Evaluation of anxiolytic activity of aqueous extract of *Coriandrum sativum* Linn. in mice: A preliminary experimental study

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ABSTRACT

Objectives: To evaluate the anxiolytic effect of *Coriandrum sativum* (CS) aqueous extract in mice. To compare the antianxiety activity of CS against standard drug diazepam (3 mg/kg). **Materials and Methods:** After obtaining Institutional Animal Ethics Committee approval, Swiss albino mice (18–25 g) of either sex were randomly divided into five groups of six animals each. Dried powder of CS leaves was boiled with distilled water, cooled, filtered, placed on a hotplate for complete evaporation, finally weighed and stored. The control group, test group, and standard drugs group received saline, CS extract (50, 100, and 200 mg/kg), diazepam (3 mg/kg), respectively, by oral feeding. The antianxiety effect was assessed by elevated plus maze (EPM) in mice. **Results:** In EPM, it implied that CS 50 mg/kg (Group III), 100 mg/kg (Group IV), and 200 mg/kg (Group V) significantly ($P < 0.001$) increases the number of entries in open arms compared to control. The time spent in open arms also increased in all the doses of CS extract significantly. **Conclusion:** The current study demonstrates statistically significant dose-dependent antianxiety activity of CS leaves.

Key words: Antianxiety effect, *Coriandrum sativum*, Diazepam, Elevated plus maze

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INTRODUCTION

The primary use of sedative–hypnotic and anxiolytic drugs is to encourage calmness (anxiolytics or sedatives) or to produce sleep (sedative–hypnotics). All people are subjected to states of emotional tension and uneasiness. For otherwise healthy individuals, these occasions are usually mild and short that pharmacological intervention is unnecessary.[1] Anxiety almost invariably accompanies many medical and surgical conditions, and it is often a symptom of psychiatric illness. When the symptoms become intolerable or interfere with the treatment of the underlying disease, and if counseling is not sufficient, drug treatment can be considered as a means of helping patients cope with their anxiety.[2]

Anxiety that results from fear caused by an acute illness or a stressful event, such as loss of a loved one, is usually self-limiting and can be of relatively short duration. The current options include various kinds of psychotherapy and pharmacotherapy such as benzodiazepines, azapirones, and antidepressants and others.[3]

The recognition of anxiolytic effects of nonbenzodiazepine azapirones agents, which acts as 5-HT1A partial agonists, such as buspirone, gepirone, and ipsapirone and their therapeutic role in clinical anxiety and mood disorders has further focused attention on the 5-HT1A receptor.[4] However, the anxiolytic effects of azapirones follow a time course observed with antidepressants where therapeutic effects are delayed for 3–4 weeks, which is unlike the rapid effects observed with benzodiazepine anxiolytics.[5] Thus, there is a need for robust anxiolytic compounds that have lesser side effects than benzodiazepines and a more immediate onset of action than currently available 5-HT1A receptor acting drugs.

The leaf of *Coriandrum sativum* (CS) Linn., is a slender, glabrous, branched, cultivated all over India, giving characteristic aroma when rubbed.[6] It is an annual herb originating from the Mediterranean.[7] The whole plant

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and especially the unriped fruit is characterized by a strong disagreeable odor, wherever the name coriander.[8-10] All parts of the plants are edible, but the fresh leaves, and the dried seeds are the most common parts used in cooking. In India, it is chiefly found in Madhya Pradesh, Tamil Nadu, Karnataka, Rajasthan, Andhra Pradesh, and Bihar.

In the Indian traditional medicine, coriander is used in disorders of digestive, respiratory and urinary system, as it has diaphoretic, diuretic, carminative, and stimulant effects. In Iranian traditional medicine, coriander has been indicated for a number of medical problems such as dyspeptic complaints, loss of appetite, convulsion, and insomnia.[11-15] This experiment was conducted to study the antianxiety (anxiolytic) effect of leaves of the plant CS in mice using elevated plus maze (EPM) test. This is a simple test used to identify the neuroprotective effects[16,17] and anxiety of the given test extracts.

