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Effect of *Solanum melongena* Linn. Leaves Extracts on Clonidine Induced Catalepsy and Milk Induced Leukocytosis and Eosinophilia in Mice

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ABSTRACT: Objective: To study the Effect of *Solanum melongena* Linn. leaves extracts on Clonidine induced catalepsy and milk induced Leukocytosis and Eosinophilia in mice. Methods: Methanolic and chloroform extracts of *Solanum melongena* Linn. leaves were prepared. Preliminary phytochemical screening of the prepared extracts was carried out. Effects of prepared extracts were studied on Clonidine induced catalepsy and milk induced leukocytosis and eosinophila in mice. Results: Maximum duration of catalepsy was observed at 90 min after the clonidine administration. There was significant inhibition ($p<0.05$) of clonidine induced catalepsy in the animals pretreated with chlorpheniramine maleate, methanol and chloroform extract of *S. melongena*. Administration of milk (4mg/kg) subcutaneous route exhibited significant increase in leucocyte and eosinophil count after 24 hrs of administration. Chloroform extract at the dose of 500mg/kg body weight showed significant inhibition ($p<0.05$) of milk induced leukocytosis and eosinophilia. Conclusions: These results suggest that *Solanum melongena* leaves extract may have the potential therapeutic value in the treatment of allergic diseases.

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INTRODUCTION

Solanum melongena Linn (Solanaceae) is an erect or suffrutescent, herbaceous, armed or unarmed plant[1]. It is a culinary vegetable, has been in use in the Indian system of medicine[2]. Besides, having many traditional uses *Solanum melongena* is reported to exhibit many important pharmacological actions. Various parts are reported to have analgesic & antipyretic[3], anti-inflammatory[4], hypolipidimic[5], Anti asthmatic[6], spasmogenic[7] and hypotensive action[8]. Flavonoids isolated from *S. melongena* showed potent antioxidant activity[9]. *S. melongena* is also a natural source of vitamin A. It would play an important role for vision and eye health[10]. The plant has been investigated for the presence of chemical constituents, quercetin 3-O-rhamnoside, kaempferol-3-O-rhamnoside[11] and alkaloidal fractions were isolated from the leaves.

Catalepsy is a condition in which the animal maintains imposed posture for long time before regaining normal posture. Catalepsy is the sign of extrapyramidal effect of drugs that inhibit dopaminergic transmission or increase histamine release in brain. Clonidine, a α_2 adrenoreceptor agonist induces dose dependent catalepsy in mice, which is inhibited by H_1 receptor antagonist but not by H_2 receptor antagonist[12].

During asthmatic inflammation leukocyte release cytokines, histamine and major basic protein promote ongoing inflammation[13]. An abnormal increase in peripheral eosinophils count more than 4% of total leukocyte is termed as eosinophilia[14]. In the present investigation we have evaluated effect of *Solanum melongena* Linn. leaves extracts on Clonidine induced catalepsy and milk induced Leukocytosis and Eosinophilia in mice.

MATERIALS AND METHODS

Collection of plant material

The leaves of *Solanum melongena* were collected from the rural areas of Baramati Dist-Pune (Maharashtra) and identified in the Department of Botany, Agricultural Development Trust's Shardabai Pawar Mahila Mahavidyalaya, Shardanagar Malegaon BkII Tal-Baramati Dist-Pune, Maharashtra, India. (Voucher specimen PASR-140)

Drugs and chemicals

The drugs used were: clonidine (Neon Lab. Ltd.,India), chlorpheniramine maleate (Pfizer Ltd.) and dexamethasone (Zydus Heathcare Ltd); all were purchased from commercial source. Chemicals used were: Methanol and chloroform (Research Lab. Industries, India)

Extract preparation and phytochemical screening

The leaves of *Solanum melongena* were dried and crushed to coarse powder. Powdered material was subjected to soxhlet extraction with methanol and chloroform as a solvent. Extracts so obtained were concentrated to dryness by evaporating the solvent. Yields were calculated. Extracts were stored at room temperature and protected from direct sunlight. Both the extracts were separately subjected to preliminary phytochemical screening using standard tests.

