

ANXIOLYTIC AND ANTICONVULSANT ACTIVITY OF ALCOHOLIC EXTRACT OF HEART WOOD OF *CEDRUS DEODARA ROXB* IN RODENTS

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ABSTRACT

The present study was undertaken to evaluate the anxiolytic and anti-convulsant activity of the alcoholic extract of heart wood of *Cedrus deodara* (ALCD). 50,100 and 200 mg/kg of alcoholic extract of *Cedrus deodara* (ALCD) were tested for its anxiolytic and anticonvulsant activity. Elevated plus maze model (EPM), Actophotometre, Light-dark model were used for testing anxiolytic activity and Pentylene tetrazole (PTZ) induced convulsions and Maximal electro shock (MES) induced convulsions models in mice were used for the assessment of its anticonvulsant activity, Pretreatment with ALCD and estimation of GABA in rat brain tissues also performed to study the effect of ALCD (30, 100 mg/kg) on GABA levels of brain. In Actophotometre test, higher doses (100 and 200mg/kg) of ALCD has showed significant CNS depression by reducing locomotor activity in mice. In EPM the 100 and 200mg/kg of ALCD has increased the time spent in the open arm and decreased time spent in the closed arm. In Light-dark model the 100 and 200mg/kg of ALCD has showed significant increase in the time spent in light zone when compare to the dark zone. In PTZ induced convulsions model 100 and 200 mg/kg of ALCD has increased the onset of clonus and tonic seizures.

In MES induced convulsions model 100 and 200 mg/kg of ALCD has decreased

duration of tonic extensor phase and also at 100 and 200 mg/kg doses the ALCD has increased the percentage protection in PTZ and MES induced convulsions. The ALCD (30 and 100 mg/kg) also showed significant modulation of GABA levels of cerebellum and whole brain other than cerebellum. In conclusion these observations suggest that 100 and 200 mg/kg doses of ALCD are having good anxiolytic and anticonvulsant activity.

Keywords: *Cedrus deodara*, Anxiolytic, Anticonvulsant, GABA estimation.

INTRODUCTION

Anxiety and depression are extremely dramatic and debilitating multifaceted disorders and it is now becoming clear that without knowledge of both clinical and biological aspects of anxiety and depression, it is impossible to offer effective treatment strategies for the patients. Over the past decades, there has been intensive study of a variety of neurobiological aspects of depression and anxiety. Mice and human share more than 90% of their genes ^[1].

Currently the most widely prescribed medications for anxiety disorders are Benzodiazepines ^[2], but the clinical applications of Benzodiazepines as Anxiolytics are limited by their unwanted side effects. Therefore the development of new pharmacological agents from plant sources is well justified ^[2]. The use of herbal medications by physicians in Europe and Asia is becoming more common and researchers are exploring the traditional remedies to find a suitable cure for these mind affecting diseases ^[3].

Cedrus is a genus of Pinacea with basically tropical and subtropical worldwide distribution, the genus is comprised of trees which are sometimes cultivated either for their usefulness to traditional cultures or for ornamental purposes. Traditionally the heartwood of *Cedrus deodara* plant was used to enhance cerebral function, balance the mind, body connection, nervous system and strengthen the brain. It was reported to possess CNS depressant and neuroleptic activity ^{[4],[5],[6]}. So the present study was undertaken to evaluate the anxiolytic and anti convulsant activity of the alcoholic extract of heart wood of *Cedrus deodara* (ALCD).

MATERIALS AND METHODS

Drugs and chemicals

Phenytoin (Sun Pharmaceuticals India.Ltd, Halol. Gujarat. India). Diazepam (Ranbaxy Laboratories Ltd, HMTD textiles, India), Pentylene tetrazole (Sigma-Aldrich, St.Louis, MO63103, USA) were used for the study. All the solvents used for the extraction process are of Laboratory grade and they are purchased from local firms.

Plant extraction

The heart wood of the plant was purchased from the local market in the month of June and authenticated by Dr.K.P.Sreenath, Reader and Taxonomist, Botany Department, Bangalore University. A sample specimen was deposited, bearing voucher number Coll.no. 2007/08.CD-I. The shade dried heart wood of the plant was powdered. The coarse powder was subjected to successive solvent extraction with petroleum ether, alcohol (70%) in soxhlet apparatus. The % yield of Petroleum ether and alcoholic extracts were found to be 13.88% and 19.44 % respectively.

