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Original Article

Sedative-Hypnotic Activity of Extracts and Essential Oil of *Coriander* Seeds

M. Emamghoreishi,
G. Heidari-Hamedani

Abstract

Background: *Coriandrum sativum* L. has been recommended for relief of insomnia in Iranian traditional medicine. However, no pharmacological studies have yet evaluated its sedative effects. The aim of this study was to determine if extracts and essential oil of coriander seeds have sedative-hypnotic activity.

Methods: The aqueous or hydro-alcoholic extracts or essential oil of coriander seeds (100, 200, 400 and 600 mg/kg) were intraperitoneally administered to male albino mice, 30 minutes before pentobarbital injection (40 mg/kg). Latency to sleep and sleep duration were recorded.

Results: Aqueous extract prolonged pentobarbital-induced sleeping time at 200, 400 and 600 mg/kg. Hydro-alcoholic extract at doses of 400 and 600 mg/kg increased pentobarbital-induced sleeping time compared to saline-treated group. The essential oil increased pentobarbital-induced sleeping time only at 600 mg/kg.

Conclusion: The extracts and essential oil of coriander seeds possess sedative-hypnotic activity. However, it is strongly suggested that the major active component(s) responsible for the hypnotic effect is mainly present in the aqueous extract.
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Keywords ● *Coriandrum sativum* ● sedative ● hypnotic ● extract ● essential oil ● pentobarbital

Department of Pharmacology,
and Psychiatry Research Center,
Shiraz University of Medical Sciences,
Shiraz, Iran.

Correspondence
Masoumeh Emamghoreishi PhD,
Department of Pharmacology
School of Medicine
Shiraz University of Medical Sciences,
Shiraz, Iran.
Tel/Fax: +98 711 2307591
E-mail: emamm@sums.ac.ir

Introduction

Coriandrum sativum L. (coriander) is an annual herb belonging to the Apiaceae (Umbellifera) family.[1] It is native to Mediterranean regions, and currently cultivated in many countries.[1] 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.[1] Pharmacological studies in animals have shown that coriander has anti-diabetic,[2,3] hypolipidemic,[4,5] and anti-cancer effects.[6]

Coriander leaves are used extensively in Iranian cookings, and coriander fruits are used as a spice, an essential ingredient in curry powder. The juice of fresh leaves and the tea of powdered fruits of coriander are recommended for relief of anxiety and insomnia in Iranian traditional medicine. Similar uses of coriander, i.e. as a sedative or for relief of nervousness, have also been indicated in other folk medicine.[7]

However, its central depressant effects have not been evaluated in scientific studies. We have recently demonstrated that the aqueous extract of coriander seeds decreased general locomotor activity in mice.[8] A decrease in spontaneous activity indicates that coriander seeds may have a sedative effect.[8] Therefore, the aim of this study was to evaluate the sedative-hypnotic activity of aqueous and hydro-alcoholic extracts and essential oil of coriander seed using prolonging pentobarbital-induced sleeping time as an index of sedative-hypnotic activity.

Material and Methods

Plant Material

Dried coriander seeds were purchased from an herbal store in Shiraz, Iran. The identity of the seeds was confirmed and for future reference a voucher specimen (#10002) was deposited at the herbarium of the Department of Biology, College of Science of Shiraz University, Shiraz, Iran.

Preparation of Aqueous Extract

Dried coriander seeds were ground to a fine powder, of which 100 grams were added to 500 ml distilled water. After 24 hrs maceration at room temperature, the mixture was heated for 30 min over the vapor of the water bath, and then allowed to infuse at ambient temperature for 15 min. The extract was filtered, concentrated by heating over the water bath and dried under vacuum,[3] with the yield of 5.9% (w/w).

Preparation of hydroalcoholic extract

The hydroalcoholic extract was prepared by percolating 100g of powdered coriander seeds with ethanol (70% v/v in water). It was then concentrated by evaporating over the water bath, and dried under vacuum. The yield was 9.8% (w/w).

