

A Review On Analgesic Activity of Coriander Fruit Extract in Mice

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ABSTRACT

Medicinal plant, *Coriandrum sativum* has a good therapeutic strategy, can be used to treat spectrum of diseases. *Coriandrum sativum* is a plant from Apiaceae (Umbelliferae) family. Numerous report indicate that Coriander sativum has positive effects on anxiety, stress, seizure, learning and memory ability, as well as Analgesic. This annual plant can also treat colitis, increase appetite, reduce blood pressure, and myocardial damage. Additionally, it improves liver and kidney function and diabetes mellitus and inhibits osteoclast activity. Among this it has good Analgesic Activity. These beneficial effects of Coriander sativum are attributed to its antioxidant and anti-inflammatory properties. We obtained analgesic activity of Coriander fruit extract in mice is positive from the present paper reviews the impacts of Coriander sativum on different body systems. Information was extracted by searching the web of science, Pub Med and Google scholar.

KEYWORDS: *Coriandrum sativum*, Analgesic activity

INTRODUCTION:

Coriander is the seed of an annual small plant like parsley which belonging the Umbelliferae family and is usually refers to spice is one of the oldest spice crops in the world. Coriander is most likely native of the eastern Mediterranean and from there spread to India, china and rest of the world. India is the largest producer of coriander which is used extensively in curry powder .The seeds of coriander are almost ovate globular and there are many longitudinal ridges on the surface. The length of seed is 3-5 mm and color, when dried, is usually brown, but may be green, straw-colored or off white.¹

Generally, the seed is sell sun dried and made available for both whole and ground. Coriander seed have a mild, sweet, slight pungent, like citrus flavor with a hint of coriander seeds are the essential oil and fatty oil. The essential oil content of dried coriander seeds varies between 0.03% and 2.6% fatty oil content varies between 9.9% and 27.7%. Other constituents, crude protein, fat, crude fiber and ash contents vary from, respectively and Main component of essential oil in seeds of coriander is linalool . and varies between 50% and 70%. The whole seeds or ground coriander is an ingredient of pickling spices also used to flavor various commercial foods, particularly prepare some instant soups and dishes, in many cakes, breads and other pastries, alcoholic beverages, frozen dairy desserts, candy, and puddings. Sugared comfits made from the coriander seeds are a traditional sweet food Its essential oil is a common ingredient in creams, detergents, surfactants, emulsifiers, lotions, and perfumes.²

The Medicinal plants as a suitable therapeutic strategy are widely prescribed by traditional reason for this is that phytochemicals presented in their extracts have fewer side effects than chemical medicines³ Medicinal plants are applied to relieve a variety of disorders and diseases such as cardiovascular diseases, psychiatric ailments, gastrointestinal disorders, metabolic syndrome, respiratory disturbances, renal and hepatic injuries, and cancer. *Coriandrum sativum* (*C. sativum*) (coriander) is an annual plant from Apiaceae family with a height of 20 cm-70 cm. Its leaves are bright green with straight, transparent, and soft stems. White flowers are located at the end of stem and the fruits are brown in color and oval in shape.⁴

All parts of *Coriandrum sativum* are edible and can be used in traditional medicine. Fresh leaves and stem of *Coriandrum sativum* possess some constituent like minerals, vitamins, and lipids and its seeds contain compounds such as linoleic acid, linalool, kaempferol, quercetin, gallic acid, and caffeic acid. *C. sativum* is reported to have antioxidant⁵. Anti-inflammatory, anti-diabetic, anti-microbial, anti-parasitic⁵, and analgesic⁵ activities.⁵ The positive effects of *C. sativum* on flatulence, diarrhea, and other gastrointestinal disorders have been also documented. The *C. sativum* extract protects nigral dopaminergic neurons against 6-hydroxydopamine. Additionally, it has anti-toxicity effects against heavy metals such as arsenic. Tousson et al. demonstrated that *C. sativum* seed extracts could alleviate carbendazim-induced testicular toxicity. In other studies, the sedative anti-aging and anticancer activities of *C. sativum* have been also reported.⁶

This review summarizes the beneficial effects of *C. sativum* extracts on diverse body systems.

