ANTI-HISTAMINIC ACTIVITY OF METHANOLIC EXTRACT OF LEAVES OF *TAMARINDUS INDICA* LINN.

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ABSTRACT

According to Ayurveda, *Tamarindus indica* Linn *(Caesalpiniaceae)* is used in treatment of asthma, inflammations, burning sensation, dysentery, vaginal and uterine complaints etc. In the present study methanolic extract of leaves of *Tamarindus indica* Linn at the doses of 175, 350 and 700 mg/kg, p.o., inhibited antigen antibody reaction and significantly reduced ($p<0.01$) antigen induced paw oedema in rats. The methanolic extract of *Tamarindus indica* Linn (217.5, 435 and 870 mg/kg, p.o.) significantly prolonged the latent period of convulsion ($p<0.01$) and protected guinea pigs in histamine induced bronchoconstriction model. Thus the present study revealed that the methanolic extract of leaves of *Tamarindus indica* Linn exhibited significant antihistaminic and anti-anaphylactic activity. The *Tamarindus indica* Linn by virtue of the said actions will prove to be very effective in the management of asthma.

Keywords: Anti-anaphylactic, Anti-histaminic, Asthma, *Tamarindus indica* Linn.

1. INTRODUCTION

Tamarindus indica Linn. (Caesalpiniaceae) is a commonly found plant in moist waste ground, lawns and open plantation. It is cultivated throughout India, self sown in waste places and forests lands in central India, Madhya Pradesh and also planted along roadsides throughout India. The phytochemical characterization shows the presence of tannins, steroids, alkaloids, triterpenes and flavonoids (Gokhle; 2002).

According to Ayurveda, *Tamarindus indica* Linn is used in treatment of asthma, inflammations, burning sensation, dysentery, vaginal and uterine complaints, fever, pile and fistula etc. (Kirtikar; 2001).

The methanolic extract of leaves contain ascorbic acid, β-carotene and is proven to be anti-lipoperoxidant and hepatoprotective. Some studies have reported immunomodulatory effect of *Tamarindus indica* Linn. (Joyeux; 1995).

Asthma is a heterogeneous disorder immunologically, physiologically and biochemicaly and its etiology is multifactorial. The present study was planned to evaluate the action of the test drug on various aspects of asthma like bronchoconstriction and allergy associated with inflammation using various animal models. There was no report on the Anti-asthmatic activity of *Tamarindus indica* Linn and therefore it was thought worthwhile to screen it for the same.

2. MATERALS AND METHOD

2.1 Plant material

The leaves of *Tamarindus indica* Linn were collected from local Nursery of Aurangabad, India. The plant specimen was authenticated by Mr. P.G. Diwakar (Scientist 'D' for Joint Director) and deposited at "Botanical Survey of India" Pune, India, (Voucher specimen no. TYP1).

2.2 Preparation of methanolic extract of *Tamarindus indica* Linn.

The leaves of *Tamarindus indica* Linn were air-dried. After 10 days of drying, the leaves were powdered using a mixer. The methanolic extract was prepared by maceration method. The extract was concentrated and dried at $40^{O}C$, (yield 8.7 % w/w) (Rangari, 2002).

2.3 Experimental animal

All experimental procedures were carried out in strict accordance with the guidelines prescribed by the Committee for the Purpose of Control and Supervision on Experimentation on Animals (CPCSEA) and were approved by the Institutional Animal Ethics Committee.

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Adult albino rats of Wistar strain weighing between 150 to 200 gm and Dunkin-Hartley Guinea pigs weighing between 350 to 400 gm. were used. The above animals of either sex were purchased from National Toxicological Center, Pune. Animals had free access to standard pellet diet (Amrut laboratory animal feed, Sangli-Maharashtra) and water.

2.4 Passive Paw Anaphylaxis in Rats:

Anti serum to egg albumin was raised in rats using aluminum hydroxide gel as an adjuvant. Animals were divided into five groups (n = 5). All the animals were given three doses of 100 mcg of egg albumin (s.c.) adsorbed on 12 mg of aluminum hydroxide gel prepared in 0.5 ml of saline on 1st, 3rd, 5-th day. On 10th day of sensitization, the blood was collected from the retro orbital plexus. The collected blood was allowed to clot and the serum was separated by centrifugation at 1500 rpm which was later used. Animals belonging to group I served as control and were administered only the vehicle (Distilled Water 10 ml/kg, p.o.). Animals belonging to group II were administered Dexamethasone (0.5 mg/kg, i.p.). Animals belonging to groups III, IV and V received methanolic extract of *Tamarindus indica* Linn 175, 350 and 700 mg/kg, p.o. respectively. The animals were passively immunized with 0.1 ml of the undiluted serum into the left hind paw. The contra lateral paw received an equal volume of saline. The drugs were administered 24 hour after immunization. One hr. after drug administration, the animals were challenged in the left hind paw with 10 mcg of egg albumin in 0.1ml of saline and the paw inflammation was measured by using a Plethysmometer (UGO Basile, 7140). The difference in the reading prior and after antigen challenge represented the edema volume and the percent inhibition of edema was calculated by using the formula (Mengi, 2003, Gokhale, 2002).