MATERIALS AND METHODS

Collection of plant material

Preparation of aqueous extract

The plant was collected from the gardens of Coimbatore. The plant was identified and authenticated by a botanist. Leaves were shade-dried, coarsely powdered. The dried CS leaves 100 g were added to 500 ml distilled water. After 24 h, maceration done at room temperature (37°C), the mixture was then heated for 30 min in the water bath at 65°C and dried under vacuum with the yield of 5.9% (w/w). The extract was stored at 4°C and used to treat animals as needed.[18]

Experimental models

Swiss albino mice of either sex weighing approximately 18–25 g (2–2.5-month-old) used for experimental purpose. They were housed in polypropylene cages in the air-conditioned room with the temperature maintained at 25 ± 3°C, and 12 h alternating light and dark cycles. The mice were provided with a nutritionally adequate diet (Hindustan Lever Limited, India) and drinking water *ad libitum* throughout the study. Approval by the Animal Ethics Committee for the experimental procedures obtained.

Acute toxicity study

Acute toxicity was generally carried out for the determination of LD_{50} value in experimental animals. The LD_{50} determination was done in mice by OECD guidelines 423. The aim of performing acute toxicity study is for establishing therapeutic index of a particular drug and to ensure safety *in-vivo*. Acute toxicity test was performed in mice. All animals were fasted overnight before treatment and were given food 1 h after aqueous extract of CS treatment. General behavior was also observed at 1, 8, and 12 h after administration. The number of animals that died after administration was recorded daily for 10 days.[19,20]

Procedure

Elevated plus-maze test

Principle

Elevated plus-maze is the most simple apparatus to study neuroprotective effects[16,17] and anxiolytic responses produced by the test drugs. It is used to test almost all types of anxiolytic agents. Exposure of animals to novel maze alley evokes an approach-avoidance conflict which is stronger in open arm as compared to enclosed arm. Rodents (rats and mice) have an aversion for high and open space and prefer enclosed arm, therefore, spend a greater amount of time in enclosed arm. When animals enter open arm, they freeze, become immobile, defecate and show fear-like movements.[21] The plasma cortisol level is also reported to be increased, as a true reflection of anxiety. Major advantages of this test procedure are: (a) It is simple, fast, and less time consuming, (b) no prior training or noxious stimuli (sound or light) is required, and (c) it is predictable and reliable procedure for studying anxiety response as well as anxiolytic action of drug.[22,23]

Procedure

Animals were weighed, numbered, and divided into five groups, each consisting six mice. One group was used as control (saline), second for standard drug (diazepam) treatment, third, fourth, and fifth group for coriandrum extract treatment (Test - 50, 100, 200 mg/kg). Animals were placed individually in the center of the maze, head facing toward open arm and stopwatch was started. The following parameters were noted for 5 min. (1) First preference of mouse to open or closed arm. (2) Number of entries in open arm (an arm entry defined as the entry of four paws into the arm). (3) Average time each animal spends in open arm (Average time = total duration in the arm/number of entries) was calculated. Saline and diazepam were injected to the control and standard groups respectively. Coriandrum extract was injected to the test groups. After 30 min, animals were placed individually in the center of the maze. Finally, we compared the preference of the animals to open or enclosed arm, average time spent in open arm and the number of entries in open arm in each group.[24,25]

Statistical analysis

Data were expressed by mean ± standard error mean. For comparison among the groups, we used analysis of variance with multiple comparisons by *post-hoc* Dunnett *t*-test method. The statistical significance of differences between the control and experimental groups was assessed by Dunnett's two-sided *t*-tests (*post-hoc* tests). Statistical analysis was done using Statistical Package for the Social

Sciences for windows (version 17.0, SPSS Inc., Chicago., USA). Statistical significance was considered $P < 0.05$ level.