Phytochemical investigation

The alcoholic extract of heart wood of *Cedrus deodara* (ALCD) was subjected to preliminary qualitative investigations^[7].

Experimental animals

Swiss albino mice of either sex (18-25g) were procured from Bioneds, Bangalore and all were acclimatized for 7 days in the animal house of P.E.S. College of Pharmacy,

Bangalore. Male Wistar albino rats (120-150g) were obtained from National Toxicology Centre, Pune and were acclimatized at the animal house of Poona College of Pharmacy, Pune. All the animals were maintained under standard conditions, i.e. room temperature $26 \pm 1^{\circ}\text{C}$, Relative humidity 45-55% and 12:12 h light- dark cycle.

The experimental protocols were approved by the Institutional Animal Ethics Committee (IAEC) of PES College of Pharmacy, Bangalore and all the experiments were conducted according to the guidelines of Committee for the Purpose of Control and Supervision on Experiments on Animals (CPCSEA).

Pharmacological activities

I. Acute toxicity studies

Acute oral toxicity of alcoholic extract of heart wood of *Cedrus deodara* was determined by using female, nulliparous and non pregnant mice weighing 18-22 g. The animals were fasted for 3 hrs prior to the experiment. OECD guideline no. 425 (Up and down procedure) was adopted for toxicity studies. Animals were administered with single dose of extract and observed for their mortality during 48 hours study period (short term) toxicity. LD₅₀ was calculated as per OECD guidelines 425 using AOT 425 software^[8].

II. Anxiolytic activity

Elevated Plus Maze

The Elevated plus-maze test is described elsewhere. The apparatus comprises of two open arms (35 cm × 5 cm) and two closed arms (30 cm × 5 cm × 15cm) that extend from a common

central platform (5 cm ×5 cm). The floor and walls of the closed is painted black. The entire maze is elevated to height of 50 cm above the floor level. Mice of 18-22g weight were housed in pair for 10 days prior to testing in the apparatus. During this time the mice are handled by the investigator on alternate days to reduce stress. A group consisting of 6 mice was used for each dose level. One hour after oral administration of the vehicle or standard or extract, each mouse was placed in the center of the maze facing towards one of the open arm.

During a five minutes session, the following parameters were noted; Number of entries into open arm, Number of entries into closed arm, Time spent in the open arm, and Time spent in the closed arm ^{[9],[10],[11]}.

Light-dark model

Natural aversion of animal for brightly lit places was evaluated in light-dark transition model. Light dark box is a rectangular box of 46 x 27x 30cm (l x b x h), which is divided into 2 compartments. 1/3rd is for the dark compartment and 2/3rd is served as light compartment. for this Male Swiss albino mice weighing between 18-25g were divided into five groups, each group comprising of six animals were used . Vehicle or standard or extract was administered orally, One hour after oral administration; the each mouse was placed individually in the illuminated part of the Light dark box . The following parameters were recorded during the test session of 5 min; Latency to the first crossing to the dark compartment, Number of crossings between the light and dark area, Total time spent in the illuminated part of the cage and Total locomotion ^[12].

Actophotometer

The locomotor activity can be easily studied with the help of actophotometer, for this Male Swiss albino mice weighing between 18-25g were divided into five groups, each group comprising of six animals, each animal was placed individually and the basal activity score was recorded for all the animals. 30 min, 60 min and 120 min after the oral administration of the vehicle or Standard or extract each mouse was retested for activity for 10 min.

The difference in the activity was recorded considering before treatment values and after vehicle or standard or extract treatment values. Finally percentage decrease in locomotor activity was calculated ^[13].

III. Anticonvulsant activity

Pentylenetetrazole induced convulsion

Male swiss albino mice weighing between 18-25g were divided into five groups, each group comprising of six animals, One hour after vehicle or standard or extract treatment, PTZ (pentylenetetrazole 80 mg/kg) was administered by intraperitoneally to all the animals. Each animal was placed in to individual plastic cage and observed initially for 30min and later up to 24 hrs. The following parameters were recorded during test session of initial 30min and up to 24 hrs; Latency (onset of clonus), Onset of tonic convulsions, Status of animal after 24 hrs, Percentage protection ^[14].

