

Research Article

Anti-Inflammatory Activity of Organic Extract of Leaves of *Sida Cordifolia* Against Egg Albumin, Cotton Pellet-Induced Granuloma in Albino Wistar Rats

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Abstract

Background: *Sida cordifolia* Linn is one of the most important tree species for the environment and commerce in arid and semi-arid parts of the world. *Sida cordifolia* is a member of the Malvaceae family. To assess the methanolic extract of dried *Sida cordifolia* Linn leaves' anti-inflammatory properties.

Methodology: Adult male Wistar rats weighing between 100 and 150 grams were used in this study. Healthy albino rats were administered *Sida cordifolia* Linn. methanolic extract orally at doses of 300 mg/kg for the egg albumin-induced paw oedema model and 200 and 400 mg/kg body weight to evaluate the cotton pellet-induced granuloma approach.

Results: The results of the egg albumin-induced paw oedema showed that the methanolic extract of *Sida cordifolia* leaves at 300 mg/kg⁻¹ showed 55.80% inhibition, while idomethacin showed 56.09%. The results of the cotton pellet-induced granuloma showed that the extract of *Sida cordifolia* at 200 mg/kg⁻¹ showed 26.3% inhibition, 40.5% inhibition, and idomethacin showed 45.5%. ANOVA and Dunnett's test were used to examine the data, with significance set at $p < 0.05$.

Conclusion: Methanolic extract of *Sida cordifolia* Linn. Possesses analgesic activity in a dose-dependent manner in thermal induced model.

1. Introduction

Using medicinal plants is essential to preserving community and individual health. Medicinal plants are a potential source of medical aid and have contributed significantly to worldwide health systems for both humans and animals, both in the event of illness and as a way to maintain good health [1].

A biological reaction to tissue damage or infection is inflammation. It is pathological to have persistent inflammation. This study used a cotton pellet-induced granuloma model in albino Wistar rats to assess the anti-inflammatory properties of methanolic extract from *Sida cordifolia* leaves.

The World Health Organization recommended nations to effectively utilize indigenous knowledge of herbal treatments for sickness prevention and health promotion in the early 1970s [2]. The World Health Organization (WHO) has shown a keen interest in documenting how indigenous people around the world use medicinal herbs [3].

Sida cordifolia, also known as "malva branca," is a plant used in Ayurvedic medicine. In Brazilian traditional medicine, it is used to treat oral mucosal inflammation, blennorrhoea, asthmatic bronchitis and nasal congestion, stomatitis, asthma, and nasal congestion. In many parts of Africa, it is used to treat a variety of illnesses, especially respiratory issues. It has been studied for its potential to reduce inflammation,

stop cell division, and promote liver regeneration. Its ephedrine content gives it psychoactive qualities that impact the heart and central nervous system.

2. Methods

2.1. Materials Required

The following lists the materials needed for the planned study: Glassware, Soxhlet equipment, distillation set, methanol, indomethacin drug and the solvents.

2.2. Plant Material

Sida cordifolia, also known as "ilima," "flannel weed," "bala," "country mallow," or "heart-leaf sida," is a perennial subshrub that is indigenous to India and belongs to the Malvaceae family. The heart-shaped leaf is referred to by the specific name, cordifolia [4–6]. The flowers have a hairy 5-lobed calyx and 5-lobed corolla, and they are dark yellow with occasionally a darker orange core. It invades overgrazed and cultivated fields as a weed, polluting hay and competing with more desirable species [7–10]. The plant has not been found to contain any tannin or glycosides.

The alkaloid ephedrine, which is often found in the several species of the gymnosperm genus Ephedra, is present in the roots and stems [11].

2.3. Animals

The animal house of Virchow Biotech Private Limited in Hyderabad provided adult albino wister rats of both sexes (150–200 g) at ages 6–8 weeks. For the excision and incision wound models, the rats were maintained in groups of four and five (n=5) at random in clean cages with a wire mesh top that contained a hygienic bed of sawdust that was changed every three days. The cages were kept in a well-ventilated environment with a temperature of $25 \pm 1^\circ\text{C}$ and a humidity of $55 \pm 5\%$. All animal procedures were performed in accordance with guidelines for the responsible handling and care of lab animals and with consent from the Institution of Animal Ethics Committee (IAEC) [12].

