



Research Article

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EVALUATION OF ANXIOLYTIC ACTIVITY OF AQUEOUS EXTRACT OF *CORIANDRUM SATIVUM* SEEDS ON SUB-ACUTE ADMINISTRATION USING DARK/LIGHT ARENA IN SWISS ALBINO MICE

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ABSTRACT

The prevalence of anxiety disorders poses a significant burden on the world population. Existing pharmacotherapy for treating anxiety disorders is spearheaded by the Benzodiazepine class of drugs that have considerable side effects. *Coriandrum Sativum* seeds are used as herbal medication in Ayurveda and have proven CNS activity. The present study was undertaken to evaluate the anxiolytic activity of sub-acute administration of aqueous extract of *Coriandrum sativum* seeds in male Swiss Albino mice using the Dark/Light arena paradigm. 30 male Albino Swiss mice, weighing 30- 35 g were divided into 5 groups (n = 6). Group I received normal saline (10 ml/kg) i.p. as control. Group II received standard drug Diazepam (1.0 mg/kg) i.p. Groups III, IV and V received aqueous extract of *Coriandrum sativum* seeds in the doses of 25 mg/kg, 50 mg/kg and 100 mg/kg i.p respectively. All drugs were administered once a day for 10 days. On the 10th day, 30 minutes after administering normal saline/Diazepam/test drugs, animals were evaluated for their anxiolytic activity in the Dark/Light arena. Aqueous extract of *Coriandrum sativum* seeds at the doses of 25 mg/kg (Group III) and 50 mg/kg (group IV) increased the time spent, number of entries into and the number of rears in the bright arena when compared to the control group (Group I). This suggests that sub-acute administration of aqueous extract of *Coriandrum sativum* seeds produced anxiolytic activity in male Swiss Albino mice when subjected to the dark/light arena experimental paradigm.

Keywords: Anxiety, *Coriandrum sativum*, Dark light arena, Diazepam.**INTRODUCTION**

The word anxiety is derived from the Latin “anxietas” (to choke, throttle, trouble, and upset) and as a normal emotional response, it encompasses behavioral, affective and cognitive responses to the perception of danger¹. However, its presence in the form of anxiety disorders poses a global burden affecting 4.5 % of the world population in the year 2010². This clinical focus received by anxiety disorders over recent decades has helped for a heightened comprehension of the underlying mechanisms and lead to advances in pharmacotherapy which are an important and centralized aspect in their management¹. The DSM-IV (American Psychiatric Association) has categorized the anxiety disorders³. The symptoms described clearly indicate the episodic or chronic presentation adopted by each of the categories³. Thus the duration of treatment should be taken into consideration in managing all anxiety disorders. Among the various classes of anxiolytic drugs that have been developed and are used in clinical practice today, perhaps, the most important are the Benzodiazepines (BZDs). Although widely used in clinical settings, short term use of the drugs are associated with adverse effects such as impaired motor coordination, drowsiness and impaired thinking. The side effect profile is further compounded on long term use, showing dependence and withdrawal effects⁴. Coriander (*Coriandrum sativum*) which belongs to family Apiaceae (Umbelliferae) is a herb which in addition to being a commonly used spice in cooking; also possesses nutritional and medicinal properties⁵. Both leaves and seeds of the plant have medicinal properties⁵. In Ayurveda, the use of the *Coriandrum sativum* seed for treating CNS diseases (vertigo and memory loss) and also

a multitude of other conditions including stomatitis, conjunctivitis, cough, dyspepsia and lymphadenopathy has been well documented^{6,7}. *Coriandrum sativum* seeds have shown anxiolytic property in an acute experimental setting⁸. Regardless, the need for anxiolytic drugs that have no/lesser side effect profiles and are effective in sub-acute doses correlating with clinical presentation of anxiety disorders forms the basis of our study. The purpose of this study is to evaluate the anxiolytic activity of aqueous extract of *Coriandrum sativum* seeds (AECSS), upon sub-acute administration in mice, using the dark/light arena (DLA) experimental paradigm.

MATERIALS AND METHODS**Site of the study**

The study was conducted at A.J. Institute of Medical Sciences, Mangalore, India. The experimental protocol was approved by the Institutional Animal Ethics Committee (Approval No. IAEC/02/2011/CPCSEA) dated 19/11/2011. All experimental procedures were conducted in accordance with CPCSEA and OECD guidelines.

Animals

Inbred male Albino mice (Swiss strain), around 3 months of age, weighing between 30-35 g were used for the study. The animals were procured from the central animal house at the institution. The animals were housed at 24 ± 2°C with 12:12 hour light and dark cycle. They were provided free access to food and water *ad libitum*. The animals were acclimatized for a period of 7 days before the study.

Control and standard drugs used

Normal saline was used as a control (vehicle) in the study. The standard anxiolytic drug used was Diazepam (Abbott Pharmaceuticals), procured from the institutional pharmacy.

Test drug and preparation of plant extract

The test drug used was aqueous extract of *Coriandrum sativum* seeds (AECSS) in doses of 25 mg/kg, 50 mg/kg and 100 mg/kg. The dried seeds were purchased from Jimmy Enterprises at Mangalore, India and their authenticity was verified by the Department of Pharmacognosy, Srinivas College of Pharmacy, Mangalore, India. AECSS was prepared by the Department of Pharmacognosy, Srinivas College of Pharmacy, Mangalore, India. Dried coriander seeds were homogenized to a fine powder. Hundred grams of powdered coriander were infused in 500 ml cold distilled water for 24 hours, brought to the boil, then removed from the heat source and allowed to infuse for 15 minutes. The extract was then filtered, concentrated over the water bath and brought to dryness under vacuum⁸. Upon extraction, 250 g of dried seeds of *Coriandrum sativum* yielded 4 g of aqueous extract which was viscous in consistency and brown in colour. The concentrations required of the coriander extract were prepared by serial dilution from a stock solution of 50 mg/ml of the extract in normal saline. All solutions were prepared freshly on test days and administered intraperitoneally (i.p.) in a volume of 0.1 ml/10 g body weight of mice.

