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Research Article

CHRONIC ANXIOLYTIC-LIKE ACTIVITY OF AQUEOUS EXTRACT OF CORIANDRUM SATIVUM SEEDS USING ELEVATED PLUS MAZE TEST IN SWISS ALBINO MICE

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ABSTRACT

Anxiety disorder is increasingly recognized as a highly prevalent and chronic disorder. Long term use of the commonly prescribed anxiolytics, Benzodiazepines has been associated with adverse effects such as withdrawal effects and dependence. Herbal medications used in traditional medicinal systems are a potential avenue for developing newer drugs with desirable profiles. In Ayurveda, the seeds of *Coriandrum Sativum* have been employed for treating various neurological diseases. The present study was undertaken to assess the anxiolytic-like property seen on chronic administration of aqueous extract of *Coriandrum Sativum* seeds (AECSS) in Swiss Albino mice using the elevated plus maze test. 30 inbred adult male Swiss Albino mice were divided into 5 groups (n=6). The test groups received AECSS in doses of 25 mg/kg, 50 mg/kg and 100 mg/kg. Standard and control groups received Diazepam and normal saline, respectively. All drugs were administered intraperitoneally once daily for 10 days. On the 10th day, 45 minutes post-administration, the exploratory and disinhibitory behaviour of the animals were evaluated for a 5 minute period each in the elevated plus maze. AECSS in doses of 25 mg/kg and 50 mg/kg significantly ($p<0.05$) increased the time spent in open arms, number of rears in open arms, as well as open and total arm entries when compared to control group. Chronic administration of AECSS has displayed anxiolytic-like property in mice subjected to the elevated plus maze paradigm. The present study indicated the potential for use of AECSS as an adjuvant in the treatment of anxiety.

Keywords: Anxiety, *Coriandrum sativum*, Diazepam, Elevated plus maze.

INTRODUCTION

Anxiety is a common emotion encountered in our day to day encounters, presenting as a response to a negative situation [1]. It is advantageous during physically or emotionally taxing situations where it may boost an individual's performance. But when anxiety becomes disproportionate and excessive to the situation, it interferes with performance and constitutes a psychiatric disorder which usually presents in a chronic state [2,3].

Anxiety disorder is increasingly 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% [3]. In 2007, the prevalence rate of anxiety in India was found to be 18.5 per 1000 population [4].

Benzodiazepines (BZDs), such as Diazepam, have been the most widely used anxiolytic drugs for many years [5]. Even though they are considered to be safe during short term therapy, the long term use of BZDs has been associated with adverse effects such as impaired motor coordination, drowsiness, withdrawal effects and dependence [6]. Another roadblock encountered in treating anxiety disorders with pharmacotherapy is the non-responder rate which has been reported to be as high as 40 % [7].

Since thousands of years, a large number of people across the world use herbal medications as remedies for various diseases [8]. Translation of these medications into allopathic practice will be beneficial in terms of developing adjuvants or even main therapy for various conditions such as anxiety disorders. Coriander (*Coriandrum Sativum*); an annual herb, is native to the Mediterranean region but also extensively grown in India [9].

The Sanskrit names of *Coriandrum Sativum* linn. are Dhanika, Dhana, Vittunaka. In Ayurveda, *Coriandrum Sativum* seeds have been employed to treat local swelling and pains, headache caused by pitta, lymphadenopathy, stomatitis, conjunctivitis and as a diuretic, anti dyspeptic, appetizer, digestive, astringent and also for treating cough (kaphagana). It is also used in Ayurveda as a Central Nervous System (CNS) tonic to treat vertigo, syncope and memory loss [10,11].

Emamghoreshi et al showed positive results with regards to seeds of *Coriandrum Sativum* exhibiting anxiolytic effects in an acute setting [12]. Hence the present study was conducted to evaluate the anxiolytic potential of Aqueous extract of *Coriandrum Sativum* seeds (AECSS) on chronic administration.

MATERIALS AND METHODS

The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC) of A.J. Institute of Medical Sciences, Mangalore, India.