RESULTS

It is shown in the Tables 1 and 2 and Figures 1-5. CS has dose-dependent antianxiety effect on mice.

DISCUSSION

Coriander leaf is a herb, indigenous ingredients of ayurvedic medicine. It is mainly used for its memory enhancing property, anticonvulsant, antianxiety, antidiuretic, and antiulcer properties. The present study was aimed at evaluating the antianxiety property of coriandrum in comparison with control and standard drugs using animal models.

Coriandrum sativum Linn. has been recommended for relief of anxiety and insomnia in Iranian folk medicine. The anxiolytic effect of aqueous extract (50, 100, 200 mg/kg, i.p) was examined in male albino mice using EPM as an animal model of anxiety. The effects of the extract on spontaneous activity and neuromuscular coordination were assessed using animal activity meter and rotarod, respectively. In the EPM, aqueous extract at 200 mg/kg showed an anxiolytic effect by increasing the time spent on open arms and the percentage of open arm entries, compared to the control group. Aqueous extract at 50, 100, and 200 mg/kg significantly reduced spontaneous activity and neuromuscular coordination, compared to the control group. These results suggest that the aqueous extract of CS seed has an anxiolytic effect and may have potential sedative and muscle relaxant effects.[26-29]

There is another study reveals that leaves of CS possesses both anxiolytic and central analgesic activity.[30] The EPM is currently one of the most widely used models of animal anxiety and has been validated for use with both the sexes of mice. Therefore, this test was chosen to investigate the anxiolytic potential of the aqueous extract of coriander seed. The indices of anxiety in this test are, number of entries in

Table 1: The number of entries (open and total) of mice in EPM (*n*=6)

Group	Mean±SEM		
	Number of entries in open arm	Total entries	Percentage ratio of open/ total arms entry
Control	5.83±0.54	28.00±0.63	20.70±1.51
Diazepam	33.83±0.54***	47.17±0.54***	71.74±0.93***
CS 50 mg/kg	19.50±0.62**	39.17±0.87**	49.78±0.76**
CS 100 mg/kg	25.00±0.37***	41.17±0.48***	60.75±0.89***
CS 200 mg/kg	29.17±0.75***	44.33±0.96***	65.77±0.49***

***P<0.001 when compared to controls. **P<0.01 when compared to controls. EPM=Elevated plus maze; CS=*Coriandrum sativum*; SEM=Standard error of the mean

Table 2: The time spent by mice on EPM in open and closed arms (*n*=6)

Group	Mean±SEM	
	Time spent in open arm in seconds	Time spent in closed arm in seconds
Control	34.33±0.62	265.67±0.62
Diazepam	132.33±0.96***	167.67±0.96***
CS 50 mg/kg	59.0±1.44**	241.00±1.44**
CS 100 mg/kg	93.0±0.86***	207.00±0.86***
CS 200 mg/kg	118.67±0.80***	181.33±0.80***

***P<0.001 when compared to Controls. **P<0.01 when compared to controls. SEM=Standard error of the mean; EPM=Elevated plus maze; CS=*Coriandrum sativum*