Preparation of essential oil

The essential oil (0.6% w/w) was obtained from 100 g of powdered coriander seeds by water-distillation during four hrs, using a Clevenger-type apparatus.[9,10]

Animals

Male albino mice (Animal house, Shiraz University of Medical Sciences, Shiraz, Iran) were housed in standard cages (5 mice/cage) in a temperature (22±1°C), humidity (40-60%), and light period (07.00-19.00 hr) controlled environment. They had free access to water and food pellets. Experiments were performed in conformity with the university research council guidelines for conducting animal studies. Total of 126 mice were assigned to 18 groups used in three experiments performed in this study. In each experiment, groups of seven mice were randomly assigned to six different treatment groups and tested in a counterbalanced order between 8:00 to 14:00.

Chemicals

Diazepam hydrochloride (10 mg/2ml; Darou Pakhsh, Tehran, Iran), used as a reference drug, diluted with saline to 3 mg/10ml before use, and administered intraperitoneally (ip) in a volume of 10 ml/kg, (3 mg/kg). Sodium pentobarbital (Sigma, UK) dissolved in saline and used accordingly.

Different concentrations of aqueous and hydroalcoholic extracts of coriander seeds were prepared by serial dilution from a stock solution (600mg/10ml) of extracts in saline, and administered ip in a volume of 0.1 ml per 10 g body weight . Different concentrations of essential oil were also prepared by serial dilution from a stock solution of 300 mg/ml in olive oil, and administered ip in a volume of 0.02 ml per 10g body weight. All solutions were freshly prepared on the test days.

Prolongation of pentobarbital-induced sleeping time

Mice were given a single ip dose of essential oil, aqueous or hydro-alcoholic extract of coriander seeds (100-600 mg/kg). The control animals received the vehicles of essential oil (olive oil) or of the extracts (saline). These treatments were carried out 30 min before challenging the animal with ip injection of pentobarbital (40 mg/kg). The latency of the loss of the righting reflex and the total sleeping time (the time between the loss and the recovery of the righting reflex) were determined for each mouse as stated previously.[11] The mouse was considered as being awake if it could right itself (return to upright position). Once a mouse righted itself, it was placed on its back once more and allowed to right a second time for confirmation.

Statistical analyses

All values were expressed as mean±SEM. The differences in mean of latency time to sleep and sleep duration among different treated groups were statistically analyzed by one-way ANOVA followed by Dunnett *t* test. Linear regression analysis was used to determine the dose dependency of the observed effects and $P<0.05$ was considered as statistically significant.

Results

Effect of Aqueous extract of coriander seeds on pentobarbital-induced sleeping time

Aqueous extract of coriander seeds produced dose-dependent increase in pentobarbital-induced sleeping time (slope=0.26±0.03, p<0.001). The aqueous extract significantly increased sleep duration by 127%, 175% and 213% at doses of 200, 400 and 600 mg/kg, respectively as compared to saline-treated group (Fig 1B, p<0.001). Aqueous extract of coriander seeds also decreased latency time at doses of 400 and 600 mg/kg by 17% and 20%, respectively as compared to their control group, (Fig 1A, p<0.01). Diazepam significantly increased sleep duration (236%) and decreased latency time (46%), compared to saline-treated group (Figs.1A, B).

