ORIGINAL ARTICLE

Effects of *Coriandrum sativum* extract on exploratory behaviour pattern and locomotor activity in mice: An experimental study

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Background: *Coriandrum sativum* L. (coriander) is an annual herb belonging to the Apiaceae family, used for medicinal purposes. **Objective**: To investigate the effect of the hydroalcoholic extract obtained from *Coriandrum sativum* leaves on the exploratory behaviour pattern and locomotor activity of mice. **Materials and Methods:** Elevated plus maze (EPM) and open field test (OFT) were the screening tests used to assess the anxiolytic activity of the extracts on mice. Diazepam (1 mg / kg) served as the standard anxiolytic agent. The animal receiving extracts or diazepam showed an increase in the time spent, total entries in the open arm of the EPM and increased total locomotion in the OFT, suggesting anxiolytic activity. **Results:** The crude dried extract was prepared in doses of 100, 200 and 400 mg / kg body weight and administered intraperitoneally to the mice, for evaluation of the anxiolytic activity. The 200 and 400 mg / kg body weight produced highly significant ($P < 0.01$) anxiolytic effects, in a dose-dependent manner, by increasing the time spent on and the number of entries into the open arms of the EPM and by an increase in the locomotion by mice in the OFT. Furthermore, in lower doses the extract did not affect the locomotor activity. **Conclusion:** Our findings demonstrated that the leaf extract of the plant exerted an anti-anxiety effect on mice in the elevated plus maze and open field test.

Key words: *Coriandrum sativum*, diazepam, open field test, elevated plus maze

INTRODUCTION

Anxiety and behavioural disorders have a relatively high prevalence in modern society and effects one-eighth of the total population of the world. The most well-known tranquilisers or anxiolytics are those of the benzodiazepine family, which act by modulating the GABAergic receptors, but many others are known, including buspirone and other drugs belonging to the class of azospirode canedione compounds, which act as agonists of the serotonergic receptors (5-HT_{1A}). However, the clinical use of these drugs is not without drawbacks, particularly due to the risk of side effects, such as the psychomotor impairment of other central depressant drugs.[1,2] Benzodiazepines are not recommended for long-term treatment of generalised anxiety disorders, due to the associated development of tolerance, cognitive and memory changes, physical dependence and withdrawal reaction on discontinuation.[3]

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Natural remedies possessing the same efficacy as conventional drugs, but with fewer side effects, would be a valuable addition to the treatment options for anxiety related disorders. However, the acceptance of alternative remedies has thus far been hampered by the scarcity of pharmacological studies elucidating their indications, limitations and mechanisms of action.[4-6]

Coriandrum sativum L. (coriander) is an annual herb belonging to the Apiaceae (Umbellifera) family.[7] Different parts of the plant, including the fruits and the green herbs, are used for medicinal purposes such as dyspeptic complaints and loss of appetite.[8] Pharmacological studies in animals have shown that coriander has anti-diabetic,[9,10] hypolipidemic[11,12] and anti-cancer effects.[13] *Coriandrum sativum* have been used as a drug for indigestion, against worms, rheumatism and pain in the joints.[14] The sedative–hypnotic activity of *Coriandrum sativum* seeds has been evaluated in mice.[15] Linalool, the main monoterpenoid of coriander seeds is shown to have a sedative and anticonvulsant activity[16] reversal of memory deficits[17] and *in vivo* antioxidant activities of the *Coriandrum sativum* seed.[18,19] However, the leaves of *Coriandrum sativum* have not been thoroughly studied with respect to their anxiolytic properties. Hence, considering the varied important activities of this plant, as reported in the traditional system of medicine, it was planned to study the effects

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of the extract of the leaves of *Coriandrum sativum* L on the exploratory behaviour pattern and locomotor activity in mice.

MATERIALS AND METHODS

Plant Material

Coriandrum sativum L. (coriander) was collected from the local market of Mysore, India. The *Coriandrum sativum* leaves were washed with clean distilled water and allowed to dry in the shade for three days in order for them to have the moisture content of 7.0%. This plant material was taken for further studies.