Experimental apparatus

The experimental apparatus used to evaluate anxiolytic activity in the study was the dark/light Arena (DLA). The paradigm is based on the principle that mice tend to explore a novel environment, but to retreat from the aversive properties of a brightly-lit open field⁹. The DLA contains two distinct arenas, a dark arena (25 cm long × 35 cm wide × 35 cm deep), painted black and illuminated with a 0-watt red light source and a bright arena (35 cm

long × 35 cm wide × 35 cm deep), painted white and brightly illuminated with 40-Watt white light source. The two arenas are connected through a small open doorway, (7.5 cm long × 7.5 cm wide) situated on the floor level at the centre of the partition⁸. When the animals freely move between a brightly-lit arena and the dark arena, they show more crossings and activity in bright arena after treatment with anxiolytics⁹.

Experimental design

Animals were divided into 5 groups (Control, Standard and Test drugs) containing 6 animals each, making a total number of 30 animals (Table 1). For sub-acute study, the animals received drugs or vehicle once a day for 10 days. 45 minutes after the last dose on the 10th day of drug or vehicle administration, each animal was placed in the bright arena of the DLA. All required parameters, i.e. the time spent in the bright arena (in seconds), number of entries into the bright arena and the number of rears in the bright arena were observed for each animal over a five minute period.

Statistical Analysis

All the groups were subjected to one-way Analysis of Variance using One Way ANOVA followed by Dunnett's multiple comparison test. (Software: Graphpad Instat v3.10)

RESULTS

The different extracts of the test drug were assessed in the Dark/Light experimental paradigm and AECSS in doses of 25 mg/kg and 50 mg/kg showed anxiolytic activity. AECSS in doses of 25 mg/kg (Group III) and 50 mg/kg (Group IV) significantly increased the time spent in the bright arena (in seconds), number of entries into the bright arena and the number of rears in the bright arena when compared to the vehicle treated group (Group I). The values are expressed as Mean ± SEM for 6 animals in each group and are shown in Table 2.

Table 1: Groups and dose of the drugs and number of animals in each group

Group	Drugs/Dose	Number of mice
I	Control – Normal saline (0.1 ml/10 g)	6
II	Standard – Diazepam (1.0 mg/kg)	6
III	Test – AECSS (25 mg/kg)	6
IV	Test – AECSS (50 mg/kg)	6
V	Test – AECSS (100 mg/kg)	6

Table 2: Effect of chronic administration of AECSS on various parameters in DLA paradigm

Group	Groups (n = 6)	Mean time spent in bright arena (in sec)	Mean number of entries in bright arena	Mean number of rears in bright arena
I	Normal saline	68 ± 9.61	3.33 ± 0.71	68 ± 9.61
II	Diazepam	147.1 ± 17.23***	11.83 ± 1.83**	7.83 ± 1.95**
III	AECSS 25 mg/kg	134.6 ± 12.35**	5.83 ± 1.01*	6.00 ± 1.63*
IV	AECSS 50 mg/kg	163.1 ± 6.75***	7.5 ± 1.18*	8.5 ± 0.56**
V	AECSS 100 mg/kg	67.5 ± 4.03	3.5 ± 0.42	1.5 ± 0.42

n = 6. The observation are mean ± SEM. *p < 0.05, **p < 0.01, ***p < 0.001 as compared to control (ANOVA followed by Dunnett's multiple comparison test) AECSS- Aqueous Extract of *Coriandrum sativum* Seeds

DISCUSSION

The Dark/Light Arena is a useful predictor of anxiolytic activity and possesses the advantage of being quick and easy to use without prior training of animals. Increased activity of the animal in the bright arena shows an enhancement of putative exploratory behavior and the amelioration of fear responses suggestive of anxiolytic activity possessed by the seed extract. The time spent in the bright arena and the numbers of rears in the bright arena are considered as better indicators of anxiolytic activity when compared to the number of entries into the bright arena¹⁰. The animals in Groups III and IV that received AECSS in doses of 25 mg/kg and 50 mg/kg respectively, showed a statistically significant increase in all three assessed parameters when compared to the control group (Group I). The higher dose of 100 mg/kg did not produce significant results. This may corroborate with the findings in a previous study where an acute toxicity study showed that the *Coriandrum sativum* extract at doses higher than 100 mg/kg caused a marked decrease in motor activity that interfered with an accurate evaluation of anxiolytic effect⁸. The seeds of *Coriandrum sativum* possess anticonvulsant, sedative hypnotic and antioxidant properties¹¹⁻¹³. Phytochemical analysis has shown Linalool to be among the major constituents of the essential oil of seeds of *Coriandrum sativum*¹⁴. Linalool possesses anxiolytic activity¹⁵. The anxiolysis shown by AECSS in our study may be attributed to mechanisms involving Linalool, antioxidant property or through GABA receptors. However, further research is required to establish the exact underlying mechanism, and also assess potential of developing AECSS as an anxiolytic drug used in clinical practice for the future.

CONCLUSION

We conclude that aqueous extract of seeds of *Coriandrum sativum* upon sub-acute administration has anxiolytic activity in male Swiss Albino mice using the Dark/Light arena experimental paradigm.

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