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EVALUATION OF ANTI-ASTHMATIC ACTIVITY OF *TECTONA GRANDIS* LINN. BARK

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ABSTRACT

Various extracts of *Tectona grandis* Linn. bark were screened for antiasthmatic activity by using different *in-vivo* animal models like clonidine induced catalepsy, haloperidol induced catalepsy, milk induced leucocytosis and eosinophilia. The observation of this study indicated that the *Tectona grandis* bark having antihistaminic activity inhibited clonidine-induced catalepsy and not inhibited haloperidol-induced catalepsy. The results of these studies indicated that ethyl acetate extract of *Tectona grandis* Linn. Bark showed significant ($p < 0.001$) antiasthmatic activity at the dose of 100 mg/kg. The anti-asthmatic activity of ethyl acetate extract can be attributed to antihistaminic (H_1 -antagonist), antimuscarinic, antiallergic, anti-inflammatory and adaptogenic activity suggestive of its potential in management of asthma.

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INTRODUCTION:

Bronchial asthma is a complex disease of lung characterized by reversible airways obstruction, airway inflammation, excessive mucus production and airway hyper responsiveness¹. Due to rapid industrialization and urbanization, its prevalence is predicted to increase more rapidly in the coming years. Although limited data is available on the asthma prevalence in India, according to the "Global Burden of Asthma Report", the increase is likely to be dramatic, particularly in India. A wide variation ranging from 4-19% is reported in the prevalence of asthma in school-going children from different parts of India. The prevalence of current-wheezing in children in Delhi is 16.7% and the cumulative prevalence is 20.8%. Another study conducted in Bangalore has reported the prevalence as high as 29.5%. The pathological condition results from a complex interaction between genetic and environmental factors².

For managing asthma attacks, symptomatic relief is the foremost requirement. In India various traditional systems mentioned numerous herbs for therapeutic use in asthma. *Tectona grandis* Linn. (Verbenaceae) is one of the important plants mentioned in Ayurveda for asthma. It is a large deciduous tree, distributed all over Indian. It is commonly known as sagwan (Hindi), saka (Sanskrit) and teak tree (English)³⁻⁵. Its bark is acrid and used in the treatment of bronchitis, hyperacidity, constipation, diabetes, anthelmintic, leprosy and skin diseases. Methanol extract has shown antibacterial activity⁶. Tectoionols A & B (apocarotenoids), naphthaquinone-anthraquinone glycoside, tectol, tectograndiol, lapachol, steroidal moieties and tannin are major components

reported which might be responsible for various medicinal use of herb⁷⁻¹¹. Although, there is no scientific proof of the efficacy of plant extracts for antiasthmatic activity, the aim of this study was to evaluate antiasthmatic effect of *Tectona grandis*.

MATERIALS AND METHODS:

Bark of *Tectona grandis* were collected from Ahmednagar district of Maharashtra in Sep 2008 and authenticated by Mr. P.G. Diwakar, Botanical Survey of India, and Pune, India. The voucher specimen was deposited bearing no. DGTEG1. The collected material was cleaned and air dried at 35-40^o and pulverized in electric grinder. The powder was subjected to successive solvent extraction in Soxhlet extractor using petroleum ether (60-80^o), ethyl acetate and ethanol as solvent and the marc left was macerated with water.

All the extracts were vacuum dried to yield petroleum ether extract, PEE (2.81%), ethyl acetate extract, EAE (6.48%), ethanol extract, ETE (5.19%) and aqueous extract, AQE (8.86%), respectively. Phytochemical screening revealed presence of flavonoids, tannins, glycosides, alkaloids and carbohydrates. The extracts were stored in a refrigerator for further use. Swiss albino mice of either sex weighing 20-25 g were housed under standard laboratory conditions. The animals were fed with standard pellet diet (Amrut laboratory animal feed, Sangali, India) and had free access to water. All the experiments were approved and conducted as per the guidelines of Institutional animal ethical committee.

