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Original Article

The Effect of Ethanol Extract of Senggani Leaves (*Melastoma malabathricum*) on Reducing Paw Edema in Rats Induced by Carrageenan

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ABSTRACT

Background: The extract of senggani leaves (*Melastoma malabathricum*) has attracted attention as a potential anti-inflammatory agent due to its diverse phytochemical content, including flavonoids, tannins, and other polyphenols, which have been shown to possess antioxidant and anti-inflammatory activities in several previous studies. This study aims to determine the difference in the percentage of inflammation inhibition of paw edema in rats induced by carrageenan through the administration of senggani leaves extract.
Methods: In this study, 24 rats were divided into 4 groups. Negative control group was given Na-CMC 0.5%, Positive control group was given Na-diclofenac 50 mg/kg BW. Two dosage groups were given senggani extract solution at 250 and 500 mg/kg BW. Carrageenan is used to induce local inflammation by injecting a 2% carrageenan solution in physiological NaCl subcutaneously into the subplantar region of all test animal groups to elicit an edema response. Paw thickness is measured using calipers at hour 0 before inflammation induction, followed by measurements at hours 1, 2, 3, 4, and 5.
Results: The peak inhibitory effect (62.10% and 60.41%) for both doses of senggani extract was observed at the 3rd hour, suggesting a rapid onset of action. At the higher dose (500 mg/kg BW), senggani extract exhibited comparable or even slightly superior inhibitory effects to Na-diclofenac.
Conclusion: Senggani extract has potential as a natural anti-edema agent. Further research is needed to explore its mechanism of action and optimize its therapeutic use.

INTRODUCTION

Inflammation is a complex biological response of the body to injury, irritation, infection, or disease. While it is a natural part of the immune system that helps protect the body from infection and initiate healing, uncontrolled or chronic inflammation can pose serious health risks. Acutely, inflammation often manifests as a rapid local reaction involving the release of inflammatory

mediators such as histamine, prostaglandins, and pro-inflammatory cytokines. This process leads to the classic symptoms of inflammation: redness, swelling, pain, and increased temperature in the affected area.[1] However, persistent or excessive inflammation can cause significant tissue damage and contribute to various chronic disorders and diseases, including autoimmune conditions, cardiovascular diseases, cancer, metabolic syndromes, and neurodegenerative disorders.[2]

The search for herbal remedies to treat inflammation is often driven by several factors, including safety with minimal side effects, natural abundance, potential efficacy in reducing inflammation and associated symptoms, and a holistic approach to addressing overall body balance rather than merely targeting specific symptoms.

Extracts of senggani leaves (*Melastoma malabathricum*) have gained attention as potential anti-inflammatory agents due to their diverse phytochemical content, including flavonoids, tannins, and other polyphenols, which have demonstrated antioxidant and anti-inflammatory activity in previous studies. Moreover, senggani has a long history of use in traditional medicine to address various health conditions, including inflammatory disorders.[3,4]

Carrageenan is a linear polysaccharide extracted from sea algae, such as red seaweed (*Rhodophyceae*). It is used as an experimental model to induce localized inflammation in experimental animals. The potential of senggani leaves extract as an anti-inflammatory agent in carrageenan-induced inflammation in rats is a relevant topic in pharmacology and herbal medicine research. Carrageenan has been widely used to induce inflammation in animal models, particularly in rats. While inflammation is the body's normal response to injury or infection, uncontrolled inflammation can lead to various chronic diseases. Therefore, finding effective and safe anti-inflammatory agents is essential for developing better therapeutic strategies.[4,5]

This study aims to investigate the anti-inflammatory effects of ethanol extract from senggani leaves in inhibiting edema thickness in the paws of rats induced with carrageenan.