2.4. Preparation of Plant Extract

We have produced a methanolic extract of *Sida cordifolia* using a Soxhlet device and a hot continuous extraction method. A commercially available Soxhlet equipment can be used to easily prepare crude plant extract. The medication was strong, dried, and packed. There is no need for additional manipulation because the Soxhlet device is an automated, continuous process. Because it only takes 48 hours to extract a standard-sized sample (50 g), this method is quick. The yield of the aqueous extract was 9.52%. The extract was kept in the refrigerator till further investigation was carried out [13].

2.5. Methodology

Phytochemical screening and pharmacological investigation: The pharmacological investigation for assessing Diuretic action can be performed using the following models. 1. Acute toxicity 2. Anti-Inflammatory activity.

We have selected only two models for the inflammatory activity of plant extract based on variables including lab infrastructure and availability, animal facilities, time restrictions, accuracy of results, data acquired rapidly, and cost considerations.

Acute toxicity study

Albino wister rats, weighing between 150 and 200 grams, were employed in the study following a week of acclimation to room temperature, standard rat diet, and unlimited access to tap water in polyacrylic cages. Following an overnight fast, the animals were given a single dosage of *Sida cordifolia* extract paste (2000 mg/kg BW) the following day, and they were observed in accordance with Organization for Economic Co-operation and Development (OECD) guideline 423-2002. The animals were observed for the first twenty-four hours (h), with a focus on the first four hours, and thereafter on an intermittent basis for the following fourteen days. Two additional animals participated in the experiment on the third day, and the previously mentioned observations were made.

Egg Albumin induced inflammation (ANTI-INFLAMMATORY ACTIVITY)

Egg albumin (0.1 mL, 1% in normal saline) was injected into the subplantar tissue of the right hind paw of rats to cause inflammation [14]. Prior to and 0.5, 1, 2, 3, 4, and 5 hours after the phlogistic drug was administered, the injected paw's linear diameter was measured. One hour before to the production of inflammation, a 24-hour fasting rat was given the leaf extract (250 mg/kg i.p.). 10 mL/kg of distilled water was given orally to the control group. The difference in paw circumference between the control and 0.5, 1, 2, 3, 4, and 5 hours after the phlogistic drug was administered was used to measure edema (inflammation). Vernier calipers were used to measure the average (mean) edema [15].

Experimental Design

- **Animals:** 24 albino Wistar rats (150 to 200 g) divided into 4 groups (n=6):
- **Group 1 (V Control):** Vehicle (1 Carboxy methyl cellulose solution).
- **Group 2 (Standard):** Diclo. Sodium (10 mg/kg orally).
- **Group 3 (Test - Low Dose):** Methanolic extract (200 mg/kg orally).
- **Group 4 (T - High Dose):** M. E. (400 mg/kg orally).

Cotton Pellet-Induced Granuloma

- **Procedure:** Rats were given sterile cotton pellets (10 ± 1 mg) subcutaneously in the groin area. Following implantation, treatment began right away and lasted for seven days. The pellets were taken out on the eighth day, dried for 24 hours at 60°C , and weighed to gauge the formation of granulomas [16].
- **Induction:** Under moderate anesthesia, sterilize and subcutaneously implant sterile cotton pellets (10–20 mg each) in the dorsal area.
- **Treatment:** Give an oral gavage of the *Sida cardifolia* extract, normal medication, or vehicle once a day for seven days.
- **Euthanasia:** Under anesthesia, sacrifice the rats on the eighth day.
- **Granuloma Evaluation:** Take the cotton pellets out and weigh them (wet weight). The pellets should be dried to a constant weight (dry weight) at 60°C in an oven. Determine the exudate weight by subtracting the wet weight from the dry weight [17].