Animals

Swiss albino mice (20-30gm) of either sex were obtained from National Institute of Biosciences, Pune, India. Animals were maintained in our animal house under standard laboratory condition. Animals were exposed to day night light cycle and room temperature $(24 \pm 2)^0$C. All animals are allowed free access to ready-made food pellets and water. Animals were handled according to standard protocols for the use of laboratory animals[15].The experimental protocol was approved by the Institutional Animal Ethics Committee (1214/ac/08/CPCSEA).

Acute toxicity study

Acute toxicity study was performed by oral route in mice as per OECD guidelines 423.

Clonidine induced catalepsy in mice

Bar test was performed to study effect of clonidine induced catalepsy[16-18]. Clonidine (1mg/kg, s.c.) was injected to mice (n=6). Before 1 h of clonidine treatment, group I received dist. Water (1ml/kg i.p.) group II received Chlorpheniramine maleate (10mg/kg body weight, i.p.) group III received methanolic extract (250mg/kg body weight i.p.) group IV received methanolic extract (500mg/kg body weight i.p.) group V received chloroform extract (250mg/kg body weight i.p) and group VI received chloroform extract (500mg/kg body weight i.p.) Forepaws of mice were placed on horizontal bar and time required to remove the paws for each animal was noted and duration of catalepsy were measured at 15, 30, 60, 90 and 120 min.

Milk induced Leukocytosis and Eosinophilia in mice

Swiss albino mice of either sex weighing between 20-30g were divided into six groups of five animals each. All animals received boiled (boiling temp 70ºC and boiling time 20 min) and cooled milk in dose of 4 ml/kg subcutaneously. Animal belong to group I treated as control and received distilled water 10 ml/kg. p.o. Group II received methanolic extract 250mg/kg.p.o.(MESML250), Group III received methanolic extract 500mg/kg.p.o.(MESML500) Group IV received chloroform extract 250mg/ kg.p.o.(CESML250) Group V received chloroform extract 500mg/ kg.p.o.(CESML500), whereas group VI received Dexamethasone 50mg/kg i.p. All the extracts and standard drug were administered 1h before milk injection. Blood samples were collected before and 24 h after milk administration from the retro orbital plexus, under light ether anesthesia. Difference in total leukocyte and eosinophil count before and after 24h drug administration were calculated [19].

Statistical analysis

The mean ±SEM values were calculated for each group. The statistical analysis was performed using one way analysis of variance (ANOVA) followed by Dunnett's test for individual groups comparison with control. A probability value less than 0.05 were considered as significant.

RESULTS AND DISCUSSION

Acute toxicity study

Treatment with methanol and chloroform extract up to 2000mg/kg orally to mice did not induce mortality. Hence LD_{50} was considered to be more than 2000 mg/kg. Based on acute toxicity results 250 and 500 mg/kg doses were selected.

Preliminary phytochemical screening

Table 1 represents the results of the phytochemical screening for both methanolic extract as well as chloroform extract.

Table1. Phytochemical screening of the extracts

Phytoconstituents	Methanol extract	Chloroform extract
Alkaloids	+++	+++
Flavonoids	++	+++
Saponins	+	-
Tannins	++	++
Steroids	+	+

+++: strong intensity reaction, ++: medium intensity reaction, +: Weak intensity reaction,-:Not detected

Clonidine induced catalepsy

All the groups showed maximum duration of catalepsy at 90 min after the clonidine administration. There was significant inhibition ($p<0.05$) of clonidine induced catalepsy in the animals pretreated with chlorpheniramine maleate, methanolic extract and chloroform extract (**Table 2, Figure 1 and 2**).

Table 2. Effect of various extracts of *Solanum melongena* on clonidine induced catalepsy in mice

Group	Duration of catalepsy (Sec), Mean±SEM				
	15min	30 min	60 min	90 min	120min
Control	62.00±4.465	89.33±4.828	102.00±.819	142.33±12.387	63.00±5.190
Std	4.33±0.667*	10.00±1.461*	22.00±3.367*	30.00±2.295*	20.00±1.414*
MESML 250	6.33±1.116*	22.00±3.055*	29.00±3.215*	45.167±7.692*	22.167±3.911*
MESML 500	5.00±0.856*	16.167±2.27*	23.00±2.324*	35.00±2.530*	17.00±2.422*
CESML 250	6.00±0.966*	17.00±1.317*	25.00±2.887*	35.00±2.221*	21.00±1.653*
CESML500	3.00±0.577*	18.00±1.065*	21.00±1.571*	30.00±2.422*	13.33±0.882*

*p<0.05

Figure 1. Effect of Chlorpheniramine maleate (10mg/kg body weight, i.p.) on clonidine induced catalepsy in mice.