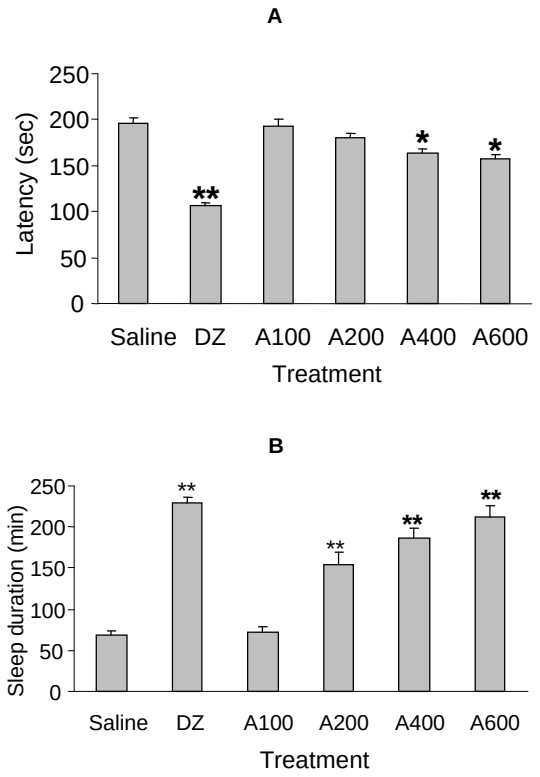

Fig 1: Effect of different doses of aqueous extract of coriander seeds (A100-A600, ip), diazepam (DZ, 3 mg/kg, ip) and saline on pentobarbital-induced sleeping time. Bars represent mean±SEM of latency to sleep (A) and sleep duration (B) of 7 mice in each group.
* p<0.01, ** p<0.001 compared to saline group.

Effect of hydro-alcoholic extract of coriander seeds on pentobarbital-induced sleeping time

Hydro-alcoholic extract of coriander seeds led to a dose-dependent increase in pentobarbital-induced sleeping time (slope= 0.21±0.04) (p<0.001) The extract significantly increased sleep duration by 95% and 189% at doses of 400 and 600 mg/kg, respectively, compared to saline-treated group (Fig 2B). Hydro-alcoholic extract of coriander seeds, at all doses used in this study caused no significant changes in latency time, relative to saline group (Fig. 2A). Diazepam significantly increased sleep duration by 246% and decreased latency time by 60%, compared to saline-treated group (Fig. 2A, B).

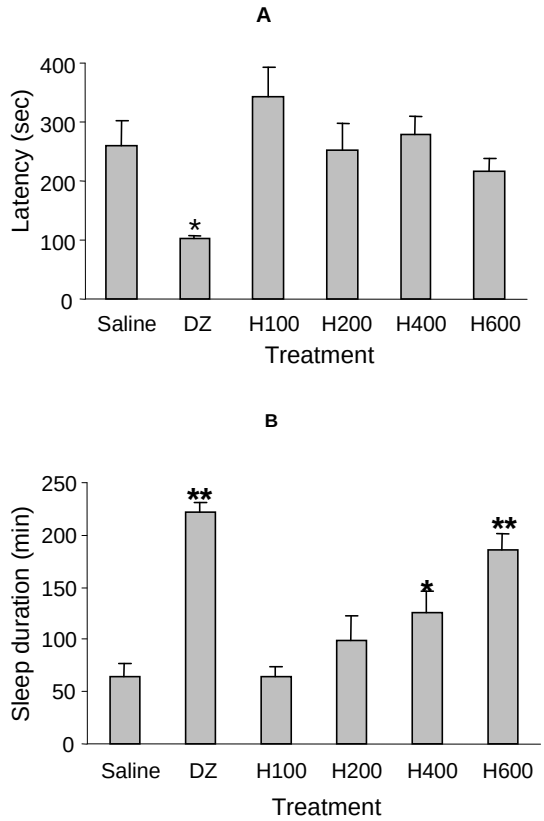

Fig 2: Effect of different doses of hydro-alcoholic extract of coriander seeds (H100-H600, ip), diazepam (DZ, 3 mg/kg, ip) and saline on pentobarbital-induced sleeping time. Bars represent mean ± SEM of latency to sleep (A) and sleep duration (B) of 7 mice in each group.
* p<0.05, ** p<0.001 compared to saline group

Effect of essential oil of coriander seeds on pentobarbital-induced sleep duration

Essential oil of coriander seeds increased sleep duration (P<0.01) in a dose dependent manner (slope= 0.17±0.05). However, the effect of essential oil on sleep duration only became significant at dose of 600 mg/kg (155%), compared to vehicle-treated group (Fig 3B). No significant changes were observed in latency time, following administration of essential oil of coriander seeds, compared to vehicle group at all doses used in this study (Fig 3A). No significant differences were found between saline and olive oil-treated groups in latency and sleep duration. Diazepam significantly increased sleep duration and decreased latency

time by 371% and 49%, respectively, compared to saline treated group (Fig 3A, B).

