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Mast Cell Stabilizing Effect of *Elaeocarpus sphaericus* (Rudraksha*fruit)*: Possible Role in Bronchial Asthma

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Abstract: *Ethanolic extract of the fruits of Elaeocarpus sphaericus was found to have protective actions against (i) histamine aerosol induced on broncho constriction (ii) mast cells degranulation induced by Compound 48/80 and (iii) active anaphylaxis. The findings are suggestive of potential use of E. sphaericus in bronchial asthma.*

Keywords: *Elaeocarpus sphaericus: Active Anaphylaxis : Mast Cell Stabilization: Bronchconstriction*

1. INTRODUCTION

Elaeocarpus sphaericus (Syn*: E.ganitrus*, Family: Elaeocarpaceae*)* **[1]**commonly known as Rudraksha is abundantly grown in the Himalayan region of India and is known for its medicinal properties**[2,3,4].**A wide range of indigenous drugs of plant origin have been recommended by Indian system of medicine for the treatment of bronchial asthma **[5].**Earlier studies from our laboratory indicated protective action of *E. sphaericus on* histamine and acetylcholine induced bronchoconstriction in Guinea –pig**[6].**

An attempt to substantiate the possible protective role of *E. sphaericus* in bronchial asthma. The present investigation was undertaken on mast cell stabilization and active anaphylaxis models in experimental animals.

2. MATERIALS AND METHODS

2.1. Plant Material

E. sphaericus fruit was obtained from the Regional Research Centre (Ay) Guwahati, Assam ,India. The vocher specimens have been preserved.

2.2. Extraction

The dried powder (1.0 Kg) *E. sphaericus* fruits were extracted with ethanol and concentrated in a steam bath to a final yield 11.0g (1.1%).The chemical test showed the presence of glycoside, alkaloids and flavonoids.

2.3. Ethical Clearance

All the experiments were conducted following the CPCSEA after the approval of Institutional Animal Ethics Committee.

2.4. Animals

Albino rat (CF strain) 100-110g and guinea –pig 300-500g of either sex, were obtained from the Central Animal House of the Institute, B.H.U . They were housed in colony cages and fed standard

Hind Lever pellet chow and kept at an ambient room temperature of 25 ^{o}± 2^{o}C and relative humidity 45-55% with 12 h light/12 h dark cycle.

2.5. Treatment

E. sphaericus extracts were suspended in 3% tween-80 in double distilled water was given either ip(intraperitoneally) or po(orally) for either 30 min or 45 min before or otherwise mentioned in table details, before experimentation.

2.6. Effect of *E. sphaericuson* Histamine Aerosol Induced Bronchospasm in Guinea-Pig

Armitage et al (1961) described that guinea-pig exposed to an aerosol of 1% histamine show progressive signs of difficulty in breathing leading to convulsion and death. The time until signs of convulsion appeared is calls pre – convulsion time. In the present experiments the critarion used was time to onset of dysponea and percent protection was calculated **[7].**

2.7. Effect of *E. sphaericus* on In-Vitro Mesenteric Mast Cell of Rats

Albino rats (CF strain) were sacrificed by cervical dislocation. The abdomen was opened and mesentery of the jejunam and ileam were carefully exposed.The mesentery along with small pieces of jejunam or ileam were removed andplaced in a petri dish containing oxygenated Ringer Locke`s solution (NaCl 9.0, KCl 0.42, $CaCl_2$ 0.24, $NaHCO_3$ 0.5 and glucose 1.0 g/L of double distilled water ph 7.4) at 37.0^{o} ± 0.5^{o}C.Tissue transferred to different dose (0.5, 1.0 & 2.0 mg/ml) for 30 min and then challenged by Comp 48/80(2.5 µg/ml) for 10 min. The tissue was then stained 0.1% Toludine blue in 4% Formaldelyde in saline for 15-20 min**[8].** The tissue was next transferred and kept in acetone (two changes) and then mounted on slides. Before mounting, excess pieces of fats were trimmed and the mesentery was stretched from the edges with the help of a needle.

Each cell was considered either disrupted or not disrupted. The term disrupted was selected instead of fragmented because granules were found around many cells which did not appear to be in fragments. The sole criterion for calling a cell disrupted was the presence of granules outside the cell. Many cell did not show extrusion of granules but appear swollen at low concentration of Comp. 48/80. For each dose concentration 100 to 150 mast cell were examined and average percentage of disruption was calculated.

