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ANTIDEPRESSANT ACTIVITY OF ESSENTIAL BARK OIL OF *CEDRUS DEODARA* IN EXPERIMENTAL ANIMAL MODELS

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ABSTRACT

The aim of the present study was designed to evaluate the antidepressant activity of "*Cedrus deodara*" bark oil using different animal models. Antidepressant activity was evaluated by using two animal models. The degree of antidepressant activity was determined by measuring the immobility time in forced swim test and tail suspension tests. Animals treated with all three doses of CDO (250,500 and 750mg/kg) witnessed a decrease in their immobility times in FST & TST which was significant when compared with control. Similarly, animals treated with imipramine (15mg/kg), as expected showed a significant decrease in the immobility time.

INTRODUCTION

Depression is a state of intense sadness and melancholy that has become disruptive to an individual's ability to function socially and complete the daily activities of life. Most people feel depressed and "down" at some point in their life; it is when these feelings are prolonged that clinical depression is suspected[1]. Incidence of depressive mood disorders is rising in the modern stressful society leading to an increased risks of self harm or suicide as well as increased mortality from related general medical conditions[1]. As many as 10-15% of individuals with this disorder exhibit suicidal tendency during their life time[2].

Mental depression affects a person's mood, thoughts, physical health and behavior. Symptoms of depression include biological and emotional components. Biological symptoms include retardation of thought and action, loss of libido, sleep disturbances and loss of appetite. Emotion symptoms include misery, apathy and pessimism, low self-esteem consisting of feeling of guilt, inadequacy and ugliness, indecisiveness and loss of motivation[3]. It is estimated that by the year 2020 if current trends for demographic and epidemiological transition continue, the burden of depression will increase to 5.7% of the total burden of disease and it would be the second leading cause of disability adjusted life years (DALYs) second only to ischemic heart disease[4].

Depression is common in people in their 20s, 30s, and 40s although depression can occur at any age[5]. Unipolar and bipolar are the two types of depression earlier occurs due to stressful life events and later due to familiar pattern[3]. Patients have symptoms that reflect decrease in brain monoamine with depression neurotransmitters, specifically norepinephrine, serotonin and dopamine[6]. Since the depressive disorders are having a huge impact on our lives, it is worth evaluating the alternative forms of medicines which can be used for its treatment. So in this study, an effort was made to investigate the antidepressant effect of *Cedrus deodara* Oil in experimental animals using different type of models of depression.

MATERIALS AND METHODS

Experimental animals

Swiss albino mice weighing 18-30 gm, were used for the study. The mice were inbred in the central animal house of the Department of Pharmacology, Karavali College of Pharmacy, Mangalore, under suitable conditions of housing, temperature, ventilation and nutrition were used for antidepressant activity. They were kept in clean dry cages week before the beginning of the experiment to acclimatize with the experimental conditions. The animals were fed with standard pelleted diet (Lipton India Ltd., Mumbai) and distilled water *ad libitum* was

maintained at 21^0C-23^0C under a constant 12hrs light and dark cycle. The animal care and experimental protocols were in accordance with CPCSEA /IAEC.

Dose preparation and administration

All the standard drug doses(imipramine) were administered intraperitoneally before 30 minutes and the test doses(CDO) were administered orally before 60 minutes.

Plant material

The wood bark of *Cedrus deodara* belonging to the family Pinaceae were collected from Nambisian's Kalpavally Stores (Dealers in Ayurvedic pharmaceuticals), Kasargod,Kerala and was authenticated by Prof.T.J.Mary Kutty, Botanist and thecertificate was presented to the departmental library for future reference.

Extraction and preparation of test sample

The wood barks were washed 2 or 3 times with tap water so that it was made free from all dust materials. They were cut into small pieces and dried under shade till they were brittle. The dried pieces of wood bark were powdered with the help of mixer grinder and 100g of powder was used for extraction. The powdered bark was extracted using Steam distillation.

Dose Fixation

A dose of 250mg/kg, 500mg/kg and 750mg/kg body weight were chosen as per the previous work[7].