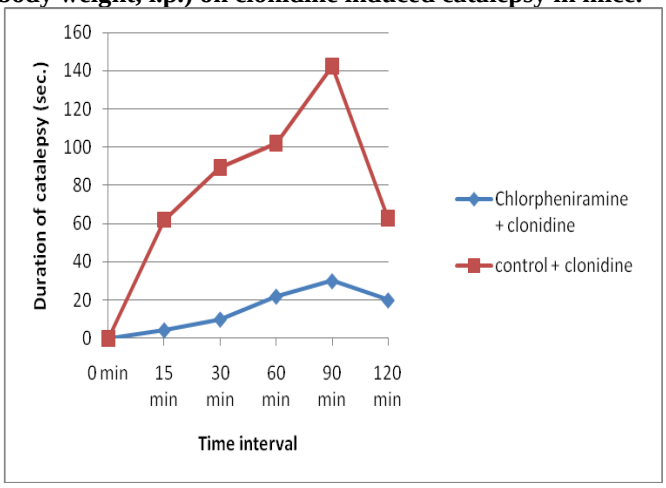
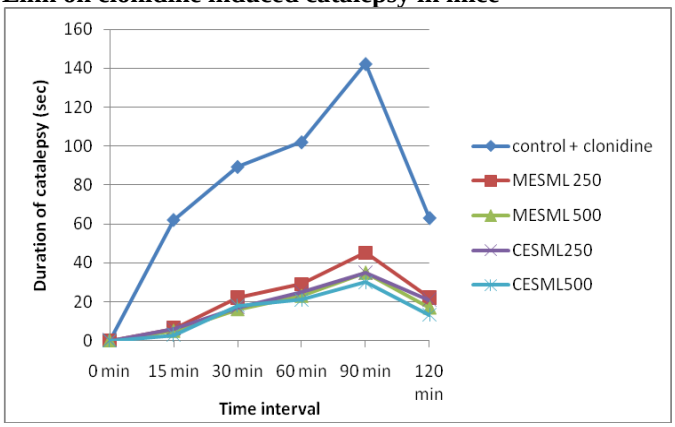


Figure 2. Effect of various extracts of *Solanum melongena* Linn on clonidine induced catalepsy in mice



Milk induced Leukocytosis and Eosinophilia in mice

Subcutaneous administration of boiled and cooled milk at dose of 4ml/kg. showed a significant increase in the leukocytes and eosinophils count after 24h as compared to leukocyte count before milk administration (**Table 3 and 4; Figure 3 and 4**).

Table 3. Effect of various extracts of *Solanum melongena* leaves on milk induced Leukocytosis in mice

Group	Treatment	Difference in Total leukocyte count (Per cu mm) (Mean ± SEM)
I	Dist. Water	2936.00 ± 487.13
II	MESML250	2386.00 ± 374.13
III	MESML500	943.00 ± 98.78*
IV	CESML250	1891.00 ± 191.19
V	CESML500	706.00 ± 172.81**
VI	Dexamethasone (50mg/kg i.p.)	476.00 ± 110.40***

*p<0.004, **P<0.003, ***p <0.001

Figure 3. Effect of various extracts of *Solanum melongena* leaves on milk induced leukocytosis in mice

