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Research Article

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Investigation into the studies on anti-histaminic and bronchodilator activity of polyherbal compound (Siringiyathi Chooranam) in albino rats

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ABSTRACT

The present study is aimed to evaluate the efficacy of anti-histaminic and bronchodilater activity of polyherbal compound (siringiyathi chooranam) through invitro and invivo in albino rats. Seven different medicinal plant materials such as Rhus succedanea, Zingiber officinale, Cyperus rotundus, Kaempferia galanga, Piper longum, Saussurea lappa, Piper nigrum were used to prepare the polyherbal compound. The results revealed that the test drug siringiyathi chooranam was found to be more effective in antagonism against histamine at 100µg/ml when compared with the standard antagonistic drug Ranitidine. From the present findings, it is manifest that the siringiyathi chooranam had shown marked antihistaminic activity in isolated albino rat ileum, and also it has significant activity in albino rat against histamine induced bronchospasm. The albino rat exposed to histamine aerosol showed signs of progressive dyspnoea leading to convulsions. The two doses of Siringiyathi chooranam significantly increase in preconvoulsion time (PCT) as compared to control following the exposure of histamine aerosol. The investigation suggest that the sidha drug polyherbal compound (siringiyathi chooranam) possess significant antihistaminic and bronchodilator activity in invitro and invivo in albino rats.

Keywords: Anti-histaminic, Bronchodilator, Polyherbal compound (siringiyathi chooranam), Albino Rats.

INTRODUCTION

Siddha medicines are being mostly utilized to treat a wide variety of diseases. Asthma is one of the chronic diseases worldwide. Bronchial asthma is defined as a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyper-responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing particularly at night or in the early morning. In spite of superlative available conventional medicines, the prevalence of bronchial asthma is increasing drastically [1- 4]. Medicinal plants have been known for millennia and are highly esteemed all over the world as a rich source of therapeutic agents for the prevention of diseases and ailments. The polyherbal preparation used in this study contains *Rhus succedanea*, *Zingiber officinale*, *Cyperusrotundus*, *Kaempferiagalanga*, *Piper longum*, *Saussurealappa*, *Pipernigrum*(siringiyathi chooranam) is the most valuable herb to take internally in respiratory ailments and for all fevers in general. The aqueous fruit extract of *Piper nigrum* shows anti-asthmatic activity in which it inhibited acetylcholine induced bronchoconstriction of isolated goat trachea [5]. *Piper longum* Linn. is used for various disorders such as asthma, tumours, spleen disorders, inflammations, piles, tuberculosis etc [6,7]. There is an ancient polyherbal blend called Trikatu churna is prepared in the combination of *Piper nigrum L. (Piperaceae), Piper longum L.(Piperaceae)& Zingiber officinale Roscoe (Zingiberaceae)* are used for anthelmintic activity by Malvankar (2012) [8]. According to Ghosh *et al* (2011) [9] *Zingiber officinale* had enormous pharmacological activities in order to protect human beings from several types of diseases and it may serve as a natural gold for

mankind. Specific studies for bronchodilator properties on isolated trachea were performed and found it is a potent bronchodilator [10]. In the present study, the effect of Polyherbal compound (siringiyathi chooranam) against antihistaminic and bronchodilator activity in invitro and invivo in albino rats.

EXPERIMENTAL SECTION

1.Collection and identification of plant materials

Seven different medicinal plant materials such as *Rhus succedanea*, *Zingibe rofficinale*, *Cyperus* r*otundus*, *Kaempferia galanga*, *Piper longum*, *Saussurea lappa*, *Piper nigrum* were purchased from the traditional herbal shop at paris, chennai, Tamil Nadu, India. The plants were confirmed and identified by Dr.G.Kathiravan, Associate professor, Vels University, Pallavaram, Chennai, Tamilnadu, India. and the voucher specimen number VUCC0003, VUCC0004, VUCC0005, VUCC0006, VUCC0007, VUCC0008 and VUCC0009 (Vels University Culture Collection) was deposited for future reference.