Extraction

Coriandrum sativum of 250 g was crushed and used for extraction. This sample was soaked overnight in 70% ethanol and filtered using Whatman No.1 paper. The process was repeated twice by adding a fresh solvent every time. The pooled extract was subjected to flash evaporation followed by lyophilization. The lyophilized sample was further analysed for its anxiolytic property.

Animal Experiment

Animal studies were conducted according to the Institutional Animal Ethical Committee regulations approved by the committee for the purpose of control and supervision of experiments on animals. Thirty male mice weighing 25 to 30 g were selected from the stock colony of the Defence Food Research Laboratory, Mysore, India, housed in an acryl fiber cage in a temperature controlled room (25±2°C). They were maintained in 12 hour light/dark cycle, with free access to food and drinking water *ad libitum*.

Experimental design

The extracts of the leaves of *Coriandrum sativum* were separately suspended in a vehicle comprising of 1% (w/v) Tween 20 in distilled water. The grouping of mice and the administration of the extracts were carried out as given below:

Group 1: Control
Group 2: Ethanol extract, 100 mg/kg body wt.
Group 3: Ethanol extract, 200 mg/kg body wt.
Group 4: Ethanol extract, 400 mg/kg body wt.
Group 5: Diazepam, 1 mg/kg body wt.

The extract of the leaves of *Coriandrum sativum* was prepared by suspending the dried extracts in the vehicle. This was administered, intraperitoneally (i.p.) to the mice, one hour before carrying out the tests. Six mice were taken in each group. The doses of the extracts were calculated, to administer 0.25 ml of the suspension of extracts to the mice. Diazepam (1 mg/kg body wt.) suspended in the vehicle was used as the standard anxiolytic drug. The suspending vehicle (0.25 ml) without any extract/drug was used as the control.

Estimation of the total flavonoid and total phenol content

The total flavonoid content was determined as described by Zou *et al*.[20] Catechin was used as a standard and the results were expressed as milligrammes of catechin equivalents (CE) per milligramme of dry extract. The total phenol content was determined by the method adapted from Singleton *et al*.[21] The total phenolic content was expressed as milligrammes of gallic acid equivalents (GAE) per milligramme of dry extract.

Phytochemical tests

The crude extract was subjected to preliminary phytochemical screening for the detection of the major functional groups.[22] Subsequently, the extract was used for pharmacological screening.

Elevated Plus-maze Test

The test procedure and scoring methodology for the elevated plus-maze test have been described by Kulkarni *et al*.[23] In brief, the apparatus consisted of two open (30×5×0.25 cm) and two enclosed (30×5 ×15 cm) arms that radiated from a central platform (5×5 cm), to form a plus sign. A slightly raised edge on the open arms (0.25 cm) provided an additional grip for the animals. The maze floor and the closed arms were covered with black adhesive tape. The plus-maze was elevated to a height of 40 cm above floor level by a single central support. The mice were injected with drugs or vehicle and 60 minutes later the trial was started, by placing the 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 arms, were counted during a five-minute test period. The open-arm entries and open-arm time were used as indices of anxiety. A mouse was considered to have entered an arm when all four paws were on the arm. The apparatus was cleaned thoroughly between trials with damp and dry towels. All behavioural recordings were carried out with the help of the ANY MAZE software.

Open field test

Spontaneous motor activity evaluated in the open field test has been described by Bhattacharya *et al*.[24] The open field apparatus is made up of black plexi glass and consists of a square, 56×56 cm. The entire floor of the apparatus was divided into 16 squares of identical dimensions. The entire room, except the open field was kept dark during the experiment. One hour after Vehicle/Standard / Extract treatment, each animal was placed at one corner of the apparatus and the behavioural aspects were noted in the next five minutes. The apparatus was cleaned thoroughly between trials with damp and dry towels. All

behavioural recordings were carried out using the ANY MAZE software.

Statistical Analysis

All data were presented as mean±SD and were analysed by one-way ANOVA. The groups treated with extracts were compared with the respective vehicle (control) group. The diazepam-treated group was compared with the control and P <0.05 and <0.001 were considered statistically significant.

RESULTS

The amount of flavonoids in 70% ethanol extract was found to be 44.5 µg of the catechin equivalent/mg extract and the total phenols were 133.74 µg of the gallic acid equivalent/mg extract. Phytochemical screening was carried out and it was found to contain alkaloids, tannins, flavonoids, glycosides and gums.