CORIANDER

Synonyms: Dhania.

Biological source: Dried ripe fruits of *Coriandrum sativum*. It contains not less than 0.3 % volatile oil .

Family: Umbelliferae

Chemical constituent- it contain an essential oil. The different parts of this plant contain linalool, camphor, coriandrin, geraniol, dihydrocoriandrin, coriandrone A-E, flavonoides, fixed oil, malic acid and tannins.

Use: It is used as a stomachic, spasmolytic and carminative which have a greater bioactive property. It also posses antioxidant activity, diuretic , anticonvulsant, antidiabetic activity, sedative, hypnotic activity , antimutagenic, antimicrobile activity. Among this due to linalool constituent its show analgesic activity.

MACROSCOPIC CHARACTER

Colour: Yellowish-brown to brown

Odour: Aromatic

Taste: Spicy and characteristics

Shape: Sub-globular cremocarpous fruit

Size: Fruits are 2-4 mm in diameter and 4-30 mm in length

Extra Features: About 10 primary ridges and 8 secondary ridges are present. Primary ridge are wavy and inconspicuous, while secondary ridge are straight.



Figure 1- coriander seed

Microscopical

characters:

1. Pericarp

- a) **Epicarp:** single layer, thickened, polygonal cells with occasional stomata and calcium of oxalate crystal, from 0.003 to 0.01 mm. in diameter, mostly in rosette aggregates, either isolated or in aleurone grains; covered by smooth cuticle.
- b) **Mesocarp:** Inner and outer layer of parenchyma with sclerenchyma in between.
- c) **Outer layer:** poorly arranged tangentially elongated non-lignified parenchyma, lacunae at dorsal side.
- d) **Middle layer:** fusiform, lignified sclerenchymatous cells in sinuous cells in tangential and longitudinal bands.
- e) **Vascular bundle:** Five vascular bundles at dorsal side, present above longitudinally elongated sclerenchyma.
- f) **Two vittae:** On the commissural surface and four lacunae on the dorsal surface.
- g) **Inner layer:** large irregular, hexagonal, lignified parenchyma.
- h) **Endocarp:** Elongated cells forming parquetry layer.

2. seed

- a) **Testa:** singal layer and yellowish in color.
- b) **Endosperm:** Thick walled, polygonal, cellulosic parenchyma cotaining oil globules and aleurone grains.

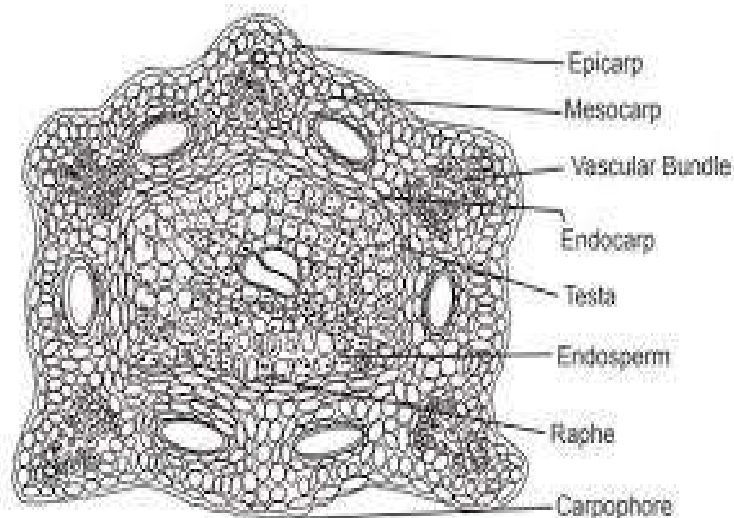


Figure 2- T .S of coriander fruit

Pharmacological Action of Coriander

- **Antioxidant:** Coriander has antioxidant properties protect against neurodegenerative diseases, cancer, and metabolic syndrome.
- **Anticonvulsant:** Coriander extracts can reduce the duration of tonic seizures.
- **Anti-Inflammatory:** Coriander can inhibit joint swelling in arthritis.
- **Neuroprotective: Coriander** can improve cognitive function and locomotor activity.
- **Anxiolytic:** Coriander can help with anxiety.
- **Antimicrobial:** Coriander can be antibacterial and antifungal.
- **Antidiabetic:** Coriander can help with diabetes.
- **Cholesterol –lowering:** Coriander can help lower cholesterol.
- **Diuretic:** Coriander can act as a diuretic.
- **Anti-ulcer:** Coriander can help with ulcers.
- **Hepatoprotective:** Coriander can protect the liver.

