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Research Article

Evaluation Of Analgesic Activity of Aqueous Extract of Cinnamomum Zeylanicum in Albino Rats

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ABSTRACT

Background: Pain is a prevalent symptom associated with various medical conditions, often requiring the use of analgesics for effective management. Severe pain, such as that resulting from cancer metastasis, typically necessitates potent centrally acting drugs like opioids. Advances in understanding endogenous peptides such as enkephalins and endorphins have provided insights into the brain's pain modulation mechanisms and the action of analgesics. *Cinnamomum zeylanicum*, commonly known as Ceylon cinnamon, is a medicinal herb claimed to have neuropharmacological properties, including analgesic potential. This study aimed to evaluate the analgesic activity of an aqueous extract of *Cinnamomum zeylanicum* in albino rats.

Methods: Albino rats were randomized into four groups, each group comprising of six rats. Group I received normal saline (0.9% NaCl, 1 ml/100 g) as control for 21 consecutive days. Group II animals were treated with Tramadol (10 mg/kg) as a standard analgesic on the day of experiment. Groups III and IV received an aqueous extract of *Cinnamomum zeylanicum* at doses of 200 mg/kg and 400 mg/kg, respectively, administered orally for 21 consecutive days. On the 22nd day, analgesic activity was assessed using Eddy's Hot Plate method. Response times for paw licking or jumping were measured at 30, 60, and 90 minutes after treatment.

Results: Rats treated with an aqueous extract of *Cinnamomum zeylanicum* demonstrated a significant increase in reaction time on the hot plate, indicating central analgesic activity. Both doses (200 mg/kg and 400 mg/kg) produced a statistically significant prolongation in latency at 30 and 60 minutes compared to the control group ($p < 0.001$), with the higher dose showing a more pronounced effect which was comparable to standard.

Conclusion: The aqueous extract of *Cinnamomum zeylanicum* exhibits significant dose-dependent analgesic activity in albino rats, suggesting its potential as a natural analgesic agent for pain management

Keywords: *Cinnamomum zeylanicum, analgesic effect, aqueous extract, hot plate test, Tramadol, albino rats.*

INTRODUCTION

Pain is a complex experience involving sensory and emotional aspects, linked to actual or potential tissue damage. It includes types such as somatic, visceral, referred, neuropathic and cancer pain. Pain perception involves chemical mediators like serotonin and prostaglandins and is triggered by nociceptors responding to harmful stimuli. The transmission of pain to the brain involves nociceptive pathways, particularly through C-fibers and Aδ fibers. Pain can be acute, serving a protective role, or chronic, persisting beyond normal healing and often associated with conditions like cancer or arthritis. Pain treatment focuses on reducing pain, improving movement, teaching stress management and promoting group activities.[1] It includes medications such as opioids, NSAIDs, cannabinoids and antidepressants, each targeting different pain aspects. Opioids relieve severe pain by mimicking natural peptides and interacting with opioid

receptors, but they can cause adverse effects like nausea and sedation[2]. In many developing nations, approximately 80% of the population turns to herbal treatments for primary health care, based on WHO data. In recent decades, interest in herbal remedies has significantly increased, particularly in the use of traditional medicinal plants to treat various neurological disorders. Some formulations have been proven to have effective analgesic activity[3].

Cinnamomum zeylanicum is an evergreen plant native to South Asia and classified under the Lauraceae family. It has long been valued as a traditional spice in South Asian cuisine and holds a prominent place in traditional medicine. Historical and ethnopharmacological evidence highlights its significance in Ayurveda and folk medicine, where it is often prepared as decoctions or infused concoctions. In addition to its culinary applications, cinnamon extract is recognized for its antioxidant properties. These antioxidant effects are thought to play a role in its increasing use in herbal treatments aimed at managing various neuropharmacological conditions[4].