Maximal electroshock induced convulsion

Male swiss albino mice weighing between 18-25g were divided into five groups, each group comprising of six animals were used , 30 mins after the oral administration of the

vehicle or standard or extract. a 60mA current was delivered transauricularly for 0.2 sec to mice via small alligator clips attached to cornea ,then the animals were placed in a rectangular plastic cage with an open top permitting full view of animal's motor responses to seizure and the following parameters were recorded during the 30 minutes test session; Tonic flexion, Tonic extension, Clonus convulsions, Stupor and Percentage protection. For recording various parameters ^[15].

IV. Estimation of Gamma-Aminobutyric Acid (GABA) levels in rat brain

Effect of ALCD on GABA levels in brain was also studied ^[16]. Briefly, after three days treatment with vehicle or standard or extract, the animals were killed by euthanasia and the body was exposed to a microwave irradiation for 4 sec.

The brain was rapidly removed ; the cerebellum and the tissue other than cerebellum was dissected on an ice-cold petri dish. The tissues were weighed and placed in pre-cooled 100ml plastic tubes.

Ice-cooled 0.1M perchloric acid (10 ml) containing valine at a concentration of 15 µg/ml (internal standard) was added to the tissue. The tissues were homogenized for one minute during which the tube was embedded in an ice bath and then centrifuged at 5000 rpm for 10 min at 4°C. The supernatants were stored at -20°C until assayed. Dansylation reaction was induced. Dansylation was carried out by adding 100µl of each supernatant of the samples or the standards to a micro-tube containing 100µl of 0.1M potassium carbonate solution. These solutions were mixed using vortex and then centrifuged using microcentrifuge at 10000 rpm for 10 min. 100µl of each supernatant was transferred into a pyrex tube containing

100µl of 0.1M sodium hydrogen carbonate solution, to which 400µl of working dansyl chloride solution (1.25 mg/ml anhydrous acetone) was added. The tubes were shaken for 30 sec using vortex and then incubated at 90°C in benchtop oven for 30 min. The tubes were not capped during the incubation to allow most of the solvent to be evaporated.

This did not appear to adversely affect the progress of the dansylation reaction and served to concentrate the samples. After getting the tubes out of the oven, they were allowed to cool down to room temperature and the dansylated derivatives were transferred to 1.5 ml microtubes and stored at -20°C until assayed.

C8 reversed-phase HPLC columns (5 µm, 250 x 3.2 mm) were used to resolve and quantify the samples. The HPLC mobile phase consisted of deionized helium degassed water-acetonitrile (HPLC grade) mixture (65:35 v/v) containing 0.15% v/v phosphoric acid. The flow rate was kept at 0.5 ml/min.

The detector excitation was at 333nm and emission at 532nm. 25µl of the dansyl derivative of the GABA samples were transferred to HPLC micro-sample vials and injected into the column. Retention time of GABA and internal standard were determined.

The peak ratios of the samples were calculated with reference to the internal standard. GABA levels were expressed as ng/g of tissue

Statistical analysis:

Values are expressed as mean ± SEM from 6 animals. Statistical differences in mean were analyzed using one way ANOVA (analysis of variance) followed by Tukey-kramer test. $p < 0.05$ was considered significant.

RESULTS

Phytochemical investigation

It was found that the alcoholic extract of *Cedrus deodara* contains alkaloids, carbohydrates, proteins, tannins and phenolic compounds.

Acute toxicity Studies

Acute toxicity studies was conducted in albino mice according to OECD guidelines no.425 and LD₅₀ of ALCD was computed to be 1098 mg/kg.

A. Assessment of Anxiolytic Activity

Elevated plus-maze model

In elevated plus-maze test (EPM), the alcoholic extract of *Cedrus deodara* at a dose of 50,100 and 200 mg/kg significantly increased the time spent and number of entries in to the open arm and decreased the time spent and number of entries in to the closed arm. The magnitude of the anxiolytic effects of 100 mg/kg and 200 mg/kg of alcoholic extract of *Cedrus deodara* was comparable to that of diazepam 3 mg/kg p.o. The results are shown in the Table no.1.

