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Anti-Inflammatory Activity Test of Mangrove Root *(Sonneratia alba)* Ethanol Extract Gel Preparation in Carragenan-Induced White Rats *(Rattus norvegicus)*

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ABSTRAK

Alam menyediakan berbagai senyawa yang dapat memberikan aktivitas sebagai antiinflamasi, salah satunya adanya senyawa yang terkandung dalam akar mangrove (Sonneratia alba). Dalam tumbuhan tersebut khususnya pada bagian akar terdapat senyawa-senyawa metabolit sekunder jenis alkaloid, flavonoid, tanin, triterpenoid dan dari berbagai hasil penelitian yang dilaporkan, flavonoid memiliki khasiat sebagai antiinflamasi. Sediaan obat yang ingin dibuat oleh peneliti adalah sediaan berbentuk gel yang digunakan untuk terapi pengobatan secara topikal. Penelitian dilakukan dengan 15 ekor tikus yang menjadi 5 kelompok uji. Kelompok kontrol positif : diberikan gel Natrium Diclofenac (Voltadex) 20 g (1%), kelompok kontrol negatif : diberikan gel tanpa ekstrak etanol, kelompok konsentrasi 2,5 % : diberikan gel ekstrak etanol 2,5 %, kelompok konsentrasi 5 % : diberikan gel ekstrak etanol 5 %, kelompok konsentrasi 10 % : diberikan gel ekstrak etanol 10 %. Data dianalisa secara deskriptif yang disajikan dalam bentuk tabel dan grafik. Hasil penelitian menunjukan sediaan gel ekstrak etanol Sonneratia alba memiliki aktivitas sebagai anti-inflamasi. Hasil penelitian menunjukan ekstrak etanol akar mangrove Sonneratia alba bisa dijadikan sediaan gel dan pada pengujiannya secara in vivo sediaan gel ekstrak etanol akar mangrove Sonneratia alba memiliki aktivitas sebagai antiinflamasi. Kelompok kontrol sediaan gel ekstrak etanol akar mangrove Sonneratia alba konsentrasi 2,5 %, 5% dan 10 % memiliki persen inhibisi bengkak yang mana berarti sediaan gel ekstrak etanol akar mangrove Sonneratia alba konsentrasi 2,5 %, 5% dan 10 % memiliki aktivitas antiinflamasi.

Kata kunci: *Antiinflamasi, gel, in vivo*

ABSTACT

Nature provides various compounds that can provide anti-inflammatory activity, one of which is the compound contained in mangrove roots (Sonneratia alba). In these plants, especially in the roots, there are secondary metabolite compounds such as alkaloids, flavonoids, tannins, triterpenoids and from various reported research results, flavonoids have anti-inflammatory properties. The medicinal preparation that the researchers want to make is a gel preparation that is used for topical treatment therapy. The research was carried out with 15 rats into 5 test groups. Positive control group: given Diclofenac Sodium gel (Voltadex) 20 g (1%), negative control group: given gel without ethanol extract, 2.5% concentration group: given 2.5% ethanol extract gel, 5% concentration group: given 5% ethanol extract gel, 10% concentration group: 10% ethanol extract gel was given. The data was analyzed descriptively and presented in the form of tables and graphs. The research results showed that the Sonneratia alba ethanol extract gel preparation had anti-inflammatory activity. The research results show that the ethanol extract of Sonneratia alba mangrove roots can be used as a gel preparation and in in vivo testing the gel preparation of Sonneratia alba mangrove root ethanol extract has anti-inflammatory activity. The control group of Sonneratia alba mangrove root ethanol

extract gel preparations of concentrations of 2.5%, 5% and 10% had a swelling inhibition percentage, which means that Sonneratia alba mangrove root ethanol extract gel preparations of 2.5%, 5% and 10% concentration had anti-inflammatory activity.