METHODS

This research is an in vivo laboratory-based experimental study using a proper experimental design with the serial post-test-only control group. A total of 24 healthy male Wistar rats (Rattus norvegicus), aged 8–10 weeks and weighing 180–220 grams, were used in this study. The rats were randomly assigned into four groups (n = 6 per group). This research was conducted at the Animal and Biomedical Laboratory of FKIK, Universitas Jambi, from August to November 2024. All animal procedures were approved by the Faculty of Medicine and Health Sciences Research Ethics Committee of Universitas Jambi, with Ethical Clearance Number 1913/UN21.8/PT.01.04/2024. Statistical analysis was conducted using One-Way ANOVA, followed by post hoc LSD. A significance level of $p < 0.05$ was considered statistically significant.

Preparation of Senggani Leaves Extract

Senggani leaves were obtained from the Mendalo area, Jambi Province, and were first identified by phenotypic morphology to confirm the species *Melastoma malabathricum*. The senggani leaves were semi-dried at room temperature for 2 weeks, then crushed into a powder and sieved using a 60-mesh sieve. The fine powder was extracted using maceration and evaporation techniques with 96% ethanol as the solvent.[6,7]

Treatment of Experimental Animal Group

Twenty-four rats were divided into four groups: the negative control group received Na-CMC 0.5%, the positive control group received Na-diclofenac at 50 mg/kg BW, and the dosage groups received senggani extract solution at 250 and 500 mg/kg BW.

Plantar Inflammation Animal Model and Foot Edema Measurement

Thirty minutes after treatment, kappa-carrageenan induces local inflammation by subcutaneously injecting a 2% carrageenan solution in physiological NaCl into the subplantar region of all test animal groups to elicit an edema response. Paw thickness is measured using calipers at hour 0 (before inflammation induction), followed by measurements at hours 1, 2, 3, 4, and 5. The percentage of edema inhibition was calculated using the formula shown in Figure 1.[8]

Leukocyte Level Measurement

Leukocyte count was measured through a routine blood test using a Sysmex KX-21 hematology analyzer at LABKESDA, Jambi Province. The principle of this method involves passing blood through a capillary gap located between two electrodes (internal and external electrodes). A laser beam is then directed through this capillary gap, generating electrical impulses that are subsequently detected by a sensor and counting device.

$$Percentage\ of\ Edema\ Inhibition = \frac{Edema\ Thickness\ in\ Control\ Group - Edema\ Thickness\ in\ Treatment\ Groip}{Edema\ Thickness\ in\ Control\ Group} \times 100\%$$

Figure 1. The formula for the Percentage of Edema Inhibition[8]

RESULTS AND DISCUSSION

The thickness of the rat paw was measured after treatment. Figure 2 illustrates the reduction in edema thickening in rat paws over a 5-hour observation period following carrageenan-induced inflammation and treatment with Na-diclofenac (50 mg/kg BW) and ethanol extract of senggani leaves at two doses (250 mg/kg BW and 500 mg/kg BW). The negative control group (Na-CMC 0.5%) showed a consistent and prominent increase in paw thickness, peaking between hour 1 to 3, which indicates a sustained inflammatory response in the absence of active treatment.