Elevated Plus Maze Test

The EPM is one of the most popular animal tests for research on behavioural pharmacology of anxiety. It involves spontaneous or natural aversive stimuli, that is, height, unprotected opening and novelty. Several plants that are used in folk medicine to diminish anxiety are reported to bring about an increase in the exploration of the open arms in the EPM test.[25] In EPM mice will normally prefer to spend much of their allotted time in the closed arms. This preference appears to reflect an aversion toward open arms that is generated by fear of open spaces. Drugs that increase open arm exploration are considered as anxiolytic and the reverse holds true for anxiogenic. In our study, we have observed that the extract at doses of 200 and 400 mg/kg (P<0.001) significantly increases the number of entries and time spent in the open arms with associated decrease in the closed arms when compared to the control-treated group [Figures 1-3]. Plant extract at 100 mg/kg had no significant effects on any of the parameters that were measured on the EPM.

Open Field Test

Confrontation with the situation induces anxiety behaviour in rodents. The data reported in the present experiment shows that exploratory and other behaviours tend to occur more in squares surrounded by walls. The larger the number of walls the more the behaviour occurs in a particular square. This indicates that thigmotaxis is a determinant factor of rat behaviour in unfamiliar places and that the rats are sensitive to the number of walls near which they can choose to be. It is known that rodents show thigmotaxic behaviour identified by spontaneous preference to the periphery of the apparatus and reduced ambulation.[26] Anxiolytic treatment decreases this anxiety-induced inhibition of exploratory behaviour. Diazepam 1 mg/kg

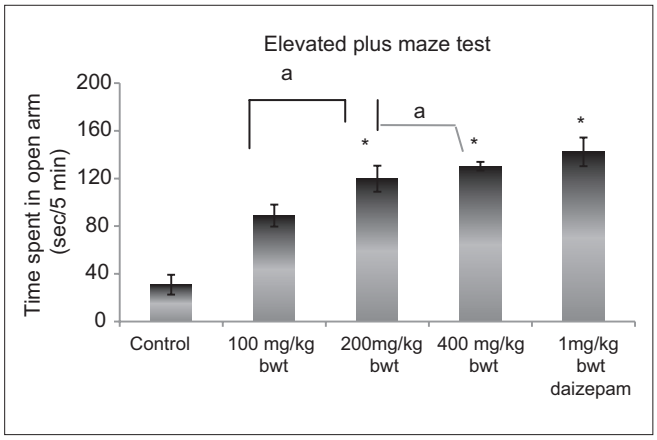

Figure 1: Effects of diazepam and the extract of *Coriandrum sativum* on the time spent in the open arms of the elevated plus-maze during a 5 min test in mice. The plant extracts, diazepam or control, were injected 60 min prior to test. Data are presented as mean values (±SD.) from group of six mice.*P<0.05 compared with vehicle-treated control. 'a' represents P<0.001.

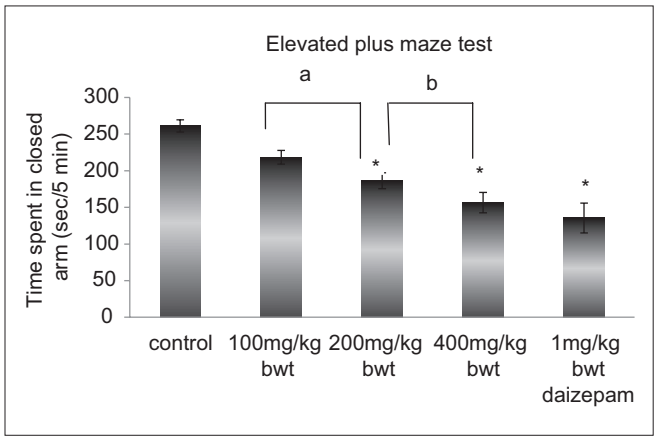

Figure 2: Effects of diazepam and the extract of *Coriandrum sativum* on the time spent in the closed arms of the elevated plus-maze during a 5 min test in mice. The plant extracts, diazepam or control, were injected 60 min prior to test. Data are presented as mean values (±SD.) from group of six mice. *P<0.05 compared with vehicle-treated control. 'a' represents P<0.001and 'b' P<0.05.