Animals

Inbred Male Albino Mice (Swiss strain), around 3 months of age, weighing between 25-35 grams were used for the study. The animals were obtained from the Animal House at our institution. The animals were housed at 24 ± 2°C with 12:12 hour light and dark cycle.

They had free access to food and water *ad libitum*. The animals were acclimatized for a period of 7 days before the study. The study was conducted in accordance with the CPCSEA guidelines.

Sample Size, Grouping and Dose of the Drugs

Animals were divided in to 5 groups (Control, Standard & Test drugs) containing 6 animals making a total number of 30 animals (Table 1).

Table 1: Drugs/dose of the drugs, groups and number of mice in each group

Drugs / Dose	Group	Number of Mice (n=6)
Control–Normal Saline (0.1ml/10gm)	I	6
Standard – Diazepam (1.0 mg/kg)	II	6
AECSS (25 mg/kg)	III	6
AECSS (50 mg/kg)	IV	6
AECSS (100 mg/kg)	V	6

Drugs and Chemicals

The standard antianxiety drug, Diazepam was obtained from our institutional pharmacy. The test drug used was AECSS. Control used was Normal Saline (Vehicle). The dried seeds were purchased from Jimmy Enterprises at Mangalore and their authenticity was verified

by the Department of Pharmacognosy, Srinivas College of Pharmacy, Mangalore.

Fig. 1: It shows Coriandrum Sativum seeds and AECSS used for the study

Preparation of extract

AECSS was prepared by the Department of Pharmacognosy, Srinivas College of Pharmacy, Mangalore. 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 vacuum.[12] Upon extraction, 250 grams of dried seeds of *Coriandrum Sativum* yielded 4 grams 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 saline. All solutions were prepared freshly on test days and administered intraperitoneally (i.p.) in a volume of 0.1ml/10 g body weight of mice.

Apparatus

Elevated plus maze test (EPMT): The EPMT apparatus consists of four arms elevated 30 cm above the floor, with each arm positioned at 90° relative to the adjacent arms. Two of the arms are enclosed with high walls (30 × 7 × 20 cm), and the other arms are connected via a central area (7 × 7 cm) to form a plus sign [12].

Behavioural assessment: For chronic 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 central arm of the Elevated plus maze, facing one of the closed arms. All required parameters, i.e. the time spent in the open and closed arms (in seconds), number of rears in the open arm and the number of open and total arm entries were observed in each arm for a five-minute period

Statistical Analysis

All data calculated were expressed as Mean ± SEM for each group. The data were analyzed by one-way ANOVA and Post-hoc comparisons were performed by applying Dunnett's multiple comparison test. P <0.05 was considered statistically significant.

RESULTS

The results given in table 2 and 3 indicate that AECSS in the dose of 50 mg/kg (Group IV) significantly increased the time spent in the open arms (in seconds), number of rears in the open arms, number of open arm entries and percentile ratio of open arm to total arm entries, when compared to the vehicle treated group (Group I).

Table 2: Effect of chronic administration of AECSS on mice behaviour in elevated plus maze

Drugs/Groups	Time spent in open arms (in sec)	Time spent in closed arms (in sec)	Number of rears in open arms
Normal Saline(0.1ml/10gm)	23.17 ± 2.02	276.83 ± 2.02	1.17 ± 0.47
Diazepam (1.0 mg/kg)	91.17 ± 2.75**	208.83 ± 2.75**	6.67 ± 0.88**
AECSS (25 mg/kg)	68.00 ± 10.55**	232.00 ± 10.55**	5.00 ± 0.57**
AECSS (50 mg/kg)	118.33 ± 6.07**	181.67 ± 6.07**	6.00 ± 0.73**
AECSS (100 mg/kg)	45.83 ± 2.63*	254.17 ± 2.63*	0.67 ± 0.33

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

Table 3: Effect of chronic administration of AECSS on mice behaviour in elevated plus maze

