

## Exploring Pharmacological Activity of Cinnamomum Plant Extracts By Biochemical Tests

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### ABSTRACT

In the present study, the alcoholic extract of *Cinnamomum verum* bark was studied for its analgesic activity and mechanism of action on rats. The alcoholic extract of *Cinnamomum verum* bark was studied for analgesic activity in rats. ANOVA was used to compare the findings to the control group, and then post hoc multiple comparisons were performed. According to the results of this investigation, the bark of *Cinnamomum verum* significantly reduces nociception in both phases. Additionally, compared to the common drug Pethidine, it demonstrates a reduction of nociception in both phases. Therefore, *Cinnamomum verum* bark may play a significant role in pain management, particularly in nations like India, where traditional drug is less readily available to the general public and has greater negative effects.

**Keywords:** Cinnamomum, Zeylanicum, Analgesic activity, Tail immersion test

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### INTRODUCTION

Pain is an unpleasant experience that happens frequently. There is no denying that pain is a warning indicator for disruptions in the body or a person's surrounding environment [1]. The main goal of pain management is the elimination or abolition of the pain's primary source [2]. However, this is not always practicable, which is why analgesics are used to manage pain in a symptomatic manner [3]. The strongest class of analgesics includes opioids, medications like morphine and Pethidine. However, they produce more adverse drug reactions than other analgesics, the majority of which are dose-dependent [4].

Increased pain in response to noxious stimulation following peripheral tissue damage requires both peripheral sensitizations increasing the sensitivity of primary afferent nociceptors at the site of injury and central nervous system excitability increasing the excitability of neurons (central sensitization) [5]. The dorsal horn neurons' thresholds to noxious stimulation are lowered, their receptive fields are increased, their

postsynaptic potentials are added, they experience a cumulative depolarization and a prolonged after discharge, or "windup," and their excitability of the flexion reflex in the responsiveness to external stimuli is improved as a result of inputs from nociceptive afferents [6]. Opioid analgesics treat severe pain, including cancer, burn, postoperative, visceral, and ischemia. They exert their effects centrally via opioid receptors. Steroids, anticonvulsants, and tricyclic antidepressants are utilized as adjuvants in managing pain. Amitriptyline, carbamazepine, and gabapentin are used to treat neuralgia [7,8].

These medications can cause side effects such as liver damage, gastric mucosal damage, pulmonary alkalosis, an increased tendency to bleed, hypersensitivity reactions, and renal disorders [9, 10]. Therefore, a quest for medications with effective therapeutic effects and low adverse effects is ongoing. Numerous demographic groups are using more plant-based products [11, 12]. An estimate states that 80 percent of people worldwide rely on plants for their medical needs. Most synthetic medications used today for analgesic and antinociceptive actions have several harmful and adverse effects [13]. Plants remain a significant untapped source of structurally unique chemicals that could be used as a starting point for creating new medications [14, 15]. Numerous medications with antinociceptive properties of plant origin have been used for a very long period without experiencing any negative effects [16, 17]. Because Assam is home to about 350 of the

1500 medicinal plant species in India, and many of these traditionally used plants have not yet undergone scientific study and validation, North East India is regarded as one of the "hotspots" for biodiversity in India [18,19].

*Cinnamomum verum* bark (Lauraceae), also referred to as cinnamon, is one of the spices frequently used as a flavoring agent. It has been demonstrated to have a wide range of pharmacological properties in addition to its use as a spice, including antidiabetic, hypolipidemic, antibacterial, and antifungal activity [20]. Additionally, it's well-accepted that cinnamon is a strong analgesic. There are no studies demonstrating the effectiveness of administering cinnamon bark as a painkiller [21]. The current study aimed to examine the analgesic activity of *Cinnamomum verum* bark in albino rats. *Cinnamomum verum* is a member of the Lauraceae family, and one of its constituents, cinnamaldehyde, has been shown to have considerable anti-allergic, anti-ulcerogenic, antipyretic, anesthetic, and anti-mutagenic properties [22]. Eastern and Western nations have historically utilized cinnamomum cassia to treat inflammatory diseases, dyspepsia, gastritis, and problems with blood circulation. Bark and leaves are used as seasonings and sauces.