2.8. Effect of *E. sphaericus on Mast Cell Degranulation in* Actively Sensitized Rats

Rats were sensitized by injecting subcutaneously 0.5 ml of horse serum with 0.5 ml of triple antigen containing 20,000 million Bordetellapertussis organism (CRI, Kasuli, India)**[9].** The sensitized rats were divided into 4 groups of 6 animals each. Rats of group I received double distilled water and served as control. Rats of group II, III and IV were administered *E. spheaericus*(0.5, 1.0 and 2.0 mg/kg, p.o.) once a day for 14 days. On day 14 rats were sacrificed 1h after treatment and the intestinal mesentery was taken for the study of mast cell. In vitro mesenteric pieces were challenged with 5% horse serum for 10 min after which the mast cells were stained and examined microscopically.

2.9. Data analysis

All the data was analyzed by student's t-test followed by ANOVA.

3. RESULTS

3.1. Effect of *E. sphaericus* on Histamine Aerosol Induced Bronchospasm in Guinea-Pig

It shows significant delay in the onset of bronchospasm with all the doses of E. spheaericus and comparable to mepyramine maleate (Table1).

3.2. Effect of *E. sphaericus* on In-Vitro Mesenteric Mast Cell of Rats

E. spheaericus pretreatment with three doses reduced mast cell degranulation significantly(Table 2).

3.3. Effectof *E. sphaericus* on Mast Cell Degranulation in Actively Sensitized Rats

All the three doses show decrease in mast cell degranulation in sensitized and horse serum challenged model (Table3).

Table1. *Effect of ethanol extract of E. sphaericus(Rudraksha) on 1% histamine induced bronchospasm in Guinea-pig.*

Treatment (mg/kg,ip,30min)	**%delay in onset of dyspnoea**
Control (3% Tween-80)	16.37 ±0.19
Meypyramine Malate 2.0	28.12±0.11 **
***E. spheaericus** 0.5*	20.87 ± 0.96 *
1.0	21.98 ± 1.37 *
2.0	23.16 ±1.08 *

Values are mean±SE of 6animals in each group.

***P<0.001,*P<0.01 in respect of control.*

Table2. *Effect of ethonol extract of E. sphaericus(0.5, 1.0 and 2.0 mg/ml) and Comp. 48/80 (2.5µg/ml) on rat mesenteric mast cell.*

Treatment (mg/ml+2.5 µg/ml *Comp. 48/80*)	**N**	**% *degranulation***	**%inhibition**
Control(3% Tween-80)	18	15.62 ± 0.16	-
Comp. 48/80	18	90.79± 0.21	-
E. spheaericus 0.5+Comp. 48/80	6	27.14 ± 0.56[a]	70.16[b]
1.0+Comp. 48/80	6	32.67 ± 2.07[a]	64.01[b]
2.0+Comp. 48/80	6	40.73 ± 1.66[a]	55.13[b]

Values are mean± SE % degranulation. Figures in parentheses indicate number of animals used.

[a]*p<0.001 in respect to control.*
[b]*p< 0.001 in respect to compound 48/80*

Table3. *Effect of mast cell degranulation in actively sensitized rats.(E. sphaericus0.5, 1.0 and 2.0 mg./kg ×14 days)*

Treatment(mg/kg,po,45 min)	**% *degranulation***
Control (3% Tween-80)	94.02 ± 0.46
***E. spheaericus** 0.5*	62.14 ± 0.16 *
1.0	67.21 ± 0.71*
2.0	75.10 ± 0.53 *

Values are mean ± SE of 6 animals in each group.
**P<0.01 in respect of Control.*

4. DISCUSSION

There has been phenomenal increased incidences of asthma leading to hospitalization and asthma related deaths .The available agents for this disease of allergic origin often limited action when used either alone or in combinations./Individual agents usually produce beneficial effect by acting as some component of pathological process of bronchial asthma. The present findings of mast cell protective effects of*E. spheaericus* in against Compound 48/80 challenge and horse serum challenge in sensitized rats are further elaborative of our earlier reported bronchoprotective action of *E. spheaericus*. However comparatively less protection at higher dose levels of *E. spheaericus* remain difficult to explain.The mast cell protective action of *E. spheaericus* may well be attributed to its alkaloids, glycoside and flavonoids components. Immunological interactions including mast cell and other excitable tissue interactive responses are dependent on glycoprotein receptors. Number of quinolone alkaloids of plant origin have glycosidase inhibitory activity and could modify glycosylation physiology and membrane interaction with ligands.*E. spheaericus* is rich in quinolizidine and indolizidine alkaloids**[10,11,12].**

The present study thus suggests possible use of *E. spheaericus* in bronchial asthma in light of present finding and earlier reported safety margin**[6].**

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