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Research Article

Antidepressant activity of the ethanolic extract of *Albizzia lebbeck* (Linn) bark in animal models of depression

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ABSTRACT

Objectives: The present study was designed to investigate the antidepressant effects of *Albizzia lebbeck* bark in various animal depression models.**Materials and Methods:** The alcoholic extract **(**70% v/v ethanol) of *Albizzia lebbeck* bark (200 & 400 mg/kg. p.o) was administered once daily for seven successive days to separate groups of young male swiss albino mice. The immobility periods of control and treated mice were recorded in two behavioral despair models forced swim test (FST), tail suspension test (TST) and the effect of extract on locomotor function of mice was studied using actophotometer. The antidepressant-like effect of tested drug was compared to that of imipramine (15 mg/ kg. p.o) and fluoxetine (20mg/kg.p.o). **Results:** The bark extract at doses of 200 and 400 mg/kg significantly decreased the duration of immobility time in a dose dependent manner in both FST and TST. The extract did not show significant effect on locomotor activity of mice. The efficacy of tested extract was found to be comparable to that of imipramine and fluoxetine. **Conclusion:** Our results suggested that the ethanolic extract of *Albizzia lebbeck* bark exerts antidepressant-like effect.

Keywords: *Albizzia lebbeck*, Depression, Forced swim test, Tail suspension test.

INTRODUCTION

Depression is a common, debilitating, life-threatening illness with an increasing morbidity and mortality. Furthermore, the World Health Organization revealed that depression is the fourth leading cause of disability worldwide, exceeded by lower respiratory infections, perinatal conditions and HIV/AIDS [1]. Current antidepressant drugs, including various monoamine reuptake inhibitors and monoamine oxidase inhibitors, have proven to be effective and are available in clinic, but they are burdened with such disadvantage as slow onset of action, relatively low response and side effects, which make the research and development of new type antidepressants urgent [2,3]. The antidepressant effect of herbs has been paid more and more attention gradually because of increasing incidence of depression and predominance of traditional herbs in therapy.

The plant *Albizzia lebbeck* Linn is a large deciduous tree belonging to the family Mimosaceae [4]. The plant possess many therapeutic activities such as in the treatment of leprosy, ulcers, ophthalmic and skin eruptions, skin diseases and CNS depressant activity [5] . In the present study, the antidepressant effect of *Albizzia lebbeck* Linn bark was assessed using well accepted and validated experimental paradigms of depression, so as to provide supportive evidence for the folklore claims. Therefore, the present study was undertaken to investigate the effect of *Albizzia lebbeck* bark on depression in mice employing forced swim test (FST) and tail suspension test (TST). Standard antidepressant drugs such as fluoxetine, a selective serotonin reuptake inhibitor, and imipramine, a tricyclic antidepressant were employed to standardize the animal models of depression and to compare the antidepressant efficacy of *Albizzia lebbeck*.

MATERIALS AND METHODS

Preparation of extract of Albizzia lebbeck

The bark of *Albizzia lebbeck* was collected from the field in Meenembakkam, Chennai district, Tamilnadu, India, in the month of

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June 2006.The plant specimen for the proposed study was collected from Chennai, Tamil Nadu. It was identified and authenticated by Dr. Sasikala, Department of Pharmacognosy, Central Drug research and Siddha institute, Chennai, where the voucher specimen was deposited (no. 168) in the Pharmacognosy herbarium, Vels University, India. The bark of *Albizzia lebbeck* Linn was shade dried and coarsely powdered. About 500 gm of powder was extracted with ethanol (70% v/v ethanol) by cold maceration method [6]. The solvent was filtered and evaporated on a rotary evaporator under reduced pressure to obtain a viscous alcoholic extract. The extract was dried in vacuum and the percentage yield was 8.5%.

Phytochemical Screening

The alcoholic extract (70% v/v ethanol) was screened for the presence of phytoconstituents by chemical methods [7], from which the extract was found to contain maximum number of phytoconstituents and was selected for the pharmacological study.

Acute toxicity study

The alcohol extract was used to test the acute and short-term toxicity in mice (20-25 g body weight) [8]. Four doses (0.25, 0.5, 0.75 and 1.0 gm/ kg) of the alcoholic extract were orally administrated to different mice groups (n=5 each). For acute toxicity, we observed mortality and general behavior of the mice for 48 hours. The parameters observed were grooming, hyperactivity, sedation, loss of righting reflex, respiratory rate, and convulsion. For the short term toxicity, we used three mice each. The behavior of the animals was observed daily for one hour in the forenoon (10 to 11 am) for 14 days.