Coriander contains many bioactive phytochemicals, including linalool, phenylpropenes , terpenoids , isocoumarins , phytosterols , and fatty acids.Linaloolis the maincompound in coriander seeds and has many health benefits.

PAIN

Pain has been described by the International Association for the Study of Pain as an “unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”.⁷Chronic pain and the inflammatory diseases are one of the major health problems in the world.² Several factors including socio-cultural, psychological and biological conditions have important roles in pain perception. Although pain is a reaction of the body to harmful stimuli, it is a protective early warning system. In medical diagnosis, pain is regarded as a symptom of an underlying condition.¹ Pain is a vital function of the human body, involving nociceptors and the central nervous system (CNS) to transmit messages from noxious stimuli to the brain.⁸

Types of pain:

Simply, pain can be divided into two types acute pain and chronic pain.

- A. **Acute pain:** Acute pain is pain of sudden onset; lasting for hours to days and disappears once the underlying cause is treated. Acute pain has a clear cause. It could result from any illness, trauma, surgery or any painful medical procedures. Acute pain is beneficial for us as it signals that something is wrong in our body and motivates us to get help soon.
- B. **Chronic pain:** Chronic pain is the pain that starts as an acute pain and continues beyond the normal time expected for resolution of the problem or persists or recurs for various other reasons. It is not therapeutically beneficial to the patient

Analgesic drugs are used in single or in combination to affect peripheral or Central Nervous System (CNS) to decrease pain sensation. Analgesics are drugs that relieve pain Without significantly altering consciousness. They relieve pain without affecting its cause. There are two groups of analgesics:

- Opioid (Narcotic analgesics)
- Non- opioid (Non-steroidal anti-inflammatory drugs)

Opioids are substances that,

When reaching opioid receptors have effects similar to those of morphine. Medically they are primarily used for pain relief, including anesthesia. Other medical uses include suppression of diarrhea, replacement therapy for opioid use disorder, reversing opioid overdose as well as suppressing cough. Morphine is the most important alkaloid of opium - the dried juice obtained from the capsules of *Papaver somniferous*. Opium contains many other alkaloids, such as codeine, thebaine, papaverine etc.

Mechanism of action of opioids: Morphine and other opioids produce their actions by interacting with various opioid receptors - mu (μ), kappa (κ) and delta (δ). They inhibit the release of neurotransmitters from the primary afferent terminals in the spinal cord as well as activate the descending inhibitory controls in the brain. This results in the sensation of pain relief as well as a relaxing and sedative effect. Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most widely used medications due to their efficacy for a wide range of pain and inflammatory conditions. However, the long-term administration of NSAID may induce gastrointestinal ulcers, bleeding, and renal disorders due to their nonselective inhibition of both constitutive (COX-1) and inducible (COX-2) isoforms of the cyclooxygenases enzymes. Therefore, new anti-inflammatory and analgesic drugs lacking those effects are being searched all over the world as alternatives to NSAIDs and opiates. The research into plants with alleged folkloric use as pain relievers, anti-inflammatory agents, should therefore be viewed as a fruitful and logical research strategy in the search for new analgesic and anti-inflammatory drug. The plant derived natural products such as flavonoids, sterols, poly-phenols, alkaloids, tannins and terpenes have gained importance in recent years due to their wide range of pharmacological activities.¹²

Coriandrum sativum Linn. (Apiaceae/ Umbelliferae) is a native plant from southern Europe and Southwestern Asia that has been naturalized in North America and acclimatized in many countries with a temperate climate. It is popularly known as coriander, Chinese parsley, or cilantro, and it has been used to add flavor, color and nutritional properties to food in many Asian countries. Parts of *C. sativum* (CS) have been used to treat many diseases and conditions, such as rheumatism/ joint pain, indigestion/ gastrointestinal disorders, anxiety etc. Its antioxidant, anti-diabetic, anticancer properties have previously been reported. This study was conducted to explore analgesic effect of leaves and seeds of *Coriandrum sativum* was assessed using hot plate method and acetic acid induced writhing method in Swiss albino mice.⁹