Grouping: Divide the rats into four groups (n=6 per group):

- **Group I:** Control (normal saline or vehicle).
- **Group II:** Standard (Diclofenac or indomethacin).
- **Group III:** Test (low dose of Methanolic extract, - 200 mg/kg B.wt).
- **Group IV:** Test (high dose of M. E, 400 mg/kg body weight).

Parameters Assessed

- Reduction in granuloma formation (dry weight).
- Inhibition of exudate formation (wet weight).
- Percentage inhibition of inflammation:

$$\text{Inhibition (\%)} = \frac{\text{Control Weight} - \text{Treated Weight}}{\text{Control Weight}} \times 100$$

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2.6. Statistical Analysis

Data analyzed using ANOVA followed by Dunnett's test, with significance at $p < 0.05$.

3. Results

3.1. Preliminary phytochemical

The methanolic extract of *Sida cardifolia* responded favorably to alkaloids, tannins, flavonoids, carbohydrates, lignins, proteins, and some active principles that are responsible for the various pharmacological activities. Tannins and triterpenes are responsible for hepatoprotective activity, antidiarrheal activity, antiulcer activity, and wound healing, while flavonoids are responsible for neuropharmacological and CNS depressants and anti-inflammatory activity.

3.2. Acute toxicity

The MESC extracts were deemed safe and non-toxic for additional pharmacological screening because they did not exhibit any toxic symptoms or mortality in the acute toxicity studies up to the dose level of 5000 mg/kg, MESC up to 4000 mg/kg, and MESC up to 3000 mg/kg body weight in rats.

3.3. Egg Albumin induced inflammation

3.4 Using the egg white-induced hind paw oedema method, the anti-inflammatory activity of the methanolic extract of *Sida cardifolia* leaves was examined. Table 1 and Figure 1 shows the effects of a methanolic extract of *Sida cardifolia* leaves on hind paw oedema caused by egg white. The findings showed that indomethacin showed 56.09% inhibition and the methanolic extract of *Sida cardifolia* leaves at 300 mg/kg^{-1} showed 55.80% Table 1.

Table 1: Methanolic extract of *Sida cardifolia* leaves has anti-inflammatory properties against paw oedema caused by egg white in albino Wistar rats

Treatment	% Increase in paw volume Mean \pm S.E (n = 6)					% Inhibition in paw volume
	Post insult time of assay (min)					
	0	60	120	180	240	
Control	19.53 \pm 1.20	81.83 \pm 5.22	88.93 \pm 3.92	95.20 \pm 7.7	99.03 \pm 7.21	-
MESC (300 mg kg ⁻¹)	19.28 \pm 0.83	70.38 \pm 4.73	63.2 \pm 2.50	58.8* \pm 3.83	55.8 \pm 2.81	55.8
Indomethacin (4 mg/kg)	14.2 \pm 0.88	33.5 \pm 1.83	38.9 \pm 2.81	41.8* \pm 3.2	58.82 \pm 2.90	56.09

*p < 0.001 Vs Control by student's 't' test. MEAS: Methanolic extract of leaves of *Sida cardifolia*

