EFFECT OF VARIOUS EXTRACTS OF *FICUS BENGALENSIS* BARK ON CLONIDINE AND HALOPERIDOL-INDUCED CATALEPSY IN MICE

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Summary

Various extracts of *Ficus bengalensis* bark were evaluated for anti cataleptic activity as the plant is having antiasthamatic activity. Aqueous extract (50 mg/kg, i.p.) of the plant significantly inhibited clonidine-induced catalepsy but not inhibited haloperidol-induced catalepsy. Thus the antihistaminic activity of *F. bengalensis* may be due to polar constituents.

Key words: *Ficus bengalensis*, cataleptic activity, antiasthamatic, clonidine, haloperidol.

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Introduction

Catalepsy is a condition in which the animal maintains imposed posture for long time before regaining normal posture. Catalepsy is a sign of extrapyramidal effect of drugs that inhibit dopaminergic transmission or increase histamine release in brain. Clonidine, a $\alpha_2$-adrenoceptor agonist, induces dose dependent catalepsy in mice, which is inhibited by histamine H$_1$ receptor antagonists but not by H$_2$ receptor antagonist. They also showed that pretreatment with L-histidine, a precursor of histamine potentiated clonidine-induced catalepsy in dose dependent manner. Muley et al., (1979) showed that intracerebroventricular injection of histamine in conscious mice induced catalepsy, which was inhibited by H$_1$ receptor antagonist but not by H$_2$ receptor antagonist. It is known that clonidine releases histamine from mast cells. Schwartz (1997) identified histamine containing mast cells in brain. Clonidine-induced release of histamine from mast cells is inhibited by $\alpha_2$-adrenoceptor blocker, prazocine. Neuroleptic agent also induced catalepsy, but by different mechanism. Neuroleptics inhibit dopamine D2 receptors in the substantia nigra.

Therefore it was our objective to study the effect various extracts of *Ficus bengalensis* bark on clonidine-induced catalepsy, as it is used traditionally in cough, asthma and inflammation. Since catalepsy is a common extrapyramidal side effect of neuroleptic agents and the effect of the plant on haloperidol-induced catalepsy is not known, we also studied their effect on haloperidol-induced catalepsy in mice.
Material and Methods

Plant Material

Bark of *F. bengalensis* were collected from Ahmednagar district of Maharashtra in May 2006 and authenticated by Dr. P.S.N. Rao, Botanical Survey of India, Pune, where a sample specimen (voucher number: TDJ1) has been deposited.

Extraction

Dried and coarsely powdered bark of *F. bengalensis* was subjected to successive solvent extraction in Soxhlet extractor using petroleum ether, chloroform, ethyl acetate, and ethanol as solvent and the marc left was refluxed with water. All the extracts were vacuum dried to produce PEE (4.81%), CLE (2.29%), EAE (3.13%), ETE (6.94%), and AQE (5.68%), respectively.

Animals

Male albino mice (Swiss strain) weighing 25-28 g were housed under standard laboratory conditions, in groups of five each. The animal had free access to food and water. The ethical committee of the institute approved the protocol of the study.

Drugs and Chemicals

The following drugs and chemicals were used. Drugs: Clonidine (Unichem, India), Haloperidol (Sunpharma, India), Pheniramine maleate (Unimark Remedies Ltd., India) purchased from commercial source. Chemicals: petroleum ether AR (60-80°C) (PCL, India), chloroform AR (PCL, India), ethyl acetate AR (PCL, India), ethanol AR (PCL, India), and tween 80 AR (PCL, India).
Assessment of Anti-cataleptic Activity

Bar test was used to study the effect of various extracts on clonidine-induced catalepsy. Clonidine (1 mg/kg, s.c.) was injected to mice (n = 5) pretreated 30 min before with vehicle (5 ml/kg, i.p.), petroleum ether, chloroform, ethyl acetate, ethanol, and aqueous extracts of *F. bengalensis* (50 mg/kg, i.p., each) or standard drug pheniramine maleate (10 mg/kg, i.p.). The dosages were selected based on preliminary studies (data not shown). The forepaws of mice were placed on horizontal bar (1 cm in diameter, 3 cm above the table) and the time required to remove the paws from bar was noted for each animal and the durations of catalepsy was measured at 0, 15, 30, 60, 90, 120, 150, and 180 min.

Effect on Haloperidol-Induced Catalepsy

The same Bar test was used using haloperidol. Haloperidol (1 mg/kg, i.p.) was injected to mice (n = 5) pretreated 30 min before with vehicle (5 ml/kg, i.p.), petroleum ether, chloroform, ethyl acetate, ethanol, or aqueous extracts of *F. bengalensis* (50 mg/kg, i.p., each). The durations of catalepsy was measured at 0, 15, 30, 60, 90, 120, 150, and 180 min.

Statistical Analysis

The data is presented as mean ± SEM. The data was analyzed by one-way ANOVA followed by Dunnet’s test. Prism Graph pad 3 was used for statistical analysis. P< 0.001 and P<0.05 was considered significant.
Results

Clonidine-Induced Catalepsy

Amongst all the extracts only ethyl acetate (P<0.05) and aqueous (P<0.001) extracts showed significant inhibition in catalepsy (Fig. 1). Results were comparable with standard drug pheniramine maleate (P<0.001).

Haloperidol-Induced Catalepsy

None of the extracts inhibited haloperidol-induced catalepsy (data not shown).

Fig. 1 Effect of various extracts of F. bengalensis on clonidine-induced catalepsy in mice

(1=0, 2=15, 3=30, 4=60, 5=90, 6=120, 7=150, 8=180 min after clonidine). *P<0.001 and #P<0.05 compared to vehicle treated group (One way ANOVA followed by Dunnett’s test)
Several drugs are known to induce catalepsy in animals. The neuroleptic agents induce catalepsy by inhibiting dopamine D2 receptors in the substantia nigra.\textsuperscript{6} Chopra and Dandiya (1975) have studied the relative role of acetylcholine and histamine in perphenazine-induced catalepsy and suggested that anticholinergic activity of antidepressant might be due to an increase in dopamine content in brain or their ability to inhibit release of acetylcholine.\textsuperscript{10} They also showed that different stages of catalepsy appear to be directly correlated with brain histamine content. Uvnas (1969) studied the mast cell degranulation and its correlation with the release of histamine after administration of mast cell degranulating agent (Compound 48/80).\textsuperscript{11} Lakdawala et al., (1980) have shown that clonidine releases histamine from mast cells in a similar manner to a selective liberator like compound 48/80.\textsuperscript{3}

The observation of this study indicated that the plant \textit{F. bengalensis} 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 aqueous and ethyl acetate extract of \textit{F. bengalensis} bark. The effect of these extracts on clonidine-induced catalepsy is probably due to their mast cell stabilizing property and the plant do not have activity on dopaminergic transmission. Aqueous extract of \textit{F. bengalensis} bark showed most potent inhibition of clonidine-induced catalepsy so it can be concluded that polar constituents may be responsible for its antihistaminic activity.
References


