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Exploring the Anti-anxiety activity of *Centratherum anthelminticum*

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Abstract

Kalijiri (*Centratherum Anthelminticum*, Family – Asteraceae) is an herbal plant that has been widely used in India traditional medicine for the treatment of different disorders (eg. Analgesic, Antipyretic, Antihelmintic, Antihyperglycemic, Antimicrobial, Antibacterial and Diuretic). Nevertheless, the available scientific information about this species is scarce and there are no reports related to its possible effect on the CNS. In this work, the effects of Methanolic extract of seeds of *Centratherum Anthelminticum* (CA) were evaluated in mice using behavioral tests sensitive to clinically effective Antianxiety compounds. The extract (100 and 200 mg/kg) administered i.p. was able to show significant effect on the anxiety as compare to the standard drug i.e. Diazepam (2 mg/kg). Present study confirms that the extract showed significant Antianxiety activity at both dose levels which is comparable with standard Antianxiety drug diazepam.

Key words: Antianxiety, *Centratherum Anthelminticum*

Introduction

In view of the fact that the beginning of human civilization, medicinal plant has been used by mankind for its therapeutic value. Nature has been a source of medicinal agents for thousands of years and an impressive number of modern drugs have been isolated from natural source. Many of these isolations were based on the uses of the agent in traditional medicine. The plant –based, traditional medicine system continues to play an essential role in health care, with about 80% of the world's inhabitants relying mainly on traditional medicines for their primary health care. India has quite a lot of conventional therapeutic systems, such as Ayurvedic and Unani, which has survived through additional than 3000 years, mostly using plant –based drugs. The material medicinal of this system contains a rich legacy of original herbal practices that have helped to keep up the fitness of most rural people of India. The olden texts like Rig Veda (4500-1600 BC) and Atharvaveda talk about the use of several plants as medicine. The book on Ayurvedic medicine such as CharakaSamhita and SushrutaSamhita refer to the use of more than 700 herbs. World Health Organization (WHO, 1977) stated that "a medicinal plant" is any plant, which in one or more of its organ contain substances that can be used for the therapeutic purposes or which, are precursors for the synthesis of useful drugs. [1]

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With the purpose of make sure the safe use of these medicines, a necessary first step is the establishment of standards of quality, safety and efficacy. Observance this fact in to consideration, the attempts were made establish physiochemical standard of the plant *Centratherum Anthelminticum* kuntze syn. Vernonia anthelmintica wild (Hindi; Kalijiri, Somraj) belonging to family Asteraceae. In India nine species of this genus are found, of which C. Anthelminticum is threadworms. The active Anthelmintic constituent is confined in the achene's (fruits) of the plant. The plant is widely distributed throughout India up to 1650m altitude in the Himalaya and Kashi hills. Seed has hot sharp test. It is an important medicinal plant used in various Ayurvedic preparations and is also reported used in Asthma, Kidney trouble and cough. It is tonic stomachic and cures phlegmatic discharge from the nostrils. It also enters into the prescription for leucoderma, psoriasis and other skin infections. The major class of chemical constituent is present in this plant are glycosides, carbohydrates, phenolic compound and tannin, flavonoids, protein, saponins, sterol, lipids, fats. [2-3]

Anxiety is a mental and physiological state characterized by somatic, emotional, cognitive, and behavioral components, associated with significant disability (including educational and occupational) which has a negative impact on the quality of life. [4] Anxiety disorder is gradually more recognized as a highly prevalent and chronic disorder with onset

during the teenage years, with an incidence of 18.1% and a lifetime prevalence of 28.8%. [5] Those are spending lot of money to rid themselves of anxiety. The charge of visits to physicians and utilization of health care in general by individuals with anxiety disorders, are double compared to those without anxiety disorders, even if the later is physically ill. [6] Anxiety has turn into a significant area of psychopharmacological research during this decade, as it affects around one-eighth of the total population of the world.