## MATERIALS AND METHODS

Wistar strain albino adult male or female (not pregnant) rats weighing 200 g were used for the investigation. The Central Animal House of the Bharath Institute of Higher Education and Research in Chennai, India, houses the animals obtained from the King Institute of Preventive Medicine in Guindy, Chennai. The animals were kept separately in polypropylene cages under temperature control and sanitary conditions. They all receive water and a typical pellet feed. The institutional animal ethics committee authorized the experimental protocol, and the Committee for the Control and Supervision of Experiments on Animals approved the animal home where the animals were kept in accordance with established procedures (CPCSEA). Cinnamon bark (*Cinnamomum verum*) was bought in Sri Lanka at the local market. The National Institute of Herbal Science in Chennai, India, identified the sample. The national institute has saved a voucher specimen (Reg. No. PARC/2010/966). In a mechanical mixer, the bark was dried and then ground finely. The (2 kilograms) dried powder is steeped in ethanol for seven days and then set aside. The solvent from the complete extract is removed after seven days. The concentrate is then dried by evaporating over a water bath until it has a consistency of syrup (150mg). This extract will be combined with 1% carboxymethyl cellulose in sterile saline before being given intra-peritoneal to rats.

### Groups

Group A: Control (Carboxymethylcellulose, 0.5ml, i.p)

Group B: *Cinnamomum verum* bark (150mg/kg)

Group C: *Cinnamomum verum* bark (300mg/kg)

Group D: *Cinnamomum verum* bark (600mg/kg)

## Part 2: Comparison of an effective dose of *Cinnamomum verum* with Pethidine, Ketorolac, *Cinnamomum verum*+ Naloxone and control group.

### Groups

Group A: Control (Carboxymethylcellulose, 0.5ml, i.p)

Group 1 (B/C/D): *Cinnamomum verum* bark (effective dose, i.p)

Group 2: Pethidine (5 mg/kg, i.p)

Group 3: Ketorolac (10 mg/kg, i.p)

Group 4: *Cinnamomum* (effective dose, i.p)

## RESULTS

When *Cinnamomum verum* 300 mg/kg, Pethidine 5 mg/kg, *Cinnamomum verum*300 mg/kg + Naloxone 1 mg/kg, and Ketorolac 10 mg/kg were compared to the control group's mean reaction time (seconds the animal spent licking the paw), it showed analgesic effect (P0.000) for both of these substances in both phases, with mean differences of 50.66 sec and 55.33 sec in phase 1. When compared to the control group in phase 1 with P values of 0.066 and 0.091, respectively, and mean differences of just 7.83 sec and 7.13 sec, respectively, the *Cinnamomum verum*300mg/kg + Naloxone 1mg/kg and Ketorolac 10mg/kg groups did not exhibit any analgesic effect, however, when compared to the control group in phase 2 with P 0.000 and mean differences of 105.16 sec and 72.33.

Among the mean reaction time (seconds animal spent licking the paw) of both the phases of *Cinnamomum verum*300mg/kg, Pethidine 5mg/kg, *Cinnamomum verum*300mg/kg + Naloxone 1mg/kg and Ketorolac 10mg/kg. *Cinnamomum verum*300mg/kg showed a similar reduction in pain (P = 0.263) compared to Pethidine 5mg/kg with a mean difference of 4.66sec for phase 1. *Cinnamomum verum*300mg/kg showed a significant analgesic effect (P<0.000) compared to *Cinnamomum verum*300mg/kg + Naloxone 10mg/kg and Ketorolac 10mg/kg with a mean difference of 42.83sec and 43.50sec respectively for Phase 1 Table 1. *Cinnamomum verum*300mg/kg showed a marked reduction in pain (P<0.05) compared to Ketorolac 10mg/kg in phase 2 with a mean difference of 34.50sec. *Cinnamomum verum*300mg/kg showed a similar reduction in pain with P values 0.872 and 0.821, respectively, to *Cinnamomum verum*300mg/kg + Naloxone 1mg/kg and Pethidine 5mg/kg with a mean difference of 1.66sec and 2.33sec respectively for Phase 2.