2. Drugs and preparation of polyherbal compound (Siringiyathi Chooranam)

Histamine dihydrochloride (Hi-media) was freshly prepared in normal saline (NaCl, 8.5g/l), carboxy methyl cellulose (2%) (LobaChemie Pvt. Ltd) was diluted with distilled water and desired concentrations were prepared. Physiological saline was widely recommended, as it is known to be compatible with human tissue and isotonicity with body fluid. Tyrode solution composition with (pH 7.4) NaCl -8.0gm , Kcl-0.2gm, $CaCl_2$ - 0.2gm, $MgCl_2$-0.1gm, $NaHCo_3$-1.0gm, NaH_2pO_4 -0.05gm, glucose – 10.0gm make upto one liter. Histamine, Salbutamol and Dexchlorpheniramine were used. All the prototypes were dissolved in minimum quantity and then the volume was adjusted to 10 ml with normal saline for making the concentration of 50 and 100 µg/ml. The test drug Siringyathi chooranam, Seven different medicinal plant materials were fine powdered and mixed uniformly in saline solution to achieve 1mg/ml as main stock solution and used in this study [11].

3. Experimental animals

Healthy adult male albino rats were obtained from Vels University animal house. Weighing 100-150gm was kept in fasting condition 18 hours prior to commencement of experiment and given water and *ad libitum.* The Institutional Animal Ethics Committee approved the experimental protocol and the conditions in the animal house approved by committee for supervision on experiments on animals. Acute toxicity study was conducted according to the IAEC guidelines. The study was undertaken after obtaining the approval of institutional ethical committee clearance. Registration no: (XIII/VELS/PCOL/67A/2000/CPCSEA/IAEC/08.08.2012). Animals were maintained under standard laboratory conditions of temperature (25 ± 2^0 C) and 12/12 hour light/dark cycle and for antihistaminic study the albino rats were sacrificed by blow to the head and exsanguinated as per CPCSEA recommended guidelines [12].

4. Experimental procedure

4.1 Acute toxicity study

The substance was administered orally to a group of experimental animals at one of the defined doses. The acute oral toxicity study was carried out as per the OECD guidelines 423 [13] (Acute toxic class method, revised Document, 2002). The substance was tested using a stepwise up and down procedure, absence or presence of drug-related mortality of the animals dosed at one step to determine the next step, no further testing was needed. The method will enable a judgment with respect to classifying the test substance to one of a series of toxicity classes. Animals were observed individually after dosing at least once during the first 30 minutes, periodically during the first 24 hours, with special attention given during the first 4 hours, and daily thereafter, for a total of 14 days except where they need to be removed from the study and humanely killed for animal welfare reasons or were found dead. All observations were systematically recorded and the observations include changes in skin and fur, eyes and mucous membranes, and also respiratory, circulatory, autonomic, central nervous systems, and somatomotor activity and behavior pattern. Attention was directed to observations of tremors, convulsions, salivation, diarrhea, lethargy, sleep and coma. One-tenth of the lethal dose was considered as therapeutic dose for further pharmacological study.

4.2 Antihistaminic activity

Albino rat was sacrificed and a segment from ileum (2 cm) was dissected from the terminal ileum and mounted in an organ bath containing Tyrode solution (10 ml) between two stainless steel hooks under 0.5 to 1 g initial tension. The lower hook was fixed at the bottom of the organ bath and upper one was connected to an isotonic transducer. It was continuously aerated and maintained at 37 ± 0.5^0C. The equilibrium period was 60 minutes and the bath solution was

refreshed every 15 minutes. After equilibrium period, a dose response curve for histamine in varient molar concentration, by maintaining 45 minutes time cycle was taken separately [10].

4.3 Evaluation of anti asthmatic activity (Bronchodilator)

Experimental bronchial asthma was induced in albino rat exposing them to histamine. Overnight fasted albino rats weighing about (100-150gms) were selected and randomly divided in to four groups each consisting of six animals, following treatment were given.

