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BRONCHODILATORY AND ANTI-ALLERGIC EFFECT OF PULMOFLEX - A PROPRIETARY HERBAL FORMULATION

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Abstract : PulmoFlex, a polyherbal anti-asthmatic formulation has been reported to possess antihistaminic, mast cell stabilizing, anti-anaphylactic and antiallergic properties in experimental animals and clinical trials. The present study was undertaken to determine the effect of PulmoFlex on isolated perfused rat lung. The lung tissues were perfused at a pressure of 50 mmHg using oxygenated Krebs solution at 37°C. PulmoFlex (1 & 2 mg/ml) increased the pulmonary perfusion flow indicating its bronchodilatory action. PulmoFlex (500 mcg) significantly prevented histamine (50 mcg), acetylcholine (50 mcg) and C–48/80 (10 mcg), induced bronchoconstriction indicating its antihistaminic, anticholinergic and mast cell stabilizing actions on pulmonary vascular beds and bronchioles, respectively. Lung tissue of sensitized (BSA) rats treated with PulmoFlex (20 mg/kg × 10 days) showed better perfusion following *Ex vivo* antigenic challenge as compared to untreated rats. This indicates the possibility of suppression of IgE mediated immune reaction by PulmoFlex. Thus, the present findings, suggest that PulmoFlex acts as an antiasthmatic by its bronchodilatory, membrane stabilizing, antihistaminic, anticholinergic and immunomodulatory (reaginic antibody mediated) effects.

Key words : pulmoFlex pulmonary perfusion

INTRODUCTION

PulmoFlex is a composite herbal formulation intended for the treatment of allergic respiratory diseases. The composition of PulmoFlex is given in Table I. It has been shown to provide symptomatic relief in patients suffering from asthma and allergic rhinitis with satisfactory tolerability (1, 2). It has also been shown to increase the ventilatory performance of lungs as indicated by increased FEV-I and PEFFR alongwith reduced airway obstruction in

TABLE I : Composition of PulmoFlex. Each 450 mg of PulmoFlex contains :

Adhatoda vasica	80 mg
Solanum xanthocarpum	120 mg
Glycyrrhiza glabra	100 mg
Sida cordifolia	30 mg
Albezia lebbeck	30 mg
Alpinia galanga	10 mg
Saussurea lappa	16 mg
Ocimum sanctum	25 mg
Piper longum	14 mg
Zingiber officinale	15 mg
Headychium spicatum	10 mg

patients with acute and chronic asthma (2, 3). Antiallergic, antihistaminic and anti-platelet aggregatory actions of PulmoFlex have been reported by various authors (4–8). The product was reported to be non-toxic (9). However, there is no report so far on this herbal product in relation to its effect on perfused lung tissues of normal and sensitized animals. Therefore, the effect of PulmoFlex on perfused lung tissues of rats was studied.

METHODS

Albino rats of Wistar strain were used.

Lung perfusion technique (10): Lungs were isolated from experimental rats and connected to a perfusion apparatus under a constant pressure of 50–52 mmHg with aerated Kreb's solution at 37°C through trachea. The perfusate was collected in a volumetric tube through a funnel after giving 2–3 fine scratches over the pulmonary lobes so that the perfusate can flow down through alveoli and bronchioles. The rate of flow (ml/min) was recorded. The test substances were either dissolved in reservoir containing perfusion fluid or injected directly into the lungs through trachea using a fine hypodermic needle, as the case may be.

Treatment groups

PulmoFlex powder was obtained from R & D Laboratory of Indian Herbs, Saharanpur.

Group–1. The effect of PulmoFlex (1 and 2 mg/ml of perfusion fluid) *per se* on pulmonary perfusion was measured after an initial control observation. Effect of PulmoFlex on perfusion flow rate in isolated lungs was recorded for 3 minutes after 5 minutes of exposure to the product.