ANTIDEPRESSANT ACTIVITY

Preparation of animals

The animals were selected in such a way that they were free from illness, injury, disease and kept in their cages for at least 5 days prior to dosing to allow for acclimatization to the laboratory conditions. Only those animals which are healthy having weights 18-30 g were selected and maintained at standard laboratory conditions.

Preparation and administration of doses

All the doses were prepared in distilled water using 5% Tween 80 solution as suspending agent and administered orally. In all cases, the concentrations were prepared in 1 ml/100g of body weight. The test substances were administered in a single dose using a gastric intubation tube after fasting for 3 to 4 h.

Observations

Animals were observed initially after dosing at least once during the first 30 min, periodically during the first 24 h. additional observations like changes in skin and fur, eyes and mucous membranes and also respiratory, circulatory, autonomic and central nervous systems and

somatomotor activity and behavioral pattern were also done. Attention was also given to observations of tremors and convulsions[8].

ANTIDEPRESSANT MODELS

Forced Swim Test[8]

Mice were individually placed into a glass cylinder filled with 15 cm of water for 6 min. As a measure of depression-like behavior, the total duration of immobility and the number of immobility episodes were recorded. Immobility is defined as the absence of movement, unless they are necessary for the animal to stay afloat (head above water).Maintained the temperature of water at 26 ± 1 ^{o}c. At this height of water, animals were not able to support themselves by touching the bottom or the side walls of the chamber with their hind-paws or tail. Water in the chamber was changed after subjecting each animal to FST because "used water" has been shown to alter the behavior.Each animal showed vigorous movement during initial 2 min period of the test. The duration of immobility was manually recorded during the next 4 min of total 6 min testing period. Mice were considered to be immobile when they ceased struggling and remained floating motionless in water, making only those movements necessary to keep their head above water. Following swimming sessions, the mice were dried with towel and placed in a cylinder heated under 60 W bulb. The animals were dried under heated cylinder for 15 minutes before returning to the home cages.

Groups of six animals were used for present study were

- Group I – Received 0.05ml/10g of Normal saline intraperitoneally.
- Group II – Received 15 mg/kg Imipramine intraperitoneally.
- Group III – Received 250 mg/kg *Cedrus deodara* Oil orally.
- Group IV – Received 500 mg/kg *Cedrus deodara* Oil orally.
- Group V – Received 750 mg/kg *Cedrus deodara* Oil orally.

Tail Suspension Test: [9, 10]

Animals were moved from their housing colony to laboratory in their own cages and allowed to adopt to the laboratory conditions for 1-2 hr. Each mice was individually suspended to the edge of a table, 50 cm above the floor by adhesive tape placed approximately 1 cm from the tip of the tail. Each animal under test was both acoustically and visually isolated from other animals during the test. Total period of immobility was recorded manually for 6 min. Animal was considered to be immobile when it didn't show any body movement, hung passively and completely motionless. The test was conducted in a dim lighted room and each mice was

used only once in the test. The observer, recording the immobility of animals was blind to the drug treatment given to the animals under study.

RESULTS AND DISCUSSION

Screening of Antidepressant activity of *Cedrus deodara* oil: Antidepressant models namely Forced Swim Test (FST), Tail Suspension Test (TST).

Forced Swim Test; In FST, Table No. 1 shows that animals treated with three doses of CDO (250, 500 and 750 mg/kg) showed decrease in their immobility times, which was significant (138.5±0.30; $p<0.05$ and 135.0±0.22, 121.0±0.17; $p<0.001$) when compared with control (140.2±0.73). Similarly, animals treated with imipramine (15 mg/kg), as expected, showed a significant decrease in the immobility time (60.3±0.17; $p<0.001$). Animals treated with high dose (750 mg/kg) and moderate dose (500 mg/kg) shows more significant decrease in immobility time when compared with low dose (250 mg/kg).