The mean reaction time (seconds animal spent licking the paw) of both the phases of Pethidine 5mg/kg showed an analgesic effect (P <0.000) when compared to *Cinnamomum verum*300mg/kg + Naloxone 1mg/kg and Ketorolac 10mg/kg with a mean difference of

**Table 1: Mean, Std. Deviation, Std. Error and 95% Confidence Interval (Reaction time in seconds) of both Phase 1 and Phase 2 in the formalin test after intra-peritoneal administered of *Cinnamomum verum*300mg/kg, Pethidine 5mg/kg, *Cinnamomum verum*300mg/kg + Naloxone 1 mg/kg, Ketorolac 10mg /kg and control group.**

Phase	DRUG	N	Mean reaction time in seconds	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
						Lower Bound	Upper Bound
Phase 1	Control	6	66.5	13.57	5.54	52.25	80.74
	<i>Cinnamomum verum</i> 300 mg/kg	6	15.83*	4.02	1.64	11.61	20.05
	Pethidine 5mg/kg	6	11.16*	2.04	0.83	9.02	13.3
	<i>Cinnamomum verum</i> 300mg/kg + Naloxone 1 mg/kg	6	58.66t	3.77	1.54	54.7	62.63
	Ketorolac 10mg/kg	6	59.33t	5.5	2.24	53.55	65.1
Phase 2	Control	6	122.33	33.71	13.76	86.95	157.71
	<i>Cinnamomum verum</i> 300mg/kg	6	15.50*	11.09	4.52	3.85	27.14
	Pethidine 5mg/kg	6	13.16*	5.56	2.27	7.32	19.00
	<i>Cinnamomum verum</i> 300mg/kg + Naloxone 1 mg/kg	6	17.16*	14.06	5.74	2.4	31.92
	Ketorolac 10mg/kg	6	50.00*6.	8.89	3.63	40.66	59.33

N Number of animals  
 \*P<0.000 when compared to Control group.  
 t P<0.000 when compared to *Cinnamomum verum*100mg/kg and Pethidine 5mg/kg group.  
 P<0.05 when compared to *Cinnamomum verum*100 mg/kg, Pethidine 5mg/kg and

**Table 2: Significance and Mean Difference (Reaction time in seconds) of Phase 1 and Phase 2 in the formalin test after intra-peritoneal administered of *Cinnamomum verum*300mg/kg, Pethidine 5mg/kg, *Cinnamomum verum*300mg/kg + Naloxone 1mg/kg, Ketorolac 10mg/kg and control group.**

DRUG (1)	DRUG (2)	Phase 1		Phase 2	
		Mean Difference	Sig.	Mean Difference	Sig.
Control	<i>Cinnamomum verum</i> 300mg/kg	50.66•	0	106.83•	0
	Pethidine 5mg /kg	55.33•	0	109.16•	0
	<i>Cinnamomum verum</i> 300mg/kg + Naloxone 1mg/kg	7.83	0.07	105.16•	0
	Ketorolac 10mg/kg	7.16	0.09	72.33•	0
<i>Cinnamomum verum</i> 300mg/kg	Control	50.66•	0	106.83•	0
	Pethidine 5mg/kg	4.66	0.26	2.33	0.821
	<i>Cinnamomum verum</i> 300mg/kg + Naloxone 1 mg/kg	42.83•	0	1.66	0.87
	Ketorolac 10mg /kg	43.50•	0	34.50•	0
Pethidine 5mg /kg	Control	55.33•	0	109.16•	0
	<i>Cinnamomum verum</i> 300mg/kg	4.66	0.26	2.33	0.82
	<i>Cinnamomum verum</i> 300mg/kg + Naloxone 1 mg/kg	47.50•	0	4	0.7
	Ketorolac 10mg/kg	48.16•	0	36.83•	0
<i>Cinnamomum verum</i> 300mg/kg + Naloxone 1 mg/kg	Control	7.83	0.07	105.16•	0
	<i>Cinnamomum verum</i> 300mg /kg	42.83•	0	1.66	0.87
		47.50•			
	Pethidine 5mg/kg		0	4	0.7
Ketorolac 10mg/kg	Ketorolac 10mg/kg	0.66	0.87	32.83•	0
	Control	7.16	0.091	72.33•	0
	<i>Cinnamomum verum</i> 300mg/kg	43.50•	0	34.50•	0
	Pethidine 5mg/kg	48.16•	0	36.83•	0
<i>Cinnamomum verum</i> 300mg/kg + Naloxone 1 mg/kg		0.66	0.87	32.83•	0