***Keywords**: Antiinflamasi, gel, in vivo*

1. INTRODUCTION

Indonesia is widely recognized as a rich source of medicinal raw materials, particularly from herbal plants that have been traditionally used for centuries in the treatment of various diseases. According to several sources, more than 9,609 plant species in Indonesia have been documented to possess medicinal properties[1]. One such medicinal plant is the mangrove *Sonneratia alba*.

Sonneratia alba is a mangrove species that thrives in coastal regions and is widely distributed across Southeast Asia and the Indian Ocean. Belonging to the family Lythraceae, it is commonly known in some regions as "Pidada Putih." Various parts of this plant have been traditionally extracted and utilized by coastal communities for natural medicinal purposes[2].

The roots of *S. alba* are known to contain several secondary metabolites, including alkaloids, flavonoids, tannins, triterpenoids, and phenolic compounds[2]. Among these, flavonoids have been widely reported to exhibit anti-inflammatory activity. Flavonoids are believed to inhibit cyclooxygenase and lipoxygenase pathways, as well as leukocyte accumulation at inflammation sites, thereby providing anti-inflammatory effects[3]. In addition, triterpenoids are thought to contribute to anti-inflammatory activity by inhibiting the release of inflammatory mediators such as histamine and kinins, or by interfering with prostaglandin biosynthesis[4].

Inflammation itself is a defense mechanism of the body that aims to neutralize or destroy invading antigens, eliminate irritants, and promote tissue repair[5]. It represents a protective response to harmful stimuli and initiates the healing process[4].

Synthetic anti-inflammatory drugs are categorized into steroidal and non-steroidal groups. However, both categories are associated with a wide range of adverse effects. SAIDs may cause peptic ulcers, reduced immune response, osteoporosis, muscle and adipose tissue atrophy, increased intraocular pressure, and hyperglycemia. NSAIDs, on the other hand, may result in gastrointestinal ulcers and bleeding, renal impairment, and anemia[6]. These side effects highlight the need to explore alternative anti-inflammatory treatments with fewer risks, particularly those derived from medicinal plants.

To develop a topical herbal anti-inflammatory formulation from *S. alba* root, ethanol extracts are prepared and combined with other pharmaceutical excipients. This study aims to create a gel-based dosage form for topical application. A trial-and-error approach was employed to determine a suitable gel formulation, as gels are widely preferred due to their favorable characteristics: they spread well on the skin, offer efficient drug release, have a clear and elegant appearance, leave a transparent film upon application, are easy to wash off, and remain stable during storage.

In the pharmacological evaluation, the anti-inflammatory activity of *S. alba* root ethanol extract was tested in vivo using white rats (*Rattus norvegicus*). Inflammation was induced via carrageenan injection into the paw to produce edema. The anti-inflammatory assessment followed a completely randomized design. Based on the aforementioned background, the objective of this study is to evaluate the anti-inflammatory activity of a gel formulation containing ethanol extract of *Sonneratia alba* root in carrageenan-induced white rats (*Rattus norvegicus*).

2. RESEARCH METHODS

Time and Location of Research

This research was conducted at the Laboratory of Pharmacology and Toxicology and the Laboratory of Pharmaceutics, Faculty of Mathematics and Natural Sciences, Universitas Kristen Indonesia Tomohon. Additional procedures were carried out at the Laboratory of Pharmaceutical Physics, Poltekkes Kemenkes Manado. The study was performed in August 2023.

Tools and Materials

Instruments:

Mortar and pestle, porcelain dish, spray bottle, 100 mL beaker glass, measuring cylinder, gauze, rat cages, grinding bowl, 200 g plastic pot, rotary evaporator, marker, 1 mL injection

syringe (One-med), stopwatch, analytical balance, watch glass, thermometer, animal scale, maceration container (jar), universal indicator, pH meter (Hanna), Bunsen burner, water bath, digital caliper.

Materials:

Thick extract of mangrove root, distilled water (aquadest), experimental animals (white rats), Carbomer 940, triethanolamine (TEA), propylene glycol, methyl paraben, sodium diclofenac (Voltadex 20 g 1%), carrageenan, and 0.9% NaCl solution.

