ANTIHISTAMINIC ACTIVITY OF *NYCTANTHES ARBORTRISTIS* BARK

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Summary

Nyctanthes arbortristis is a small tree commonly known as 'Parijat'. The plant is commonly cultivated in the gardens in many parts of the India. Traditionally plant is having antiasthmatic activity hence present work was undertaken to establish antihistaminic potential of the bark extracts. Bark of the plant was collected, authenticated, shade dried and extracted successively with petroleum ether, chloroform, ethyl acetate, ethanol and water to produce respective extracts. Antihistaminic effect was assessed by effect of extracts on clonidine-induced catalepsy and haloperidol-induced catalepsy in mice at 50 mg/kg, i.p. dose. The petroleum ether extract significantly reduced clonidine-induced catalepsy as compared to other extracts; this proves antihistaminic effect of the extract. Hence we can conclude that petroleum ether extract may be useful in the treatment of asthma.

Keywords: *Nyctanthes arbortristis,* antihistaminic, catalepsy, 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 extra-pyramidal effect of drugs that inhibit dopaminergic transmission or increase histamine release in brain. Clonidine, a α_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.[1] They also showed that pretreatment with L-histidine, a precursor of histamine potentiated clonidine-induced catalepsy in dose dependent manner. Muley *et al*. 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.[2] It is known that clonidine releases histamine from mast cells.[3] Schwatz identified histamine containing mast cells in brain.[4] Clonidine-induced release of histamine from mast cells is inhibited by α_2-adrenoceptor blocker, prazocine.[5] Neuroleptic agent also induced catalepsy, but by different mechanism. Neuroleptic agents inhibit dopamine D_2 receptor in the substantia nigra.[6,7] Therefore it was our objective to study the effect of *Nyctanthes arbortristis* bark on clonidine-induced catalepsy, as it is used traditionally in the treatment of asthma.[8] Since catalepsy is a common extra-pyramidal 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 *N. arbortristis* was collected from Ahmednagar district of Maharashtra in August 2007 and authenticated by Dr. P.S.N. Rao, Botanical Survey of India, Pune, where a sample specimen (voucher number: Nirmal-1) has been deposited.

Extraction

Dried and powdered bark of the plant was extracted successively with various solvents viz. petroleum ether, chloroform, ethyl acetate and ethanol in Soxhlet extractor. The mark left was extracted using water as solvent. Extracts were concentrated by vacuum distillation and then dried in open air to produce respective extracts.

Animals

Male albino mice (Swiss strain) weighing 25-28 g were housed under standard laboratory conditions, in groups of six 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) and Pheniramine maleate purchased from commercial source. Chemicals: Petroleum ether ($60\text{-}80^0$c) AR, chloroform AR, ethanol AR, ethyl acetate AR and tween 80 AR (PCL, India).

Assessment of Anti-cataleptic Activity

1. **Effect on clonidine-Induced Catalepsy**

Bar test was used to study the effect of various extracts on clonidine-induced catalepsy.[9] Clonidine (1 mg/kg, s.c.) was injected to mice (n = 6) pretreated 30 min before with vehicle (5 ml/kg, i.p.), petroleum ether extract, chloroform extract, ethyl acetate extract, ethanol extract, aqueous extract of *N. arbortristis* bark (50 mg/kg, i.p., each) and 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.

2. **Effect on Haloperidol-Induced Catalepsy**

The same Bar test was used using haloperidol. Haloperidol (1 mg/kg, i.p.) was injected to mice (n = 6) pretreated 30 min before with vehicle (5 ml/kg, i.p.), petroleum ether extract, chloroform extract, ethyl acetate extract, ethanol extract and aqueous extract of *N. arbortristis* bark (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 Dunnett's test. Prism Graph pad 3 was used for statistical analysis. $P<0.05$ was considered significant.