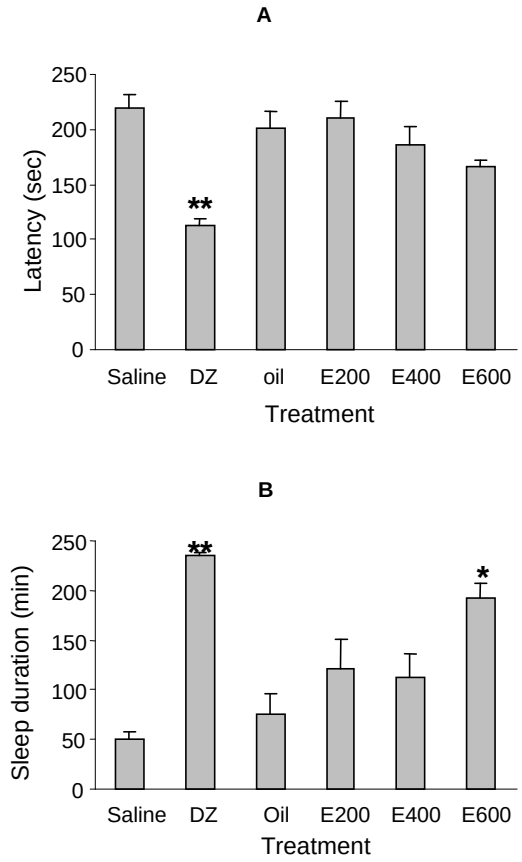

Fig 3: Effect of different doses of essential oil of coriander seeds (E200-E600, ip), diazepam (DZ, 3 mg/kg, ip) and saline on pentobarbital-induced sleeping time. Bars represent mean±SEM of latency to sleep (A) and sleep duration (B) of 7 mice in each group.
* $p<0.01$, compared to oil-treated group
** $p<0.001$, compared to saline group

Discussion

We have recently shown that the aqueous extract of coriander seed decreased general locomotor activity and neuromuscular coordination,[8] suggestive of central depressant effects of coriander. The present study, therefore, was undertaken to determine if coriander has sedative-hypnotic activity. The extracts and essential oil of coriander seeds enhanced the hypnotic effect of sodium pentobarbital, further confirming that it had sedative-hypnotic effects as claimed for this plant in traditional medicine.

Pentobarbital is a short-to-intermediate acting barbiturate that exerts its pharmacological effect on the central nervous system by enhancing inhibition of GABA-mediated neurotransmission.[12] Therefore, the potentiation of pentobarbital-induced sleeping time was used to evaluate the possible sedative-hypnotic effects of essential oil and extracts of coriander seeds. Test compounds that prolong pentobarbital-induced sleeping time are considered as sedative agents.

In agreement with the previously published reports, diazepam produced sedation at 3 mg/kg.[13,14] Aqueous extract of coriander seeds produced a substantial dose-related sedative-hypnotic effects. Its aqueous extract potentated the pentobarbital-induced sleep by decreasing the induction time and prolonging the sleep duration, which were considered to be the two aspects of a sedative effect. High dose of the aqueous extract (600 mg/kg) and diazepam were comparable in increasing hypnotic effect by 213% and 236%, respectively. However, the effect of the aqueous extract on sleep induction time was lower (20%) than that of diazepam (46%).

It is well known that benzodiazepines have anxiolytic effect at low doses and possess sedative-hypnotic effects at higher doses.[12] Aqueous extract of coriander seed at 100 mg/kg has been shown to have anxiolytic effect in mice.[8] This, together with our current observation of sedative effect of the aqueous extract of coriander at doses higher than 100mg/kg, suggest that phamacologic profile of coriander seed might resemble that of benzodiazepine receptor agonists such as diazepam.

Hydro-alcoholic extract of coriander seeds showed dose-dependent sedative activity, but lower doses of the extract (100 and 200 mg/kg) had no significant sedative-hypnotic effects. The essential oil of coriander seeds exhibited sedative-hypnotic effect only at highest doses (600 mg/kg) used in this study which was almost half of that observed with diazepam at 3 mg/kg. Neither hydro-alcoholic extract nor essential oil of coriander had any significant effect on sleep- induction time.

