECTION |
|---|---|
| CONTROL | 7.3 |
| CPM (2mg/kg) | 82.8 |
| ENC LD 100mg/kg | 61.5 |
| ENC MD 200mg/kg | 71.1 |
| ENC HD 300 mg/kg | 80 |

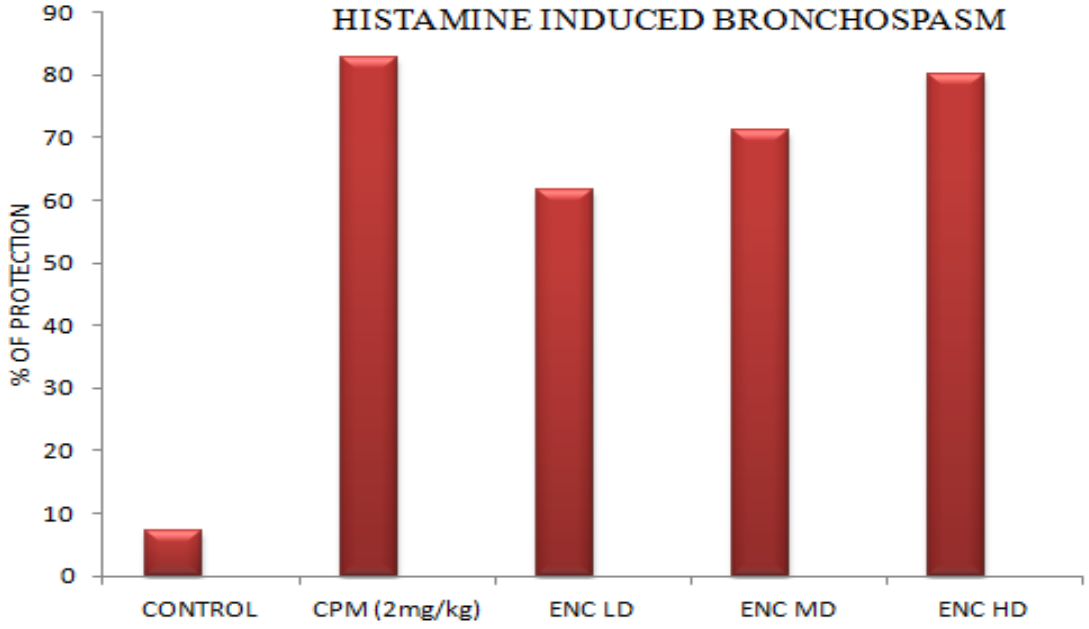


**Fig.2 Percentage of protection offered by ENC in histamine induced bronchospasm**

## 8.Discussion

The central mediator in the pathogenesis of allergic disorders is histamine and it causes bronchospasm thus precipitating bronchial asthma. Histamine act as inflammatory mediators and causes increase in mucous secretion thus resulting in a crowd of changes in the bronchial tissue and finally constriction of smooth muscles of bronchus thus reducing air flow leading to hypoxia and convulsions. There is a very close resemblance of pulmonary responses to histamine challenge in both guinea pigs and human species, as well as the anaphylactic sensitization made this species the model of choice. Inhalation of histamine and acetylcholine is a classical model of inducing bronchoconstriction which results intense smooth muscle contractions, hypoxia, and convulsion in case of guinea pig. Bronchodilators can delay the occurrence of these symptoms.[20] In this study histamine as spasmogens in the form of aerosols is used to cause immediate bronchoconstriction in guinea pigs.CPM (2mg/kg) is included as the reference standard against histamine induced bronchospasm. In this study, the trial drug ENC showed a sustained inhibitory effect on preconvulsive dyspnoea and prolonged latent period of convulsion in the guinea pigs exposed to histamine aerosols. The results of the study suggest that the trial drug ENC significantly increased the time of occurrence of PCD via dilatation of bronchial smooth muscles. Again, ENC showed a dose-dependent inhibitory effect on preconvulsive dyspnoea in sensitized guinea pigs exposed to histamine aerosols.