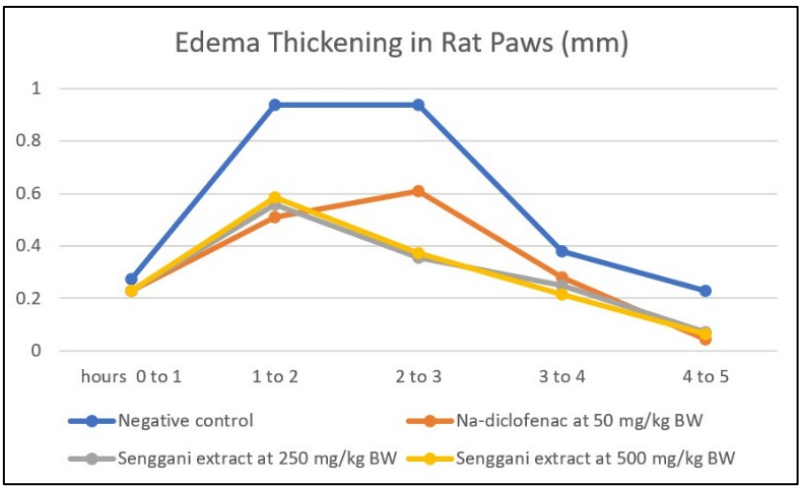

Figure 2. Reduction of Edema Thickening in Rat Paws for Each Treatment Group

Conversely, all treatment groups demonstrated a marked reduction in edema progression compared to the negative control. Notably, the Na-diclofenac and higher-dose senggani extract (500 mg/kg BW) groups exhibited the greatest suppression of edema, particularly from hour 2 onward. The 250 mg/kg BW dose also showed moderate efficacy, closely following the performance of the 500 mg/kg BW group.

The maximum edema thickness in the negative control reached nearly 1 mm, whereas treatment groups remained below 0.6 mm at peak inflammation. This suggests substantial anti-inflammatory activity of the treatments.

The edema thickening was further calculated as a percentage of edema inhibition using the formula (Figure 1), and the results are shown in Table 1. The percentage of edema inhibition observed in different treatment groups measured hourly over 5 hours following carrageenan-induced inflammation. The Na-diclofenac (50 mg/kg BW) group consistently showed a strong anti-edema effect, with the highest inhibition (80.68%) observed at hour 5, and a significant effect already evident at hour 2 (45.82%). The Senggani extract at 250 mg/kg BW also demonstrated a clear inhibitory effect, peaking at hour 3 with 62.10%, and maintaining relatively high inhibition through hour 5 (68.24%). Meanwhile, the Senggani extract at 500 mg/kg BW showed an early onset of effect similar to diclofenac, with notably high inhibition at hour 3 (60.42%) and hour 4 (42.94%), continuing to hour 5 with 71.32%.

Table 1. Percentage Difference in Edema Inhibition of Drug and Extract Dose Groups Compared to the Negative Control Group

Treatment Group	Edema Inhibition Percentage (%, SD) per Hour				
	1	2	3	4	5
Na-diclofenac at 50 mg/kg BW	16.42 (0.45)	45.82 (0.97)[b,c]	35.00 (0.51)[b,c]	25.72 (0.57)[b,c]	80.68 (0.46)[b,c]
Senggani extract at 250 mg/kg BW	16.46 (0.20)	40.46 (0.46)[a,c]	62.10 (0.38)[a,c]	34.36 (0.36)[a,c]	68.24 (0.34)[a,c]
Senggani extract at 500 mg/kg BW	16.42 (0.25)	37.66 (0.40)[a,b]	60.42 (0.49)[a,b]	42.94 (0.304)[a,b]	71.32 (0.43)[a,b]

Note: Data are significantly different from (a) Na-diclofenac at 50 mg/kg BW, (b) senggani extract at 250 mg/kg BW, and (c) senggani extract at 500 mg/kg BW at $p = 0.05$, analyzed using ANOVA followed by post hoc test.

Table 2 shows no significant trend of increase or decrease in leukocyte counts across all treatment groups compared to the control group. The leukocyte levels in all groups remained within the normal range. These results suggest that the treatments, whether Na-diclofenac or Senggani extract, did not significantly affect white blood cell counts under the conditions of this study.

Table 2. Mean of Leucocyte Levels in Rat Models of Inflammation Injected with Carrageenan

Treatment Group	Leukocyte Levels (10^3/mm^3, SD)
Negative Control	11.3 (0.8)
Na-diclofenac at 50 mg/kg BW	10.5 (3.0)
Senggani extract at 250 mg/kg BW	9.2 (2.0)
Senggani extract at 500 mg/kg BW	9.7 (1.3)

Note: The data were not significantly different at p = 0.05, as analyzed using ANOVA

The results confirm that both doses of senggani leaves extract (*Melastoma malabathricum*) possess measurable anti-inflammatory effects in an acute paw edema model. The extract's effect appears to be dose-dependent, with the higher dose (500 mg/kg BW) demonstrating efficacy

comparable to the reference drug Na-diclofenac.