Experimental Animals

Albino Swiss mice of either sex (20-30 g) were obtained from Institutional Animal Breeding House, Vels University, Pallavaram, Chennai-117. Animals were housed in plastic cages at an ambient temperature (25±2^{o}C) and relative humidity of 45-55%. A 12:12 hr light- dark cycle was maintained during the experiments. They were fed with balanced rodent pellet diet from Poultry Research Station, Nandanam, Chennai-35 and water *ad libitum* throughout the experimental period. Animals were acclimatized to their environment for atleast one week before experimentation. The animals were randomly divided into different groups. Each animal was housed separately after recording its body weight. The Institutional Animal Ethics Committee (IAEC) approved the protocol of the study. Registration No. 290 CPCSEA.

Drugs and Chemicals

Imipramine hydrochloride (Sigma-Aldrich, St. Louis, USA) Fluoxetine hydrochloride (Ranbaxy Laboratories, Gurgaon, India) and Diazepam (Calmpose inj. Ranbaxy Laboratories, India) were used in the present study.

EVALUATION OF ANTIDEPRESSANT ACTIVITY

Forced swim test (FST)

Behaviour despair was proposed as a model to test for antidepressant activity [9, 10]. Animals were divided in to four groups of six animals each. Normal control group, receiving a single dose of 0.5 mL/100g of the vehicle. Group 2 reference drug group, being treated with imipramine (15 mg/kg). Groups 3 and 4 were being treated with the ethanolic extract at two dose levels (200 and 400 mg/ kg). The treatment was continued for seven consecutive days. .On the test day mice were forced to swim individually in a glass jar (25 x 12 x 25 cm^{3}sub) containing fresh water of 15 cm height and maintained at 25°C (± 3°C). After an initial 2 min period of vigorous activity, each animal assumed a typical immobile posture. A mouse was considered to be immobile when it remained floating in the water without struggling, making only minimum movements of its limbs necessary to keep its head above water. The total duration of immobility was recorded during the next 4 min of a total 6 min test. The changes in immobility duration were studied after administering drugs in separate groups of animals. Each animal was used only once.

Tail suspension test (TST)

Animals were divided in to four groups of six animals each. Normal control group, receiving a single dose of 0.5 mL/100g of the vehicle. Group 2 reference drug group, being treated with fluoxetine (20 mg/ kg). Groups 3 and 4 were being treated with the ethanolic extract at two dose levels (200 and 400 mg/ kg). The treatment was continued for seven consecutive days. On the test day mice were suspended on the edge of a table 50 cm above the floor by the adhesive tape placed approximately 1 cm from the tip of the tail. The total duration of immobility induced by tail suspension was measured as a facile means of evaluating potential antidepressants [11]. Immobility time was recorded during a 6 min period [12]. Animal was considered to be immobile when it did not show any movement of body and hanged passively.

Study of locomotor activity using Actophotometer

Effect of test extract (200 and 400 mg/kg) on locomotor function of mice was studied using a Actophotometer (INCO, Ambala, India) to rule out the increase in locomotor performance of mice. The difference in the locomotor activity scores was noted before and after the administration of ethanolic extract of *Albizzia lebbeck*.

Statistical analysis

Statistical analysis was carried out using Graph Pad PRISM software (version 4.03). One way ANOVA was used, followed by Dunnet's multiple comparison tests (2005). A p-values <0.05 were considered significant.

RESULT

Phytochemical screening

The phytochemical screening by chemical test showed that the ethanolic extract showed positive results for steroids, proteins, flavonoids, tannins, glycosides and carbohydrates.

Acute toxicity study

Acute toxicity was tested up to a high concentration of 1 g/kg (two times more than the active dose). We note that even at this dose level, the extract did not exhibit any sign of toxicity.

Effect of ethanolic bark extract of Albizzia lebbeck on the forced swimming tests in mice

Compared to the control group, the ethanolic extract of *Albizzia lebbeck* at dose of 200 mg/kg and 400 mg/kg significantly decreased the duration of immobility time in a dose dependent manner (Table.1). Immobility time was reduced by 16.62% and 35% for the extract at the dose of 200 and 400 mg/kg respectively and 39% for imipramine at the dose of 15 mg/kg.