Group–2, 3 and 4. In these groups, the effect of Pulmoflex (500 mcg) pretreatment, on histamine (50 mcg), acetyl choline (50 mcg) and compound 48/80 (10 mcg), respectively induced bronchoconstriction was studied and the results were compared with that of 50 mcg of meclizine, atropine and disodium cromoglycate (DSCG), respectively. The dose of PulmoFlex was selected after pilot experiments. The constrictory agonists were administered exogenously 3 minutes after the administration of PulmoFlex.

Group–5. The rats were further divided into two sub groups of six animals each. They were then sensitized with FCA and BSA as described elsewhere (11). One group of rats was treated with PulmoFlex (20 mg/kg; orally) for ten days following antigen treatment, the other group remained untreated. After ten days, the lungs from each rat were perfused. The rate of perfusion was recorded before and 3 minutes after the challenging dose of antigen (100 mcg/ml).

Group–6. These rats were sensitized with antigen as described above. After ten days the lungs were isolated and perfused. The flow rate of perfusion was recorded 3 minutes after antigen challenge in presence and absence of PulmoFlex (500 mcg/ml) and DSCG (50 mcg/ml) in the perfusion fluid.

Statistical analysis: The results were expressed as mean ± SE and analysed using Student's t–test.

RESULTS

In the present study, PulmoFlex significantly increased the rate of perfusion flow of isolated rat lung as compared to control (Fig. 1). Pre-treatment of the system with PulmoFlex provided significant antagonism against histamine, acetyl choline and comp 48/80 induced bronchoconstriction. The results were comparable with meclizine, atropine and DSCG, respectively although they produced nearly equivalent effect at lower concentration than PulmoFlex (Fig. 2, 3, 4).

Treatment of the sensitized rats with PulmoFlex exerted significant protection against challenging dose of antigen induced bronchoconstriction. The rate of perfusion flow was compared between pre and post antigen challenge in the same group of animals (Fig. 5). PulmoFlex also

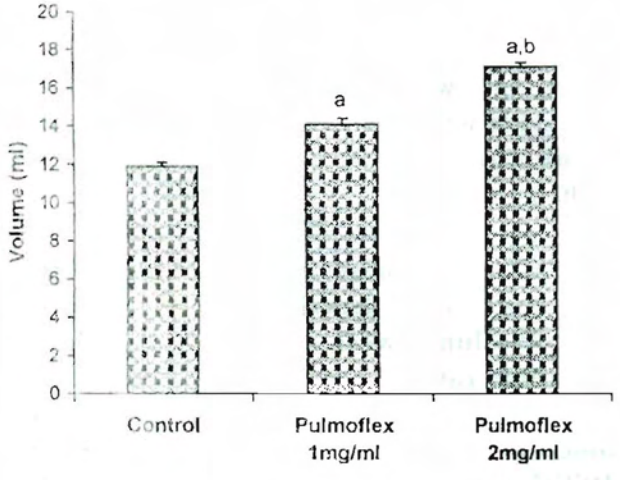

Fig. 1 : Effect of Pulmoflex on perfusion flow rate of isolated rat lungs. (n=10).
a=Significant difference ($P \leq 0.05$) form control;
b=Significant difference ($P \leq 0.05$) form pulmoflex (1 mg/ml) treatment.