Clonidine-induced catalepsy^{12, 13}:

Animals were divided into six groups (n=6). Control group received vehicle (5% tween 80 in normal saline) and other

groups PEE, EAE, ETE and AQE received single dose (as 100 mg/kg, p. o., each). Chlorpheniramine maleate (10 mg/kg, i. p.) was used as positive control. All the groups received clonidine (1 mg/kg, s. c.) 1 hr after the drug administration and duration of catalepsy was measured at 0, 30, 60, 90, 120, 150, and 180 min. (Graph 1)

Haloperidol-induced catalepsy^{12, 14}:

Animals were divided into six groups (n=6). Control group received vehicle (5% tween 80 in normal saline) and other groups PEE, EAE, ETE and AQE received single dose (as 100 mg/kg, p. o., each). Chlorpheniramine maleate (10 mg/kg, i. p.) was used as positive control. All the groups received haloperidol (1 mg/kg, s. c.) 1 hr after the drug administration and duration of catalepsy was measured at 0, 30, 60, 90, 120, 150, and 180 min. (Graph 2)

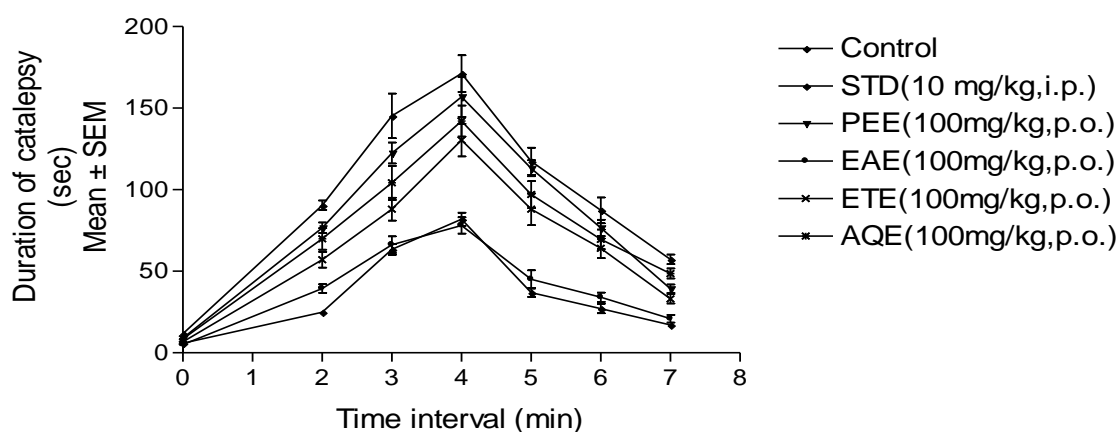
Milk-induced leucocytosis and eosinophilia in mice^{15, 16}:

Animals were divided into seven groups (n=6). Control group received vehicle (5% Tween 80 in normal saline) and other groups PEE, EAE, ETE and AQE received single dose (as 100 mg/kg, p. o., each). Dexamethasone (1 mg/kg, i. p.) was used as positive control. Only milk received group served as an intoxicant. After 1 h of drug treatment except control all groups received boiled and cooled milk injection in dose of (4 ml/kg, s. c.). Total leukocyte count was done in each group before drug administration and 24 h after milk injection. (Graph 3 and 4)

RESULTS AND DISCUSSION:

The present study dealt with screening of antiasthmatic activity of various extracts of bark of *Tectona grandis* Linn. Bronchial asthma is a chronic inflammatory disease, characterized by both bronchoconstriction and airway inflammation which leads to bronchial, hyper-responsiveness to various

GRAPH 1: Effect of various extracts of *Tectona grandis* bark on clonidine induced catalepsy.

