International Journal of Research in Pharmacy and Life Sciences

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Research Article Open Access

Antinociceptive activity of methanolic extract of *Cordia Subcordata* Lam. (*Boraginaceae*) in animal models of nociception

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A B S T R A C T

Antinociceptive activity of methanolic extract of whole plant of cordial subcordata was studied by peripheral or non-narcotic model of nociception like formalin induced writing test and central or narcotic model like hotplate method. The methanolic extract of plant of the plant, administered orally and the standard drug produced significant analgesic activity in formalin induced writhing syndrome as compared to the vehicle treated control group. In the hot plate analgesic test, in cordia subcordata at different doses and the standard drug treated group. The plant possesses significant anti nociceptive property as evidenced in all animal models of nociception. It is possible through diverse mechanism that may involve both central and peripheral pathways. The preliminary phytochemical investigation revealed the presence of alkaloids, terpenoids, and tannins in the methanolic extract of cordial subcordata which may be responsible for its antinociceptive activity.

Keywords: *Cordia Subcordata*, hot plate, nociception, formalin, pain.

A R T I C L E I N F O

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Article History: Received 21 March 2015, **Accepted** 15 June 2015, **Available Online** 24 November 2015

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PAPER-QR CODE

Citation: C. Madhavi Latha. Antinociceptive activity of methanolic extract of *Cordia Subcordata* Lam. (*Boraginaceae*) in animal models of nociception. *Int. J. Res. Pharm, L. Sci.*, 2015, 3(2): 342-345.

1. Introduction

Analgesic choice is also determined by the type of pain: For neuropathic pain, traditional analgesics are less effective, and there is often benefit from classes of drugs that are not normally considered analgesics, such as tricyclic antidepressants and anticonvulsants pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. In many pathological conditions, tissue injury is the immediate cause of pain which results in the local release of a variety of chemical agents. These chemical agents are known to act on the nerve terminals, either activating them directly or enhancing their sensitivity to other forms of stimulation. Pain is the main symptom in many medical conditions, and can significantly interfere with a person's quality of life and general functioning Nociceptive pain may be classified further three types that have distinct organic and felt qualities. Superficial somatic pain is caused by injury to skin or superficial tissues. Deep somatic pain originates from ligaments, tendons, bones, blood vessels and muscles. Visceral pain originates from the viscera, or organs.

2. Materials and Methods

The whole plant of *Cordia subcordata Lam.* will be collected from Tirumala hills and was authenticated by the department of botany, the authentified plant material where shade dried and powdered coarsely. It will be passed through the 40 mesh sieve. The coarsely powdered drug were extracted separately in soxhlet apparatus in sufficient volume of redistilled water and methanol at 48-50^{0}c for 24 hrs. The filtrate were collected and evaporated to dryness at 45^{0}c on rotary evaporator. The solid masses were collected carefully and weighed. Their yield were calculated and then stored in sealed glass bottles at 5^{0}c for further experimental work.

Acute oral toxicity study:

Male albino mice weighing 30-40 gm were used for the study. The starting dose level of methanol extract of *Cordia subcordata.lam.* was 2000 mg/kg body weight p.o as most of the crude extracts posses LD_{50} value more than 200 mg/kg p.o. Dose volume was administered 0.2ml per 100gm body weight to overnight fasted mice with were *ad libitum.* Food was with held for a further 3-4 hours after administration of methanol extract *Cordia subcorta.lam* and observed for signs for toxicity.

The body weight of the mice before and after administration were noted that changes in skin and fur, eyes, mucous membranes, respiratory, circulatory, autonomic and central nervous system and motor activity and behavior pattern were observed and also sign of tremors, convulsions, salivation, diarrhea, lethargy, sleep and coma were noted. The onset of toxicity and signs of toxicity also noted.

Formalin induced pain:

Male Albino mice weighing 20-25g will be divided into five groups of six animals each. All groups of animals will be injected subcutaneously with 20µl of formalin into the dorsal hind paw. The time the mice spent licking or biting the injected paw or leg will be recorded. Two distinct periods of intensive licking activity will be identified and scored separately. The first period (early phase) will be recorded 1- 5min after the injection of formalin and the second period (late phase) will be recorded 20–40 min after the injection. The percentage inhibition of licking will be calculated by the formula: (C−T)/C×100 where C represents the vehicle treated control group value for each phase and T represents the treated group value for each phase.