Group I: Control (treated with normal saline)
Group II: Test 1 (Siringiyathi chooranam 250mg/kg)
Group III: Test 2 (Siringiyathi chooranam 500mg/kg)
Group IV: Standard (Salbutamol 5mg/kg)

All the doses were given orally. Prior to drug treatment each albino rats were exposed to an atomised fine mist of 2% W/V histamine dihydrochloride aerosol (dissolved in normal saline) using a nebulizer in the histamine chamber. Albino rat exposed to histamine aerosol showed progressive signs of difficulty in breathing leading to convulsions, asphyxia and death. The time until signs of convulsion appeared is called pre-convulsion time (PCT) and was determined from the time of exposure to onset of convulsions [14].

As soon as pre convulsion time was noted, animals were removed from the chamber and placed in fresh air to recover. The percentage protection offered by treatment was calculated by using the following formula:

Percentage protection = $(1-T_1-T_2)$ X 100

Where; T_1 = the mean of PCT of control group animals.
T_2 = the mean of PCT of test group animals.

5. Statistical analysis

Ileum contractions induced by agonist were assumed as 100% and reductions induced by test drug calculated. Percentage of ileum contraction was expressed as mean $\pm$SEM. Results were analysed using one-way analysis of variance (ANOVA). Probability values less than 0.05 were considered as significant. For bronchodilator activity, the data were expressed as Mean $\pm$SEM. Differences between groups were analysed by one way analysis of variance (ANOVA) followed by Dunnet "t" test. Differences were considered significant when $P<0.05$ and very significant when $P<0.01$.

RESULTS

Toxicity study was reported in Table 1 Positive results were observer at all the doses of Sirinigyathi chooranam for Alertness, Grooming, Touch response, Decreased motor activity, Hypnosis, and Respiration. 500 mg/Kg dose of Siringiyathi chooranam on histamine induced shown significant result on bronchoconstriction in Albino rats. The compounds presence in Siringiyathi chooranam showed significant inhibition in histamine induced albino rat ileum contraction. Siringiyathi chooranam reduce the contraction of albino rat ileum preparation induced by histamine, the real mechanism may be by calcium ions. As the contraction of the Siringiyathi chooranam was decreased when compared to standard, a more pronounced relaxant effect was observed in Table 2 and Figure 1.

DISCUSSION

Invivo study of siringiyathi chooranam have been also shown significant increase in pre convulsion time due to pre treatment at the dose of 250 and 500 mg/kg of albino rat when the albino rat where exposed to histamine the result of siringiyathi chooranam suggested that it is effective in reducing the symptom of bronchial asthma and also in improve the lung function parameters of asthmatic subject.

In the present albino rats were used because of the extreme sensitivity of the airways to the primary mediators of bronchoconstriction including histamine and leukotrienes and their ability to be sensitized to foreign proteins although they are various model of asthma albino rat airways react to histamine acetyl choline leukotrienes and other bronchoconstriction in a manner similar to that seen in human. Thus the albino rats model resembles the human

allow the pathology in several aspect, especially in terms of mediator release. Histamine antagonists from the conveniently recognized and assayed by the ability to protect albino rats against lethal effect of histamine induced bronchospasm. Medicinal herbs is a powerful drug used for asthma treatment [15], hence this herbs (siringiyathi chooranam) provides a natural source, supports our health and pharmaceutically prescribed to treat respiratory disease. The investigation suggests that the sidha drug polyherbal compound (siringiyathi chooranam) possess significant antihistaminic and bronchodilator activity in invitro and invivo in albino rats.

Table 1: Dose finding experiment of Sirinigyathi chooranam and its behavioral signs of toxicity

S.No	Dose mg/Kg	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1	500	+	-	-	+	-	+	+	-	-	-	-	-	+	-	-	-	-	-	+	-
2	1000	+	-	-	+	-	+	+	-	-	-	-	-	+	-	-	-	-	-	+	-
3	2000	+	-	-	+	-	+	+	-	-	-	-	-	+	-	-	-	-	-	+	-
4	5000	+	-	-	+	-	+	+	-	-	-	-	-	+	-	-	-	-	-	+	-