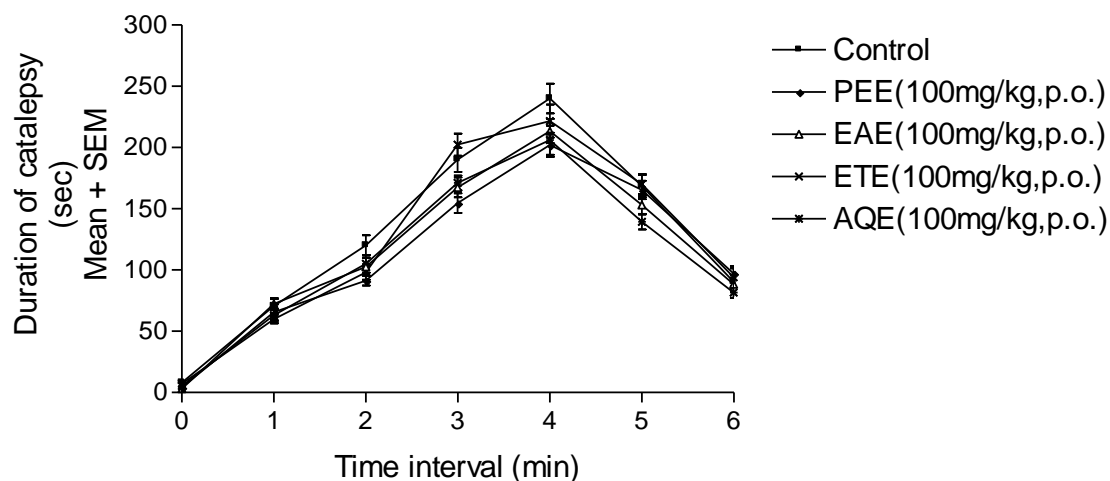


All the values are expressed as mean \pm SEM of a sample size of n=6;

P<0.001 Compared with control treated group by One way ANNOVA followed by Dunnett's Test.

Std= Chlorpheniramine maleate

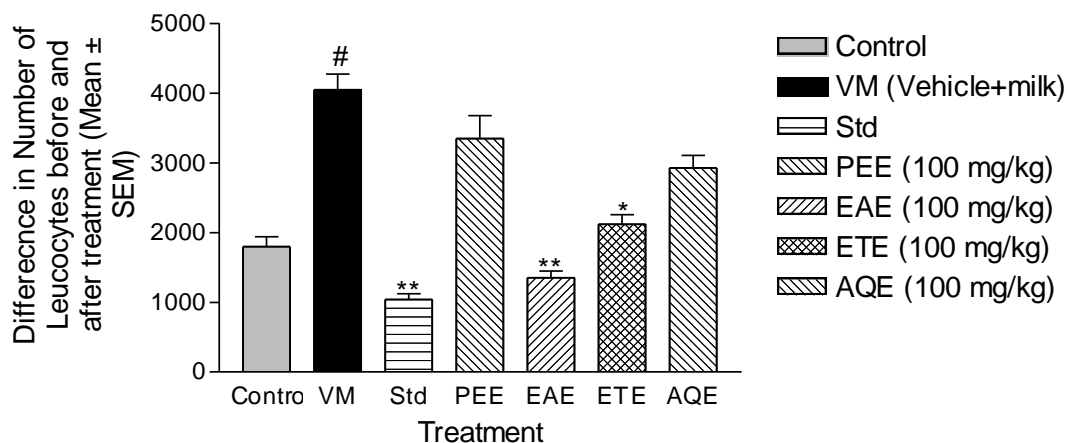
GRAPH 2: Effect of various extracts of *Tectona grandis* bark on Haloperidol induced catalepsy.



All the values are expressed as mean \pm SEM of a sample size of n=6;

* $P < 0.05$, Compared with control treated group by one way ANNOVA followed by Dunnett's Test.

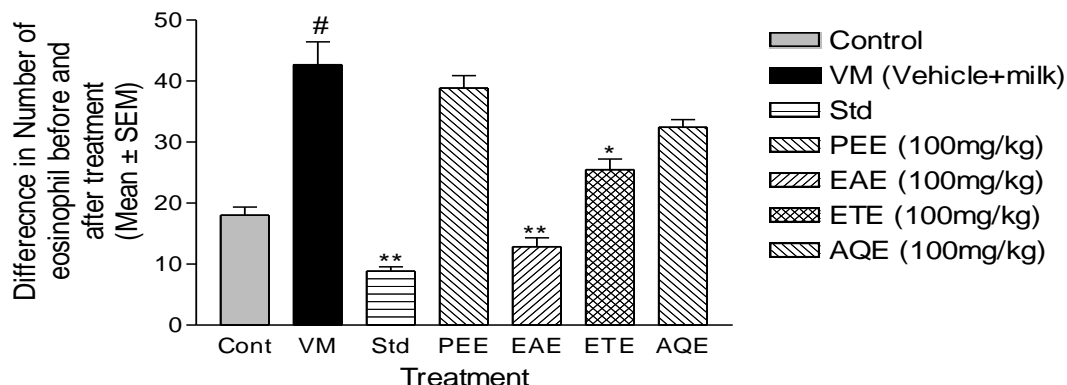
GRAPH 3: Effect of various extracts of *Tectona grandis* bark in milk induced leucocytosis.