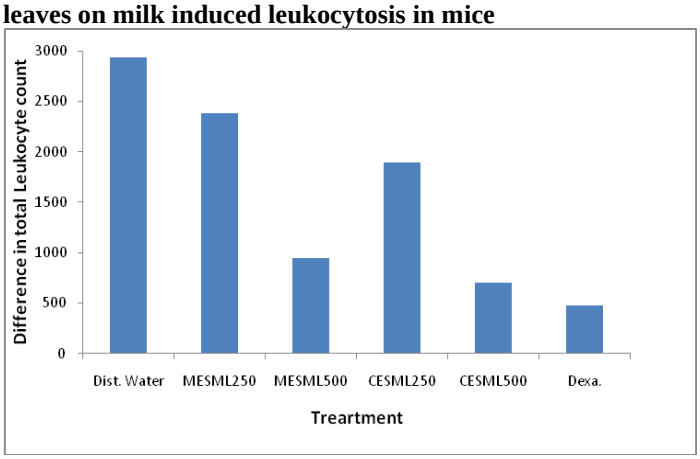
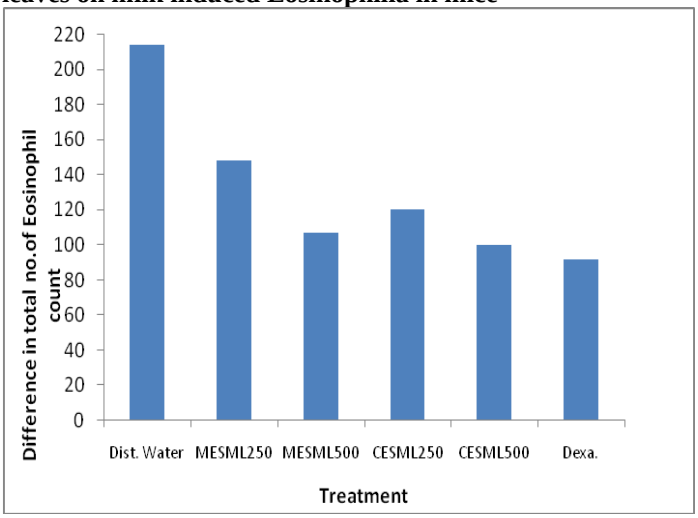


Table 4. Effect of various extracts of *Solanum melongena* leaves on milk induced Eosinophilia in mice

Group	Treatment	Difference Total eosinophil count (Per cu mm) (Mean ± SEM)
I	Dist. Water	214.00 ± 38.64
II	MESML250	148.00 ± 15.29**
III	MESML500	107.00 ± 11.35
IV	CESML250	120.00 ±18.16
V	CESML500	100.00 ± 22.36*
VI	Dexamethasone (0.5mg/kg i.p.)	92.00 ± 22.00***

*p<0.03, **P<0.029, ***p <0.025

Figure 4. Effect of various extracts of *Solanum melongena* leaves on milk induced Eosinophilia in mice



It is known that clonidine releases histamine from mast cells[20]. Clonidine induced release of histamine from mast cells is inhibited by α_2 adrenoceptor blocker. In the present investigation, all groups showed maximum duration of catalepsy at 90 min after the clonidine administration. There was significant inhibition ($p<0.05$) of clonidine induced catalepsy in the animals pretreated with *Solanum melongena* extract. This indicates antihistaminic activity of the *Solanum melongena*.

After parentral administration of milk there is increase in total leukocyte and eosinophil count, this stressful condition can be normalized by administration of an antistress or adaptogenic drug. The involvement of eosinophil in bronchial mucosa, in which allergic inflammation occurs, is a critical contributor to the late asthmatic reaction of congestion and mucus hypersecretion. In the late phase, especially in the development of allergic asthma, eosinophil plays role as inflammatory cell. Eosinophil secrets mediators such as eosinophil cationic protein, tumor necrosis factor, eosinophil derived neurotoxin and prostaglandin results in epithelial shedding, bronchoconstriction and promotion of inflammation in respiratory tract often allergic. In the present study it has been found that, parenteral administration of milk at a dose of 4ml/ kg significantly induced the total leukocyte and eosinophil count ($p<0.001$) after 24 hours. Animals of the group treated with chloroform extract (500mg/ kg body weight) of *S. melongena* significantly inhibited increase in number of total leukocyte and eosinophil count.

CONCLUSION

The results of present study revealed that *Solanum melongena* leaves extract inhibit the clonidine induced catalepsy and milk induced leukocytosis and eosinophilia in mice, suggests its potential antihistaminic and antiallergic activities. However we are screening *Solanum melongena* leaves extract for other animal models of asthma to evaluate its efficacy in the management of asthma. We are also working on phytochemical investigation of these extracts to pin point the chemical constituents responsible for the activity

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CONFLICT OF INTEREST

The authors have no conflict of interest.

FUNDING SOURCE

There is no source of funding.

DATA AVAILABILITY

Not declared.

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