ANTIHISTAMINIC EFFECT OF *CITRULLUS COLOCYNTHIS LINN* SCHARD LEAVES.

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Summary

Citrullus colocynthis (L) Schrad leaves are used in the treatment of asthma traditionally, so present work was undertaken to prove it scientifically using suitable animal models. Antihistaminic principles are useful in the treatment of asthma; hence in present work antihistaminic activity of various extract of *C. colocynthis* (L) Schrad leaves were checked using clonidine-induced catalepsy and haloperidol-induced catalepsy in Swiss albino mice at the dose of 50 mg/kg, i.p. Results showed that Petroleum ether extract inhibited clonidine-induced catalepsy but there is no effect on haloperidol-induced catalepsy. This shows that the inhibition is through antihistaminic action and there is no role of dopamine. Hence it is concluded that Petroleum ether extract is having significant antihistaminic activity and the nonpolar constituents from Petroleum ether extract of leaves of *C. colocynthis* may be responsible for antihistaminic activity and may have potential role in the treatment of asthma.

Keywords: *Citrullus colocynthis*, antihistaminic, catalepsy, clonidine, asthma.

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.*, (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.[2] It is known that clonidine releases histamine from mast cells.[3] Schwatz (1997) 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 various extracts of *Citrullus colocynthis* Linn. leaves 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

Fresh Leaves of *C.colocynthis* were collected from Ahmednagar district of Maharashtra in September 2009 and authenticated by Mr. S.C. Majumdar, Botanical Survey of India, Pune, where a sample specimen (Voucher number: BSI/ 501) has been deposited.

Extraction

Dried and coarsely powdered Leaves of *C. colocynthis* were subjected to successive solvent extraction in Soxhlet extractor using petroleum ether, ethanol as solvent and the marc left was refluxed with water.

Animals

Male albino mice (Swiss strain) weighing 22-25 g were housed under standard laboratory conditions, in a group of six each.

Drugs and chemicals

The following drugs and chemicals were used.

Drugs: clonidine, haloperidol, pheniramine maleate

Chemicals: Petroleum ether, Ethanol and Tween 80

Anticataleptic 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 Petroleum ether extract (50 mg/kg, i.p.), ethanol extract (50 mg/kg, i.p.), Aqueous extract (50 mg/kg, i.p.) and standard drug pheniramine maleate (10 mg/kg, i.p.). 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 duration 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. [9] Haloperidol (1 mg/kg, i.p.) was injected to mice (n=6) pretreated 30 min before with Petroleum ether extract (50 mg/kg, i.p.), ethanol extract (50 mg/kg, i.p.), Aqueous extract (50 mg/kg, i.p.) and standard drug pheniramine maleate (10 mg/kg, i.p.). The duration of catalepsy was measured at 0, 15, 30, 60, 90, 120, 150, and 180 min.