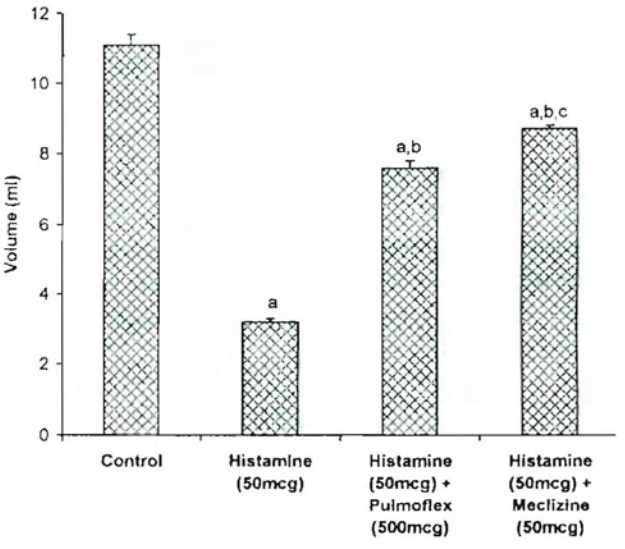

Fig. 2 : Effect of Pulmoflex on histamine induced bronchoconstriction in siolated perfused rat lungs. (n=10).
a=Significant difference ($P \leq 0.05$) form control
b=Significant difference ($P \leq 0.05$) form histamine treatment;
c=Significant difference ($P \leq 0.05$) form histamine + pulmoflex treatment.

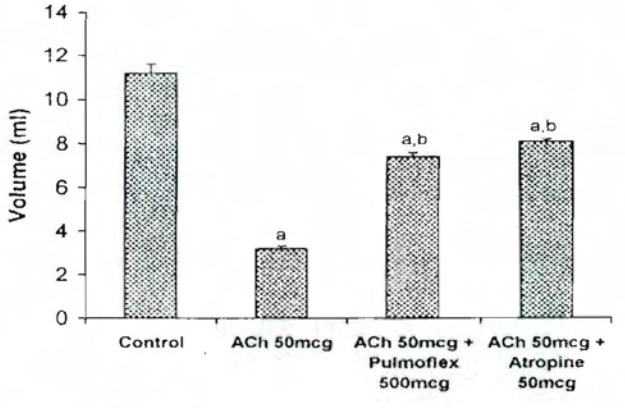

Fig. 3 : Effect of Pulmoflex on acetylcholine induced bronchoconstriction in siolated perfused rat lungs. (n=10).
a=Significant difference ($P \leq 0.05$) form control;
b=Significant difference ($P \leq 0.05$) form acetylcholine treatment.

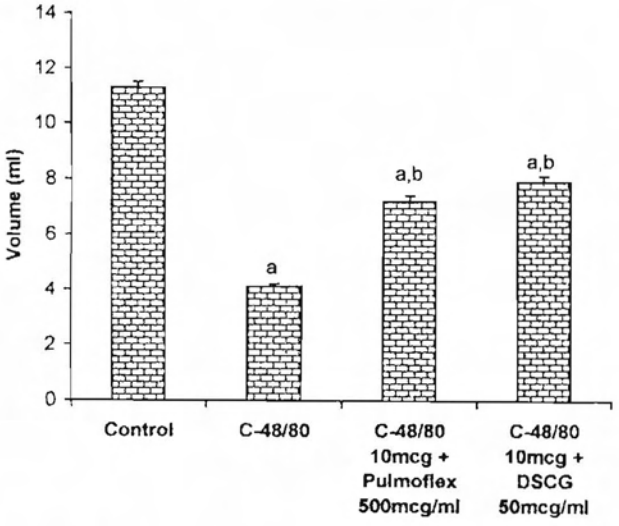

Fig. 4 : Effect of Pulmoflex on compound 48/80 induced bronchoconstriction in siolated perfused rat lungs. (n=10).

a=Significant difference ($P \leq 0.05$) form control;

b=Significant difference ($P \leq 0.05$) form C-48/80 treatment.

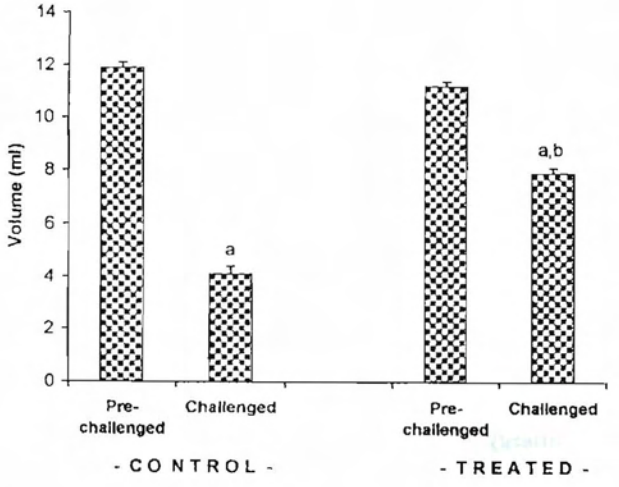

Fig. 5 : Effect of antigen challenge on perfusion flow of Pulmoflex treated sensitized rat lungs. (n=10).