Light-dark model

In Light-dark test (LDT), 50, 100 and 200 mg/kg dose of ALCD has increased the latency to enter into the dark compartment and time spent in light compartment, confirming anxiolytic activity of alcoholic extract of *Cedrus deodara* at 100 mg/kg and 200 mg/kg. The results are shown in the **Table no.2.**

Actophotometer

In Actophotometer, 100mg/kg and 200mg/kg dose of ALCD significantly reduced locomotor activity and 50mg/kg has showed slight reduction in the locomotor activity which may be due to the CNS depressant property of the drug. The results are shown in the **Table no.3.**

B. Assessment of Anticonvulsant Activity

Pentylenetetrazole (PTZ) Induced Convulsions

In Pentylene tetrazole (PTZ) induced convulsion model, ALCD 50, 100 and 200 mg/kg, p.o doses significantly increased both the onset of clonus and onset of tonic convulsions induced by PTZ and also showed significant increase in percentage protection at 100 and 200 mg/kg doses. The effect was dose dependent. The results are shown in the **Table no.4.**

MES (Maximal Electro Shock) Induced Convulsions

In Maximal electroshock (MES) induced convulsions model 50, 100 and 200 mg/kg doses of ALCD exhibited significant anticonvulsant effect, the extract has showed significant decrease in the duration of extensor phase with increase in the latency of clonus in both acute and chronic studies and also showed significant increase in percentage protection at 100 and 200 mg/kg doses. The results are shown in the **Table no.5.**

C. Estimation of GABA levels in rat brain

Pretreatment with ALCD (30 and 100 mg/kg, p.o) for seven days had increased the GABA levels in cerebellum and whole brain other than cerebellum. Similar effect was observed with diazepam (2 mg/kg). However, the effect of ALCD was less than diazepam. The results are shown in the **Table no.6.**

Table.1. Effect of ALCD on number of entries and time spent in Elevated Plus-Maze Model

| Sl.no | Treatment | Number of entries (counts/5min) | | Time spent (counts/5min) | | Time spent in neutral zone counts/5min) |
|-------|----------------------------|------------------------------------|--------------|-----------------------------|-----------------|---|
| | | Open arm | Closed arm | Open arm | Closed arm | |
| 1 | Control (3%Tween 80) | 6± 0.930 | 11.67 ± 2.16 | 53.67 ± 7.491 | 190.33 ± 8.50 | 56 ± 14.76 |
| 2 | Diazepam (3 mg/kg, p.o) | 10.67±0.88 ^{***} | 12.67 ± 0.84 | 105.66±24.43 ^{***} | 178.833± 4.79 * | 16.5 ± 2.40 ^{**} |
| 3 | ALCD (50 mg/kg, p.o) | 11.17±0.94 ^{***} | 11.67 ± 1.38 | 88.334±13.86 ^{***} | 195.17 ± 5.72 | 15.83 ± 3.49 ^{**} |
| 4 | ALCD (100 mg/kg,p.o) | 12.67±1.22 ^{***} | 10.5 ± 0.67 | 107.33±2.98 ^{**} | 187.83 ± 8.15 * | 6.17 ± 2.07 ^{**} |
| 5 | ALCD (200 mg/kg,p.o) | 12.17±1.35 ^{***} | 10.5 ± 0.67 | 114 ±20.342 ^{**} | 178.83± 8.15 * | 7.17± 2.07 ^{**} |

(Observation period: 5min for all parameters)

Values are expressed as mean ± SEM, from 6 mice. Significant at * $P < 0.05$, ** $P < 0.01$ and *** $P < 0.001$ as compare to control using One way ANOVA followed by Turkey's post hoc test.

Table.2. Effect of ALCD on various parameters in Light-Dark Model

| Sl.N | Treatment | Number of entries(Sec) | Time spent in light box (Sec) | Total locomotion (Counts/5min) | Defecation (Counts/5min) | No. of rearings in Light box |
|------|------------------------|-------------------------|-------------------------------|--------------------------------|--------------------------|------------------------------|
| 1 | Control (3%Tween-80) | 9.834 ± 0.7923 | 65.8 ± 5.63 | 291.67 ± 8.460 | 5.834 ± 1.72 | 6.5 ± 0.670 |
| 2 | Diazepam (5 mg/kg, po) | 4.5 ± 0.428*** | 176.8±5.68*** | 131.67±2.69*** | 2.5 ± 0.341*** | 2.667 ± 0.6022*** |
| 3 | ALCD (50mg/kg, po) | 5.34 ± 0.667*** | 124.5± 8.62*** | 287.5 ± 4.59 | 4.34 ± 0.61 | 4.167 ± 0.307* |
| 4 | ALCD (100mg/kg,po) | 4.167 ± 0.47*** | 164.8±5.09*** | 157.5 ± 5.75** | 2.833± 0.30** | 3.167 ± 0.307*** |
| 5 | ALCD (200mg/kg,po) | 3.834± 0.75*** | 171 ± 4.25*** | 147.5 ± 5.75** | 2.334±0.21*** | 2.167 ± 0.307*** |