Drugs/Groups	Number of open arm entries	Number of total arm entries	Percentage ratio of open/total arms
Normal Saline(0.1ml/10gm)	1.83 ± 0.40	6.83 ± 0.40	27.36 ± 6.21
Diazepam (1.0 mg/kg)	6.00 ± 0.51**	13.67 ± 1.08**	46.23 ± 7.13*
AECSS (25 mg/kg)	3.00 ± 0.68	9.17 ± 1.57	50.40 ± 1.82
AECSS (50 mg/kg)	6.50 ± 0.50**	13.00 ± 1.15**	45.69 ± 5.23**
AECSS (100 mg/kg)	2.17 ± 0.30	3.83 ± 1.01	40.16 ± 2.76*

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

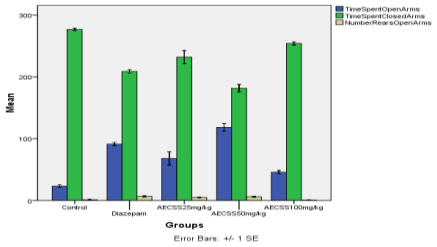

Fig. 2: It shows the Mean duration of time spent in open and closed arms (in seconds) and mean number of rears in open arms in all groups receiving Normal saline (0.1ml/10g), Diazepam (1.0mg/kg) and AECSS at doses of 25 mg/kg,50 mg/kg and 100 mg/kg:

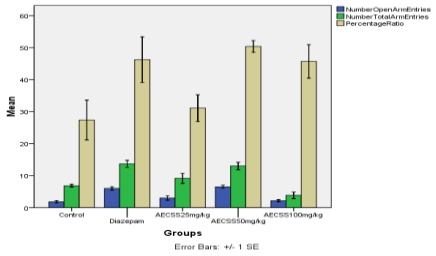

Fig. 3: It shows the Mean number of open and total arm entries and mean percentage ratios for all groups receiving Normal saline (0.1ml/10g), Diazepam (1.0mg/kg) and AECSS at doses of 25 mg/kg,50 mg/kg and 100 mg/kg

DISCUSSION

With a considerable populace under its umbrella, anxiety is a mental disorder that has received substantial focus over the past few decades in terms of research [13]. The current armamentarium of medications used to treat anxiety is spearheaded by the Benzodiazepine class of drugs [6]. The adverse effects associated with BZDs have galvanized the search for medications that possess more desirable safety profiles. The herbal drugs employed in traditional medicine for treating neurological disorders are an unexplored avenue which needs to be researched for demonstrating drugs with anxiolytic potential [14].

In the present study using the EPMT, it was observed that AECSS at a dose of 50 mg/kg (Group IV) showed a statistically significant increase in parameters such as time spent in the open arms (in seconds), number of rears in the open arms, number of open arm entries and percentile ratio of open arm to total arm entries when compared to the control group (Group I). However, at a dose of 25 mg/kg (Group III), AECSS increased the time spent in the open arms and the number of rears in the open arms. This is clearly indicative of the anxiolytic-like potential of the test drug.

The seeds of *Coriandrum Sativum* have shown therapeutic potential as a diuretic [15], antidiabetic [16] and anthelminthic [17]. In CNS studies, the seeds have also shown positive results when screened for their antioxidant [17,18], anticonvulsant [19] and sedative hypnotic [20] properties. Linalool (67.7%) and flavinoids (16.6%) are major phytochemical constituents of *Coriandrum Sativum* seeds [21]. Linalool has shown to possess anxiolytic property [22,23]. The mechanism of anxiolytic action displayed by Coriandrum Sativum may be attributed to the flavinoids, which have structural similarity to Diazepam (that acts via Gamma amino butyric acid [$GABA_A$] receptor complex) [24].

CONCLUSION

The present study shows that chronic administration of AECSS has anxiolytic-like activity when demonstrated in the Elevated plus maze test. However, further research needs to be conducted to identify the exact mechanism of anxiolysis involved and to determine the use of *Coriandrum Sativum* seeds as an adjuvant to BZDs for treatment in humans.

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