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Evaluation of analgesic activity of aqueous extract of *Cinnamomum zeylanicum* bark extract in mice

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Abstract

The present study aims to evaluate the analgesic activity of aqueous extract of *Cinnamomum zeylanicum* bark in mice by using acetic acid induced writhing and formalin - induced paw licking models. The results showed a significant reducing in the number of writhing responses and a significant reduction in duration of paw-licking in both early and late phase comparing to the control group. We conclude that aqueous extract of *C. zeylanicum* possess analgesic activity.

Keywords: *Cinnamomum zeylanicum, analgesic activity, aqueous extract*

Introduction

Pain has been Pain has been defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage (Manuel, 2006).

Acute pain often serves an essential protective function by associating potentially damaging noxious stimuli with an unpleasant sensation. When acute pain fails to resolve, it will be chronic, a more useful definition for chronic pain is that chronic pain is said to be present when the pain continues beyond the stage where it is useful to protect the region or is persistent and may not have a clearly identifiable cause (Laxmaiah *et al*., 2001; Zakir and Joy, 2014).

Somatic pain occurs when an injured body part is involved in covering or support of the body, such as skin, bone, tendon, joint, or muscle (Mary and Margaret, 2002; Karas *et al*., 2008).

Visceral pain arises from internal organ dysfunction and can be result from inflammation, ischemia occlusion of flow resulting in capsular or organ distension or from functional (Schmidt, 1989; Goldman and Andrew, 2012).

In animals, assessment of pain is done by different methods. Some of them depend on the use of thermal, mechanical or electrical stimuli, while the others involved injection of chemically noxious substance (Karas *et al*., 2008).

Cinnamomum zeylanicum (Lauraceae family) is an evergreen tree widely used in the food industry as spice because of its special aroma. *C. zeylanicum* is commonly used in folk medicine as a remedy for respiratory and digestive ailments. It also indicated as antipyretic agent against cold, fever and headache (Ali *et al*., 2016; Habibe *et al*., 2013; Shen *et al*., 2000; Snehlata *et al*., 2014).

Although *C. zeylanicum* bark is used as analgesic for Menstrual cramps in folk medicine, there are no enough studies to evaluate this biological activity. So the present study aims to estimate the analgesic activity of aqueous extract of *C. zeylanicum* bark in experimental animals.

Materials and methods

Plant materials

Dried *C. zeylanicum* bark was collected from local markets of Al- Nasiriyah city, Thi-Qar province, Iraq. The dried bark was grinded to fine powder.

Preparation of plant extraction

Twenty grams of bark powder was suspended with 200 ml of distilled water, and well mixed using stirrer hot plate for 4 hours. Bark suspension was allowed to stand for 30 min. The extract was filtered using Whatman's Number one filter paper. The extract was dried at room temperature (Harborne, 1984).

Experimental animals

Two month old BALB/c female mice weighting about 20-25 g were purchased from college of veterinary medicine/ University of Basrah. Animals were treated according the local animal care ethics committee of Thi-Qar University/ College of Science. They were housed under standard hygienic conditions at 20°C ± 2°C with a 12-hour day/night cycle.

Analgesic activity

Analgesic activity using acetic acid induced writhing test

Mice were randomly into four groups of six animals each. After acclimation they set to receive

Group1, control group, delivered orally 0.5 ml of distilled water.

Group 2, standard group, intraperitoneally injected 20 mg/kg of diclofenac sodium

Group 3, orally received *C. zeylanicum* extract (100 mg/kg) in 0.5 ml of distilled water

Group 4, orally delivered *C. zeylanicum* etract (200 mg/kg) in 0.5 ml of distilled water.

Each animal was placed separately into a cage and allowed to acclimate for at least 10 minutes. Mice were given vehicle, diclofenac sodium or *C. zeylanicum* etract suspensions according its group 30 min prior to induction of visceral pain by intraperitoneal injection of a 0.6% volume per volume (10 mL/kg) glacial acetic acid solution in normal saline. The animal was

returned to its cages and observed for writhing behavior, indicated by stretching of the abdomen with simultaneous stretching of at least one hind limb. The number of writhing responses was counted for 15 minutes, starting directly after the acidic saline injection (Sharma *et al*., 2011).