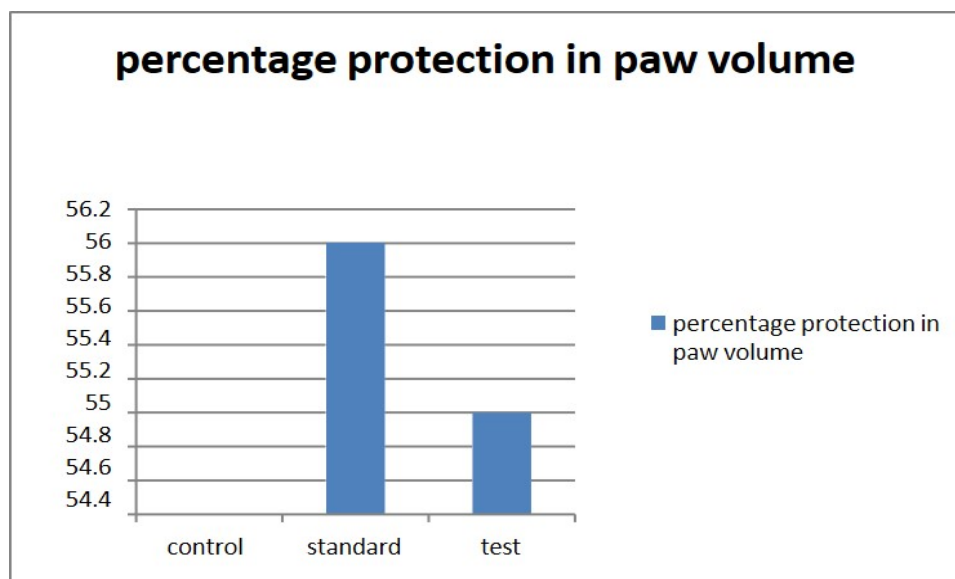


Figure 1: Methanolic extract of *Sida cardifolia* leaves has anti-inflammatory properties against paw oedema caused by egg white in albino Wistar rats

3.4. Cotton Pellet-Induced Granuloma

The Cotton Pellet-Induced Granuloma technique was used to examine the potential of the methanolic extract of *Sida cardifolia* leaves. Table 2 and Figure 2 shows the outcomes of *Sida cardifolia* leaf methanolic extract in Cotton Pellet-Induced Granuloma. According to Table 2, the methanolic extract of *Sida cardifolia* leaves demonstrated 26.3% inhibition at 200 mg/kg⁻¹, 40.5% inhibition at 400 mg/kg⁻¹, and 45.5% inhibition at idomethacin.

Table 2: *Sida cardifolia* leaf methanolic extract's anti-inflammatory properties against cotton pellet-induced granuloma in albino Wistar rats

Group	Wet Weight (mg)	Dry Weight (mg)	Exudate Weight (mg)	% Inhibition of Granuloma
Control	110.5 ± 5.3	55.3 ± 3.1	55.2 ± 2.2	%
MESC (200 mg kg ⁻¹)	85.4 ± 4.5*	40.8 ± 2.6*	44.6 ± 1.9	26.3%
MESC (400 mg kg ⁻¹)	72.1 ± 3.8**	32.9 ± 1.8**	39.2 ± 1.5**	40.5%
Indomethacin (10 mg/kg)	65.3 ± 3.5**	30.1 ± 1.5**	35.2 ± 1.3**	45.5%**

Values are Mean ± S.E. (n=6), *Significant at $p < 0.05$ compared to control, **Highly significant at $p < 0.01$ compared to control