$$\% \text{ Inhibition} = 1-(V_t / V_c) \times 100$$

V_t - Mean relative change in paw volume in test group.

V_C - Mean relative change in paw volume in control group.

2.5. Histamine induced Bronchoconstriction in Guinea pig:

Bronchospasm was induced in guinea pigs by exposing them to histamine aerosol (0.2%) produced by an ultra-sound nebulizer in an aerosol chamber (24×14×24 cm) made of Perspex glass. The time required for appearance of pre-convulsive dyspnoea caused by the histamine was recorded for each animal. (Rajesh, 2000, Singh, 1990)

Fasted guinea pigs were randomly divided into four groups, (n=5). Group-I received Chlorpheniramine maleate (2 mg/kg, p.o.), Group-II, Group-III and Group-IV received methanolic extract of *Tamarindus indica* Linn 217.5, 435 and 870 mg/kg, p.o. respectively. Prior to drug treatment each animal was placed in the histamine chamber and exposed to 0.2 % histamine aerosol. The preconvulsion time (PCT) (The time of aerosol exposure to the onset of dyspnoea leading to the appearance of convulsion) was noted. As soon as preconvulsive dyspnoea commenced, animals were removed from the chamber and placed in fresh air to recover. This time for preconvulsive dyspnoea was taken for basal value. Guinea pigs were then allowed to recover from dyspnoea for 4 hours. After 4 hr., the animals of group II, III and IV were administered the test drug extract and group I received Chlorpheniramine maleate. These animals were again subjected to histamine aerosol later at interval of 1 hr, 4 hr and 24 hr and time for preconvulsion (PCT) was determined (Mitra, 1999). The protection offered by the treatment was calculated by using the following formula:

$$\% \text{ Protection} = \frac{T_2 - T_1}{T_2} \times 100$$

Where, T_1 = The mean of PCT before administration of test drugs.

T_2 = The mean of PCT after administration of test drugs at 1hr, 4hr and 24 hr.

2.6 Statistical Analysis

All observations were presented as Mean ± SEM. The data was analyzed by Student't'-test or one-way ANOVA followed by Dunnett's test. $p<0.05$ was considered as significant.

3. RESULTS AND DISCUSSION

3.1 Effect of methanolic extract of *Tamarindus indica* Linn on passive paw anaphylaxis in rat:

The methanolic extract of *Tamarindus indica* Linn inhibited the paw edema in dose dependant manner. In the passive paw anaphylaxis model, the methanolic extract of *Tamarindus indica* Linn at the doses of 175, 350 and 700 mg/kg, p.o. showed significant inhibition ($p<0.01$) of paw edema. Paw edema inhibiting activity of the methanolic extract of *Tamarindus indica* Linn started within 0.5 hour and prolonged up to 4 hrs after challenge with egg albumin. In the vehicle treated group, egg albumin increased the paw volume in the sensitized

animals, which was measurable up to the time period of 4 hrs. The group pretreated with Dexamethasone (0.5 mg/kg, i.p.) significantly reduced the paw volume at 0.5, 1, 2, 3 and 4 hrs time interval ($p<0.01$).

3.2 Effect of methanolic extract of *Tamarindus indica* Linn on histamine induced Bronchospasm.

The methanolic extract of *Tamarindus indica* Linn (217.5, 435 and 870 mg/kg, p.o.) significantly prolonged ($p<0.01$) the latent period of convulsions as compared to control following exposure to histamine aerosol at 1st and 4th hour, where as *Tamarindus indica* Linn (870 mg/kg, p.o.) exhibited significant ($p< 0.05$) action at 24th hour also.