The mean difference is significant at the 0.05 level.

47.50sec and 48.16sec respectively in Phase 1. Pethidine 5mg/kg showed marked reduction (P<0.05) compared to Ketorolac 10mg/kg in phase 2 with a mean difference of 36.83sec. Pethidine 5mg/kg showed a similar reduction in pain with a P value of 0.699 to *Cinnamomum*

*verum*300mg/kg + Naloxone 1mg/kg with a mean difference of 4.00sec in phase 2.

Comparing the average reaction time (seconds the animal spent licking the paw) in both phases of *Cinnamomum verum*300 mg/kg + naloxone 1 mg/kg

and ketorolac 10 mg/kg revealed no reduction in pain with a P value of 0.871 and mean difference of 0.66sec in Phase 1 and with a reduction in pain (P 0.05) and mean difference of 32.83sec in Phase 2. For each of these five groups, the one-way ANOVA value F and significance for Phases 1 and 2 were 84.68, 41.40, and P0.000, P0.000, respectively, with a degree of freedom 3 Table 2.

### DISCUSSION

The rat formalin test was used in this work to objectively evaluate the efficacy of *Cinnamomum verum* bark in treating two different forms of nociception. The majority of research that was reportedly used biting and licking as a way to gauge nociception. It has been claimed that major alteration of the central system neurons also occurs in addition to the peripheral activity. Dorsal horn neurons have a lowered threshold for stimulation brought on by inputs from afferent neurons, an expansion of their receptive fields and a summation of slow postsynaptic potentials. This causes cumulative depolarization and a protracted after-discharge in the dorsal horn neurons. "Wind up" is the term used to describe the later 18. The substances responsible for this central nervous system phenomenon are still being studied, including amino acids and N-methyl-D-aspartate antagonists. 19 In addition to their other recognized central nervous system modes of action, opioid analgesics may also be involved in modifying this process.

We administered Naloxone, an opioid receptor antagonist, along with *Cinnamomum verum* to check if it blocked the opioid receptor since it had similar effects to Pethidine, an opioid receptor agonist, in the formalin test. *Cuminum verum* 300 mg/kg plus Phase 1 nociceptive behavior was unaffected by Naloxone and was comparable to that of the control group. But compared to the control group, it decreased the nociceptive behaviour in phase 2. Phase 2's reduction in nociception is comparable to Pethidine and *Cinnamomum verum* 300mg/phase kg's 2 responses. Naloxone blocks the first phase of *Cinnamomum verum* activity, as seen by the response to its administration. Phase 1 of the formalin test is brought on by contact with the central nervous system's opioid receptors.

### CONCLUSION

The formalin test indicates that opioid receptors probably mediate the major effect. Phase 1 nociceptive behaviour significantly increased when Naloxone was administered in addition to the test drug as compared to the test medication administered alone and Pethidine. This suggests that the anti-nociceptive action of *Cinnamomum verum* bark is mediated by endogenous opioid peptides.

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