The 3 neurotransmitters primarily implicated in anxiety are GABA, serotonin and noradrenaline. [7] Verification of GABAergic participation in modulating anxiety is that assured classes of drugs such as the benzodiazepines, barbiturates and alcohol all bind to GABA receptors to increase its post-synaptic inhibitory effect and reduce anxiety. Benzodiazepines attach allosterically to the GABA receptor and have their own binding site. Additionally, benzodiazepine inverse agonists such as flumazenil decrease effects of GABA and cause anxiety. [8] Benzodiazepines are the prime class of compounds used in anxiety and they have remained the most commonly prescribed treatment for anxiety, but they can cause deterioration of cognitive functioning, sedation, muscle relaxation, ataxia, psychomotor impairment, confusion, anterograde amnesia, physical dependence and tolerance. [9-10] For these reasons, newer anti-anxiety drugs with better efficacy and decreased side effect profile is needed[11].

Material and Method

Procurement of the plant parts

The seed of the *Centratherum Anthelminticum* was collected from the local market, Indore, Madhya Pradesh.

Treatment and Preparation of the aqueous extracts

The seed were washed with the water and keep dried for 2 hr.The seed of *Centratherum Anthelminticum* was extracted with the help of soxhlet apparatus. The soxhlet solvents extracts were obtained by soxhlet extraction of 25g of dried seeds in 100ml-200ml of solvents at 65° C using soxhlet apparatus. The extract was concentrated to 10ml on a water bath and dried at room temperature. Percentage yield of various extracts were noted in each solvent.

Phytochemical evaluation

The phytochemical evaluation of methanolic extract of Barringtonia Racemosa seed were carried out as per standard methods .The presence of flavonoids will determined by lead acetate test, tannins by acetic acid test, saponins by foam test and steroids will determine.

Pharmacological Methods

Animals

Wistar albino mice, weighing 25-30 gm, were obtained from the animal house of the Department of Pharmacology of the Swami Vivekanand College of Pharmacy, Indore, India. Animals were housed at four per cage, allow free access to water and food, and maintain under constant temperature (23±1 0C) and humidity (60±10%) under a 12-h light/dark cycle (light on 07.30–19.30 h). Animal treatment and maintenance was conducted in accordance with the Principles of Laboratory Animal Care (NIH publication no. #85-23 revised 1985).

Experimental design

A total number of 24 mice were divided into four groups of six mice each:

Group I: control (Normal Saline, 2ml/kg)

Group II: standard (Diazepam, 2mg/kg)

Group III: Test (Methanolic extract of C. Anthelminticum, 100mg/kg)

Group IV: Test (Methanolic extract of C. Anthelminticum, 200mg/kg)

Procedure

1. The Wistar albino mice, weighing between 25-30 gm of either sex were selected for the experiment.
2. Prior to experiment the mice were divided randomly in to four groups. Each group contains 6 mice.
3. First group was treated as control (Normal Saline) and second and third groups were treated with the Methanolic extract of *Centratherum Anthelminticum*(100 mg/kg and 200mg/kg). Fourth group was treated with Diazepam (2mg/kg).

Elevated plus-maze apparatus

The elevated plus-maze comprises two open (50 cm×10 cm×25 cm) and two enclosed (50 cm×10 cm×40 cm) arms that radiated from a central platform (10 cm×10 cm) to form a plus sign. The maze will construct of black painted wood. A slight raises edge on the open arms (0.25 cm) provide additional grip for the animals. The plus-maze will elevate to a height of 50 cm above floor level by a single central support. Four 25W red fluorescent lights arrange as a cross at 100 cm above the maze will use as the source of illumination. The experiment will conduct during the dark phase of the light cycle (9:00–14:00 h). The trial will start by placing an animal on the central platform of the maze facing an open arm. The number of entries into, and the time spent in, each of the two types of arm, will count during a 10 min test period. The percentage open arm entries and

percentage open arm time will use as indices of anxiety. A mice will consider to have entered an arm when all four paws will on the arm. The apparatus will clean thoroughly between trials with damp and dry towels. All behavioral recordings will carry out with the observer unaware of the treatment the mice has received.

