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Dose-dependent effect of *Coriandrum sativum* Linn. seeds on thermal pain stimulus

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Abstract

Aim- To evaluate the analgesic activity of the aqueous and ethanolic extracts *Coriandrum sativum* (*C. sativum*) seeds by thermal pain stimulus. **Materials & methods-** After an acute toxicity study performed as per OECD-425 Guidelines, doses of 100 mg/kg, 250 mg/kg and 500 mg/kg of each extract were selected. Wistar albino rats of either sex (100-200 g) were tested for the mean response time by Eddy's hot plate method. Statistical significance ($p<0.05$) was analyzed using ANOVA with post-hoc Dunnett's test. **Results-** Both the aqueous and ethanolic extracts showed significant and dose-dependent analgesic activity. The activity of aqueous extracts peaked at 30 min with the mean response time increasing to 5.90s, 5.92s and 6.10s with the 100 mg/kg, 250 mg/kg and 500 mg/kg doses respectively while the activity of ethanolic extracts peaked at 60 min with the mean response time increasing to 5.02s, 6.52s and 6.75s with the 100 mg/kg, 250 mg/kg and 500 mg/kg doses respectively. **Conclusion-** *Coriandrum sativum* is a plant with analgesic potential. However, further evaluation is required for analysis of the phytochemical constituents responsible for this activity.

Keywords: *Coriandrum sativum*, Coriander seeds, Analgesic, Aqueous, Ethanolic.

Introduction

A highly reputed medicinal herb belonging to family Umbelliferae is Coriander (*Coriandrum sativum* Linn.), commonly called Dhaniya. It originated from the Mediterranean and is now cultivated all over India, Italy, Netherlands, Central and Eastern Europe, China and Bangladesh.[1]

It is used in the preparation of many household medicines to cure cold, seasonal fever, nausea, vomiting, helminthic infestations, rheumatism and pain in the joints.[2] In Ayurvedic system of medicine, it has been used to treat local swelling and pain, headache, burning sensation, lymphadenopathy, stomatitis, conjunctivitis, vertigo, syncope, memory loss, digestive disorders, bleeding disorders, cough, dyspnoea and as a diuretic.[3-5]

In the ancient text of the Sushruta Samita, coriander is referred to as *Kustumvari*, which was commonly used raw and undried for digestion, as a demulcent, for thirst and to relieve burning sensations of the skin. The bitter and pungent taste was believed to purify the body and to relieve all three doshas in Indian medicine.[6]

The predominant use of *Coriandrum sativum L.* (C. sativum) in painful, inflammatory conditions and scarcity of reports on its analgesic activity motivated us to investigate

the anitnociceptive potential of its seeds.

Materials & Methods

Plant material

The seeds of *C. sativum* obtained from the local market of Aligarh, India were washed and shade-dried. The sample was authenticated by Dr. Mohd. Badrazzun Siddique, Associate Professor, Dept. of Botany, A.M.U., Aligarh and the sample voucher specimen number 47796 was obtained.

Preparation of the extracts

100 g of the seeds were finely powdered in a grinder and utilised for preparation of aqueous and ethanolic extracts each with the help of a soxhlet apparatus. The aqueous extract was a light thick, brownish semi-solid material and the ethanolic extract was an oily, greenish-brown semi-liquid material with a yield of 27.10% and 17.42% respectively. The extracts were sealed in an air-tight manner and preserved at 4^0C till further usage.

Experimental animals

Wistar albino rats of either sex (100-200 g) were housed under standard conditions (Temperature = 27 ± 2^0C, Humidity = 30-70%) with a 12 hr light-dark cycle. Standard laboratory pellet diet and water ad libitum was provided. The diet was withheld for 12 hours prior to the administration of standard and test drugs. They were acclimatized to laboratory conditions for 7 days prior to the experiments. The study protocol was approved by the Institutional Animal Ethics Committee (8335/CAH, dated 16 April 2013) and performed as per CPCSEA guidelines.