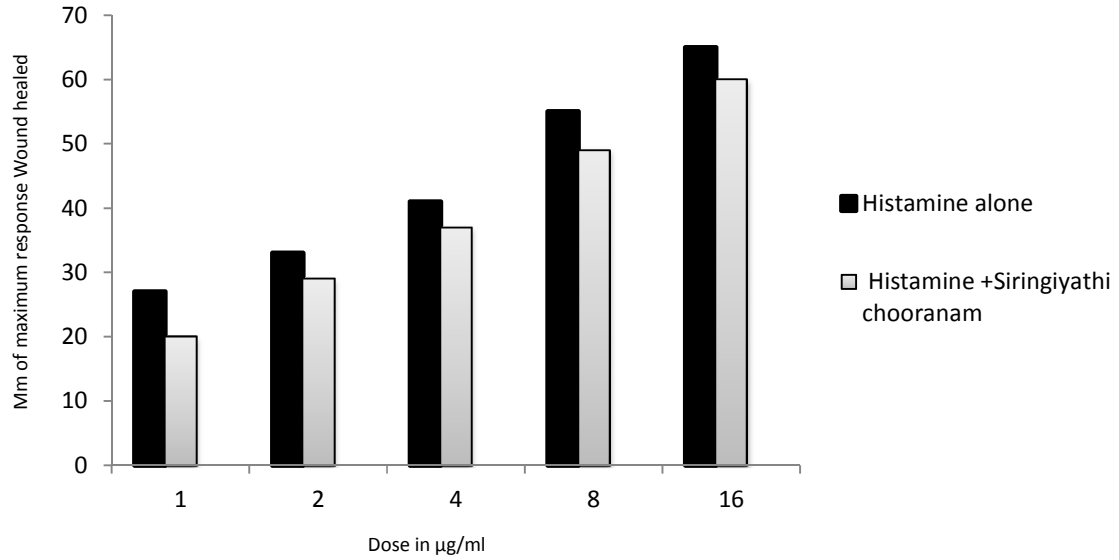
1. Alertness, 2. Aggressiveness, 3. Pile erection, 4. Grooming, 5.Gripping, 6. Touch response, 7. Decreased motor activity, 8.Tremors, 9.Convulsion, 10. Muscle spasm, 11.catatonia, 12. Muscle relaxant, 13. Hypnosis, 14.Analgesia, 15.Lacrimation, 16.Exophthalmos, 17.Diarrhea, 18.Writhing, 19.Respiration, 20.Mortality.

Table 2: Effect of Siringiyathi chooranam on histamine induced bronchoconstriction in albino rats

		Pre-Convulsion Time (PCT) in hours			
Groups	**Treatment and Dose**	**Before**	**1st hour**	**2nd hour**	**4th hour**
Control	Normal saline	130.8±2.11	122 ± 2.00	128 ± 2.14	110 ± 1.88
Test 1	Siringiyathi chooranam 250mg/kg	120 ± 2.00	186±1.92**	207±2.48**	144±2.00**
Test II	Siringiyathi chooranam 500mg/kg	122 ± 2.38	220±2.10**	238±2.40**	147±2.80**
Standard	Salbutamol 5mg/kg	122 ± 2.00	321±2.70**	349±2.88**	210±2.18**

*Values are in mean ±SEM; statistical analysis done by using One-way ANOVA followed by Dunnet ' t'- Test. **p<0.01, compared to control; n=5; control=histamine (0.2%, aerosol).*

Figure 1. Antihistaminic effect of Siringiyathi chooranam on isolated albino rat ileum preparation (In vitro study)



CONCLUSION

The results demonstrate that the test drug siringiyathi chooranam was found to more effective in antagonism against histamine at 100µg/ml when compared with the standard antagonistic drug Ranitidine. From the present findings, it is manifest that the siringiyathi chooranam had shown marked antihistaminic activity in isolated albino rat ileum. And also it is suggested that siringiyathi chooranam significantly protected the albino rat against histamine induced bronchospasm.The albino rat exposed to histamine aerosol showed signs of progressive dyspnoea leading to

convulsions. The two doses of Siringiyathi chooranam significantly increase in preconvoulsion time (PCT) as compared to control following the exposure of histamine aerosol.

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