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Evaluation of Anti-inflammatory activities of *Sida cordifolia* Linn in Albino rats

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ABSTRACT

Sida cordifolia Linn, herb belonging to Malvaceae family is extensively used in traditional folk remedies for a variety of conditions like rheumatism, wound healing, gonorrhoea, spermatorrhea and in intermittent fever etc. This study evaluates ethanolic extract of *Sida cordifolia* Linn for acute & sub-acute anti-inflammatory property in albino rats and compared with the reference drug indomethacin. The 80% ethanolic extract of *Sida cordifolia* Linn was prepared using soxhlet apparatus. Crude extract was suspended in 1% carboxy methyl cellulose for administration into albino rats. For acute anti-inflammatory study, the carrageenan induced rat paw oedema inhibition method was used and for sub-acute anti-inflammatory study, cotton pellet granuloma method was used. Data was statistically analysed by one factor ANOVA followed by Newman – Keul's studentized range test. Ethanolic extract of *Sida cordifolia* Linn showed statistically significant acute & sub- acute anti-inflammatory effects matching to that of control group at doses of 100 mg/kg and 200 mg/kg ($p < 0.05$). It was found that percentage reduction in the paw-oedema was 58.13% with Indomethacin, 48.83% and 53.48% with 100 mg/kg and 200 mg/kg *Sida cordifolia* Linn respectively. Percentage reduction in the granuloma formation was 60.2% with Indomethacin, 54.7% and 56% with 100 mg/kg and 200 mg/kg *Sida cordifolia* Linn respectively. *Sida cordifolia* Linn could be a source of valuable anti-inflammatory drugs, in addition to currently available steroidal and nonsteroidal anti-inflammatory agents.

Key words: *Sida cordifolia* Linn; anti-inflammatory; Rat paw oedema method; Cotton pellet granuloma method.

INTRODUCTION

Inflammation is a pathophysiological response of living tissue to injury that leads to local accumulation of plasmatic fluid and blood cells. Although it is a defence mechanism that helps

body to protect itself against infection, burns, toxic chemicals, allergens or other noxious stimuli. The complex events and mediators involved in the inflammatory reaction can induce, maintain or aggravate many diseases [1].

Traditional and folk remedies have provided us with important drugs in the treatment of many diseases and are being increasingly subjected to scientific study. The family of anti-inflammatory drugs is of no exception, to this salicylate had their origin in the 'willow bark' of folk medicine paracetamol, cortisone, gold salts, and phenylbutazone made their way into clinical medicine serendipitously [2]. Inflammatory diseases such as rheumatoid arthritis, inflammatory bowel disease, multiple sclerosis and other connective tissue diseases are a major cause of morbidity. Anti-inflammatory agents have been traditionally evaluated by studying their effects on inflammation produced in animals by injecting foreign or noxious agents [3]. It is believed that current analgesia inducing drugs such as opiates and NSAIDS are not useful in all cases, because of their side effects like gastrointestinal irritation, liver dysfunction and many others [4]. Thus there is still a need to develop newer and safer anti-inflammatory drugs. This need has evoked extensive search for new anti-inflammatory drugs in the hope of being able to bridge the short comings of currently available therapies.

Sida cordifolia Linn is a herb belonging to the family Malvaceae [5]. This plant is used in folk medicine for the treatment of stomatitis, blenorrhea, asthmatic bronchitis, and nasal congestion [6]. However systematic study of this plant has not been carried out for these properties. The objective of present study was to evaluate the anti-inflammatory activity of *Sida cordifolia* Linn in albino rats using established anti-inflammatory rodent models and to compare it with reference drug indomethacin with regard to acute and sub-acute anti-inflammatory properties, visible side effects if any (eg. sedation, tremors, convulsions etc)

EXPERIMENTAL SECTION

Preparation of extract

***Sida cordifolia* Linn:** The leaves of *Sida cordifolia* were shade dried and powdered. Subsequently an 80% ethanolic extract of the leaves was obtained using Soxhlet apparatus. The extract was concentrated under reduced pressure. The crude extract obtained was suspended in 1% carboxy methyl cellulose for oral administration in albino rats.