Experimental design

The animals were divided into 6 groups (n=6) as follows - Group 1 (Distilled water 1 ml/kg p.o.), Group 2 (Standard drug - Pentazocine 30 mg/kg i.p.), Group 3, 4, 5 (Aqueous, 100 mg/kg, 250 mg/kg, 500 mg/kg p.o. respectively), Group 6, 7, 8 (Ethanolic, 100 mg/kg, 250 mg/kg, 500 mg/kg p.o. respectively).

Eddy's Hot Plate

The analgesic activity was evaluated as described by Eddy and Leimbach.[7] The standard drug used was Pentazocine (Inj. Fortwin, Ranbaxy Lab. Ltd., India) 30 mg/kg i.p. They were placed individually on an electrically heated aluminium plate (Temperature = 55˚- 56˚C) in the analgesiometer (Orchid Scientifics, India). They were first screened for an initial reaction time of 6 seconds and those responding later than that were discarded. After oral administration of the control and test drugs, the response (licking of the paws) was observed at 0, 15, 30, 60, 90 and 120 minutes. The cut-off time for the reaction was 15 seconds so as to avoid injury to the paw. The plate was wiped clean with saline each time after urination/defecation by rats.

Acute Toxicity Study

This study was performed on healthy, adult female rats (150-200 g) as per OECD Guidelines 425. The animals were observed for acute (24 hrs) and subacute (14 days) toxicity.

Statistical analysis

The data is expressed as Mean ± S.E.M. and analysed using One-way ANOVA with post hoc Dunnett's test. P value <0.05 was considered significant.

Results

Acute Toxicity Study

The LD_{50} was found to be more than 2000 mg/kg for both aqueous and ethanolic extracts of *C. sativum*. There was no change in animal behavior/weight either.

Effect of extracts of *C. sativum* seeds on Eddy's Hot Plate test in rats

As shown in Table 1, the rats in the control group responded at all intervals (0, 15, 30, 60, 90, 120 min) by 6 seconds. The Standard group showed highly significant results ($p<0.001$) at 15, 30, 60, 90 and 120 min with the mean response time being 6.15s, 8.32s, 13.41s, 14.17s and 13.79s respectively. The 100 mg/kg aqueous extract treated group showed significant results at 15, 30 and 60 mins with increase in mean response times being 4.99s ($p<0.01$), 5.96s ($p<0.001$) and 5.28s ($p<0.01$). The 250 mg/kg and 500 mg/kg aqueous extracts showed significant results at 15, 30 and 60 mins with increase in mean response times being 5.11s ($p<0.01$), 5.92s ($p<0.001$), 5.18s ($p<0.01$) and 5.25s ($p<0.01$), 6.10s ($p<0.001$) and 5.24s ($p<0.01$) respectively.

Table 1: Analgesic effect of aqueous and ethanolic extracts of *Coriandrum sativum* seeds on Eddy's hot plate method in rats

Group (n=6)	Mean Reaction time (seconds)					
	0min	**15min**	**30min**	**60min**	**90min**	**120min**
DW 1 ml/kg	4.04±0.24	4.10±0.09	4.03±0.01	4.00±0.26	4.04±0.08	4.10±0.03
Pentazocine 30 mg/kg	3.73±0.33	8.32±0.75 [b]	12.92±1.53 [b]	14.17±0.82 [c]	14.55±0.44 [c]	13.41±0.74 [c]
AECS 100 mg/kg	4.01±0.21	4.99±0.23 [b]	5.90±0.39 [c]	5.28±0.18 [b]	4.44±0.10	4.25±0.22
AECS 250 mg/kg	4.09±0.31	5.11±0.13 [b]	5.92±0.21 [c]	5.18±0.16 [b]	4.38±0.14	4.27±0.12
AECS 500 mg/kg	3.93±0.10	5.25±0.21 [b]	6.10±0.18 [c]	5.24±0.24 [b]	4.61±0.10	4.33±0.10
EECS 100 mg/kg	3.74±0.14	4.08±0.23	4.67±0.09	5.02±0.25 [a]	4.68±0.11	4.31±0.11
EECS 250 mg/kg	3.93±0.10	4.21±0.14	4.99±0.20 [a]	6.52±0.31 [c]	6.09±0.39 [c]	4.38±0.13
EECS 500 mg/kg	3.74±0.11	4.30±0.13	5.27±0.20 [b]	6.75±0.16 [c]	6.55±0.18 [c]	4.91±0.06 [a]

Data were expressed as Mean ± S.E.M. Statistical significance elicited by ANOVA with post hoc Dunnett's test is expressed as a P<0.05, b P<0.01, c P<0.001 when compared to control. DW- Distilled Water; AECS- Aqueous Extract of *C. sativum*; EECS- Ethanolic Extract of *C. sativum*.