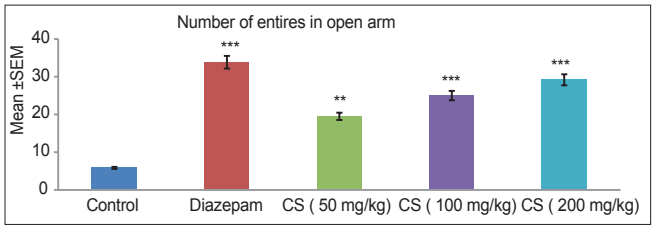

Figure 1: Effect of *Coriandrum* shows antianxiety effect in open arm entries

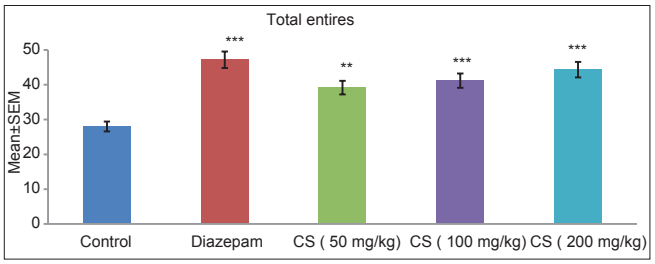

Figure 2: Effect of *Coriandrum* shows antianxiety effect in total entries

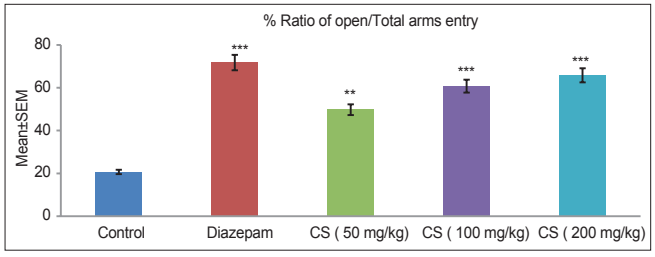

Figure 3: Effect of *Coriandrum* shows antianxiety in % ratio of open/ total arms

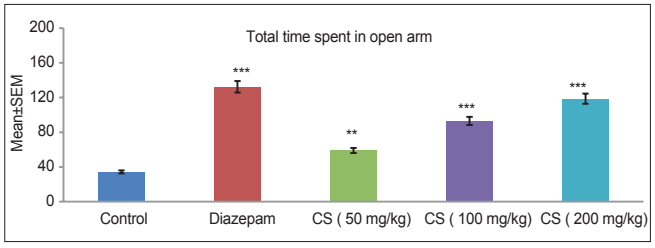

Figure 4: Time spent by mice with *Coriandrum sativum* on elevated plus maze in open arm (n = 6)

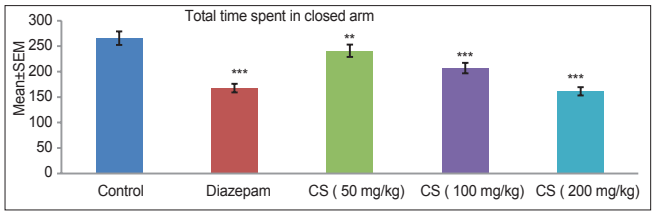

Figure 5: The time spent by mice with *Coriandrum sativum* on elevated plus maze in closed arm (n = 6)

open arm and closed arm. The sensitivity to agents acts via the gamma-aminobutyric acid receptor complex, justifying the use of diazepam as a positive control in this study. Diazepam increased the entries of open arm and the time spent in the open arms confirming its anxiolytic effects.[30-33]

The aqueous extract of coriander seed had similar effects on these parameters. The effect of 200 mg/kg coriander on the EPM test was almost equivalent to that of 0.3 mg/kg diazepam. These observations clearly indicate that coriander seed exerts an anxiolytic activity. In this study, the anxiolytic activity of the coriander seed extract occurred at a dose of 50, 100, and 200 mg/kg in mice.[31,34] The above effects may be due to the presence of sterols, tannins, and flavonoids in the extract.[35-37]

In our study, coriandrum leaf aqueous extract was used in a dose of 50, 100, and 200 mg/kg for identifying antianxiety. In these doses, coriandrum extract increases the number of entries in open arm as compared to control in dose-dependent manner effectively and significantly decreased the number of entries in closed arm compared to that of control in a dose-dependent manner. As the dose of coriandrum increases, the effect also increased, but in all the three doses, there was significant antianxiety effect was seen. Hence, in our study, coriandrum showed significant anxiolytic activity with 50, 100, and 200 mg/kg compared to the control group but has less activity when compared to that of standard drug diazepam.