Selection of animals, caring and handling: This was done as per the guidelines set by the Indian National Science Academy New Delhi, India. Healthy Wistar rats (150–200 g), aged twelve weeks of either sex, bred locally in the animal house of J.J.M Medical College, Davangere were selected for the study. They were housed under controlled conditions of temperature of $23\pm 2^{\circ}\text{C}$, relative humidity of 30–70% and 12 h light–12 h dark cycle. The animals were housed individually in polypropylene cages containing sterile paddy husk (procured locally) as bedding throughout the experiment. All animals were fed with sterile commercial pelleted rat chow supplied by Hindustan Lever Ltd. (Mumbai, India) and had free access to water ad libitum. Animals were kept under fasting for overnight and weighed before the experiment. The study was undertaken after obtaining approval of Institutional Animal Ethics.

Study design:

- 1) For acute inflammation: Carrageenan induced rat paw oedema inhibition method.
- 2) For sub-acute inflammation: Cotton pellet granuloma method.

Carrageenan induced rat paw oedema inhibition method: Wistar albino rats were divided into 4 groups each containing 6 rats

- Group I: Control treated with normal saline per orally (0.1 ml).
 Group II: Indomethacin (20 mg /kg) per orally.
 Group III: Test group A: *Sida cordifolia* (100 mg/kg) per orally.
 Group IV: Test group B: *Sida cordifolia* (200 mg/kg) per orally.

Acute inflammation was produced by injecting 0.1ml of 1% carrageenan suspension in normal saline into the subplantar region of right hind paw after 30 minutes of drug administration. A mark was made on the leg at the malleous to facilitate uniform dipping at subsequent readings. The volume of paw oedema volume was measured with the help of plethysmograph by mercury displacement method immediately before and three hours after the drug administration. The percentage inhibition of oedema in various treated groups was then calculated by using statistical analysis.

Cotton Pellet Granuloma Method: Rats were divided into 4 groups as earlier, each group consisting of 6 rats. Under light ether anaesthesia, the hair in the axillary and groin region were cut and sterile cotton pellets of 10mg each were implanted in the subcutaneous tissue on either sides of axilla and sterile grass pith (25 x 2mm) in the groin region. Wounds were then sutured and animals were caged individually after recovery from anaesthesia. The rats then received treatments as described earlier. The scheduled drug administration was started on the day of implantation and repeated every twenty four hours, regularly for 7 days. During the 7 days any change in food intake, motor activity and diarrhoea, if any were noted.

On the 8th day, the rats were sacrificed and cotton pellets and grass piths removed. The pellets free from the tissue were dried overnight to their dry weight. Net granuloma formation was calculated by subtracting the initially weight noted (i.e.10 mg). The grass piths were served in 10% formalin for histopathological studies.

Statistical analysis:

One factor ANOVA followed by Newman – Keul’s studentized range test was used for comparing with control at different time intervals. Fisher’s exact test was used to compare the ulcer incidence.

Table 1: Showing Oedema Volumes (MI) In Carrageenan Induced Rat Paw Oedema Inhibition Test

Groups	Dose/route	Paw oedema ml (%) Mean ± S.E.M	Inhibition %	P value
Group I Control	0.1ml po	0.43 ± 0.30	---	–
Group II Indomethacin	20 mg/kg po	0.18 ± 0.33	58.13	0.05*
Group III Test group A	100mg/kg po	0.22 ± 0.30	48.83	0.05*
Group IV Test group B	200 mg/kg po	0.20 ± 0.36	53.48	0.05*

po: per orally, S.E.M: Standard error of mean

RESULTS

Effect on carrageenan induced paw edema inhibition test (Table -1, Graph-1)

In carrageenan induced rat paw edema test, the doses of 100mg/kg and 200 mg/kg ethanolic extract of *Sida cordifolia* Linn plant showed statistically significant ($P < 0.05$) inhibitory effect on “mean increase in paw volume”. *Sida cordifolia* Linn showed acute anti inflammatory activity higher than control group, but it did not show so strong effect as Indomethacin, which produced significant inhibition (58.13%) ($P < 0.05$). It was found that reduction in the inflammation was 48.83 % ($P < 0.05$) with 100mg/kg *Sida cordifolia* Linn and 53.48 % ($P < 0.05$) with 200 mg/kg *Sida cordifolia* Linn.