Research Type

This research was a laboratory experimental study using a completely randomized design (CRD).

Research Procedure

1. Sample Preparation
   The harvested *Sonneratia alba* roots underwent both wet and dry sorting. The dried simplicia were air-dried for three days to prevent mold growth during long-term storage. This drying process is crucial to preserve the stability of the bioactive compounds (Luliana et al., 2016). The dried roots were then chopped into smaller pieces and subjected to maceration extraction.
2. Preparation of *Sonneratia alba* Extract
   A total of 1.5 kg of the sample was weighed and macerated in 95% ethanol. The sample was soaked for 5 days (120 hours) with occasional stirring, repeated twice. The resulting mixture was filtered using filter paper to obtain three filtrates, which were then evaporated using a rotary vacuum evaporator to yield a concentrated extract.
3. Preparation of *Sonneratia alba* Gel Formulation
   Three gel formulations were prepared with extract concentrations of 2.5%, 5%, and 10%, respectively[7].

Table 1. Gel Formulation Composition

No	Ingredients	Formula			
		Negative	**2.5%**	**5%**	**10%**
1	*S. alba* Extract	0%	2.5%	5%	10%
2	Carbomer 940	1%	1%	1%	1%
3	Triethanolamine (TEA)	2%	2%	2%	2%
4	Propyl Paraben	0.18%	0.18%	0.18%	0.18%
5	Methyl Paraben	0.05%	0.05%	0.05%	0.05%
6	Propylene Glycol	5%	5%	5%	5%
7	Distilled Water (Ad)	to 100 mL	to 100 mL	to 100 mL	to 100 mL

4. Preparation Steps:
   a. Weigh all ingredients.
   b. Disperse Carbomer 940 in a portion of pre-heated distilled water and grind to form Gel Base I (MI).
   c. Dissolve methyl and propyl parabens in another portion of distilled water and heat (MII).
   d. Once cooled, add propylene glycol to MII to obtain MIII.
   e. Add mangrove root extract to MI and grind until homogeneous (MIV).
   f. Combine MIII with MIV and mix thoroughly. Add triethanolamine and the remaining distilled water, grind until a homogeneous gel is formed.
5. Stability Testing of *Sonneratia alba* Gel
   a. **Organoleptic Evaluation:** Visual inspection was conducted to assess the color, clarity, and odor of the gel. A good gel formulation should appear clear with a semi-solid consistency[8].
   b. **Homogeneity Test:** Gel homogeneity was assessed by spreading a small amount of gel onto a glass slide. A homogeneous formulation was indicated by the absence of coarse particles, suggesting even distribution of the extract and excipients[9].
   c. **pH Test:** Ten grams of gel were dissolved in 50 mL of distilled water, then diluted to 100 mL and stirred until homogeneous. The pH was measured using a standardized pH meter and recorded[8].
   d. **Spreadability Test:** A 0.5 g sample of gel was placed between two glass plates and left for 1 minute. The average diameter was measured from multiple directions. Additional weights of 50, 100, 150, and

300 g were successively applied for 1 minute each, and the spread diameter was measured three times. Gels with a spread diameter of 5–7 cm are considered semi-fluid, while those with <5 cm are classified as semi-rigid[10].

e. **Viscosity Test**: Approximately 100 mL of gel was placed into a beaker, and a viscometer with spindle No. 64 was used. The spindle was immersed in the gel, and the rotation speed was set to 60 rpm[8].