MATERIALS AND METHODS

Experimental animals

Healthy Albino rats of either sex weighing 150-250 grams were obtained from CCSEA approved Central Animal House of LLRM Medical College, Meerut. The selected rats were housed in polypropylene cages under controlled conditions of temperature (25°C) with alternating periods of light and darkness of 12 hours each. The rats were provided unrestricted access to a standard pellet diet and tap water *ad libitum.* After one week of acclimatization, the animals were rendered suitable for study. Pregnant female rats were not included in the study.

Ethics approval

This was an experimental study conducted on albino rats, in Department of Pharmacology, LLRM Medical College, Meerut (U.P) from January 2024 to December 2024. The study was commenced after getting approval from Institutional Animal Ethics Committee (approval letter no. IAEC/2023/02 dated 12/12/2023) of Lala Lajpat Rai Memorial Medical College, Meerut, India, registered under CCSEA India (Registration No. 819/Go/ReRcBiBt/S/04/CCSEA).

As per OECD guidelines, doses of aqueous extract of *Cinnamomum zeylanicum* to be used in the study were calculated on the basis of previously documented LD50 on rats (OECD-423).

Method of preparation of extract

Fresh bark of *Cinnamomum zeylanicum* was sourced from a local market and cleaned thoroughly using distilled water to remove surface contaminants. The cleaned bark was then air-dried in a shaded, well-ventilated area to preserve its phytochemical integrity. After complete drying, the bark was finely powdered using a mechanical grinder. A 5 g portion of the powdered bark was extracted with 150 ml of distilled water using a Soxhlet apparatus for a continuous hot percolation process lasting 4 to 5 hours. The resultant extract was sequentially filtered through muslin cloth and Whatman No. 1 filter paper to remove particulate matter. The clear filtrate was concentrated on a water bath and then subjected to freeze-drying to obtain a stable, crude aqueous extract. A stock solution (40 mg/ml) was made by dissolving the freeze-dried extract in distilled water and used for dosing in albino rat[5].

ANALGESIC EFFECT

Eddy's Hot Plate Method

Eddy and Leimbach (1944) has been adapted by several researchers. Here's a suitable modification:
Each experimental group comprised of six albino rats of either sex, weighing between 150 and 200 grams. Analgesic response was assessed using a commercially available hot plate apparatus equipped with an electrically heated surface, maintained at a constant temperature of 55–56°C. Each rat was individually placed on the hot plate, and the latency to a nociceptive response—such as paw licking or jumping—was measured using a stopwatch. Baseline reaction times were recorded prior to administration of the test or reference substance. Subsequent measurements were taken at 30, 60, and 90 minutes following administration, which was carried out either orally or via intraperitoneal injection[7].

MATERIALS

The commercially available injectable preparation of tramadol (manufactured by Torrent pharmaceuticals Pvt Ltd) was used.

EXPERIMENTAL STUDY DESIGN

Albino rats were separated into four groups, each group comprising of six rats.

Group I - The experimental animals of this group (Control group) were given 0.9% NaCl solution in oral dose of 1ml/100gm b.w./day for 21 days.

Group II - In addition to pellet diet and tap water *ad libitum* the experimental animals of this group were given Tramadol in a single dose of 10mg/kg b.w. i.p on the day of experiment.

Groups III - This group was given aqueous extract of *Cinnamomum zeylanicum* [AECZ] per orally in 200mg/kg/day dose consecutively for 21 days[6].

Groups IV - This group was given aqueous extract of *Cinnamomum zeylanicum* [AECZ] per orally in 400mg/kg/day dose consecutively for 21 days[6].

On 22nd day analgesic activity was explored by Eddy's hot plate method. Rats were placed on the surface of "Eddy's Hot Plate" in which temperature was maintained at 55-56ºC and observed for either paw licking or jumping reaction. The reaction time was taken as the interval from the instant the animal reached the hot plate until the moment the animal licked its feet or jumped out. The reaction time was recorded using stopwatch before and after treatment with different drugs.