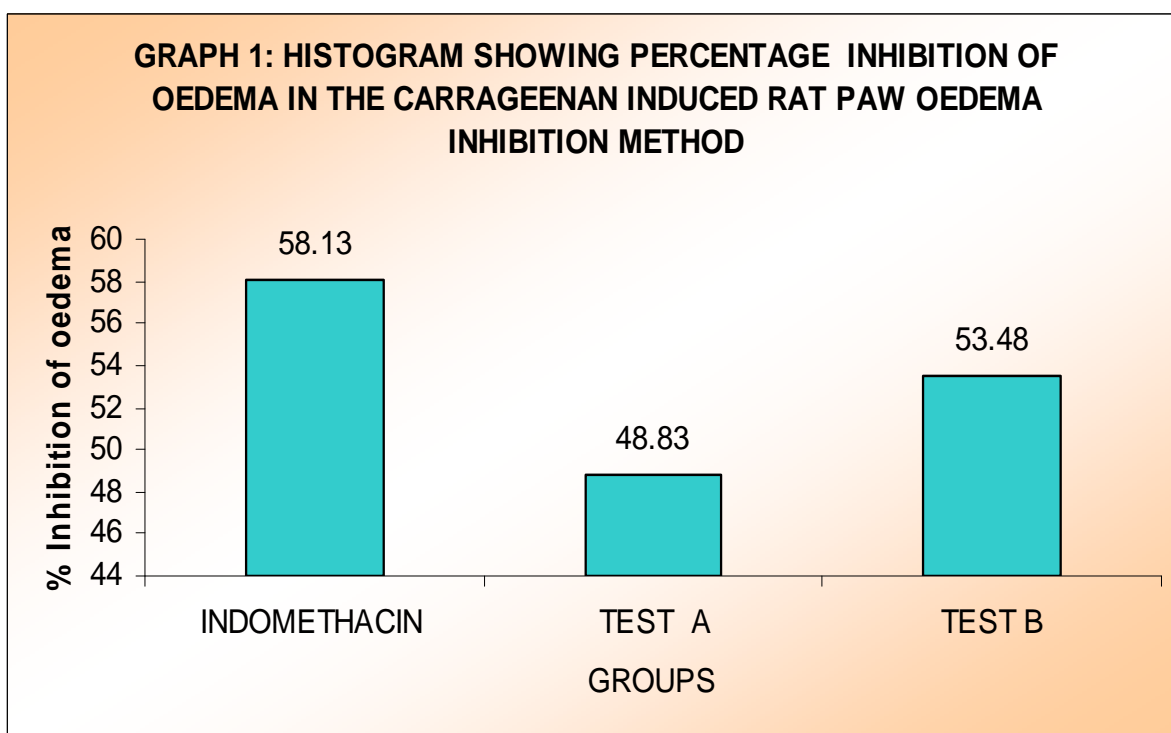


Table 2: Dry weight of cotton pellet in the cotton pellet granuloma method

Groups	Dose/route	Weight of dry cotton pellet granuloma (mg) Mean \pm S.E.M	Inhibition %	P value
Group I Control	0.1ml po	18.27 \pm 0.32	---	—
Group II Indomethacin	20 mg/kg po	7.27 \pm 0.18	60.20	0.05*
Group III Test group A	100 mg/kg po	8.27 \pm 0.34	54.70	0.05*
Group IV Test group B	200 mg/kg po	8.03 \pm 0.27	56	0.05*