Analgesic activity using formalin - induced paw licking model

In this test, animals were divided into 4 groups (6 animals each) and received distilled water (group 1), standard drug (diclofenac,sodium 20 mg/kg *i.p*) (group 2) and 100 and 200 mg/kg of *C. zeylanicum* extract (group 3 and group 4 respectively). Thirty minutes after treatment, 20 µl of 1% formalin was injected subcutaneously under dorsal surface of the hind paw and the time spent for licking the paw injected with formalin was counted for 30 min post formalin injection and considered as indicative of the pain stimuli. The formalin test has two distinctive phases possibly reflecting two different types of pain. The first phase peaked at 5 min and the second phase at 30 min after formalin injection (Hunskaar and Hole, 1997).

Results and Discussion

The analgesic effect of *C. zeylanicum* extract in the acetic acid-induced writhing model is shown in Table 1. The number of writhing responses was significantly reduced in the animal groups treated with 100 and 200 mg/kg of *C. zeylanicum* extract. Diclofenac caused comparable decreases in the number of writhing responses in mice; the effect of diclofenac was significantly greater than that of *C. zeylanicum* extract.

C. zeylanicum extract and standard drug caused a significant reduction in duration of paw-licking as compared to the control group in both early and late phase (Table 2)

Table 1: Number of writhing responses induced by acetic acid

Groups	Mean ± S.D.
Group 1	26.6 ± 2.16 [a]
Group2	2.4 ± 0.51 [d]
Group3	9.4 ± 0.93 [b]
Group4	5.6 ±0.79 [c]
LSD	**3.11**

Values represent mean ± SEM. Values with non-identical superscripted letters (a–d) are considered significantly different ($P < 0.05$).

Table 2: Anti-nociceptive activity of in *C. zeylanicum* extract albino mice in formalin induced paw-licking test

Groups	Early phase (Duration of paw licking in seconds)	Late phase (Duration of paw licking in seconds)
Group 1	57.66±1.70[a]	147.00±2.84[a]
Group 2	12.33±1.52[d]	22.66±1.38[d]
Group 3	33.16±1.57[b]	52.16±1.53[b]
Group 4	22.83±1.68[c]	32.00±10.33[c]
L.S.D.	4.78	5.40

Values represent mean ± SEM. Values with non-identical superscripted letters (a–d) are considered significantly different ($P < 0.05$).

The acetic acid-induced writhing method is used to evaluate the effect of analgesics (for example nonsteroidal anti-inflammatory drugs) on visceral pain by releasing endogenous mediators that stimulate nociceptors. These mediators include cytokines, such as interleukin-1β and interleukin-8, prostaglandins and lipooxygenase products released into the peritoneum. Cytokines are released by resident peritoneal macrophage and mast cells (Collier *et al.*, 1968; Ribeiro *et al.*, 2000; Ghosh *et al.*, 2011; Prabhu *et al.*, 2011).

The formalin-induced paw licking model comprises of two phases, early phase and late phase. The early phase (starts immediately after injection) seems to be caused by C-fiber activation due to the peripheral stimulus. The late phase (starting approximately 20 min after formalin injection) appears to depend on the combination of an inflammatory reaction, activation of N-methyl-D-aspartate (NMDA) and non-NMDA receptors and Nitric oxide (NO) cascade in the peripheral tissue and the functional changes in the dorsal horn of the spinal cord (Abbott et al., 1995; Davidson and Carlton, 1998).

Anti-inflammatory drugs increased pain threshold, because many endogenous chemical mediators of inflammation (histamine, serotonin and prostaglandins)

play a role in generating pain impulses, while other mediators such as bradykinin and cytokines are involved the prolongation of the sensation of the pain (Besson, 1997).

Ethanol and aqueous extracts of *Cinnamomum verum* leaf galls have a potential analgesic activity via inhibition of phospholipase as alleged mechanism for cinnamon tannins and polyphenols (Newall *et al*., 1996; Fine, 2000; Pandy and Chandra, 2015).

Two main constituents of *Cinnamomum osmophloeum* essential oil, namely l-borneol and l-bornyl acetate exhibited excellent anti-inflammatory effects. *C. osmophloeum* extracts also inhibit interleukin-8 expression in human gastric epithelial cells which explain the antinociceptive effect of this plant extracts (Tung *et al*., 2008).

We conclude that aqueous extract of *C. zeylanicum* possess analgesic activity. However, further study is warranted to identify the active constituent.

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