MATERIAL AND METHOD

The analgesic effect of leaves and seeds of *Coriandrum sativum* was assessed using Eddy's hot plate method and acetic acid induced writhing method in Swiss albino mice. The animals were treated with the ethanolic extract of leaves and seeds of *Coriandrum sativum* administered orally

at two doses of 100, 500 mg/kg body weight after electric heat and acetic acid induced pain in mice. This study was carried out in lab.¹⁰

Animals

Swiss Albino mice (*Mus musculus*) either sex weighing 23-32mg (four weeks of age) were kept in the animal house in the lab. All the animals were housed in clean polypropylene cages and were maintained at standard conditions of temperature ($25 \pm 1^\circ\text{C}$) and 12:12 hour light/ dark cycles. They were fed with standard pellet diet and had free access to water ad libitum.¹¹

Plant material

The aerial parts of the leaves and seeds of *Coriandrum sativum* were collected from various regions. The selected plant was identified.¹²

Preparation of extract

The aerial parts of the leaves and seeds of *Coriandrum sativum* collected were washed thoroughly with water and air dried under shade at room temperature. Then, the dried plant materials were chopped into small pieces and finely ground to give powder form of crude drug. The drug was extracted using ethanol as solvent by continuous hot percolation with the help of Soxhlet apparatus. The duration of extraction was 48 hours. The extract was reduced to dryness using rotary apparatus. The seed and leaves were extracted separately using the same method.^{12/13}

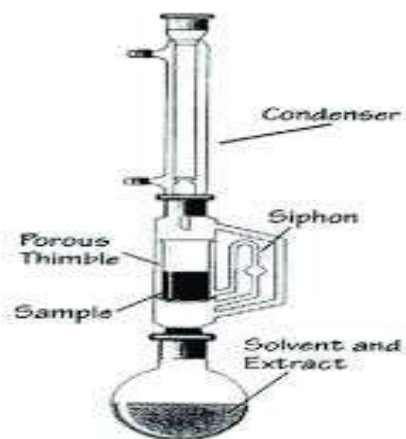


Figure 3- soxhlet apparatus

Phyto-chemical screening

Phyto-chemical screening was carried out for the determination of different secondary metabolites (Carbohydrate, glycosides, saponin, sterols, tannins, terpenoids, flavonoids,¹⁴ and alkaloids) present in the leaves and seed extract of *Coriandrum sativum*.

Dose selection

Lethal dose 5000 ml/kg selected and two doses of 100 ml/kg and 500 ml/kg body weight of ethanolic extract of *Coriandrum sativum* leaves and seeds was selected as low dose and high dose as per the acute oral toxicity studies.¹⁵

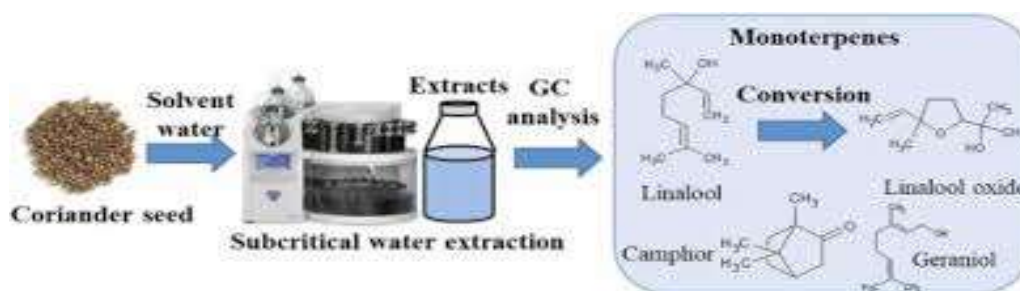
Experimental design

The mice were randomly divided into four groups each for leaves and seeds extract. So total groups are six including negative control and standard (n=5 mice per group). Thus, 30 mice were used for the evaluation of analgesic effect of *Coriandrum sativum* leaves and seed.¹⁶

Experimental design groups for seed extraction.