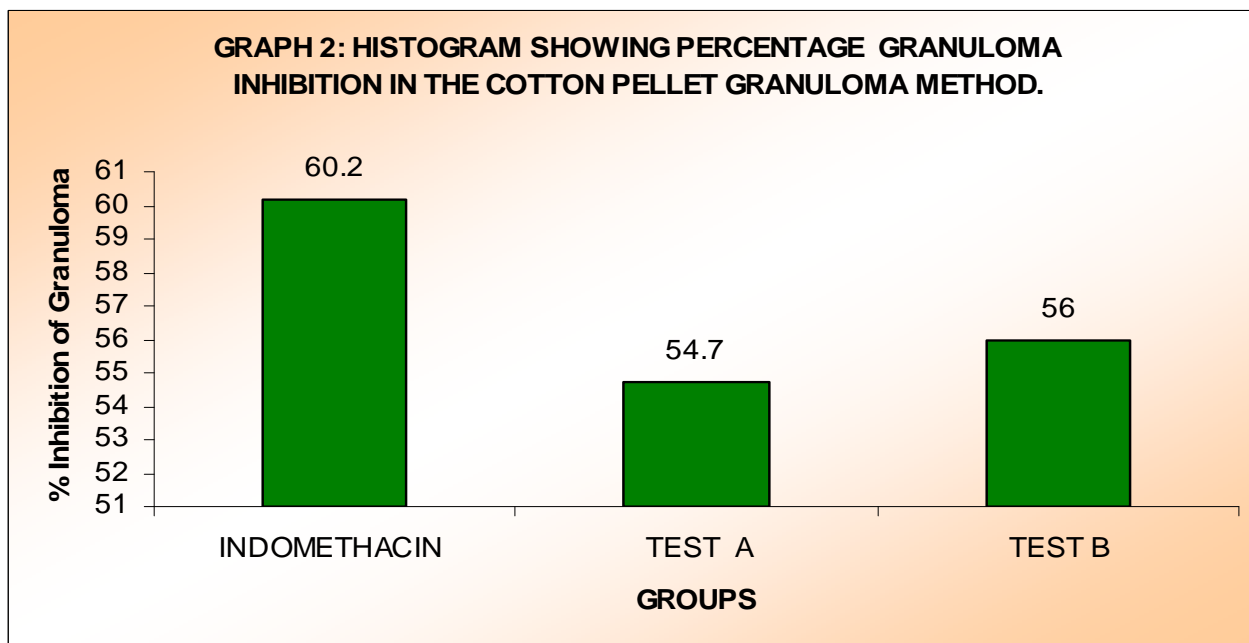
po: per orally, S.E.M: Standard error of mean

* $P < 0.05$: Significant with respect to control group

Effect on Cotton pellet granuloma inhibition method: (Table -2, Graph-2)

The dry weight of cotton pellet granuloma in control, two different doses of *Sida cordifolia* Linn and Indomethacin treated groups is shown in the Table 2, Graph 2. It can be noted that the two doses of *Sida cordifolia* Linn 100 mg/kg and 200 mg/kg, and Indomethacin showed significant

($P < 0.05$) activity in inhibiting dry weight of granuloma. The extract administered at 200 mg/kg, p.o. had a greater anti-granulation (56 %) effect but less than indomethacin (60.2 %).



Sida cordifolia Linn also showed lower percentage of ulcers compared to indomethacin. (Table - 3, Graph-3)

