ANALGESIC ACTIVITY OF METHANOL EXTRACT OF CORIANDRUM SATIVUM LINN FRUIT

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ABSTRACT
The analgesic activity of 75 % methanol extract fruit of Coriandrum sativum Linn were tested against Eddy’s hot plate method and tail flick method. Animals were treated with distilled water, paracetamol and 100, 200,400 mg/kg body weight 75 % methanol extract of C.sativum. In hot plate method, the reaction time (in seconds) or latency period was determined as the time taken for the rats to react to the thermal pain by either Paw licking or jumping. The reaction time was recorded before (0 min) and at 30, 60, 90, 120 and 150 min after the administration of the treatments. In tail flick method, the response time was noted as the sudden withdrawal of the tail from the hot water. The reaction time was recorded before (0 min) and at 30, 60, 90, 120 and 150 min after the administration of the treatments. The result in the hot plate study shows that 100 mg/kg is very effective when compared to 200 and 400 mg/kg extract and in tail flick method 400 mg/kg had better effect when compared to 100 and 200 mg/kg extract. The above results suggest the analgesic activity of the 75 % methanol extract of fruit of C.sativum.

KEYWORDS: Coriandrum sativum, analgesic activity, Eddy’s hot plate method, tail flick method, paracetamol

INTRODUCTION
Reverse pharmacology is gaining importance to treat most of the common ailments since the available remedies in modern medicine are known to cause side effects. During 1980s exhaustive studies on plant products were carried out, however, on plant principles. World
Health Organization (WHO), then insisted on the identification of active principles followed by investigations on pharmacological actions. Unfortunately, significant outcome was not reported. One of the contributing factors for this may be the loss of activity during isolation of active principles with various polar/ non-polar solvents. In order to overcome this hurdle, WHO recommended that scientific support for the herbal products for use in humans could be provided only by using the recommended formulations in the ancient medicine and allowed its use in human being.\textsuperscript{[1,2]} A significant momentum gained after this created a renewed interest in herbal research.

One of the most common ailments for which humans seek remedy to alleviate is pain. Many over the counter drugs such as paracetomol, is used frequently besides, the use of non steroidal anti-inflammatory drugs are also used. Unfortunately, all the available analgesic and anti-inflammatory agents induce side effects\textsuperscript{[3]}. Therefore it is essential to identify a suitable safe analgesic drug from the herbal source having minimal side effects.

Coriander [\textit{Coriandrum sativum} Linn.] an annual of the Apiaceae family is one of the valuable medicinal and seasoning plant. This species comes from the Mediterranean region and it is grown all over the world. The coriander fruit and essential oil isolated from it are used for medicinal purpose.\textsuperscript{[4,5]} \textit{C. sativum} is widely used in traditional medicine to treat anxiety, dizziness, headache, edema, fever, digestive disorders, respiratory diseases, allergies, and burns.\textsuperscript{[6,7]} The fruits are used as astringent, anthelmintic, emollient, stomachic, antibilious, digestive, appetizer, constipating, diuretic, antipyretic, refrigerant, tonic, expectorant, anodyne, antidiabetic and dyspepsia. The phytochemical screening of \textit{Coriandrum sativum} showed that it contained essential oil, tannins, terpenoids, reducing sugars, alkaloids, phenolics, flavonoids, fatty acids, sterols and glycosides. It also contained high nutritional values including proteins, oils, carbohydrates, fibers and wide range of minerals, trace elements and vitamins. The previous pharmacological studies revealed that it possessed anxiolytic, antidepressant, sedative-hypnotic, anticonvulsant, memory enhancement, improvement of orofacial dyskinesia, neuroprotective, antibacterial, antifungal, anthelmintic, insecticidal, antioxidant, cardiovascular, hypolipidemic, anti-inflammatory, analgesic, antidiabetic, mutagenic, antimutagenic, anticancer, gastrointestinal, deodorizing, dermatological, diuretic, reproductive, hepatoprotective, detoxification and many other pharmacological effects.\textsuperscript{[8-12]}
Silver nanoparticles were synthesized using methanol and aqueous extract of fruit of *C. sativum* and its antioxidant activity were reported.\[^{[13]}\] We have reported better activity with 75 % methanol extract of fruit of *C. sativum* and HPTLC data also showed that 75 % methanol extract has more number of phytoconstituents than all other extract. In the light of the above information, the present investigation was under taken to evaluate the analgesic activity with this concentration using Eddy’s hot plate method and tail flick method.

**MATERIALS AND METHODS**

**Plant material**

The *Coriandrum sativum* fruits were collected from local market in Bangalore, Karnataka, India and it was identified and authenticated by Botanist, Natural Remedies Pvt Ltd., Bangalore. A voucher specimen was deposited in The Oxford College of Pharmacy, Bangalore. The fruits were dried in shade and powdered coarsely, passed through sieve no. 40 and stored in air tight container for further use.