Light dark test

The equipment has an essential feature of two 20 cm×10 cm×14 cm plastic boxes: one was dark and the other was transparent. The mice were allowed to move from one box to the other through an open door between the two boxes. A 100W bulb positioned 30 cm higher than the floor of the transparent box was the only light source in the room. A mouse was put into the light box facing the hole. The alteration among the light and the dark box and time spent in the light box were recorded for 5 min immediately after the mouse stepped into the dark box. The apparatus was cleaned thoroughly between trials. All behavioral recordings were carried out with the observer unaware of the treatment the mice had received.

Statistical Analysis

All the data represent mean±S.E.M. values. The data were analyzed by means of analysis of variance (ANOVA). Whenever ANOVA was significant, further multiple comparisons were made using Tukey's test as the post hoc test. All analyses were performed using the SPSS statistical software. The levels of statistical significance ranged from$p<0.05$ to $p<0.001$.

Results and Discussion

Table 1: Indicating presence of various phytochemical constituents.

S. No.	Test	Positive/ Negative
1.	Carbohydrate	+
2.	Terpenoids	-
3.	Flavone Glycoside	+
4.	Phenolic Compound	+
5.	Flavonoids	+
6.	Saponins	-
7.	Sterols	+

Note:- + = Present; - = Absent

Table 2: Anti anxiety activity of *Centratherum Anthelminticum* on mice by using Elevated plus-maze model

Group	Treatment	Dose	No. of entries in open arm	Time spent in open arm (Sec)
I	Control	2 ml	4.25±0.35	215±8.5
II	Diazepam	2 mg/kg	7.45±0.57	356±7.5
III	Test(Methanolic extract of *Centratherum Anthelminticum*)	100 mg/kg	5.97±0.41	246±6.3
IV	Test(Methanolic extract of *Centratherum Anthelminticum*)	200 mg/kg	6.27±0.31	275±6.2

All value are given in mean±SEM, *$P < 0.05$, **$P < 0.01$ as compare with the control group (one way ANOVA followed by Dunnett's test).

Table 3: Anti anxiety activity of *Centratherum Anthelminticum* on mice by using Light-dark test

Group	Treatment	Dose	No. of entries in light chamber	Time spent in light chamber (Sec)
I	Control	2 ml	2.27±0.32	211±6.4
II	Diazepam	2 mg/kg	4.35±0.41	344±6.2
III	Test(Methanolic extract of *Centratherum Anthelminticum*)	100 mg/kg	3.20±0.45	248±5.9
IV	Test(Methanolic extract of *Centratherum Anthelminticum*)	200 mg/kg	3.47±0.47	267±5.6

All value are given in mean±SEM, **P* < 0.05, ***P* < 0.01 as compare with the control group (one way ANOVA followed by Dunnett's test).

Fig. 1: Effects of C.A extract in the elevated plus-maze test in mice. Results are expressed as means±S.E.M. (*n* = 6). The following parameters are shown: no of entries in open arm. **P* < 0.05, ***P* < 0.01, compared with vehicle-treated animals.

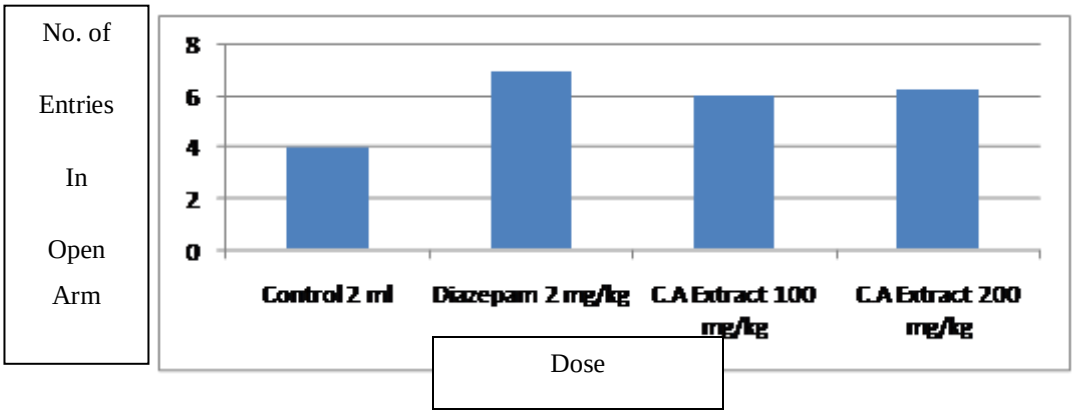


Fig. 2: Effects C.A Extract in the elevated plus-maze test in mice. Results are expressed as means±S.E.M. (*n* = 6). The following parameters are shown; time spent in open arms. **P* < 0.05, ***P* < 0.01, compared with vehicle-treated animals.

