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Evaluation of Anti-Asthmatic Activity of Siddha Drug Thalaga Kuligai against Histamine Induced Rodents

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ABSTRACT

This preclinical study was designed to evaluate the Anti-asthmatic activity of the Siddha drug Thalaga kuligai by using *in-vitro* and *in-vivo* methods on different animal models. The asthmatic activity was evaluated by Histamine and acetylcholine induced constriction on isolated rat colon and guinea pig ileum by *in-vitro* method and histamine induced bronchospasm in guinea pig by *in-vivo* method. The pre-convulsion dyspnoea time at 0^{th} and 7^{th} days at the dose of 200 mg/kg in guinea pig, the smooth muscle relaxation at the dose of 100 mg/kg on isolated guinea pig ileum was evaluated and compared with the standard groups. The present study showed that the drug Thalaga kuligai was effective against histamine and acetylcholine induced contraction on guinea pig ileum and rat colon on dose dependant manner.

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INTRODUCTION

Asthma is an inflammatory disease of the small airways characterized by episodic, reversible bronchial obstruction, polyphonic wheeze, dyspnoea, and cough which may be relieved spontaneously or as a result of therapy[1]. The prevalence of asthma has significantly increased in recent decades, that is, nearly 7% - 10% of the world population were affected in each year. In urban areas, this problem is increasing due to increase in environmental smoke and air pollution resulting from urbanization. It can be triggered by various factors like allergens, drugs, respiratory infection, dust, cold air, exercise, emotions, occupational stimuli, chemicals, histamine and also hereditary[2]. Between 100 and 150 million people around the globe suffer from Asthma. In India 15-20 million people get affected. WHO recognize Asthma as a disease of major public health importance and place a unique role in the co-ordination of international efforts against the disease.

Asthma cannot be cured but it could be controlled[3]. Despite the availability of a wide range of Anti-asthmatic drugs, the relief offered by them is mainly symptomatic and short lived with more or less side effects. Assessing the current status of health care system, there has been an alarming increase in number of diseases or disorders caused by synthetic drugs promoting a switch over to traditional medical system[4,5].

Siddha system is a traditional medical system in South India. It is the most primitive medical system. This art of healing incorporates a variety of holistic practices and remedies which were established by the eminent powers called Siddhars, out of their intuitions. Hence it is named as Siddha Medicine. In Siddha system the symptoms of Bronchial asthma can be correlated with the symptoms of Swasakasam as quoted by Yugi muni[6]. The present study was undertaken to investigate the effect of the herbo-mineral formulation of Siddha drug Thalaga kuligai quoted in the text Agasthiyar Vaithiya Kaviyam-1500[7] for its Anti-asthmatic activity against Histamine and acetylcholine induced Rodents.

MATERIALS AND METHODS

Materials:

Histamine dichloride, acetylcholine chloride were used drugs, were purchased from Sigma chemical, USA. Histamine and acetylcholine was dissolved in distilled water and desired

concentration was prepared. The interventional drug Thalaga kuligai was prepared in Government Siddha Medical College, Chennai.

Animals:

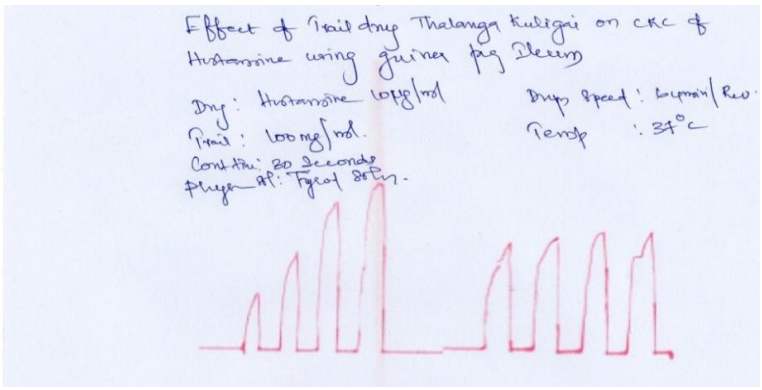
Wister albino rats (150-200 gm) and Guinea pigs (400- 600 gm) of either sex housed in standard conditions of temperature 24-28^{0}C and standard light cycle (12 hours light/dark cycles) were used. They are fed with standard pallet diet and water *ad libitum*. The experimental protocol was approved by Institutional Animal Ethical Committee as per the guidance of CPCSEA and the approval no is KKCP/2013/005/CPCSEA.