The findings in Table 1 reinforce the anti-inflammatory potential of senggani leaves extract when compared to the reference drug Na-diclofenac. Notably, the 250 mg/kg BW dose achieved the highest inhibition percentage at hour 3, even exceeding the response of diclofenac at the same time point, suggesting a strong peak-phase anti-inflammatory effect.

However, the 500 mg/kg BW dose demonstrated more stable and sustained inhibition across the later time points (hours 3 to 5), indicating a dose-dependent, prolonged effect. The extract's action appears to peak during the prostaglandin-mediated late phase of inflammation, aligning with the pharmacodynamics of many polyphenol-rich plant extracts.

The differences in timing and magnitude of peak inhibition across doses suggest different pharmacokinetic profiles or threshold concentrations for optimal efficacy. The fact that both doses showed significant effects compared to the control, and were comparable or better than diclofenac at certain points, supports the therapeutic promise of senggani extract.

Mechanistically, these effects are likely mediated by flavonoids, tannins, and polyphenols in the extract, which have been reported to: (a) Inhibit COX enzymes (similar to NSAIDs like diclofenac); (b) Reduce oxidative stress via free radical scavenging; (c) Modulate inflammatory cytokines (e.g., TNF-α, IL-1β), and (d) Stabilize membranes and reduce capillary permeability.[9,10]

The anti-inflammatory activity of senggani leaves extract (*Melastoma malabathricum*) can be attributed to several synergistic mechanisms. Firstly, its bioactive constituents—primarily flavonoids and tannins—are known to inhibit cyclooxygenase (COX) enzymes, particularly COX-2, similar to the mechanism of action of nonsteroidal anti-inflammatory drugs (NSAIDs) such as diclofenac. This inhibition leads to decreased synthesis of prostaglandins, which are central mediators in inflammation, pain, and swelling.[11.12] In addition, senggani's antioxidant compounds act as potent free radical scavengers, thereby reducing oxidative stress, which is a key amplifier of inflammation. By neutralizing reactive oxygen species (ROS), the extract helps prevent oxidative damage to cellular membranes and tissue structures.[13]

Moreover, these phytochemicals also modulate the production of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-1 beta (IL-1β), which play crucial roles in amplifying the inflammatory response. Suppressing these cytokines leads to the attenuation of leukocyte recruitment and inflammatory signaling cascades.[14,15] Finally, the extract contributes to membrane stabilization and reduced capillary permeability, which minimizes fluid leakage and tissue swelling—hallmarks of inflammation. This effect is likely due to the astringent properties of tannins and the regulatory influence of flavonoids on endothelial barrier function.[16,17] Taken together, these multi-target actions position senggani extract as a promising natural anti-inflammatory agent capable of both symptom relief and molecular pathway modulation.

As shown in Table 2, the mean leukocyte levels across all treatment groups remained within the normal range for Wistar rats (6.0–18.0 × 10^3/mm^3).[18] Statistical analysis revealed no significant differences between the negative control, Na-diclofenac, and both doses of senggani extract. These findings indicate that neither the standard drug nor the plant extract had a substantial systemic effect on total leukocyte count.

The lack of significant variation suggests that the anti-inflammatory effects observed in paw edema measurements were likely localized rather than systemic. This is consistent with previous research showing that plant-based anti-inflammatory agents like *Melastoma malabathricum* act primarily through modulation of local inflammatory mediators without drastically altering hematological parameters.[19,20]

CONCLUSION

The findings support the potential therapeutic use of senggani extract in managing edema-related conditions. Both senggani extract doses are effective in reducing edema, with the 250 mg/kg BW dose achieving peak inhibition earlier, and the 500 mg/kg BW dose offering a more sustained effect. However, these results are preliminary and derived from preclinical models, therefore, cannot yet be directly applied to human use. Further research is essential to elucidate the extract's mechanisms of action, determine optimal dosing, and thoroughly assess its long-term safety and efficacy in animal and human clinical trials.

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