Table 1. Experimental design groups each for leaves and seeds extract

| Leaves extract | | Seed extract | |
|------------------------------|----------------------------------|------------------------------|----------------------------------|
| Animal Group | Dose | Animal Group | Dose |
| Negative control | Disease induced and vehicle only | Negative control | Disease induced and vehicle only |
| Standard (Diclofenac sodium) | 10 mg/kg | Standard (Diclofenac sodium) | 10 mg/kg |
| Test-1 | 100 mg/kg | Test -1 | 100 mg/kg |
| Test-2 | 500 mg/kg | Test-2 | 500 mg/kg |



Nociceptive test

To assess nociceptive responses, hot plate method was used. The mice were placed on the hot plate with temperature setting controlled at 55 ± 0.20 C. Cut-off time was 60 s. Nociceptive response was defined as licking forepaws or moving hind paws. Time duration between placing the animals on hot plate and licking fore paws or moving hind paws was considered as the reaction time. The hot plate test was performed as a base record 10 min before injection of the

drugs and consequently it was repeated 5 times, every 10 min after injection. Analgesic effects of the extracts or vehicle were calculated as maximal possible effect (MPE) [MPE (%) = [(test response time-basal response time)/(cutoff time-basal response time) × 100%] (1- 3, 27-29).^{17/18}

Statistical analysis

All data were expressed as Mean ± SEM and analyzed by using ANOVA followed by Tukey's post hoc comparison test. P values less than 0.05 were considered to be statistically significant.¹⁹

Collection of Crude Drug: Dried seeds of coriander were purchased from a commercial source in North Maharashtra (Nashik). The identity of the seed was confirmed by the Botanical Survey of India, Koregaon Park, Pune (Maharashtra). A voucher specimen was kept in our laboratory for future reference.²⁰

Preparation of Aqueous Extract

Dried coriander seeds were homogenized to a fine powder. Hundred grams of powdered coriander was infused in 500 ml cold ethanol for 24 h, brought to the boil, then removed from the heat source and allowed to infuse for 15 min. The extract was filtered, may concentrated over the water bath and brought to dryness under vacuum. The yield of the extract was 7.9%.²¹

Analgesic Effect

Method- hot plate method

Equipment- Eddy's hot plate

Principle

Analgesia is defined as state of reduced awareness to pain, and analgesics are substances which decrease pain sensation (pain-killers) by increasing threshold to painful stimuli. The commonly used analgesics are aspirin, paracetamol (nonnarcotic type) and morphine (narcotic type). Painful reaction in experimental animals can be produced by applying noxious (unpleasant) stimuli such as (a) thermal (radiant heat as a source of pain), (b) chemical (irritant such as acetic acid and bradykinin) (c) physical pressure (tail compression). In the laboratory, commonly used procedures are tail –flick (tail withdrawal from radiant heat) method using analgesiometer, hot plate (jumping from hot plate at 55 C) method and acetic acid- induced writhing 20. Animals -- Albino mice Weight -- 22 to 28 gms. Sex -- either sex.²²

Sample Preparation

1. **Control** - Saline solution.

2. **Standard** - Morphine sulphate (5mg/kg i.p) was Prepared as stock solution containing 0.5 mg/ml of the drug & injected 1ml/100 g of body weight of the mouse.

3. **Test-** Coriander extracts 50, 100 & 200 mg/kg.

Animal groups

Each group was containing 5 animals Group-I: was received Control (Saline) solution.

Group-II: was received Std. (Morphine) drug.

Group-III: was received Test-1 (Coriander extract-50mg/kg) drug.

Group- IV: was received Test-2 (Coriander extract-100mg/kg) drug.

Group- V: was received Test-3 (Coriander extract-200mg/kg) drug.²³

Procedure

1. Animals were weighed, numbered & divided them into six groups each containing of 5 mice. One group was used as control (saline), second for drug (Morphine sulphate) std. treatment & third, fourth & fifth group for coriander extract treatment (Test).