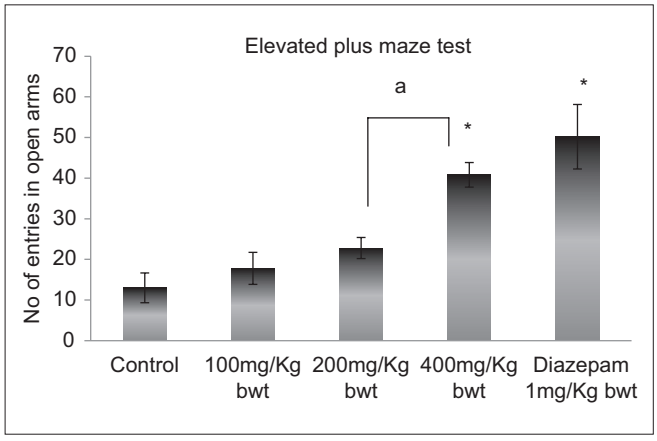

Figure 3: Effects of diazepam and the extract of *Coriandrum sativum* on the number of open arm entries of the elevated plus-maze during a 5 min test in mice. The plant extracts, diazepam or control, were injected 60 min prior to test. Data are presented as mean values (±SD.) from group of six mice. P<0.05 compared with vehicle-treated control. 'a' represents P<0.001.

significantly (P<0.001) increases the ambulation, activity at the centre and total locomotion. Similar results are exhibited by the extracts in the OFT. The *Coriandrum sativum* extract at 200 and 400 mg/kg shows a significant (P<0.001) increase in the total locomotion [Figure 4] and increase in the number of line crossings [Figure 5]. However, no significant effects are produced by the administration of 100 mg/kg of the plant extract of *Coriandrum sativum* leaves.

Correlation of the activity of the animals in the open field test and elevated plus maze test was represented in the Doughnut graph [Figure 6]. There was also a positive correlation in all the studies between exploratory movements and open arm entries, probably reflecting the fact that mice in the open field would choose to move at distances away from the walls. Correlation indicates that mice actively exploring one environment tend to do the same in another.

DISCUSSION

The incidence of pathological anxiety in the community is very high and is associated with a lot of morbidity. Lifetime prevalence in women is 30.5% and in males 19.2%.[27] Hence, it is very important to address the problem of anxiety and find effective remedies. Although several drugs are available, all are associated with some limitations. Anxiety and depression are among the symptoms most frequently reported by patients seeking complementary and alternative medical treatments and natural remedies.[28-31]

A comparison of the data for the two test models shows the anxiolytic-like effects of *Coriandrum sativum*. This may be due to different reasons. A first possibility is that the two tests explore distinct behavioural aspects that are affected in different ways by the remedies. The elevated plus maze test is widely used, with mice as a model, for screening anxiolytic or anxiogenic drugs, based on the innate aversion of mice to height and the spontaneous exploratory behaviour of rodents in response to mild stressors, such as a novel environment.[26] Elevated plus maze is the most appropriate device for assessing 'state anxiety', whereas, the free exploratory paradigm can be used for 'trait anxiety'.[32-37] Our data represents that dosages of 200 and 400 mg of hydroethanol extract of *Coriandrum sativum* leaves/kg body weight has a highly significant anxiolytic effect, similar to diazepam. Mice treated with the extracts of *Coriandrum sativum* exhibit less time in the periphery and more time in the centre of the field compared to the corners. As seen in the earlier study, *Coriandrum sativum* extracts at 200 and 400 mg/kg body weight demonstrate a significant increase in the time spent at the centre of the field and a significant increase in the number of line crossings.