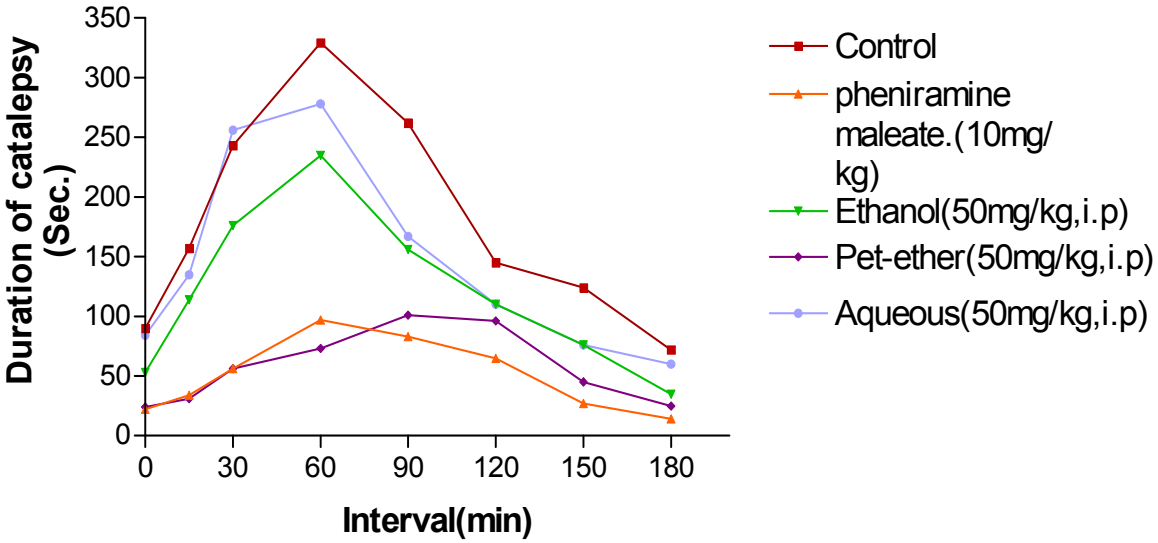
Statistical Analysis

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. $P<0.05$ was considered significant.

Results

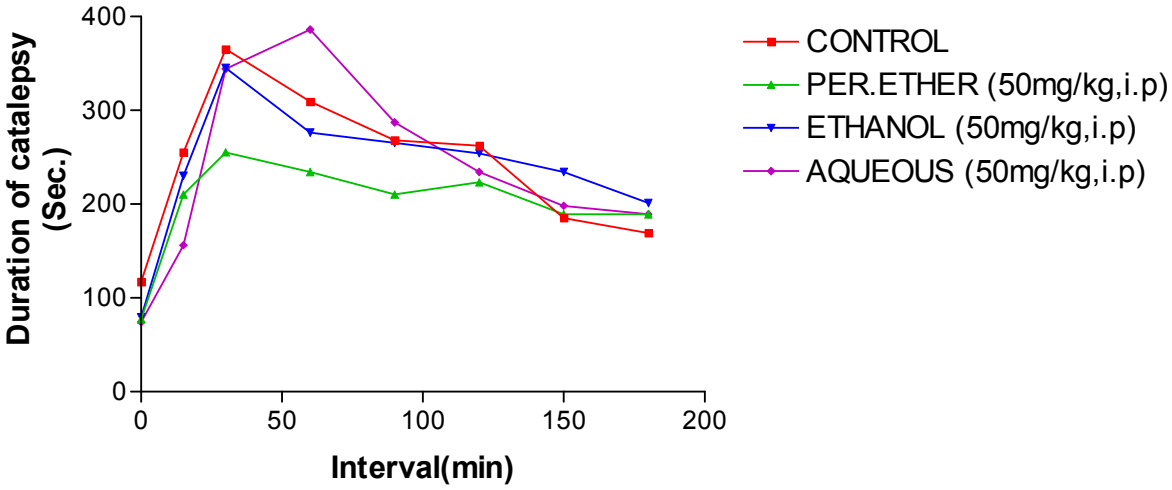
Result showed that petroleum ether extract of *C.colocynthis* (50 mg/kg, i.p.) inhibited clonidine-induced Catalepsy (Fig.1) but not haloperidol-induced Catalepsy (Fig.2). The inhibition of catalepsy was comparable with standard drug pheniramine maleate.

Figure 1: Effect of various extracts of leaves of *C.colocynthis* on clonidine induced catalepsy in mice.



*P<0.001 compared to vehicle treated group (One way ANOVA and Dunnett's test)

Figure 2: Effect of various extracts of leaves of *C.colocynthis* on haloperidol induced catalepsy in mice (50 mg/kg)



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 (1975) 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 (1969) 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*., (1980) have shown that clonidine releases histamine from mast cell in a similar manner to a selective liberator like compound 48/80.[3]

The observation of this study indicated that the petroleum ether extract of leaves of *C.colocynthis* 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.

Conclusion

As petroleum ether extract of leaves of *C.colocynthis* (50 mg/kg, i.p.) significantly inhibited clonidine-induced catalepsy but not inhibited haloperidol-induced catalepsy, we can conclude that nonpolar constituents of the plant can be used as antihistaminic and can be useful in the treatment of asthma.

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