***In vitro* Evaluation**

Isolated guinea pig ileum preparation[8,9]

Guinea pigs weighing (300-500 g), starved overnight with water *ad libitum*. The animal was killed by a blow on the head and the neck was exsanguinated. The abdomen was cut open and a suitable length of the ileum (approximately 2 cm long) was placed on a petridish containing Tyrode solution. The composition of the Tyrode solution in mM was NaCl 137 mM, $NaHCO_3$ 12 mM, NaH_2PO_4 0.3 mM, KCl 2.7 mM, $MgCl_2$ 1.0 mM, $CaCl_2$ 1.0 mM and d- glucose 5.6 mM.

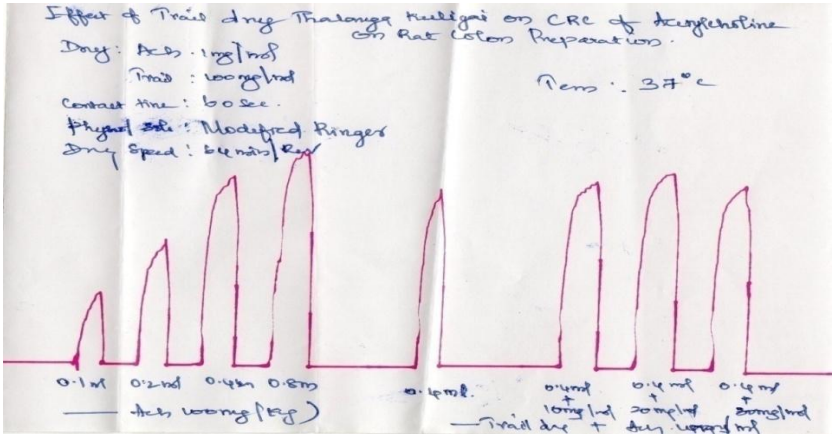
Experiments were performed in a 30 ml organ bath containing Tyrode solution maintained at 37ºC under a tension of 0.5 gm and gassed with air mixture (O_2+CO_2). Isometric contractions were recorded on a kymograph paper with frontal writing lever. After an equilibration period of 30 min during which the Tyrode solution was changed at intervals of 10 minutes, contractile responses were recorded for histamine (10 µg/ml). The contact time of 30 sec recorded at 5 min time cycle is kept for proper recording of the responses. The trial drug - tissue contact time was 1 min before the addition of histamine. Thus, the effect of the extract on histamine induced contractions was recorded. The percentage inhibition of the trail drug on contraction induced by histamine was calculated.



Isolated rat colon preparation

Wistar rats weighing (150-200 g) were starved overnight with water *ad libitum*. The animals were killed by cervical decapitation. The abdomen was cut open and the stomach was exposed. The colon was identified and transferred it to the petridish containing Tyrode solution. The composition of the Tyrode solution in mM was NaCl 137 mM, $NaHCO_3$ 12 mM, NaH_2PO_4 0.3 mM, KCl 2.7 mM, $MgCl_2$ 1.0 mM, $CaCl_2$ 1.0 mM and d- glucose 5.6 mM. The strip was suspended in atropinized Tyrode solution (3.5x10-7M).

The experiments were performed in a 30 ml organ bath containing Tyrode solution maintained at 37^0C under a tension of 1.0 gm and gassed with air mixture (O_2+CO_2). Isometric contractions were recorded using a frontal writing lever. After an equilibration period of 60 min, contractile responses were recorded (acetylcholine 1 mg/ml). The contact time of 30 sec, and 5 min time cycles are kept for proper recording of the responses. Trail drug- tissue contact time was 1 min before the addition of acetylcholine. The effects of the extract on acetylcholine induced contractions were recorded.



***In vivo* pharmacological evaluation**

Effect of Thalaga kuligai on histamine induced bronchospasm in guinea pigs

The effect of Thalaga kuligai on histamine induced bronchospasm was studied in guinea pigs. Guinea pigs of either sex (400-600 g) were housed under uniform environmental conditions. They were divided into two groups of six animals each and the following regimen of treatment was followed -

Group I (n =6) Animals received 200 mg/kg, p.o of Thalaga kuligai. This group served as test group in which six animals were exposed to histamine aerosol.

Group II (n =6) Animals received 2 mg/kg, p.o of chlorpheniramine maleate. This group served as standard group in which six animals were exposed to histamine aerosol.

Procedure

Prior to drug treatment, the animals were placed in the histamine chamber and exposed to micro aerosol of histamine acid phosphate (1% w/v) using a nebulizer under constant pressure of 40 mm/Hg. The animals exposed to the asthmatic agents showed progressive dyspnoea. The end point preconvulsive dyspnoea (PCD) was determined from the time of aerosol exposure to the onset of dyspnoea leading to the appearance of convulsions. As soon as the PCD was noted, the animals were removed from the chamber and placed in fresh air. 0-day values of PCD were taken before treatment. The animals were administered with the formulation and drugs as described above. On day 7, two hours after the last dose, the time for the onset of PCD was recorded as on day 0. The animals, which withstood exposure to histamine aerosol for 10 min, were considered to be completely protected.