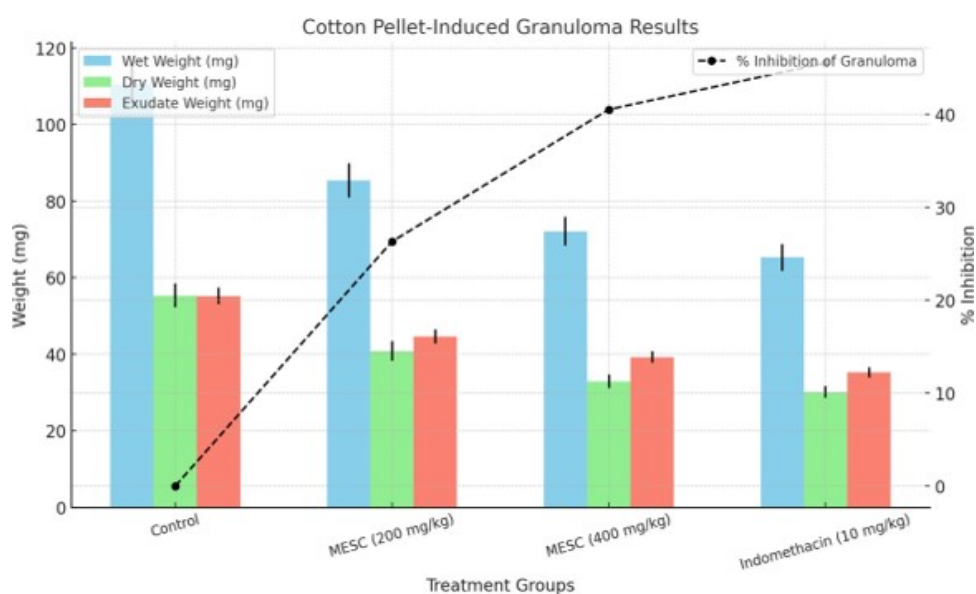


Figure 2: Methanolic extract of *Sida cardifolia* leaves has anti-inflammatory properties against cotton pellet-induced granuloma in albino Wistar rats

4. Discussion

Additionally, the extract prevented oedema caused by egg albumin, indicating that it can reduce inflammation by preventing the release of two mediators that egg albumin releases: histamine and 5-HT [18]. It has been proposed that a number of inflammatory mediators, including complement, histamine, kinins, prostaglandins, and pro-inflammatory cytokines, are involved in the mechanism of inflammation. On the other hand, ASA, a cyclooxygenase inhibitor, considerably decreased the oedema caused by egg albumin. Plants' anti-inflammatory properties have been linked to flavonoids [19].

It has been discovered that the extract contains these. The methanolic extract of *Sida cardifolia* leaves is thought to block at least some of these mediators. Based on its pathophysiology, the inflammation can be classified into three types: allergic, nonspecific, and infectious [20]. The following generic animal models are typically utilized in research of anti-inflammatory drugs: cotton pellet granuloma in rats, carrageenan, egg albumin, or histamine-induced rat paw edema [21]. In order to study chronic inflammation, which has both a transudative and a proliferative phase, cotton pellet granuloma in rats is a great model [22]. The cotton pellet granuloma experiment makes it easy to identify an inflammatory response by granuloma formation, extravasations, and different biochemical exudates. There is a strong correlation between the amount of granulomatous tissue development and the dry weight of the implanted cotton pellet [23]. MESC may prevent the proliferative stages of inflammation by lowering the dry weights of implanted cotton pellets.

Oedema is a biphasic occurrence that follows inflammation caused by carrageenan [24]. The release of serotonin and histamine is responsible for the first stage. Kinin-like compounds are responsible for the oedema that persists between the first and second phases. The egg white is said to have a significant effect on the mast cells. Histamine and serotonin seem to be involved in the oedema it causes. Antihistaminic and anti-serotonin substances reduce inflammatory processes in rats where mast cells play a major role.

Cotton pellet-induced inflammation is followed by oedema, a biphasic event [24]. The first stage is caused by the release of histamine and serotonin. The oedema that lasts between the first and second phases is caused by kinin-like substances. The mast cells are reported to be significantly impacted by the egg white. The oedema it induces appears to be caused by histamine and serotonin. Antihistaminic and anti-serotonin drugs lessen inflammatory processes in rats, which are largely mediated by mast cells [25].

5. Conclusion

For thousands of years, traditional medicines have been utilized as natural medicinal cures all throughout the world, and it is generally acknowledged that their effectiveness is due to a variety of elements. The results of this trial showed that MESC has anti-inflammatory properties and is safe to use. The screening of *Sida cardifolia* leaves reveals the presence of steroids, triterpenoids, flavanoids, tannins, reducing sugar, and saponins. These pharmacological activities offer pharmacological evidence for the traditional use of *Sida cardifolia* for treatment.

This anti-oedematous effect may be caused by the extract's steroids, alkaloids, and triterpenoids. Therefore, more research is necessary to precisely understand the mechanism of action of the methanolic extract of *Sida cardifolia* leaves' anti-inflammatory properties as well as to fractionate, purify, and identify the active principle or principles pre-setting this extract.

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Disclaimer (Artificial Intelligence): The author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.), and text-to-image generators have been used during writing or editing of manuscripts.

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