All the values are expressed as mean \pm SEM of a sample size of n=6;

[#] $P < 0.05$ vehicle+ milk compare with control and ^{**} $P < 0.001$, ^{*} $P < 0.05$, test groups compare with vehicle+ milk, One way ANNOVA followed by Dunnett's Test.

Std= Dexamethasone

GRAPH 4: Effect of various extracts of *Tectona grandis* bark in milk induced eosinophilia.

All the values are expressed as mean \pm SEM of a sample size of n=6;

[#]P<0.05, vehicle+ milk compare with control and ^{**} P<0.001, ^{*}P<0.05, test groups compare with vehicle+ milk, one way ANNOVA followed by Dunnett's Test.

stimuli, in which many cell types play a role, more important being mast cells, eosinophils and T- lymphocytes¹⁷. Clonidine, a α_2 adrenoreceptor agonist induces, dose dependant catalepsy in mice, which is inhibited by histamine H₁ receptor antagonist but not by H₂ receptor antagonist¹⁸. At a dose of 100 mg/kg p.o. body weight, ethyl acetate extract show significantly decrease in (p<0.001) duration of catalepsy. Haloperidol inhibits dopamine D₂ receptor in substantia nigra. Since catalepsy is a common extra pyramidal side effect of haloperidol¹⁴. In our present study it was found that none of the extracts inhibited haloperidol-induced catalepsy.

The observation of this study indicated that the *Tectona grandis* bark having antihistaminic activity inhibited clonidine-induced catalepsy and not inhibited haloperidol-induced catalepsy. From the present study we can conclude that the cataleptic effect of clonidine in the mouse is mediated by histamine release from mast cells and the clonidine-induced catalepsy was inhibited by ethyl acetate extract at a dose of 100 mg/kg.

The effect of ethyl acetate extract on clonidine-induced catalepsy is probably due to their mast cell stabilizing property and the plant does not have activity on dopaminergic transmission.

Most allergic and non-allergic asthmatics, including those with mild asthma, have bronchial eosinophilia and there is a significant association between eosinophil activation and asthma severity as well as bronchial hyper-responsiveness. The involvement of eosinophils into bronchial mucosa in which allergic inflammation occurs is a critical contributor to the late asthmatic reaction of congestion and mucus hypersecretion. When these cells arrive, they degranulate and perpetuate underlying airway inflammation¹⁹.

After parental administration of milk, there is increase in total leukocytes count, and this stressful condition can be made normalized by administration of an anti-stress drug. Furthermore, leukocytes during asthmatic inflammation release the inflammatory mediators like cytokines, histamine, and major basic protein, which promote the ongoing inflammation. An abnormal increase in peripheral

eosinophil to more than 4% of total leukocyte count (Eosinophilia) associated with respiratory disorder, often allergic in nature together with pulmonary infiltrates²⁰⁻²². Ethyl acetate extracts significantly reduced eosinophils, thus these extracts are useful as antiallergic in asthmatic condition. Total leucocytes count is immunological response, ethyl acetate extract exhibit significant ($p < 0.001$) decrease in leucocytes at dose of 100 mg/kg.

Thus, all the finding obtained in the present investigation that *Tectona grandis* Linn. possess significant anti-asthmatic activity. The anti-asthmatic activity of ethyl acetate extract of bark of *Tectona grandis* Linn. can be attributed to antihistaminic (H_1 -antagonist), antimuscarinic, antiallergic, anti-inflammatory, mast cell stabilizing and adaptogenic activity, suggestive of its potential in management of asthma. Drug effective in asthma are mostly steroidal in nature. Ethyl acetate extract contains steroidal nucleus, glycosides and flavonoids. So antiasthmatic activity showed by *Tectona grandis* might be because of these chemical moieties.

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