The results of this study is indicating that the sedative-hypnotic effect of aqueous extract of coriander seed started at a lower dose (200 mg/kg) than of its hydro-alcoholic extract (400 mg/kg) or essential oil (600 mg/kg). In addition, the highest dose of the aqueous extract, examined in this study, caused a greater increase (213%) in sleep duration compared to those of its hydro-alcoholic extract (189%) or essential oil (155%). It is also important to mention that only the aqueous extract could decrease the sleep induction time. These results strongly suggest that the phytoconstituent responsible for sedative-hypnotic effect of coriander seeds is present in the aqueous extract in high concentrations. Therefore, future studies for isolating the active components of coriander seeds should be focused on this extract.

The aqueous extract of coriander seeds contains predominantly hydrosoluble substances. In addition, a decrease in the polarity of extracting solvent from water to 70% ethanol or extraction of volatile oils decreased its sedative effect. Taken together, it is suggested that the phytoconstituents accountable for its sedative activity are hydrosoluble.

In the present study, the route of administration of extracts or essential oil of coriander seeds were ip which was different from its traditional oral route in human. Since the route of administration may affect the pharmacokinetics of the active components, the therapeutic doses and the extent of sedative effects of coriander preparations obtained here can not be extrapolated to human. Nevertheless, these results support the traditional use of coriander as a sedative-hypnotic medicine.

The active sedative constituents of coriander seeds are unknown. Further studies are needed to isolate and identify these active components. Nevertheless, several compounds, such as flavonoids, quercitin and isoquercitrin, found in the coriander seeds may account for such sedative activity. Quercitin has been shown to have sedative effect,[15] and isoquercitin glycosides isolated from *Albizzia Julibrissin* prolongs the sleep time of pentobarbital in mice.[16] In addition, many traditionally herbal medicines used as sedative-hypnotic agents like *Passiflora coerulea* or *Matricaria chamomilla* contain flavonoids such as chrycin and apigenin which have depressant effects on the central nervous system.[17,18]

Linalool, the main monoterpenoids of coriander seeds,[1] may also have sedative activity. Linalool is shown to have sedative and anticonvulsant activity in animal studies,[19] and anxiolytic and sedative activity in human studies.[20] In addition, some traditional herbs used as hypnotics, such as lavender contain linalool.[1] Other monoterpenoids such as limonene and myrcene, present in coriander seeds,[1] are shown to possess sedative and muscle relaxant effects in mice.[21,22] These compounds may also be considered as other candidates for the observed effects of coriander seeds.

The mechanism by which coriander exerts its effects has to be addressed in future studies. Compounds that acting through $GABA_A$-chloride ion channel complex prolongs pentobarbital-induced sleep duration, therefore, an involvement of GABAergic system may be suggested. Future studies using flumazenil, a benzodiazepine receptor antagonist, will address this possibility.

Conclusion

The extracts and the essential oil of coriander seeds produce central nervous depression. However, the aqueous extract of coriander seeds has much profound effects than of its hydro-alcoholic extract or essential oil. The results of this study support the use of coriander seeds as a sedative, as claimed in traditional medicine.

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References

1 Blumenthal M, Goldberg A, Brinkmann J. Coriander seed. In: Herbal Medicine-Expanded Commission E Monographs. 1st edition, Integrative Medicine Communications, Newton, MA, USA; 2000. p. 75-7.

2 Swanston-Flatt SK, Day C, Bailey CJ, Flatt PR. Traditional plant treatments for diabetes. Studies in normal and streptozotocin diabetic mice. *Diabetologia* 1990; 33: 462-4.

3 Gray AM, Flatt PR. Insulin-releasing and insulin-like activity of traditional anti-diabetic plant Coriandrum sativum. *Br J Nutr* 1999; 81: 203-9.

4 Chithra V, Leelamma S. Hypolimedic effect of coriander seeds (Coriandrum sativum): mechanism of action. *Plant Foods Human Nutr* 1997; 51: 167-72.