Tail Suspension Test; Animals treated with three doses of CDO showed decrease in their immobility times, which was significant (158.63 ± 0.49; $p<0.05$, 157.98 ± 0.07; $p<0.01$ and 118.78 ± 0.30; $p<0.001$) when compared with control (160.95 ± 0.40). Similarly, animals treated with imipramine (15 mg/kg) as expected showed a significant decrease in the immobility time (72.23 ± 0.68; $p<0.001$). Animals treated with high dose (750 mg/kg) showed more significant decrease in immobility time (Table No. 2).

Table No 1. Effect of CDO on Immobility time in FST:

Group No.	Drug Treatment	Dose (mg/kg)	Immobility period
I	Control	0.05 ml/10 g	140.2±0.73
II	Imipramine	15	60.3±0.17***
III	CDO	250	138.5±0.30*
IV	CDO	500	135.0±0.22***
V	CDO	750	121.0±0.17***

Values were mean ± S.E.M. for (n=6) expressed as the time (in sec) of 6 animals each group. Data analysis was performed using Dunnett's test. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$

Table No 2. Effect of CDO on Immobility time in TST:

Group No.	Drug Treatment	Dose (mg/kg)	Immobility period
I	Control	0.05 ml/10 g	160.92 ± 0.40
II	Standard	15	72.23±0.68***
III	CDO	250	158.63±0.49*
IV	CDO	500	157.98±0.07**
V	CDO	750	118.78±0.30***

Values were mean ± S.E.M. for (n=6) expressed as the time (in sec) of 6 animals in each group. Data analysis was performed using Dunnett's test. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$ vs. control

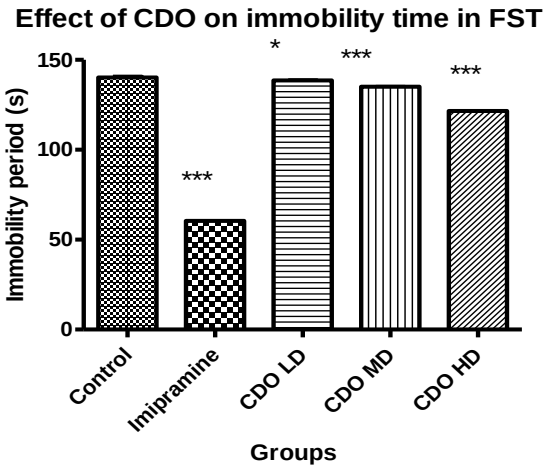

Figure 1: Comparative profile of immobility parameter in FST after oral administration of 250, 500 & 750 mg/kg of *Cedarus deodara* oil (CDO).

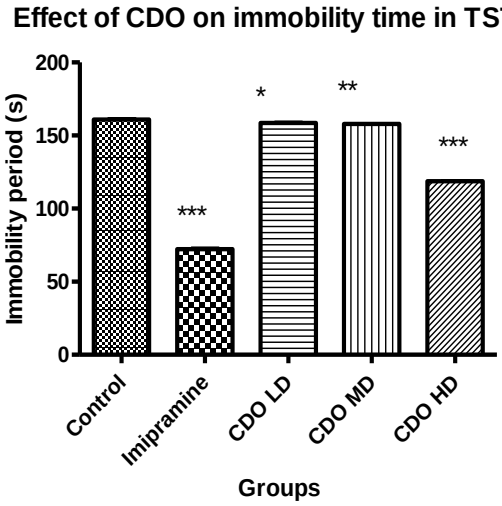

Figure 2: Comparative profile of immobility parameter in TST after oral administration of 250, 500 & 750 mg/kg of CDO.

CONCLUSION

The present study was aimed to expose the antidepressant activity of *Cedrus deodara* Oil in swiss albino mice using Forced swim test and Tail suspension test respectively. The data obtained was satisfactory in conclusion the present data indicate that the administration of *Cedrus deodara* oil to mice has shown significant dose dependant antidepressant activity supporting folk information regarding antidepressant activity of the essential oil, relatively sub-chronic study may be necessary to arrive at a better picture. The exact mechanism underlying antidepressant effect is not clear but it may be apparently related to active compounds present in *Cedrus deodara* oil. Hence further studies would be necessary to evaluate the contribution of active chemical constituents for the observed antidepressant activity as it still remains to be determined which components were responsible for these effects.

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