**Preparation of fruit extract**

Coarsely powdered fruits of *C. sativum* 200 g was extracted with 75 % methanol [1500 ml] in soxhlet apparatus till the complete exhaustion, filtered. The methanol extract was concentrated by rotary vacuum evaporator and evaporated to dryness.

**Chemicals used**

The drug paracetamol was procured from M/s yucca enterprises, Mumbai and all other chemicals and solvents used were of analytical grade.

**Animals**

Mature Albino rats of both the sexes obtained from the Animal house of The Oxford College of Pharmacy, Bangalore were used for the studies. Rats were maintained under standard conditions (27 ± 2°C; relative humidity 60 ± 5 %, light dark cycle of 12 hrs) and fed with standard pellet diet and water *ad libidum*. Prior to the experiment the animals were fasted for 12 h with water *ad libitum* given and weighed. All procedures described were reviewed and approved by Institutional Animal Ethics Committee.

**Acute Toxicity Study**

The toxicity study reveals the safety of *Coriandrum sativum* in Rat. There was no marked change in the general behavior up to 2000 mg/kg., body weight of *C. sativum*. No mortality was observed during the observation period as per literature study.\[^{[14]}\]
Analgesic Activity
Analgesic activity of *C. sativum* were determined by following methods.

**Eddy's Hot Plate Method**
Evaluation of analgesic activity of the extract was carried out using hot plate method.\(^{[15]}\) The animals were divided into five groups of six animals each. Group I served as control. Group II served as standard and were given orally paracetamol (100 mg/kg). Group III, IV and V were treated orally with 75% methanol extract of *C. sativum fruit* at the dose of 100, 200 and 400 mg/kg body weight, respectively. The rats were placed on a hot plate maintained at 55°C within the restrainer. The reaction time (in seconds) or latency period was determined as the time taken for the rats to react to the thermal pain by either Paw licking or jumping. The reaction time was recorded before (0 min) and at 30, 60, 90, 120 and 150 min after the administration of the treatments. The Cut off period was fixed at 15 sec to prevent any injury to the tissues of the paws. If the reading exceeds 15 sec, it would be considered as maximum analgesia.

**Tail Flick Method**
The animals were divided into five groups of six animals each. Group I served as control. Group II served as standard and were given orally paracetamol (100 mg/kg). Group III, IV, and V were treated orally with 75% methanol extract of *C. sativum* fruit at the dose of 100, 200 and 400 mg/kg body weight, respectively. After one hour, the tip of tail was dipped up to 5 cm into hot water maintained at 58°C. The response time was noted as the sudden withdrawal of the tail from the hot water. Cut off time of 10 seconds was maintained to avoid damage to the tail for all groups. The time required for flicking of the tail, was recorded, to assess response to noxious stimulus.\(^{[16]}\)

**Statistical analysis**
The data is expressed as Mean ± S.E.M. and analysed using One-way ANOVA with with Tukey Kramer multiple comparison test. P value < 0.5 was considered significant.

**RESULTS AND DISCUSSION**
Analgesics are drugs that act on peripheral or central nervous system to selectively relieve pain without significantly altering consciousness.\(^{[16]}\) Centrally acting analgesics act by raising the threshold for pain and also altering the physiological response to pain. On the other hand, peripherally acting analgesics act by inhibiting the generation of impulses at chemoreceptor
site of pain. The animal models employed for screening of analgesic activity in this study are pain-state models using thermal stimuli which include tail-flick and hot plate methods. Both methods are useful in illustrating centrally mediated antinociceptive responses which focus generally on changes above the spinal cord level. While the tail-flick method mediates a spinal reflex to a nociceptive stimulus, hot plate method involves higher brain functions and is regarded a supraspinally organized response.

Hot plate method produces two measurable behavioural components in response to thermal pain, with regard to their reaction times. Responses such as paw licking and jumping in rats are considered to be supraspinally integrated. The results of the analgesic effect of the methanol extract of the seeds of *C. sativum* using hot plate method are presented in Table no. 1 and Fig: 1. The results showed that there was no significant difference on the thermal stimulus in rats treated with normal saline (negative control) throughout the 150 min observation. There was no increase in reaction time at all time points compared to baseline values (0 min) within the same treatment groups. However, the analgesic activity in Paracetamol and extracts treated animals is noted from 30 minutes onwards till 150 min which peaked at 60 minutes for paracetamol and for extracts it was 90 minutes. The result in the hot plate study shows that 100 mg/kg is very effective when compared to 200 and 400 mg/kg extract.