STATISTICAL ANALYSIS

Statistical analysis was performed using one-way analysis of variance (ANOVA), followed by Dunnett's post hoc test to identify significant differences between groups. Statistical significance was assumed when the p-value was less than 0.05. All comparisons between test groups, standard drug treatments, and the control group were made at corresponding time intervals using SPSS software (Version 22, 2010).

RESULTS

The analgesic activity was evaluated by Eddy's hot plate, measuring the percentage increase in mean reaction time as compared with the control group (treated with normal saline) set as 100% reaction time. The reaction time before and after drug administration, at intervals of 30, 60 and 90 minutes was observed (Table I, Figure 1). Group 1 (1ml/100gm of normal saline) exhibited no significant increase in the reaction time to noxious stimuli induced by the hot plate throughout the 90-minute study period. The results revealed that Tramadol (10 mg/kg, i.p), significantly increased the pain latency at all time points (30, 60 and 90 minutes). A statistically significant prolongation ($p<0.001$) in reaction time was noted at 30min and 60min after oral administration of AECZ at doses of 200mg/kg and 400mg/kg, respectively.

Table I: Effect of aqueous extract of *Cinnamomum zeylanicum* (AECZ) on Algesia induced by hot plate method in albino rats (n=6).

Treatment	Daily Dose and Route	Reaction time (seconds) (mean ± SE)			
		Before treatment	After treatment		
			30 min	60 min	90 min
Normal saline (control)	1ml/100gm, p.o	6.67 ± 0.42	6.83 ± 0.30	7.50 ± 0.42	8.00 ± 0.36
Tramadol (standard)	10mg/kg, i.p	6.50± 0.42	11.33 ± 0.21	15 ± 0.36	13.33 ± 0.33
AECZ200	200mg/kg, p.o	6.17 ± 0.30	7.17 ± 0.30	7.33 ± 0.33	6.83 ± 0.30*
AECZ400	400mg/kg, p.o	6.50 ± 0.34	8.67± 0.33	10.50 ± 0.42	9.16 ± 0.30**

Data are expressed as mean ± SE, with six animals per group (n = 6).
*p<0.01 significant in comparison to control
**p<0.001 significant in comparison to control

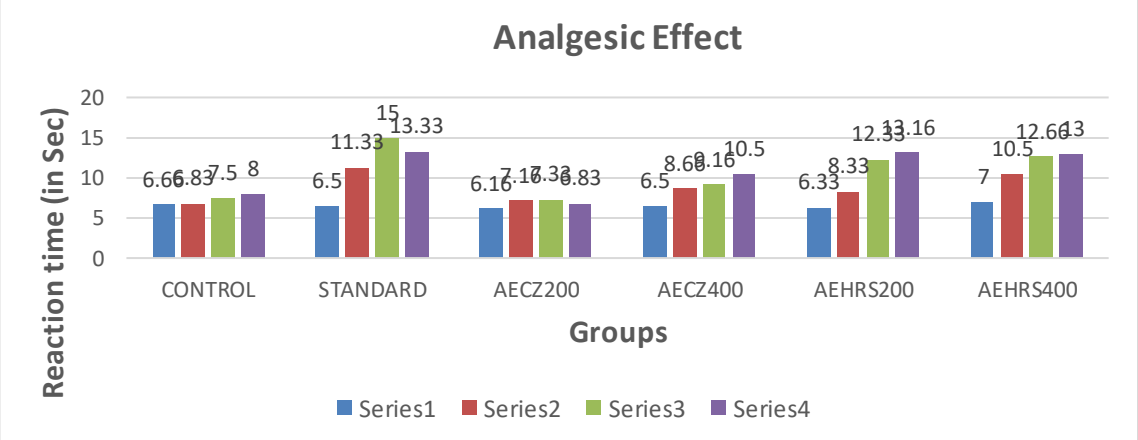

Figure 1: Effect of aqueous extract of *Cinnamomum zeylanicum* (AECZ) on Algesia induced by hot plate method in albino rats (n=6).