The protection offered by the treatment was calculated by the following formula.

$$\textbf{Percentage protection} = \left\{1 - \frac{T_1}{T_2}\right\} \times 100$$

Where,

T_1 is time for PCD onset on day 0

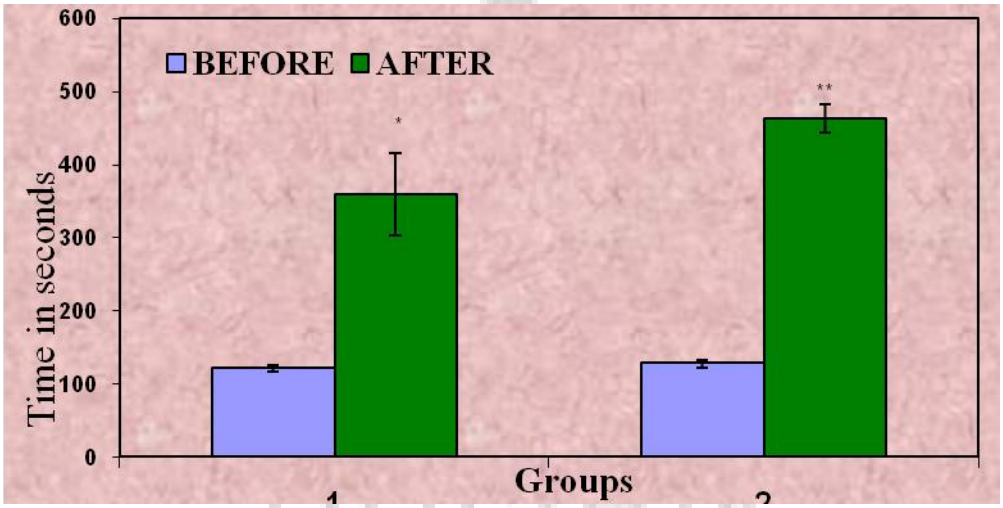
T_2 is the time for PCD onset on day 7.

RESULTS

Groups	Treatment	Time of preconvulsive dyspnoea in sec		% Protection
		Before	After	
I	Thalaga Kuligai (200 mg/kg, p.o)	121.8 ± 4.39	358.8 ± 56.07*	66.05
II	Chlorpheniramie maleate (2 mg/kg, p.o)	128 ± 5.07	463.3 ±19.38**	72.37

Values are mean ±SEM from 6 animals in each group.

*p<0.01, **p<0.001 When compared with untreated control group



DISCUSSION

Bronchial asthma is commonly characterized by increased airway reactivity to different spasmogens. An initial attack of asthma was triggered by the release of inflammatory mediators like histamine, acetylcholine, leukotrienes, prostaglandins, or specific exposure of allergens, which reflected the signals of acute bronchoconstriction[10,11]. Thalaga Kuligai was evaluated for antiasthmatic activity using different screening models as asthma various types of mediators. The close resemblance of pulmonary responses to histamine challenge in both guinea pigs and humans, as well as the anaphylactic sensitization made this model of choice.

The animals treated with Thalaga Kuligai showed significantly ($p<0.01$) delayed the onset of preconvulsive dyspnoea time against histamine induced aerosol. The percentage protection was found to be 66.05% in Thalaga Kuligai treated animals, when compared with the untreated control group. The standard group also showed significantly ($p<0.001$) delayed the onset of preconvulsive dyspnoea time and the percentage protection was found to be 72.37%, when compared with untreated control group.

The effect of Thalaga Kuligai on isolated Guinea pig ileum was evaluated by suspending in Tyrode solution. Contractile profile of isolated ileum was brought by histamine. Histamine induced contraction was inhibited on a dose dependant manner by Thalaga Kuligai at the dose level of 100 mg/kg. Pre-treatment with Thalaga Kuligai has produced smooth muscle relaxation. Thalaga Kuligai has also produced a dose dependant inhibition of contraction in isolated rat colon and Guinea pig ileum.

CONCLUSION

In conclusion, the results of this study suggest that the test drug Thalaga Kuligai is found to have smooth muscle relaxation property which is attributed by the percentage of inhibition against histamine and acetylcholine and significantly protect the Guinea pig against histamine induced broncho-spasm. Thus our findings suggest that the interventional drug Thalaga Kuligai possess significant Anti-asthmatic activity.

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