a=Significant difference ($P \leq 0.05$) form corresponding pre-challenged value;

b=Significant difference ($P \leq 0.05$) form control challanged value.

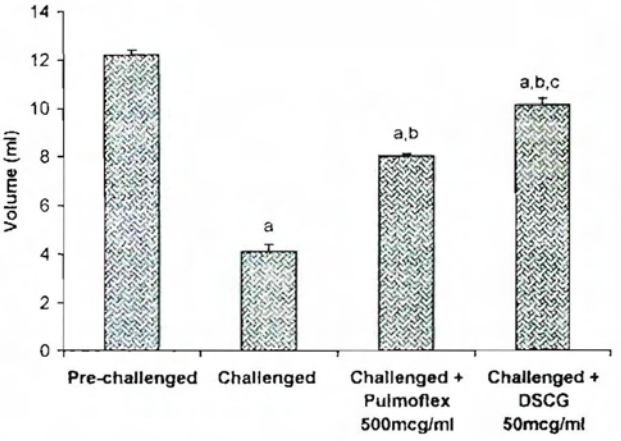

Fig. 6 : Effect of Pulmoflex (*ex vivo*) on perfusion flow in isolated sensitized rat lungs. (n=10).

a=Significant ($P \leq 0.05$) difference form pre-challenged value;

b=Significant ($P \leq 0.05$) difference form challanged value;

c=Significant ($P \leq 0.05$) difference form challanged + Pulmoflex value.

provided significant protection against bronchoconstriction in perfused lungs of sensitized rats by challenging dose of antigen when the product was used *ex vivo* (Fig. 6). DSCG exerted better protection in this experimental model as compared to PulmoFlex.

DISCUSSION

Increase in the rate of flow of normal lung perfusion by PulmoFlex in present study indicates bronchodilatory effect of this product. PulmoFlex antagonized histamine, acetyl choline and comp 48/80 induced reduction in pulmonary perfusion flow which clearly indicates its anti-histaminic, anticholinergic and mast cell stabilizing actions on pulmonary vascular beds. These action of PulmoFlex were demonstrated earlier in different experimental models

namely, guineaping tracheal chain, histamine aerosol induced collapse of guineapigs and rat peritoneal mast cells (4–7). PulmoFlex exerted similar action in pulmonary vascular beds in the present study.

Treatment of sensitized rats with PulmoFlex also prevented subsequent antigen induced bronchoconstriction and thereby maintained the nearly normal pulmonary perfusion flow. This indicates the possibility of suppression of IgE mediated immune function by PulmoFlex. The action may also be due to mast cell stabilization. Earlier, PulmoFlex was reported to increase the survival rate of mice against antigen induced anaphylactic bronchospasm and provided protection against passive foot anaphylaxis in mice (4). The probable suppression of reaginic antibody mediated immune response by PulmoFlex indicates potential for use in allergic respiratory diseases.

PulmoFlex also showed a mast cell stabilizing action in the present study. It protected the sensitized lungs of rats against challenging dose of antigen induced bronchoconstriction when administered *ex vivo*. Mast cell stabilizing as well as antihistaminic actions of PulmoFlex have been reported earlier also (4–7).

Thus, the present study demonstrates that PulmoFlex possesses bronchodilatory, membrane stabilizing, antihistaminic, anticholinergic and immunomodulatory (reaginic antibody mediated) properties which may be responsible for anti-asthmatic effect of this herbal product.

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