6. Preparation of 1% Carrageenan Solution (Inflammation Inducer)
   Weigh 100 mg of carrageenan and homogenize it in 0.9% physiological NaCl solution. Transfer the mixture to a 10 mL volumetric flask and make up the volume to 10 mL with NaCl solution. Heat and stir until fully expanded, then leave overnight. Each rat was subplantarly injected with 0.1 mL of 1% carrageenan into the left hind paw[11].
7. Observed Variables
   Measurements were taken every hour for 6 hours. The percentage of swelling was calculated using the formula[12]:

$$\textbf{Swelling} = \frac{\mathrm{Tt} - \mathrm{T0}}{\mathrm{T0}}\ x\ 100\%$$

The inhibition percentage was then calculated using swelling values from the negative control (a) and treatment groups (b) as follows[12]:

$$\textbf{Swelling } \boldsymbol{Inhibition} = \frac{\mathrm{a} - \mathrm{b}}{\mathrm{a}}\ x\ 100\%$$

Data Analysis

The data were analyzed descriptively and presented in tables and graphs.

3. RESULTS AND DISCUSSION

Determination of *Sonneratia alba*

The plant under study was first identified before being collected as a sample. This determination process aimed to verify the accuracy of the plant being studied and to avoid errors in material collection and the possibility of mixing it with other plants. The identification of the mangrove root plant (*Sonneratia alba*) was conducted at the Basic Biology Laboratory, Department of Biology, Faculty of Mathematics and Natural Sciences, Sam Ratulangi University.

Yield Calculation of *Sonneratia alba* Root Extract

The yield was calculated by comparing the mass of the dry extract (in grams) with the initial mass of the raw material before the extraction process (in grams). This calculation aimed to determine the percentage of sample remaining after the extraction process. The yield percentage of the *Sonneratia alba* root extract, based on a thick extract weight of 91 grams and an initial simplicia weight of 1,500 grams, was 6.06%.

$$\%\ \textbf{Yield} = \frac{\text{Thick Extract (grams)}}{\text{Initial Simplicia (grams)}}\ x\ 100\%$$

$$= \frac{91}{1.500}\ x\ 100\%$$

$$\%\ \textbf{Yield} = 6.06\%$$

Formulation of *Sonneratia alba* Root Extract Gel Preparation

Table 2. Modified Formula of *Sonneratia alba* Root Extract Gel Preparation

No	Ingredients	Formula			
		Negative	**2.5%**	**5%**	**10%**
1	*Sonneratia alba* Extract	0%	2.5%	5%	10%
2	Carbomer 940	0.5%	0.65%	1%	1%
3	TEA (Triethanolamine)	2%	2%	2%	2%
4	Methyl Paraben	0.18%	0.18%	0.18%	0.18%
5	Propyl Paraben	0.02%	0.02%	0.02%	0.02%
6	Propylene Glycol	1.6%	3%	5%	5%
7	Distilled Water	q.s. to 100 ml	q.s. to 100 ml	q.s. to 100 ml	q.s. to 100 ml

Carbomer was chosen due to its ease of dispersion in water, even at low concentrations. Propylene glycol functions to enhance the properties of carbomer, especially when it binds too tightly to the drug, by increasing the solubility of the active ingredient. Increased solubility facilitates the drug's release from the base, thereby improving its effectiveness[13].

Triethanolamine was selected because it creates an alkaline environment for carbomer, resulting in a thick and clear gel[14]. Ooptimal concentrations for gel base ingredients include carbomer 940 at 0.5%–2%, methyl paraben at 0.18%, propyl paraben at 0.02%, TEA at 2%–4%, and propylene glycol at 0.3%–5%. A combination of 0.02% propyl paraben and 0.18% methyl paraben provides strong antimicrobial preservative activity[15].

The initial gel formula in Table 1 was developed through a trial-and-error process by modifying the concentration of gelling agents to obtain an optimal formulation for *Sonneratia alba* root extract gel, as shown in Table 2. The addition of gelling agents aimed to achieve formulation characteristics in accordance with desired specifications/parameters. The type and concentration of excipients and extract can affect the physical stability of a preparation, thus a physical stability test of the optimal formulation for *Sonneratia alba* gel must be performed. This test ensures that the preparation retains the same properties after production and continues to meet quality parameters during storage[16].