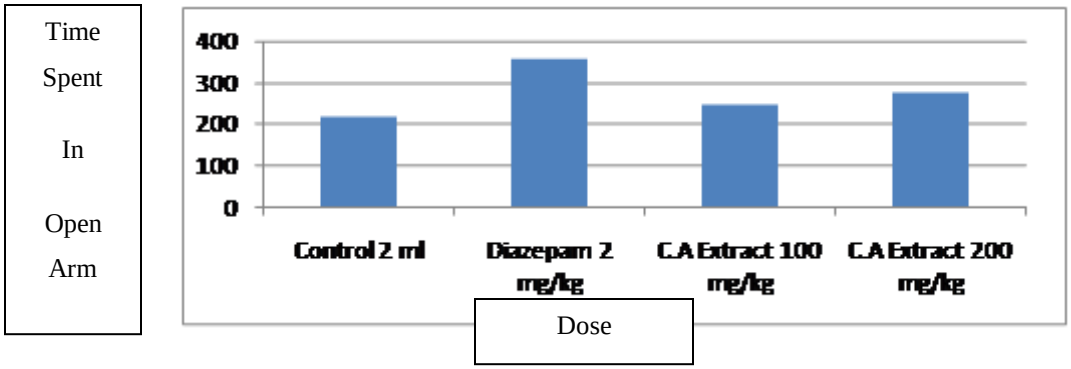


Fig. 3: Effects of C.A Extract in the light-dark test in mice. Results are expressed as means±S.E.M. (*n* = 6). The following parameters are shown; no of entries in light chamber. **P* < 0.05, ***P* < 0.01, compared with vehicle-treated animals

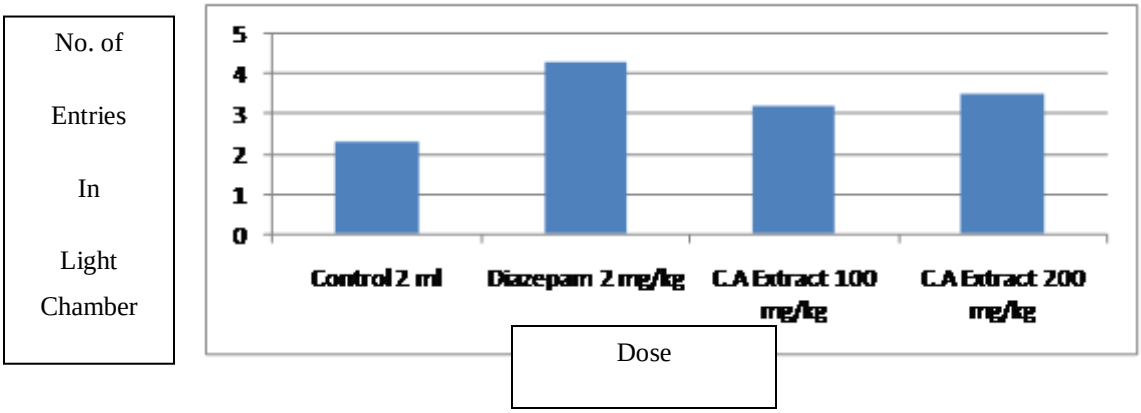
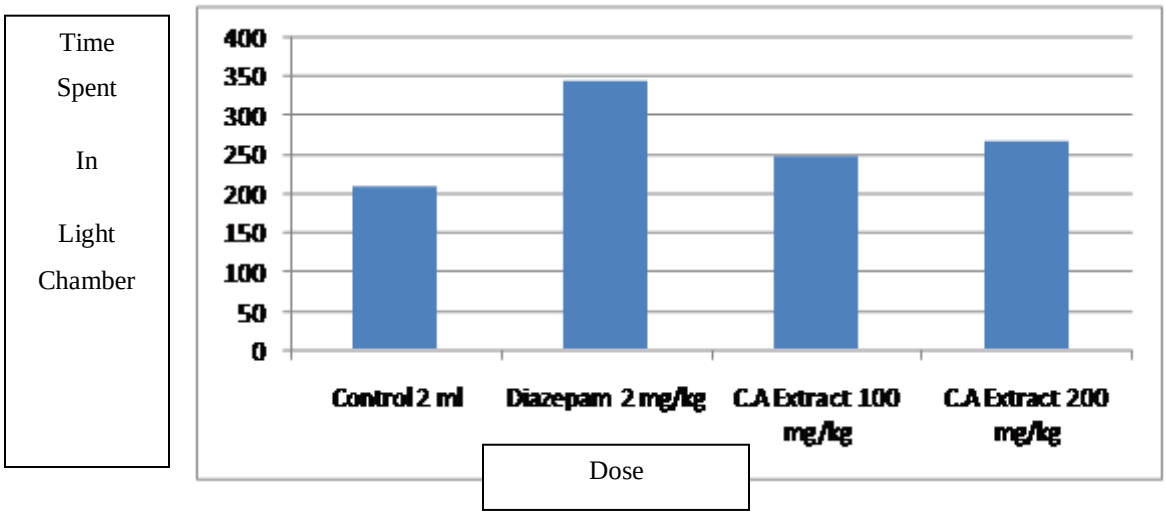