5 Chithra V, Leelamma S. Coriandrum sativum-mechanism of hypoglycemic action. *Food Chemistry* 1999; 67: 229-31.

6 Chithra V, Leelamma S. Coriandrum sativum: Effect on lipid metabolism in 1, 2-dimethylhydrazine induced colon cancer. *J Ethnopharmacology* 2000; 71: 457-63.

7 Duke JA. Handbook of Medicinal herbs/ James A. Duke, with Bogenschutz-Godwin M, duCellier J, Duke PK. 2nd ed. CRC press LLC, Boca Raton, Florida; USA; 2002. p. 222-3.

8 Emamghoreishi M, Khasaki M, Fath-Aazam M. Coriandrum sativum: Evaluation of its anxiolytic effect in the elevated plus-maze. *J Ethnopharmacolgy* 2005; 96: 365-70.

9 Atta-ur Rahman, Choudhary MI, Farooq A, et al. Antifungal activities and essential oil constituents of some spices from Pakistan. Third International Electronic Conference on Synthetic Organic Chemistry (ECSOC-3), www.reprints.net/ecsoc-3.htm, September 1-30, 1999.

10 de Figueiredo RO, Marques MOM, Nakagawa J, Ming LC. Composition of coriander essential oil from Brazil. ISHS Acta Horticulturae 629: XXVI International Horticultural Congress: The Future for Medicinal and Aromatic Plants. www.actahort.org/books/629/629_18.htm, 2004.
11 Turner RA. Screening procedures in pharmacology. Academic Press, New York; USA; 1972.
12 Charney DS, Mihic SJ, Harris RA.. Hypnotic and sedatives. In: Hardman JG, Limbird LE, Gilman AG eds. Goodman & Gilman's, The pharmacological basis of therapeutics. 10th ed, Mac Graw-Hill, New York; 2001. p. 399-427.
13 Helton DR, Berger JE, Czachura JF, et al. Central nervous system characterization of new cholecystokinin B antagonist LY288513. *Pharmacol Biochem Behav* 1996; 53: 493-502.
14 Nogueria E, Vassilieff VS. Hypnotic, anticonvulsant and muscle relaxant effects of *Rubus Brasiliensis*. Involvement of $GABA_A$ system. *J Ethnopharmacol* 2000; 70: 275-80.
15 Picq M, Cheav SL, Pringent AF. Effect of two flavonoi compounds on central nervous system. Analgesic activity. *Life Science* 1991; 49:1979-88.
16 Kang TH, Jeong SJ, Kim NY, et al. Sedative activity of two flavonol glycosides isolated from the flowers of Albizzia julibrissin Durazz. *J Ethnopharmacol* 2000; 71: 321-3.
17 Wolfman C, Viola H, Paladini AC, et al. Possible anxiolytic effects of chrycin, a central benzodiazepine receptor ligand isolated from Passiflora coerulea. *Pharmacol, Biochem and Behav* 1994; 47: 1-4.
18 Avallone R, Zanoli P, Puia G, et al. Pharmacological profile of apigenin, a flavonoid isolated from Matricaria chamomilla. *Biochem Pharmacol* 2000; 59:1387-94.
19 Elisabetsky E, Brum LF, Souza DO. Anticonvulsant properties of linalool in glutamate-related seizure models. *Phytomedicine* 1999; 6: 107-13.
20 Sugawara Y, Hara C, Tamura K, et al. Sedative effect on humans of inhalation of essential oil of linalool. Sensory evaluation and physiological measurement using optically active linalool. *Anal Chim Acta* 1998; 365: 293-9.
21 do Vale TG, Furtado EC, Santos JG Jr, Viana GS. Central effects of citral, myrcene and limonene, constituents of essential oil chemotype from *Lippia Alba* (Mill) n.e. Brown. *Phytomedicine*, 2002; 9:709-14.
22 da Silva VA, de Freitas JC, Mattos AP, et al. Neurobehavioral study of the effect of beta-myrcene on rodents. *Braz J Med Biol Res* 1991; 24: 827-31.