Hot plate reaction time in mice:

Mice will be screened by placing them on a hot plate maintained at 55 ± 1 ˚C and will be recorded the reaction time in seconds for licking of hind paw or jumping. A cut-off time of 40s will be selected to avoid tissue damage.

3. Results and Discussion

Anti nociceptive activities:

Effects *of C.subcordata on the formalin test in mice:*

The formalin induced paw licking model was used to study the analgesic effects during early and late phase (table-1).The administration of standard drug asprin significantly ($p<0.01$)inhibiting the licking response the methanolic extract of cordial subcordata failed to produce any significant suppression in the licking response during the early phase of formalin test in the late phase of the formalin test, the administration of standard drug highly significantly ($p<0.001$)inhibited the paw licking response as compared to the control group .the methanolic extract of cordial subcordata significantly ($p<0.05$) suppressed the paw licking in the late phase as compared to control group.

Hot plate reaction time in mice:

While evaluating analgesic activity of different extracts by hot plate method, it was observed that Morphine sulphate showed significant analgesic effect at 30, 60,120 and 180 minutes. Peak effect was observed at 120 minute. Normal 1% DMSO solution (group-1) did not have any significant change in basal reaction time. The different dose of methanolic extract of *c.subcordata showed* highly significant effect ($P<0.0001$) at 30, 60,120 and 180 minutes as compared with control group. As compared to standard drug, the methanolic extract at a dose of 200mg/kg was found to have no significant differences ($P<0.05$) in basal reaction time at different time periods. The methanolic extract at a dose of 200mg/kg showed peak effect 12.9± 0.182 at 120 minute.

4. Conclusion

In the present study, the antinociceptive effect of methanolic extract of cordial subcordata was evaluated in different models of pain. Finally I conclude that the plant having analgesic activity against the non narcotic model like formalin induced writhing in rats and narcotic model like hot plate test. The results of the present study clearly demonstrated that the methanolic extract of C. Subcordata possessed a definite dose dependent antinociceptive activity as observed by significant increase in reaction time in formalin induced writhing syndrome, hot plate test as compared to the control group.

Table 1: Effects of standardized methanolic extract of *C.subcordata*on early phase and late phase of the formalin test in mice

Group	Dose (mg/kg)	Early phase		Late phase	
		Licking time(sec)	%Inhibition of licking response	Licking time(sec)	%Inhibition of licking Response
Control	-	91.67± 2.50	-	64.50±17.04	-
Asprin	300	75.00± 4.79	14	0.00±0.00	100
Morphine	10	0.00± 0.00	100	0.00±0.00	100
C.subcordata	150	67.33± 4.75	29	13.80±5.67	75
	300	60.55±3.90	35	8.30±4.87	88
	600	50.81±2.32	47	2.53±2.21	95

Values are expressed as mean ± S.E.M., n = 6. * Significantly different from control, $p<0.05$.

Table 2: Evaluation of analgesic activity of chloroform and methanol extracts of *C.subcordata* whole plant by hot plate method.

Group	Treatment	Dose (mg/kg bw)	Basal reaction time	Reaction time(in sec) after administration of drugs at different time (minutes)			
				30	60	120	180
1	Control(1%DMSO)	10	4.2±0.112	5.0±0.205	4.5±0.147	4.8±0.155	5.0±0.155
2	Morphine sulphate	5	4.5±0.112	9.5±0.055	12.5±0.112	12.9±0.110	12.4±0.112
3	Methanol extract	50	4.5±0.100	5.1±0.100	6.2± 0.115	6.6± 0.055	7.0± 0.100
4		100	5.0±0.100	5.4±0.173	9.8 ±0.173	10.8 ±0.301	11.1± 0.155
5		200	4.5±0.100	6.1± 0.057	10.9±0.179	12.9±0.182	12.5 ±0.055

All values are expressed in Mean ± SEM, n=6; †p< 0.0001, ‡p< 0.001 and _p< 0.05compare with control and '#'- Indicates there is no significant difference between standard and test drug at P< 0.05 significant level.

5. Acknowledgement

We express our sincere thanks to the Management and Madhusudhan Reddy, Honorable Chairman, Jagan's College of Pharmacy, jangalakandriga, Nellore, for providing necessary facilities and financial support for this study.

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