The tail-flick method is based on the observation that morphine-like compounds are selectively able to prolong the reaction time of typical tail-withdrawal effect in rats. Analgesic drugs which are centrally acting elevate pain threshold of animals towards heat and pressure. The results of the analgesic effect of the methanol extract of the seeds of *C. sativum* using tail flick method are presented in Table no. 2 and Fig :2. The results showed that there was no significant difference on the thermal stimulus in rats treated with normal saline (negative control) throughout the 150 min observation. There was no increase in reaction time at all time points compared to baseline values (0 min) within the same treatment groups. However, the analgesic activity in Paracetamol and extracts treated animals is noted from 60 minutes onwards till 120 min which peaked at 90 minutes for paracetamol and for extracts. The result in the tail flick study shows that 400 mg/kg is very effective when compared to 100 and 200 mg/kg extract. Findings from this study demonstrated that the methanol extract at the dose of 100 mg/kg prolonged the reaction time in the hot plate method but showed an apparent less effect in the tail-flick method. Taken together, the differences in
sensitivity of both methods as well as the mechanism involved may explain the analgesic effects observed in this study. However the 75% methanol extract showed good analgesic activity in both model.

Eddy’s Hot plate method is a better method to evaluate analgesic activity compared to Tail immersion method. This observation is in agreement with findings of which reported that the extract of *C. sativum* produced a significant elongation of reaction time in hot plate method but not in Tail immersion method reaction time. Both treatments produced comparable reaction times, suggesting that the fruit of *coriander sativum* could be a better natural alternative for mild pain relief.

**Table 1: Analgesic activity of methanol extract of *Coriandrum sativum* fruit by hot plate method**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Reaction time in seconds</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 min</td>
</tr>
<tr>
<td>Control</td>
<td>3.67 ± 0.51</td>
</tr>
<tr>
<td>Paracetamol 100 mg/kg</td>
<td>3.67 ± 0.51</td>
</tr>
<tr>
<td>CS 100 mg/kg</td>
<td>4.00 ± 0.63</td>
</tr>
<tr>
<td>CS 200mg/kg</td>
<td>4.17 ± 0.40</td>
</tr>
<tr>
<td>CS 400 mg/kg</td>
<td>3.80 ± 0.44</td>
</tr>
</tbody>
</table>

Data were expressed as Mean ± S.E.M. Statistical significance elicited by ANOVA with Tukey Kramer multiple comparison test and is expressed as <sup>a</sup>P<0.05;  <sup>b</sup>P<0.01;  <sup>c</sup>P<0.001 when compared to control. CS-75 % methanol extract.

**Table 2: Analgesic activity of methanol extract of *Coriandrum sativum* fruit by tail flick method**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Reaction time in seconds</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 min</td>
</tr>
<tr>
<td>Control</td>
<td>4.17 ± 0.75</td>
</tr>
<tr>
<td>Paracetamol 100 mg/kg</td>
<td>4.33 ± 1.86</td>
</tr>
<tr>
<td>CS 100 mg/kg</td>
<td>3.83 ± 0.98</td>
</tr>
<tr>
<td>CS 200mg/kg</td>
<td>3.83 ± 0.75</td>
</tr>
<tr>
<td>CS 400 mg/kg</td>
<td>4.20 ± 0.44</td>
</tr>
</tbody>
</table>

Data were expressed as Mean ± S.E.M. Statistical significance elicited by ANOVA with Tukey Kramer multiple comparison test and is expressed as <sup>a</sup>P<0.05;  <sup>b</sup>P<0.01;  <sup>c</sup>P<0.001 when compared to control. CS- 75 % methanol extract.
CONCLUSION

Renewed interest on the use of herbal products is gaining importance. This is because the World Health Organization has agreed for reverse pharmacology as described in the review of literature. Globally, many herbal products are being used as food supplements for prophylaxis of common ailments such as hypertension, diabetes etc.

Prior to the pharmacological investigation of any herbal product it is mandatory to investigate the safety profile of these herbal products. It is documented that if a herbal substance is free from side effects or adverse effects up to 2000 mg/kg, it is considered safe for clinical use, the absence of acute toxicity is observed thus proving the safety profile of C. sativum

The 100 mg/kg dose of C. sativum 75% methanol extract showed better activity when compared to 200 and 4000mg /kg dose in hot plate method. The 400 mg/kg dose of 75% methanol extract showed better activity when compared to 100 and 200 mg /kg dose in tail flick method. The above results suggest the analgesic activity of the 75 % methanol extract of fruit of C. sativum and it could be a better natural alternative for pain relief.
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Conflict of Interest
None to be declared

REFERENCES