Although we should be cautious in extrapolating the dose obtained from animal studies to human subjects, it may be suggested that the effective dose for a 75 kg adult man would be 7.5 g dry extract of coriander leaf.[31,34] This corresponds to an infusion of approximately 20 g of coriander seed in100 ml water, considering the yield of the extract. This is in the range of the coriander doses empirically used in traditional medicine. However, the optimum therapeutic dose for human would require further studies, evaluating the effect of the extract in a clinical situation.

CONCLUSION

The present study demonstrated that the aqueous extract of leaves of CS Linn. possess dose-dependent anxiolytic activity. Further, there is need to isolate, characterize, and screen the active principles from the different parts of CS Linn. that are responsible for its anxiolytic activity. Furthermore, there is need to find out the exact mechanism by which the plant exerts above effects. Further studies are needed to separate and confirm the active components and its effect on anxiety.

REFERENCES

1. Eisenberg DM, Davis RB, Ettner SL, Appel S, Wilkey S, Van Rompay M, *et al.* Trends in alternative medicine use in the United States, 1990-1997: Results of a follow-up national survey. JAMA 1998;280:1569-75.
2. Lader M, Morton S. Benzodiazepine problems. Br J Addict 1991;86:823-8.
3. Griffiths RR, Ator NA, Roache JD, Lamb RJ. Abuse liability of triazolam: Experimental measurements in animals and humans. Psychopharmacol Ser 1987;3:83-7.
4. Kunovac JL, Stahl SM. Future directions in anxiolytic pharmacotherapy. Psychiatr Clin North Am 1995;18:895-909.
5. Lowry CA, Johnson PL, Hay-Schmidt A, Mikkelsen J, Shekhar A. Modulation of anxiety circuits by serotonergic systems. Stress 2005;8:233-46.
6. Evans WC. Treas: Pharmacognocy. 15th International edition. Edinburgh, London, New York: W.B. Saunders; 2002. p. 262.
7. Vaidya VM. Ayurvedic Pharmacology and Therapeutic Uses of Medicinal Plants. 1st ed. Mumbai, India: Dravyagunavigyan Press; 2000. p. 405-6.
8. Gruenwalded J. PDR-HM Physicians' Desk Reference for Herbal Medicine. Vol. 8. New Jersey: Medical Economics; 2004. p. 378-84.
9. British Pharmacopoeia. Introduction General Notices Monographs, Medicinal and Pharmaceutical. Vol. 1. London: British Pharmacopeia Commission; 2003. p. 542-43.
10. Monograph of the 1[5th]h edition of European Pharmacopoeia (2004). Stationary Office on Behalf of the Medicines and Healthcare Products Regulatory Agency (MHRA). London: The Stationary Office; 2008. p. 617.
11. Benjumea D, Abdala S, Hernandez-Luis F, Pérez-Paz P, Martin-Herrera D. Diuretic activity of Artemisia thuscula, an endemic Canary species. J Ethnopharmacol 2005;100:205-9.
12. Maghrani M, Zeggwagh NA, Haloui M, Eddouks M. Acute diuretic effect of aqueous extract of *Retama raetam* in normal rats. J Ethnopharmacol 2005;99:31-5.
13. Mir H. *Coriandrum sativum*. In: Application of Plants in Prevention and Treatment of Illnesses. Persian 1992;1:257-52.
14. Zargari A. *Coriandrum sativum* L. In: Herbal Medicine. Persian 1991; 1: 586-90.
15. Duke JA. Handbook of Medicinal Herbs. 2nd ed. Boca Raton, Florida, USA: CRC Press LLC; 2002. p. 222-3.
16. Sunanda BP, Latha K, Rammohan B, Uma Maheswari MS, Surapaneni KM. Evaluation of the neuroprotective effects of curcumin (turmeric) against scopolamine induced cognitive impairment in mice. Int J Pharm Phytochem Res 2014;6:133-6.
17. Sunanda BP, Latha K, Rammohan B, Uma Maheswari MS, Surapaneni KM. Evaluation of the neuroprotective effects of centella asiatica against scopolamine induced cognitive impairment in mice. Indian J Pharm Educ Res 2014;48:31-4.
18. Gray AM, Flatt PR. Insulin-releasing and insulin-like activity of the traditional anti-diabetic plant *Coriandrum sativum* (coriander). Br J Nutr 1999;81:203-9.