Fig. 4: Effects of C.A Extract in the light-dark test in mice. Results are expressed as means±S.E.M. (*n* = 6). The following parameters are shown; times spend in light chamber. **P* < 0.05, ***P* < 0.01, compared with vehicle-treated animals



Summary and Conclusion

The Methanolic extract of *Centratherum Anthelminticum* (200 mg/kg) shows significant antianxiety activity in elevated plus maze apparatus and light dark test. The plant (*C. Anthelminticum*) containing carbohydrates, flavone glycosides, Phenolic compound, Flavonoids and sterols were identified. Flavonoids may be responsible for the neuropharmacological activity of the plant. In the present study, we used the EPM & light dark model of anxiety to evaluate the anxiolytic effects of the methanolic extract of *C. Anthelminticum* this is a model which uses the natural fear of rodents to avoid open and elevated places. As projected, diazepam shown significant increases in time spend and in number of entries into the open arms & light chamber. Diazepam also increased the total number of entries. These data are in agreement with the results of other studies, where diazepam and other

benzodiazepines have been shown to produce anxiolytic effects in a variety of anxiolytic screening procedures, including EPM and light dark model. The behavioral alterations induced by the *C. Anthelminticum* plant extract in the EPM provided anxiolytic effect because the *C. Anthelminticum* seeds extract at a dose of 200 mg/kg significantly increased the arm entries in open arms and decreased the time spent and arm entries in the closed arms in a similar fashion; diazepam increased the time spent and arm entries in the open arms and the Light-dark model also provided anxiolytic effect because *Centratherum Anthelminticum* seeds extract at a dose of 200 mg/kg significantly increased the entries in light chamber and decreased the time spent and entries in the dark chamber in a similar fashion, diazepam increased the time spent and entries in the light chamber. On the other hand, different a lot of other plant extracts where an anxiolytic effect was accompanied by sedative action, increase in the dose of *C. Anthelminticum* exerted stimulation rather than sedation. In this study, the number of entries into open arm and time spent into open arm were taken & the number of entries in light chamber and time spent in light chamber were taken as a measure of anxiety by elevated plus maize and light dark method. The findings in this study suggest that the *C. Anthelminticum* possess Anti- anxiety activity. The results have been obtained carefully from the controlled experiments model with laboratory animals. The statistical validity of the findings has been proven and they provide a scientific foundation for the use of the biologically active ingredients of *C. Anthelminticum* in anxiety for explain the clinical importance of the *C. Anthelminticum*.

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