Allergic asthma is a chronic inflammatory process occurring due to exposure of allergen resulting in the activation of T-lymphocytes with subsequent release of inflammatory mediators. Immuno-modulating agents are useful in the treatment of asthma by virtue of inhibiting the antigen-antibody (AG:AB) reaction thereby inhibiting release of inflammatory mediators. Administration of egg albumin (s.c.) to rat raises the antiserum to egg albumin in the plasma and sub plantar injection of plasma containing these antibodies, then challenged with egg albumin leads to passive paw anaphylaxis in rats (Mengi, 2003). The present study revealed that in the animals pretreated with methanolic extract of *Tamarindus indica* Linn, there was significant reduction ($p<0.01$) in the paw volume at all the time intervals. The beneficial effect of *Tamarindus indica* Linn could be due to either inhibition AG: AB or anti-histaminic activity.

The histamine induced bronchoconstriction model of asthma is characterized by allergen-induced immediate airway constriction and late airway reactivity to a pharmacological vasoconstrictor-histamine. Histamine is a central mediator in the pathogenesis of allergic and inflammatory disorders (Uvnas, 1969). In the present study methanolic extract of *Tamarindus indica* Linn prolonged the latent period of convulsion (PCT) in guinea pigs following exposure to histamine aerosol. This is suggestive of bronchodilating and antihistaminic activity of *Tamarindus indica* Linn.

4. CONCLUSION:

Thus, it can be concluded from the results obtained in the present investigation that *Tamarindus indica* Linn possess significant antiasthmatic activity. The anti-asthmatic activity of *Tamarindus indica* Linn can be attributed to bronchodilating, antihistaminic (H_1-antagonist) and anti-inflammatory, suggestive of its potential in treatment and prophylaxis of asthma. Hence further detailed study needs to be conducted to evaluate the clinical efficacy in the treatment of asthmatic patients.

Table No 1 : Effect of *Tamarindus indica* Linn on passive paw anaphylaxis in rats.

Group	Paw Edema Volume (ml) at Mean ± SEM				
	0.5 hr	1 hr	2 hr	3 hr	4 hr
I	0.48 ± 0.047	0.44 ± 0.018	0.42 ± 0.036	0.40 ± 0.017	0.37 ± 0.010
II	0.26 ± 0.070**	0.21 ± 0.005**	0.18 ± 0.007**	0.15 ± 0.009**	0.10 ± 0.005**
III	0.36 ± 0.007**	0.32 ± 0.058**	0.30 ± 0.013**	0.27 ± 0.009**	0.25 ± 0.010**
IV	0.30 ± 0.044**	0.26 ± 0.005**	0.21 ± 0.013**	0.19 ± 0.010**	0.17 ± 0.011**
V	0.28 ± 0.007**	0.23 ± 0.004**	0.20 ± 0.013**	0.18 ± 0.007**	0.15 ± 0.008**

n=5, Values are mean ± SEM. Group II, III , IV and V compared with Group I (ANOVA followed by Dunnet's test). **$p < 0.01$

Table No 2 : Effect of *Tamarindus indica* Linn against histamine induced bronchoconstriction in guinea pigs.

Group	Treatment	Latent Period of Convulsion			
		Before	After 1 hr	4 hr	24 hr
I	CPM (2 mg/kg, p.o.)	43.6 ± 1.66	71.2 ± 1.65***	86.6 ± 1.56***	53.0 ± 1.44*
II	*Tamarindus indica* Linn (217.5 g/kg,)	48.0 ± 2.68	58.6 ± 5.29**	80.0 ± 1.00**	44.4 ± 1.67**
III	*Tamarindus indica* Linn (435 mg/kg, p.o.)	51.4 ± 1.69	68.0 ± 2.50**	83.4 ± 1.77**	47.0 ± 2.21**
IV	*Tamarindus indica* Linn (870 mg/kg, p.o.)	40.4 ± 1.36	70.2 ± 2.47**	85.6 ± 2.90**	49.8 ± 2.35*

Values are mean ± SEM. n=5 Statistical analysis done by Student 't' test *$p<0.05$, **$p<0.01$, ***$p<0.001$

Table No 3 : Effect of *Tamarindus indica* Linn on passive paw anaphylaxis in rat.