2. Basal reaction –time were noted by observing hind paw licking or jump response (whichever appears first) in animal when placed on the hot plate maintained at constant temp (55C). Normally animals show such response in 6 -8 sec. a cut off period of 15 sec was observed to avoid damage to the paws.

3. Saline, Morphine & coriander extract were injected as per animals groups & reaction time of animals was noted on the hot plate at 15, 30, 60, & 120 min after the drug administration.

4. Percent increase in reaction time (as index of analgesia) at each time interval was calculated. PIP was calculated using following formula

$$= \frac{T_t - T_c}{T_c} * 100 .$$

Where , T_c = Time required to lick a paw in control animal

T_t = Time required to lick a paw in treated animal.²⁴

STATISTICAL ANALYSIS

The statistical significance was assessed using one –way analysis of variance (ANOVA) followed by Dunnet comparison test. The values are expressed as mean \pm SEM .²⁴

Analgesic Activity**Hot plate Method**

AECS produced significant analgesic activity ($P < 0.001$) against Hot Plate method was in dose dependent manner. The Analgesic effects of the AECS by the hot plate method in mice were

summarized in (Table 5). Pretreatment with the extract significantly increased reaction time in comparison to control. At a dose of 200

mg/kg of AECS exhibited analgesic effect and reaction time was 5.281 sec. while standard drug Morphine 5 mg/kg i.p. had reaction time of 6.282 sec. At a dose of 200 mg/kg AECS shows more than 50% Pain Inhibition Percentage (PIP) as compared to control.²⁵

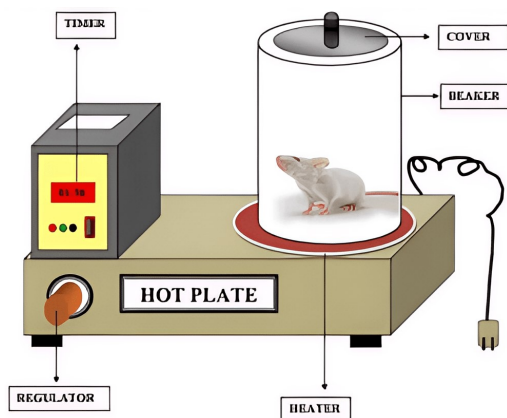


Fig 4- Hot Plate Method

Table 2 : Effect of alcoholic Extract of *Corianderum sativum* L

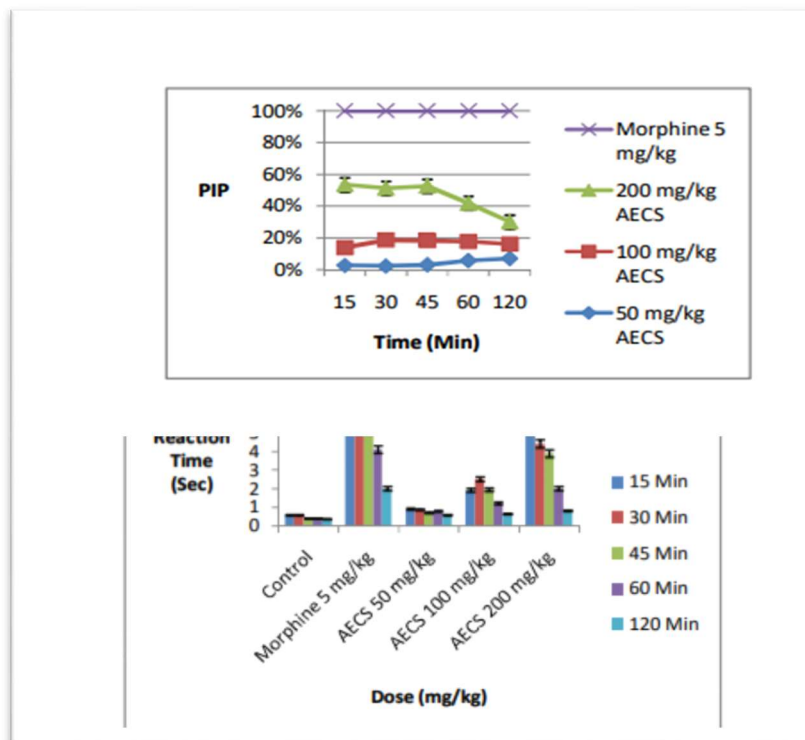


Fig 5- Effect of alcoholic extract of coriander sativum. On hot plate method in mice. (pain inhibition percentage)

Observation

When acetic acid is injected into the mice they exhibit a characteristic writhing behavior as a reaction to the pain. This behavior is used in a screening tools to assess the anti-inflammatory or analgesic properties of various agents. This test is known as acetic acid induced abdominal writhing test.