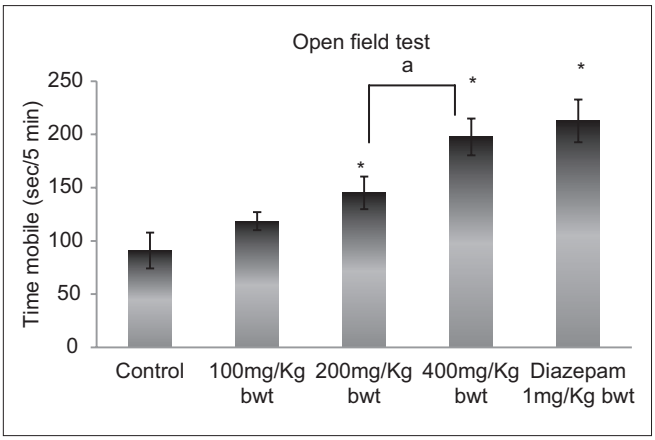

Figure 4: Effects of *Coriandrum sativum* leaves ethanolic extract on total locomotor activity in mice. The plant extracts, diazepam or control, were injected 60 min prior to test. Data are presented as mean values (±SD.) from group of six mice. *P<0.05 compared with vehicle-treated control. 'a' represents P<0.001

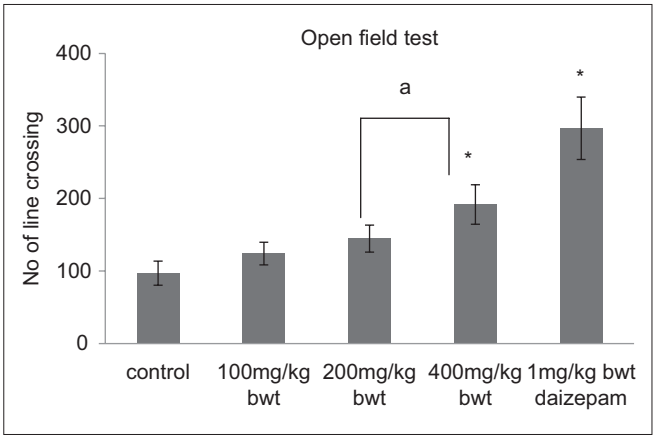

Figure 5: Effects of *Coriandrum sativum* leaves ethanolic extract on number of line crossing activity in mice. The plant extracts, diazepam or control, were injected 60 min prior to test. Data are presented as mean values (±SD.) from group of six mice. *P<0.05 compared with vehicle-treated control. 'a' represents P<0.001

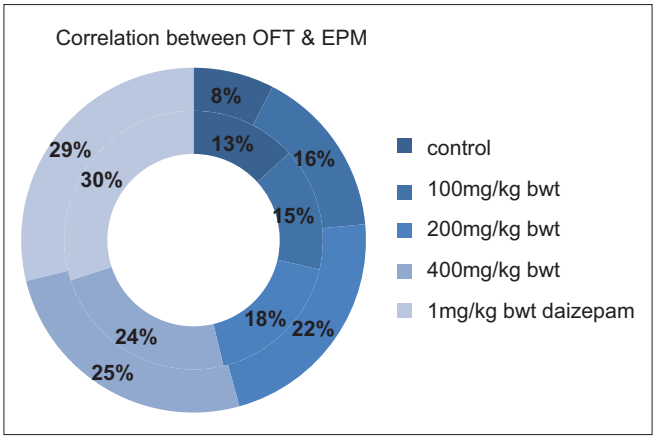

Figure 6: Doughnut graph representation shows correlation between open field test and elevated plus maze test. Activities of animals are represented in percentage. The *Coriandrum sativum* leaves extracts, diazepam or control, were injected 60 min prior to test. Data are presented as mean values (±SD.) from group of six mice. P<0.05 compared with vehicle-treated control

Rge anxiolytic activity of *Coriandrum sativum* is likely to be associated with its rich contents of phytochemicals, namely, alkaloids, tannins, flavonoids, glycosides and gums. The linalool, a monoterpene, is found in some species of aromatic plants, including *Coriandrum sativum*, as a major component.[38] In a recent study, in the light/dark box test, inhalation of linalool oxide led to an increase in the time spent by the mice in the brightly-lit chamber and the number of times the animal crossed from one compartment to another, without affecting the performance on the rotarod.[39] Further pharmacological and chemical investigations are required to elucidate the exact mechanism of action of this extract.

CONCLUSION

In the study reported here, the exploratory behaviour pattern and locomotor activities of mice were assessed by using the elevated plus maze and open field test models in which *Coriandrum sativum* leaf extracts at the levels of 200 and 400 mg/kg body weight showed a significant effect. Overall, the present study suggests the anxiolytic effects of the ethanol extract of *Coriandrum sativum* probably due to its rich content of linalool.

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