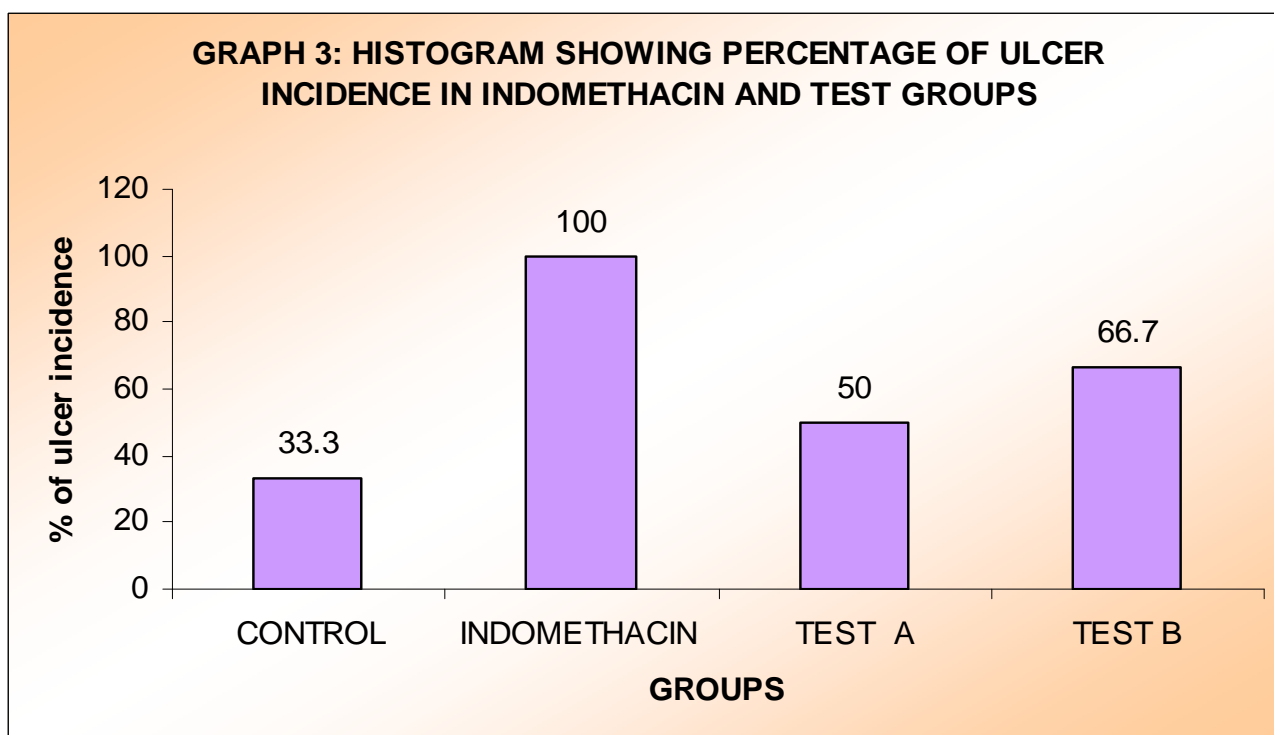


Table 3 : Ulcer Index Of Indomethacin And Test Compound

Groups	Ulcer incidence		P* Value	
	Rats with ulcer	%	With Control	With Indomethacin
Group I Control	2 (6)	33.3	-	P>0.05
Group II Indomethacin	6 (6)	100	P<0.05	-
Group III Test group A	3 (6)	50	P>0.05	P>0.05
Group IV Test group B	4 (6)	66.7	P>0.05	P>0.05

*P < 0.05: Significant, *P > 0.05: Not Significant

DISCUSSION AND CONCLUSION

The current study was done to screen ethanolic extract of *Sida cordifolia* Linn for acute and sub acute anti-inflammatory effects. They were also tested for their probable ulcerogenic properties. This study shows that ethanolic extract of *Sida cordifolia* Linn possesses anti-inflammatory activity in albino rats.

The carrageenan-induced paw edema model in rats is known to be sensitive to cyclooxygenase inhibitors and has been used to evaluate the effect of non-steroidal antiinflammatory agents, which primarily inhibit the cyclooxygenase involved in prostaglandin synthesis [7]. The development of oedema in carrageenan induced rat-paw oedema model follows a biphasic response [8]. The first phase that occurs between 0 to 2.5 h after injection has been attributed to histamine or serotonin release. The second phase occurs at 3 hrs and is caused by the release of bradykinin, protease, prostaglandin and lysosome [9]. On the basis of the time of action of *Sida cordifolia* Linn, Sutradhar et al. inferred that chloroform & methanol extracts of *Sida cordifolia* Linn exhibited sufficient inhibition of paw oedema [5]. The aqueous extract (AE) also showed a significant inhibition at a dose of 400 mg/kg administered orally, but did not block the oedema induced by arachidonic acid [10]. A new alkaloid, 1,2,3,9-tetrahydro-pyrrolo [2,1-b] quinazolin-3-ylamine isolated from *Sida cordifolia* Linn produced inhibition of paw oedema at the doses of 25 and 50 mg/kg [11]. In present study extract of *Sida Cordifolia* Linn at a dose of 100mg/kg & 200mg/kg showed 48.83% & 53.48% inhibition ($p < 0.05$) of rat-paw oedema respectively .

Cotton pellet granuloma model was used to evaluate sub acute anti -inflammatory activity of *Sida cordifolia* Linn. Sub acute inflammation includes proliferation of fibroblasts and the infiltration of neutrophils and exudation. Sub acute inflammation occurs by means of the development of proliferative cells. These cells can either be spread from granuloma form [12]. Efficacy of anti-inflammatory agents in sub acute inflammatory states is indicated by their ability to inhibit the increase in the number of fibroblasts and synthesis of collagen and mucopolysaccharides during granuloma tissue formation [13]. *Sida cordifolia* Linn showed significant ($P < 0.05$) anti-inflammatory activity by reducing granulomatous tissue in cotton pellet granuloma method and thus found to be effective in sub acute inflammatory condition.

Sida cordifolia Linn also showed lower percentage of ulcers compared to indomethacin. Thus, this could be an added advantage with respect to other anti-inflamatory drugs. On the basis of these findings, it may be inferred that ethanolic extract of *Sida cordifolia* Linn has acute and sub acute anti-inflammatory activities. These results corroborate the potential traditional use of the plant in folk medicine. At present, there are less reports on investigation to identify the active

components present in ethanolic extract of *Sida cordifolia* Linn. Further investigations are anticipated to identify the active components and lead to their further clinical use.

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