DISCUSSION

Cinnamomum zeylanicum is a commonly utilized medicinal plant known for its wide range of therapeutic properties. It is integrated into traditional and modern medical practices across the world. Numerous studies have documented its pharmacological activities, including anti-diabetic, antimicrobial, antioxidant, anti-inflammatory, and anticancer effects, all of which play a vital role in promoting human health. The plant is rich in various bioactive compounds like eugenol, cinnamaldehyde, cinnamyl acetate and camphor. Its botanical features, chemical composition and medicinal applications have been extensively investigated in scientific literature[8].

Pain is a multifaceted experience that involves both sensory perception and emotional response, arising from actual or potential injury to body tissues. It can be classified into several types, including somatic pain, visceral pain, referred pain, neuropathic pain, and cancer-related pain. Pain perception involves chemical mediators like serotonin and prostaglandins and is triggered by nociceptors responding to harmful stimuli. Nociceptive fibers, including C-fibers and Aδ fibers, transmit these signals to the brain. Pain can be acute, serving a protective role, or chronic, persisting beyond normal healing and often associated with conditions like cancer or arthritis[1]. Analgesics are agents used to alleviate pain by modulating signals in the peripheral or central nervous system, typically without altering the state of consciousness. These drugs are broadly classified based on their site of action. Centrally acting analgesics modulate pain perception by raising the pain threshold and altering the central processing of pain signals. In contrast, peripherally acting analgesics alleviate pain by blocking the initiation and propagation of pain signals at the site of peripheral nerve endings. Tramadol is a centrally acting analgesic with a unique dual mechanism of action that distinguishes it from conventional opioids. It exerts mild agonistic activity at the μ-opioid receptors, with minimal affinity for κ and δ receptors. Additionally, tramadol inhibits the reuptake of norepinephrine (NA) and serotonin (5-HT), thereby enhancing their synaptic availability. This facilitates the activation of descending monoaminergic pathways, which contribute to spinal inhibition of pain transmission. This multimodal mechanism underlies tramadol's analgesic efficacy and reduced potential for opioid-related adverse effects.

In this study, animal models were employed to assess analgesic activity, specifically through the use of thermal stimuli, utilizing the hot plate method. Eddy's hot plate model is effective for studying centrally mediated pain relief responses, primarily focusing on processes above the spinal cord level. In this study, AECZ was found to increase the reaction time of rats in the hot plate test, indicating a potential analgesic effect. The extract-treated groups exhibited statistically significant differences in mean reaction times compared to the control group at all observation periods. Tramadol, a known analgesic, demonstrated detectable analgesic effects at 30, 60 and 90 minutes. The extract also showed significant differences when compared to the control, suggesting it too has analgesic properties. Since the extract elicited these responses, its analgesic effect may operate through central nervous system mechanisms rather than solely at the peripheral level. In conclusion, the aqueous extract of CZ appear to have analgesic properties, acting likely at the supraspinal level, and this effect was comparable to tramadol in reducing pain in rats[9]. The concluded results of present study were also supported by similar studies done by Soni D. *et al*., 2011[10] and Jain S. *et al*., 2019[6].

CONCLUSION

In established animal models of algesia, pre-treatment with aqueous extracts of *Cinnamomum zeylanicum exhibited statistically significant analgesic activity through Eddy's hot plate method (centrally mediated analgesic action) in albino rats.* This study also paves the way for further evaluation of *Cinnamomum zeylanicum* across various dose levels, as well as testing with different durations and extract forms. Future research could focus on identifying the phytochemicals or bioactive compounds in these plants that contribute to their neuroprotective effects. While many of the bioactive compounds responsible for these properties have already been isolated and identified, it is important to note that these compounds can vary depending on the plant's variety, environmental factors and the analytical methods used for characterization. Therefore, there is potential for discovering more powerful antioxidant compounds in *Cinnamomum zeylanicum.*

Although this plant is currently used primarily as a spice and in traditional medicine, it holds promise as a potential source of compounds for clinical trials aimed at evaluating its efficacy and potential to prevent specific diseases.

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