The ethanolic extracts of the 100 mg/kg group showed a significant increase in mean response time to 5.02s ($p<0.05$) at 60 min. The 250 mg/kg and 500 mg/kg groups demonstrated peak analgesic activity at 60 min, significantly increasing the mean response time to 6.52s ($p<0.001$) and 6.09s ($p<0.001$) at 60 and 90 min respectively and 6.75s ($p<0.001$), 6.55s ($p<0.001$) and 4.91s ($p<0.05$) at 60, 90 and 120 min respectively.

Discussion

The current research article deals with the analgesic activity of the aqueous and ethanolic extracts of *C. sativum* seeds in an established animal model.

The extracts showed significant and dose-dependent results in Eddy's hot plate test with the peak effect of aqueous extracts at 30 min and ethanolic extracts at 60 min. The aqueous extracts demonstrated quick onset of analgesic action which lasted for a brief duration while the ethanolic extracts showed a later onset and longer duration of action. The ethanolic extract 500 mg/kg treated group also produced the largest increase in mean response time (6.75s) among all the extracts. Our findings corroborate with other studies which reported analgesic activity of aqueous extracts of seeds using thermal pain models.[8, 9] No similar reports on analgesic activity of the ethanolic extracts of its seeds are available as yet.

Opiate receptors are probably involved in the mechanism of analgesia of *C. sativum* seeds as administration of the opioid receptor antagonist, Naloxone, reversed the anti-nociceptive effect and this was partially attributed to the presence of Linalool.[9] A major monoterpene compound called Linalool is reported to be present in *C. sativum*.[10, 11] In a similar study done by Paena *et al*, 2003 using Linalool, a complete reversal of its analgesic effect was seen with Naloxone.[13] Therefore, certain constituents of C.sativum extracts like Linalool may be exhibiting an opioid-like effect.

(-)-linalool is the natural occurring enantiomer of the essential oils of several aromatic plant species. Its antinociceptive effect has been ascribed to the stimulation of the cholinergic, opioidergic and dopaminergic systems, to its local anaesthetic activity and to the blockade of N-Methyl-d-aspartate receptors.[13] Based on experiments with rats using (14) C-labelled substance, linalool is rapidly absorbed from the intestinal tract following oral uptake and judging from the delay in fecal excretion, intestinal absorption is complete.[14] Subsequent to absorption, linalool is metabolized rapidly, with urinary excretion of (14)C activity starting without delay.[14]

Coriandrum sativum seeds contained about 79% Linalool when determined through Soxhlet extraction, 77.9% through hydrodistillation and 82.9% through subcritical water extraction.[15] Analysis of coriander seed essential oil by Gas chromatography and Mass spectrometry techniques showed the presence of more than 52 components, the major being linalool (75.30%).[16] Fatty acid oil is different (contains oleic, petroselinic and linolenic fatty acids and not linalool) and therefore, should not be confused with essential oil of coriander.[11] Hence, it is possible that the aqueous extracts contain a higher amount of Linalool as compared to the ethanolic extracts, explaining their faster and shorter-lasting action.

Apart from Linalool, other major constituents like γ-terpinene, camphor, α-pinene, geraniol and geranyl acetate may have a role to play in its anti-nociceptive action.[2]

Therefore, we would conclude this study by reporting that the extracts of *C. sativum* possess significant and dose-dependent analgesic activities. Moreover its use in painful, inflammatory conditions since ancient times demands further exploration of its analgesic potential.

Conflict of interest statement

We declare that we have no conflict of interest of any kind.

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