(Observation period: 5min for all parameters)

Values are expressed as mean ± SEM, from 6 mice. Significant at * $P < 0.05$, ** $P < 0.01$ and *** $P < 0.001$ as compare to control using one-way ANOVA followed by Tukey-kramer's post hoc test.

| Sl.No | Groups | Photocell counts | | | | | |
|-------|--------------------------|--------------------------------|-----------------|---------------------------|--------------|-------------------------------|--------------|
| | | 30 min | % Inhibition | 60 min | % Inhibition | 120 min | % Inhibition |
| 1 | Control (3% Tween-80) | 294.5 ±16.69 | -- | 281±11.43 | -- | 289±6.23 | -- |
| 2 | Diazepam (3mg/kg) | 80.6±15.36 ^{***} | 72.60 | 60 ^{***} ±9.21 | 78.64 | 64.3±4.29 ^{***} | 77.73 |
| 3 | ALCD (50mg/kg) | 149.1±12.66 ^{**} * | 49.34 | 130.1±3.59 ^{***} | 53.67 | 151.5±6.42 [*] ** | 47.57 |
| 4 | ALCD (100mg/kg) | 167± 19.84 ^{***} | 3.29 | 114.5±7.53 ^{***} | 59.25 | 109±6.88 ^{***} | 62.28 |
| 5 | ALCD (200mg/kg) | 103.3±20.52 ^{**} * | 64.91 | 72.5±9.95 ^{***} | 74.19 | 73.6±8.08 ^{***} | 74.50 |

Table 3. Effect of ALCD on Locomotor activity (Actophotometer) in mice at different time intervals(min).

(Observation period: 10 min for all parameters)

Values are expressed as mean ± SEM, from 6 mice. Significant at * $P < 0.05$, ** $P < 0.01$ and *** $P < 0.001$ as compare to control using One way ANOVA followed by Tukey-kramer's post hoc test.

Table.4. Effect of ALCD on Pentylenetetrazole induced convulsions

| Sl.N | Treatment | Latency (Onset of clonus) (Sec) | Onset Of Tonic (Sec) | Status of animal (24 hrs, No. of animals Alive) | %Protection (24h) |
|------|------------------------------|---------------------------------------|-------------------------|--|-------------------|
| 1 | Control (3% tween80) | 49.33 ± 5.32 | 368.33 ± 17.97 | 0 | 0 |
| 2 | Diazepam (5 mg/kg) | No clonus | No Tonic | ALL | 100 |
| 3 | ALCD (50 mg/kg, p.o.) | 175 ± 27.29** | 672 ± 69.46 ** | 1 | 16.66 |
| 4 | ALCD (100 mg/kg, p.o.) | 265 ± 27.29*** | 980 ± 131.15 *** | 5 | 83.33 |
| 5 | ALCD (200 mg/kg, p.o.) | 265 ± 27.29*** | 980 ± 131.15 *** | ALL | 100 |

Values are expressed as mean ± SEM, from 6 mice. Significant at ** $P < 0.01$ and *** $P < 0.001$ as compare to control using One way ANOVA followed by Tukey-kramer's post hoc test.

Table.5. Effect of ALCD on Maximal Electroshock induced convulsions

| Sl.no | Treatment | Duration of tonic flexion(sec) | Duration of tonic extensor (sec) | %protection (24h) |
|-------|-----------------------|--------------------------------|----------------------------------|-------------------|
| 1 | Control (3% Tween 80) | NO | 14.17 ± 0.872 | 16.66 |
| 2 | Phenytoin (25 mg/kg) | 5.83 ± 0.9804 | NO *** | 100 |
| 3 | ALCD (50 mg/kg, po) | NO | 8 ± 0.577 | 33.33 |
| 4 | ALCD (100 mg/kg, po) | NO | 7.83 ± 0.60* | 83.33 |
| 5 | ALCD (200 mg/kg, po) | NO | 3.83 ± 0.60* | 100 |

Values are expressed as mean ± SEM, from 6 mice. Significant at * $P < 0.05$ and *** $P < 0.001$ as compare to control using one way ANOVA followed by Tukey-kramer's post hoc test.