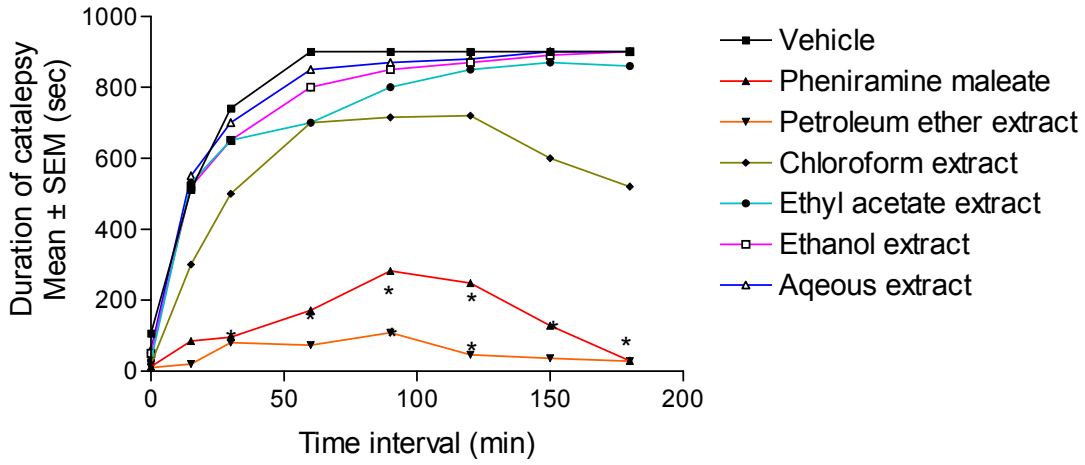
Results

Results showed that amongst all the extracts, petroleum ether extract of *N. arbortristis* bark (50 mg/kg, i.p.) inhibited clonidine-induced Catalepsy (Fig.1) but not haloperidol-induced catalepsy (Fig.2). The inhibition of catalepsy was comparable with standard drug pheniramine maleate.

Discussion

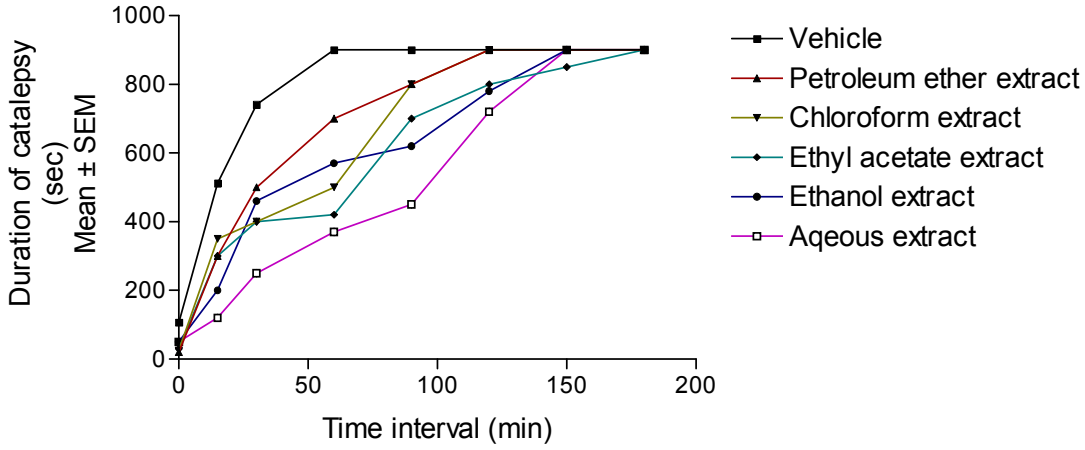
Several drugs are known to induce catalepsy in animals. The neuroleptic agents induce catalepsy by inducing dopamine D_2 receptor in the substantia nigra.[6] Chopra and Dandiya have studied the relative role of acetylcholine and histamine in perphenazine-induce catalepsy and suggested that anticholinergic activity of antidepressant might be due to an increase in dopamine content in brain or their ability to inhibit release of acetylcholine.[10] They also showed that different stages of catalepsy appear to be directly correlated with brain histamine content. Uvnas studied the mast cell degranulation and its correlation with the release of histamine after administration of mast cell degranulating agent (Compound 48/80).[11] Lakdawala *et al* have shown that clonidine releases histamine from mast cell in a similar manner to a selective liberator like compound 48/80.[3]

Figure 1. Effect of various extracts of *N. arbortristis* bark on clonidine-induced catalepsy in mice.



*P<0.05 compared to vehicle treated group (One way ANOVA followed by Dunnett's test).

Figure 2. Effect of various extracts of *N. arbortristis* bark on haloperidol-induced catalepsy in mice.



The observation of this study indicated that the plant *N. arbortristis* 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. The effect of this extracts on clonidine-induced catalepsy is probably due to their mast cell stabilizing property and the plant does not have activity on dopaminergic transmission. It can be concluded that nonpolar constituents may be useful as antihistaminic and may be used in the treatment of asthma.

Acknowledgement: Authors are thankful to BCUD, University of Pune, Pune for providing financial support (Letter No. BCUD/OSD/217, Dated 15/07/09).

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