Table 1: Effects of ethanol bark extract of *Albizzia lebbeck* and imipramine on the forced swimming test in mice

Group	Treatment	Dose (mg/kg)	Duration of immobility (sec)
Group I	Control	0.5ml/100g	179.8 ± 4.3
Group II	Imipramine	15	109.64 ± 3.8**
Group III	Ethanol extract	200	149.9 ± 7.3*
Group IV	Ethanol extract	400	117.0 ± 4.7**

Each value represents the mean ± SEM of six observations.*p<0.05, **p<0.01 vs. Control (ANOVA followed by Dunnett's test).

Effect of ethanolic bark extract of Albizzia lebbeck on the tail suspension tests in mice

The results indicated that *Albizzia lebbeck* bark extract administrated acutely at dose of 200 and 400 mg/kg, significantly decreased the duration of immobility time in comparison to the control group when mice were tested in the tail suspension test. The reductions of the immobility time were 33% and 57% for the extract at 200 and 400 mg/kg respectively.

Table 2: Effects of ethanol bark extract of *Albizzia lebbeck* and imipramine on the tail suspension test in mice

Group	Treatment	Dose (mg/kg)	Duration of immobility (sec)
Group I	Control	0.5ml/100g	130.2 ± 5.3
Group II	Fluoxetine	20	58.67 ± 2.8**
Group III	Ethanol extract	200	86.9 ± 4.3*
Group IV	Ethanol extract	400	56.17 ± 5.7**

*Each value represents the mean ± SEM of six observations.*p<0.05, **p<0.01 vs. Control (ANOVA followed by Dunnett's test).*

Effect on locomotor activity

There was no significant effect on locomotor activity of mice (396 ± 9.7 and 378.6 ± 5.8) when treated with ethanolic extract of *Albizzia lebbeck* bark (200 and 400 mg/kg) for seven successive days as compared to control (before treatment) (430.78 ± 7.3).

DISCUSSION

The antidepressant effect of herbs has been paid more attention gradually because of increasing incidence of depression and predominance of traditional herbs in therapy. The effective components of herbs that have antidepressant- like effect include flavonoid, oligosaccharide, polysaccharide, alkaloid and organic acid, etc [13, 14, 15].

In the present study, ethanolic extract of *Albizzia lebbeck* bark (200 and 400 mg/kg, p.o.) produced significant antidepressant-like effect in mice in both FST and TST. Both these models of depression are widely used to screen new antidepressant drugs [16, 17]. These tests are quite sensitive and relatively specific to all major classes of antidepressant drugs including tricyclics, serotonin-specific reuptake inhibitors, monoamine oxidase (MAO) inhibitors and atypical [18]. In FST, mice are forced to swim in a restricted space from which they cannot escape, and are induced to a characteristic behavior of immobility. This behavior reflects a state of despair that can be reduced by several agents, which are therapeutically effective in human depression. The TST also induces a state of immobility in animals like that in FST. This immobility, referred as behavioural despair in animals, which is claimed to reproduce a condition similar to human depression [19]. It has been argued that the TST is less stressful than FST and has greater pharmacological sensitivity [20].

The antidepressant-like effect of ethanolic extract of *Albizzia lebbeck* bark (200 and 400 mg/kg, p.o.) seems not to be associated with any motor effects, since it did not show significant change in locomotor function of mice as compared to control indicating that extract had no excitatory or inhibitory action on central nervous system in effective dose range, which eliminated the probability of false-positive results in forced swimming test and tail suspension test. Initial hypothesis of depression was formulated about 40 years ago, proposing that the main symptoms of depression were due to the functional deficiency of cerebral monoaminergic transmitters such as norepinephrine (NE), serotonin (5HT), and/or dopamine (DA) located at synapses [21]. As is well known, synaptic concentration of 5-HT and/or NE can be increased by commercial antidepressants. The precise mechanisms by which *Albizzia lebbeck* produced antidepressant-like effect are not completely understood.

CONCLUSION

Thus, it may be concluded that *Albizzia lebbeck* produced antidepressant-like effect in mice in both FST and TST. The efficacy of the *Albizzia lebbeck* was comparable to that of imipramine and fluoxetine. Further work was necessary to elucidate the mechanism of action involved in the antidepressant activity of *Albizzia lebbeck* with special references to phytochemicals.

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