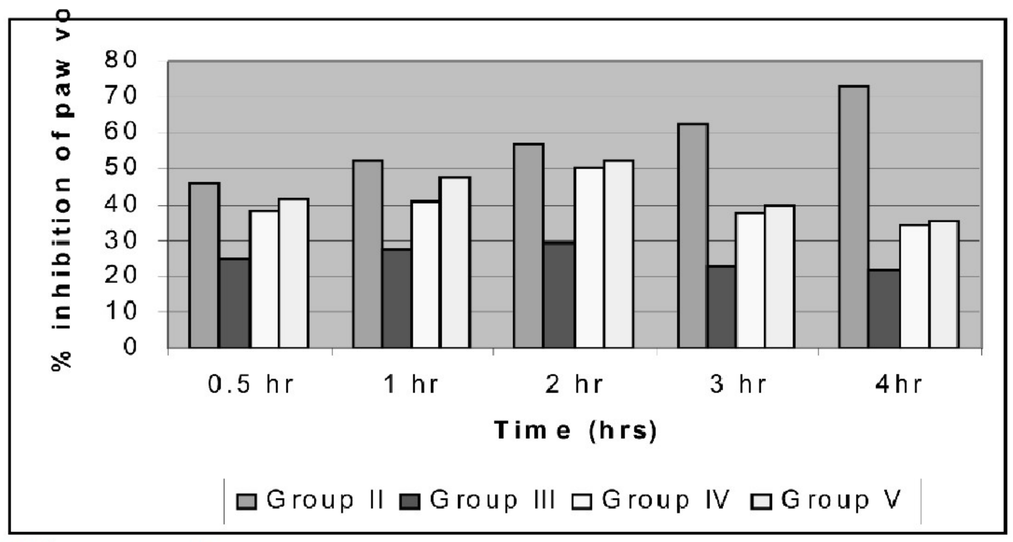
GR Group OUP	Percentage Inhibition of Paw Edema				
	0.5 hr	1 hr	2 hr	3 hr	4 hr
II	45.8	52.2	57.1	62.5	72.9
III	25.0	27.7	29.5	22.5	21.6
IV	37.8	40.9	50.4	37.5	34.2
V	41.5	47.7	52.3	40.0	35.1

Table No 4 : Effect of *Tamarindus indica* Linn against histamine induced bronchoconstriction in guinea pigs

Group	Treatment	% Protection		
		After 1 hr	4 hr	24 hr
I	CPM (2 mg/kg, p.o.)	38.76	49.65	20.17
II	*Tamarindus indica* Linn (217 (217.5 mg/kg, p.o.)	18.08	40.00	10.31
III	*Tamarindus indica* Linn (43 (435 mg/kg, p.o.)	24.41	44.52	13.36
IV	*Tamarindus indica* Linn (870 mg/kg, p.o.)	42.45	48.22	18.87

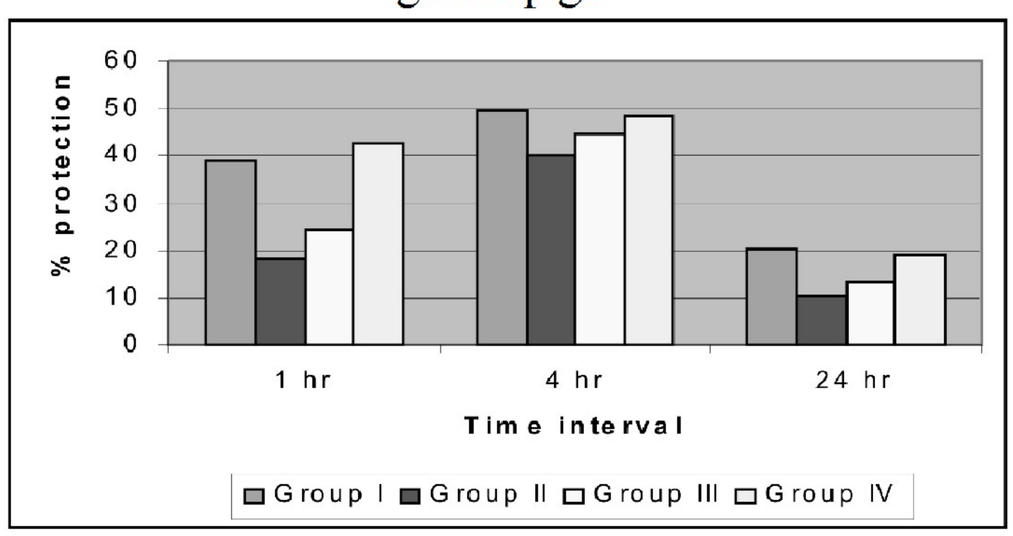
CPM= Chlorpheniramine

Figure no. 1: Effect of *Tamarindus indica* Linn on Passive paw anaphylaxis in rats.



Where n=5

Figure no. 2: Effect of *Tamarindus indica* Linn against histamine-induced bronchoconstriction in guinea pigs



Where, n=5

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