NOTE:

The study highlights the efficacy of "natural herbal source" which is an ancient tradition, used in some parts of India. This ancient concept should be carefully evaluated in the light of modern medical science and can be utilized partially if found suitable

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

REFERENCE

1. WHO Traditional medicine strategy 2014-2023 page no 25. Pub; World Health Organization, Geneva

2. Thirunarayanan T, Introduction to Siddha Medicine Pub Centre for Traditional Medicine and Research, Chennai 2012.
3. Holgate ST, Polosa R. Treatment strategies for allergy and asthma. Nat Rev Immunol 2008;8:218-30.
4. Sagar R, Sahoo HB, Kar B, Mishra NK, Mohapatra R, Sarangi SP. Pharmacological evaluation of Calendula officinalis L. on bronchial asthma in various experimental animals. Int J Nutr Pharmacol Neurol Dis 2014;4:95-103.
5. Jones J.V. The nature of the pulmonary receptors excited by antihistamines. *Br. J. Pharmacol. Chemother.* 1952;7:450–454. doi: 10.1111/j.1476-5381.1952.tb00712.x. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
6. Tucker A., Weir E.K., Reeves J.T., Grover R.F. Histamine H1- and H2-receptors in pulmonary and systemic vasculature of the dog. *Am. J. Physiol.* 1975;229:1008–1013. doi: 10.1152/ajplegacy.1975.229.4.1008. [PubMed] [CrossRef] [Google Scholar]
7. Ichinose M., Barnes P.J. Inhibitory histamine H3-receptors on cholinergic nerves in human airways. *Eur. J. Pharmacol.* 1989;163:383–386. doi: 10.1016/0014-2999(89)90212-4. [PubMed] [CrossRef] [Google Scholar]
8. Kay L.J., Suvarna S.K., Peachell P.T. Histamine H4 receptor mediates chemotaxis of human lung mast cells. *Eur. J. Pharmacol.* 2018;837:38–44. doi: 10.1016/j.ejphar.2018.08.028. [PubMed] [CrossRef] [Google Scholar]
9. Curry J.J. The effect of antihistamine substances and other drugs on histamine bronchoconstriction in asthmatic subjects. *J. Clin. Investig.* 1946;25:792–799. doi: 10.1172/JCI101765. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
10. The Pharmacopoeia of siddha medicines- Dr.M.Shanmugavelu & dr.G.D.Naidu. Published by Dr.G.D.Naidu Industrial labour welfare association ltd, Coimbatore.
11. The Pharmacopoeia of siddha medicines- Dr.M.Shanmugavelu & Dr.G.D.Naidu.Published by Dr.G.D.Naidu Industrial labour welfare association ltd, Coimbatore.
12. Dr.R.Thyagarajan,(Gunapadam Thadhu Jeeva Vaguppu, Indian medicine and Homoeopathy, Chennai-106,Ed - 4 1992 )
13. Saraku suthisei muraiyagal
14. International Journal of Advanced Multidisciplinary Research (IJAMR) ISSN: 2393-8870 www.ijarm.com Volume 3, Issue 6 -2016 34-38
15. International Journal of Advanced Research in Biological Sciences ISSN: 2348-8069 www.ijarbs.com Volume 3, Issue 6 – 2016 106-112
16. Armitage AK, Boswood J, Large BJ. Thioxanthines with potent bronchodilator and coronary dilator properties. Br Pharm Chemother 1961;16:59-76 (isolated tissue, HISTAMINE)
17. . Bosquet J., Jeffery P.K., Busse W.W. Asthma: From bronchoconstriction to airway inflammation and remodeling. *Am.J.Respi.Care.Med*. 161 : 1745-1749 (2000)
18. Horwitz R. J., Busse W.W. Inflammation and asthma. *Clin. Chest. Med*. 16 : 583-620 (1995).
19. Shah G. B., Parmar N. S. Antiasthmatic property of polyherbal preparation E-721. *B. Phytother.Res*. 17 :1092-1097 (2003

20. Stephen OO, Gerald IE, Ifeanyi HA, Ogochukwu LI, Dickson OU, Viona O, et al. Evaluation of the anti-asthma activity of aqueous root bark extract of Ficus exasperata Vahl (Moraceae). Int J Health Res 2012;5:5-12.