Table 6: Effect of ALCD on GABA levels in brain

| Sl.No | Treatments | In cerebellum (ng/g of tissue) | In whole brain other than cerebellum (ng/g of tissue) |
|-------|--------------------------|------------------------------------|--|
| 1 | Control (3% Tween 80) | 430.215 ±12.54 | 2228.83±48.01 |
| 2 | Diazepam (2mg/kg) | 1873.81±120.75*** | 5884.55±124.32*** |
| 3 | ALCD (30 mg/kg) | 767.42 ±34.75*** | 3083.31±195.15*** |
| 4 | ALCD (100 mg/kg) | 990.45±43.21*** | 3571.97±204.03*** |

Values are expressed as mean ± SEM, from 6 mice. Significant at * $P < 0.05$ and *** $P < 0.001$ as compare to control using one way ANOVA followed by Tukey-kramer's post hoc test.

DISCUSSION

Fear and anxiety are defined as the response of a subject to real or particular threats that may impair its homeostasis, this response may include physiological or/and behavioral. Measuring anxiety like behavior in mice has been mostly undertaken using a few classical animal models of anxiety such as the elevated plus maze and Light dark model. All these procedures are based upon the exposure of subject to unfamiliar aversive place ^[17].

Epilepsy is one of the most common serious neurological conditions. Seizure refers to a transient alteration of behaviour due to disordered, synchronous and rhythmic firing of populations of brain neurons ^[18]; the frequency and importance of epilepsy can hardly be overstated from the epidemiologic studies. However, in most studies, the overall incidence of epilepsy in developed societies has been found to be around 50 cases per 100,000 persons per year, and rises steeply in older age ^[19]. For measuring the anticonvulsant activity in mice has been mostly undertaken using a few classical animal models such as the PTZ induced convulsions and MES induced convulsions ^{[20],[21]}. Studies have proved that the agents which increase the brain GABA content and administration of centrally active GABA mimetic agents have been used as an effective therapeutic approach for treatment of epilepsy.

Hence to see the effect of the extract on GABA levels different parts of the brain, the animals are treated with the extracts and GABA levels are estimated by HPLC method ^[16].

The heart wood extracts of *Cedrus deodara* which have been not studied so far for its anxiolytic and anticonvulsant activity. In present study the heart wood extracts of *Cedrus deodara* was studied for anxiolytic and anticonvulsant activity by three experimental models namely Elevated plus maze test, Light dark model, locomotor activity by actophotometer and anticonvulsant activity was studied by using Pentylene tetrazole induced convulsions and MES induced convulsions and Pretreatment with ALCD followed by estimation of GABA in rat brain tissues was performed to study the effect of ALCD on GABA levels of brain.

The elevated plus maze is currently one of the most widely used models of animal anxiety [9],[10],[11], the test is principally based on the exposure of animal to an elevated maze array evokes an approach-avoidance conflict that is considerably stronger than that evoked by exposure to an open maze array. The animals being exposed to the new environment tend to avoid open entries and prefer to stay in closed arm due to fear. In our study the ALCD at 50,100 and 200mg/kg doses has significantly increased the time spent and number of entries in to the open arm indicating the test drugs could reduce the fear and anxiety in the mice. In Light dark model, ALCD (50,100,200mg/kg) has increased the time spent and number of entries in to the light compartment. Anxiolytics should reduce the natural aversion to light, the essential feature of this model is that anxiolytic drugs increase the number of crossings and/or the time spent in the light compartment.

These results suggests that extract administration could reduce the aversion fear and produce anxiolytic activity.

In pentylene tetrazole induced convulsions model^[14] the ALCD (100, 200 mg/kg) has significantly increased the onset of clonus, onset of tonus and percentage protection when compare to control group and in MES induced convulsions model ^[15] ALCD (100, 200 mg/kg) has significantly decreased the duration of tonic extensor and increased the percentage protection when compare to the control group.

GABA appears to play an important role in the pathogenesis of several neuropsychiatric disorders. Many of the traditional agents used to treat psychiatric disorders are known to act, at least in part, by enhancing GABA activity, while some of the newer agents may exert their therapeutic effects exclusively via GABAergic actions. In our present study, seven days treatment with ALCD (30 mg/kg, 100mg/kg.p.o.) and further GABA estimation in brain showed significant enhancement of GABA levels in cerebellum and whole brain other than cerebellum compared to control group.

In conclusion, these findings suggest that the alcoholic extract of heartwood of *Cedrus deodara* possess significant anxiolytic and anticonvulsant activity through modulation of GABA levels in brain.

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