19. Ecobichon DJ. The Basis of Toxicity Testing. 2nd ed. New York: CRC Press; 1997. p. 43-60.
20. Ghosh MN. In: Fundamental of Experimental Pharmacology. Kolkata: Scientific Book Agency; 1984. p. 156-7.
21. Pellow S, Chopin P, File SE, Briley M. Validation of open: Closed arm entries in an elevated plus-maze as a measure of anxiety in the rat. J Neurosci Methods 1985;14:149-67.
22. Gerhard Vogel H. Drug Discovery and Evaluation: Pharmacological Assays. 2nd ed., Vol. 434. Berlin: Springer; 2002. p. 696.
23. Emamghoreishi M, Khasaki M, Aazam MF. *Coriandrum sativum*: Evaluation of its anxiolytic effect in the elevated plus-maze. J Ethnopharmacol 2005;96:365-70.
24. Gupta SK. Drug Screening Methods: Preclinical Evaluation of New Drugs. Vol. 2. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd.; 2009. p. 234-8.
25. Ghosh MN. Fundamentals of experimental pharmacology. Indian J Pharmacol 2007;39:216.
26. Kubo I, Fujita K, Kubo A, Nihei K, Ogura T. Antibacterial activity of coriander volatile compounds against Salmonella choleraesuis. J Agric Food Chem 2004;52:3329-32.
27. Emamghoreishi M, Heidari-Hamedani G. Sedative-hypnotic activity of extracts and essential oil of Coriander seeds. Iran J Med Sci 2006;31:22-7.
28. Momin AH, Acharya SS, Gajjar AV. *Coriandrum sativum*-Review of advances in phytopharmacology. Int J Pharm Sci Res 2012;3:1233-9.
29. Harsha SN, Anilakumar KR. Effects of *Coriandrum sativum* extract on exploratory behaviour pattern and locomotor activity in mice: An experimental study. Int J Green Pharm 2012;6:157-63.
30. Pathan AR, Kothawade KA, Logade MN. Anxiolytic and analgesic effect of seeds of *Coriandrum sativum* Linn. Int J Res Pharm Chem 2011;1:1087-99.
31. Moser PC. An evaluation of the elevated plus-maze test using the novel anxiolytic buspirone. Psychopharmacology (Berl) 1989;99:48-53.
32. Michel B, Martine H. The mice light/dark maze test. Mood and anxiety related phenotypes in mice. Neuromethods 2009;42:197-223.
33. Mahendra P, Bisht S. Anti-anxiety activity of *Coriandrum sativum* assessed using different experimental anxiety models. Indian J Pharmacol 2011;43:574-7.
34. Eguchi J, Inomata Y, Saito K. The anxiolytic-like effect of MCI-225, a selective NA reuptake inhibitor with 5-HT3 receptor antagonism. Pharmacol Biochem Behav 2001;68:677-83.
35. Ravindran A, Manohar VR, Rai M, Rraveendran N, Naik H. Chronic anxiolytic-like activity of aqueous extract of *Coriandrum sativum* seeds using elevated plus maze test in swiss albino mice. Int J Pharm Pharm Sci 2014;6:93-5.
36. de Almeida ER, Rafael KR, Couto GB, Ishigami AB. Anxiolytic and anticonvulsant effects on mice of flavonoids, linalool, and-tocopherol presents in the extract of leaves of *Cissus sicyoides* L. (Vitaceae). J Biomed Biotechnol 2009;2009:274740.
37. Linck VM, da Silva AL, Figueiró M, Caramão EB, Moreno PR, Elisabetsky E. Effects of inhaled Linalool in anxiety, social interaction and aggressive behavior in mice. Phytomedicine 2010;17:679-83.

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