

EVALUATION OF ANTI-ASTHMATIC ACTIVITY OF ERAIPPU NOI CHOORANAM (ENC)

Abstract

Background

Every human race has its own traditional system of medicines. Siddha system of medicine is unique and ancient of its kind originating from Tamil Nadu in India. Siddha system could be considered as the crown of all the traditional arts of the ancient Tamil. 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 & Objective:

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 anti asthmatic 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 100,200 and 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 system²

A rise in the occurrence of allergic diseases, has reported in the last few decades. Both the diseases have a significant impact on the economic burden of the people and also they affect the quality of their life. Approximately worldwide 300 million people are suffering from asthma and this is proposed to increase to 400 million by year 2025. Approximately 500,000 hospitalizations each year occurs on account of asthma, with around 250,000 deaths annually attributed to the disease. The percentage of school children suffering from bronchial asthma in India doubled in the last 10 years and has reached its highest level ever. A study conducted on children from urban and rural areas in the state Tamil Nadu in the age group of 6-12 years elicit the prevalence of wheeze to be 18%.

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, dyspnoea, 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 oedema. 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 histamine⁹.

Despite the availability of a wide range of anti-asthmatic 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 flatulence¹⁰. 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 Histamine 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 Standard operating procedure of the drug Eraippu Noi Chooranam¹¹:

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 Analysis¹⁴

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, flavonoids, amino acids, carbohydrates, terpenoids, phenolic compounds and tannin.

5.Toxicity Study of ENC¹⁵

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 bronchospasm¹⁶

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 $22\pm 3^{\circ}\text{C}$ 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 was 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,

$$\text{Percentage protection} = \{1 - T1/T2\} \times 100$$

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.

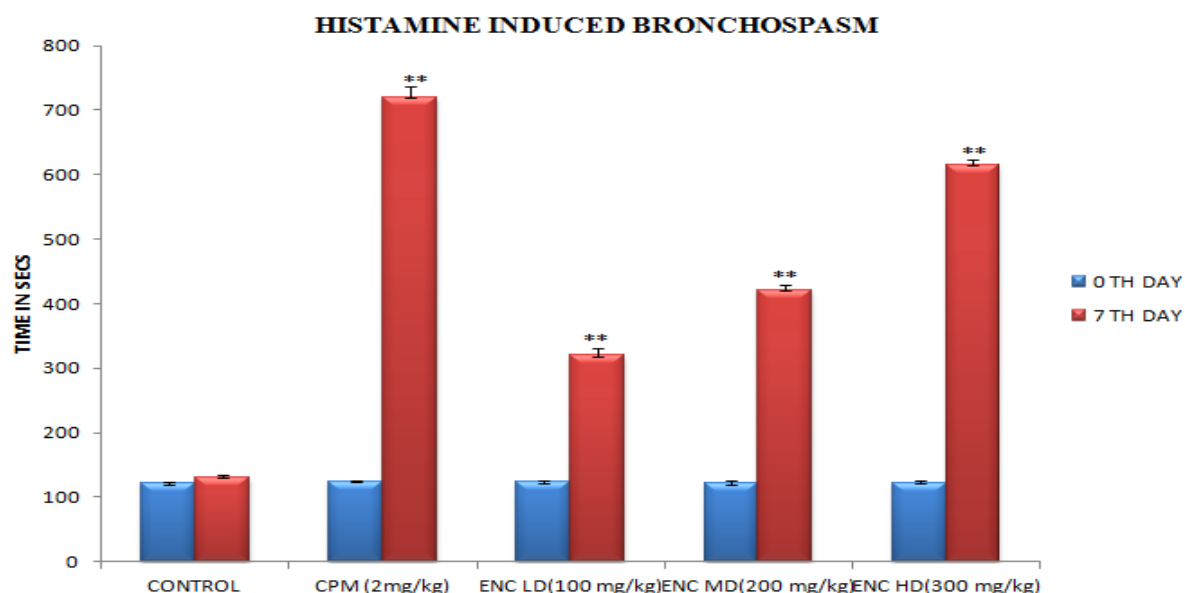


Fig.1 Effect of ENC on Histamine induced bronchospasm

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

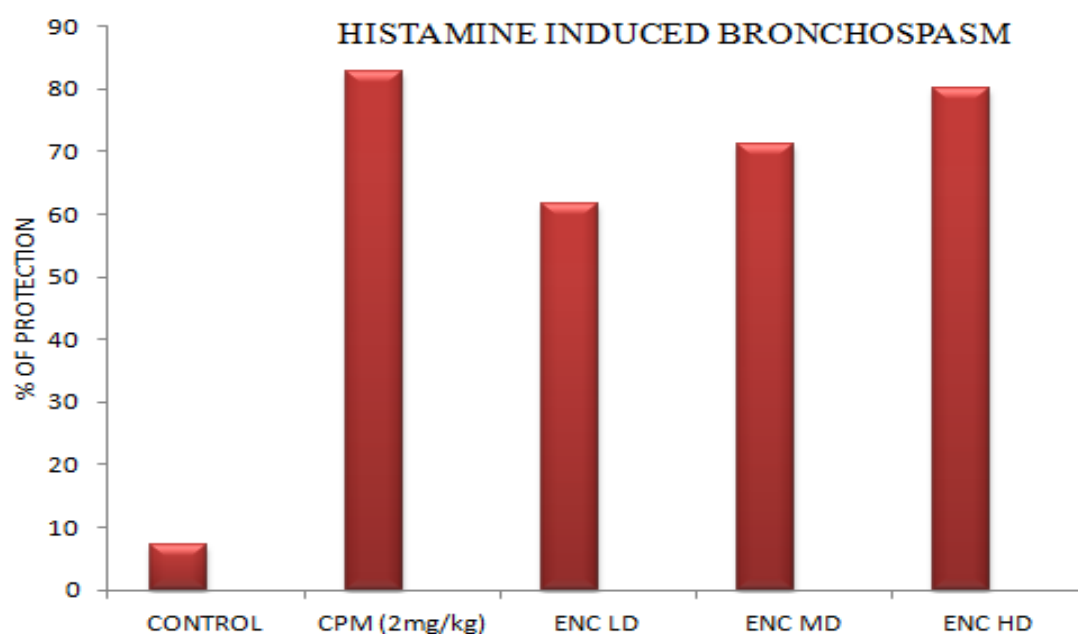


Fig.2 Percentage of protection offered by ENC in histamine induced bronchospasm

8. Discussion

Histamine induced broncho-constriction is the traditional immunological model of antigen induced airway obstruction. Histamine when inhaled causes hypoxia and leads to convulsion in the guinea pigs and causes very strong smooth muscle contraction, profound hypotension, and capillary dilation in the cardiovascular system. A prominent effect caused by histamine is severe bronchoconstriction in the guinea pigs that causes asphyxia and death. Broncho dilators can delay the occurrence of these symptoms.

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. The outcomes of the present study showed that latent period of PCD in guinea pigs is prolonged by the test drug ENC following histamine aerosols. Due to the presence of a number of phytoconstituents like Phyto sterols, flavonoids and others, 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. Again, ENC showed a dose-dependent inhibitory effect on preconvulsive dyspnoea in sensitized guinea pigs exposed to histamine aerosols. The result of this study proves that the possible mechanism of action appears to be the broncho constriction produced by histamine was antagonized strongly by ENC possessing significant anti asthmatic activity

Conclusion:

From the result obtained, it can be concluded that the aqueous extract of the trial drug ENC has antiasthmatic activity and have beneficial effect in asthma.

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

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