How the test is performed

A 3% solution of acetic acid in sterile distilled water is injected into the peritoneal cavity of the mice. When acetic is injected into mice, they exhibit a characteristic writhing response as a result of intense pain.

Writhing

A mouse’s response to the pain a series of writhing movements, including stretching tension to one side, extending the hind legs, or contracting the abdomen.

Inflammation

Acetic acid causes an inflammatory response in the abdominal cavity, which activates nociceptors.

Nociceptors

The pain signals transmitted to the central nervous system cause the release of mediators like prostaglandins. Which increases sensitivity to nociceptors, generally pain is caused by the release of substance that include prostaglandins, cyclooxygenase (cox) pathway product and endogenous mediators

The result of present study showed that extract (aqueous ethanolic) of *Coriandrum sativum* had analgesic effects. The analgesic effects of the extracts was comparable to morphine and was attenuated by naloxone pretreatment.

Linalool a terpene alcohol found in coriander has been reported to the main constitute that is responsible for some therapeutic value of coriander.

Coriander seeds have compounds such as linoleic acid and cineole which are well known for analgesic antiarthmic and properties .

Linalool is a monoterpene alcohol and is not an alkaloid or flavonoid. coriander extract can reduce the production of chemical mediator that are released during inflammation and cause pain. Such as cox-2, pro-IL, -B.

It might be suggested that the beneficial effects of the extracts which were observed in the present study are at least in part due to linalool which is a main compound in coriander.

Results

The study showed that ethanolic extract of leaves and seeds of *Coriandrum sativum* presented significantly and analgesic activity in mice simultaneously. The data wear analyzed by one-way ANOVA followed by dunett's multiple comparison test. The results demonstrate that ethanolic extract of leaves and seeds of *Coriandrum sativum* has got analgesic potential.

CONCLUSION

1. The present study demonstrated that the ethanolic extract of seeds and leaves of *Coriandrum sativum* possess analgesic activity. The above effects may be due to the presence of flavonoids, linalool, borneol, camphor, tannins and sterols in the extracts.
2. The present study demonstrated that the alcoholic extract of seeds of *Coriandrum sativum* L. possess and analgesic activity..
3. The central analgesic action of the *Coriandrum sativum* was probably mediated through inhibition of central pain receptors.
5. The above effects of it may also be due to the presence of sterols, tannins and flavanoids in the extract.

DISCUSSION

The Present study reveals that seeds of *Coriandrum sativum* possesses and Analgesic activity. Has been validated for use with both rats and mice Therefore, we chose this test to investigate the analgesic potential of the aqueous extract of coriander seed. The indices of anxiety in this test, percent of open arm entries and time spent in the open arm are sensitive to agents .The aqueous extract of coriander seed had similar effects on these parameters. These observations clearly indicate that coriander seed exerts an analgesic activity. In the present study, the analgesic activity of the coriander extract occurred at a dose of 200 ml/kg in mice. Seed this corresponds to an infusion of approximately 20 g of coriander seed in 100 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. The results of hot- plate test showed that Coriander Extract provide significant protective effects on thermic pain stimuli. Such an effect is a characteristic of the central analgesic effect, like morphine, while peripheral analgesic is known to being active on this kind of painful stimuli.

Further there is need to isolate, characterize and screen the active principles from the different parts of *Coriandrum sativum* L. that are responsible for its Anxiolytic and analgesic activity. Also there is need to find out the exact mechanism by which the plant exerts above effects. Active principles from the different parts of *Coriandrum sativum* L. may be evaluated for following activities.

Lacomotor activity

Muscle -relaxant activity.

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