Gelling agents, humectants, and alkalizing agents are critical components that greatly influence the physical properties and stability of a gel formulation. The relevant physical properties include viscosity, spreadability, pH, and organoleptic characteristics, while stability refers to changes in viscosity, pH, and syneresis. In this gel preparation, carbomer was used as the gelling agent, propylene glycol as the humectant, and triethanolamine as the alkalizing agent[14]. Propylene glycol serves as a humectant to maintain the stability of the formulation by absorbing moisture from the environment and reducing water evaporation from the product. Additionally, humectants indirectly help maintain skin moisture, preventing dryness. Methylparaben and propylparaben function as preservatives necessary for gel formulations due to their high water content, which can lead to microbial contamination. Distilled water serves as a solvent in the gel formulation[17].

Stability Test of Gel Preparation
Organoleptic Test

Table 3. Organoleptic Test

No	Formula	Odor	Color	Form
1	Negative Control	Odorless	Clear	Semi-solid
2	2.5% Extract Gel	Characteristic Aromatic	Brown	Semi-solid
3	5% Extract Gel	Characteristic Aromatic	Brown	Semi-solid
4	10% Extract Gel	Characteristic Aromatic	Brown	Semi-solid

The results of the organoleptic test for the negative control, 2.5% concentration, 5% concentration, and 10% concentration showed that all formulas had the same organoleptic properties, namely a semi-solid dosage form, brownish color, and a characteristic odor of *Sonneratia alba* extract. The organoleptic properties of the gel preparation resulted from the combination of ingredients used, including carbomer 940, methyl paraben, and propyl paraben in powder form, and TEA, propylene glycol, and distilled water in liquid form. With the right composition, a semi-solid preparation with specific consistency can be obtained. The brown color of the preparation was due to the thick *Sonneratia alba* extract, as the other ingredients are either white or colorless. The odor was also attributed to the thick *Sonneratia alba* extract, which has a strong and distinctive smell, while the other ingredients are odorless.

Homogeneity, pH, Viscosity, and Spreadability Test

Table 4. Homogeneity, pH, Viscosity, and Spreadability Test

No	Formula	Homogeneity	pH	Viscosity (m.Pas)	Spreadability (cm)
1	Negative Control	Homogeneous	7.881	9,260	4.6
2	2.5% Extract Gel	Homogeneous	7.694	3,610	5.2
3	5% Extract Gel	Homogeneous	7.230	1,740	5.2
4	10% Extract Gel	Homogeneous	6.584	820	6.0

The results of the homogeneity test for the negative control, 2.5%, 5%, and 10% extract concentrations showed that all formulations were homogeneous with no visible particles. This indicates that the extract and other ingredients were well dissolved and evenly mixed, fulfilling the homogeneity criteria. A homogeneous preparation ensures a consistent amount of active substance in each dose.

The pH test results for all four gel formulas (negative control, 2.5%, 5%, and 10% extract concentrations) fall within the acceptable pH range specified by SNI 16-4399-1996 for topical preparations (4.5–8.0) and are compatible with the natural pH of the skin (4.5–7.5). Topical formulations should ideally match the skin's pH to allow effective diffusion. A formulation that is too alkaline may cause dry skin, while one that is too acidic may trigger irritation. These results indicate that all four gel formulas are safe for use on the skin and are unlikely to cause irritation[14]. The differences in pH levels among the formulas are due to the base used, which is a result of neutralizing a strong acid with a strong base. Using 0.5–1% carbopol produces a base with pH 3, which, when neutralized with triethanolamine (TEA), results in a neutral base[18]. The higher the concentration of *Sonneratia alba* extract, the more acidic the gel becomes. A lower pH also correlates with a more fluid consistency and wider spreadability[19].

The viscosity test aims to determine the thickness of the gel formulation. Gel thickness is influenced by the gelling agent used, in this case, carbopol 940. A good viscosity range for gel preparations is between 500–10,000 mPas[20]. The table shows that the viscosity values of the formulas vary due to differences in the concentrations of carbopol and TEA. Higher concentrations of these components lead to higher viscosity. Viscosity is also influenced by the formulation's pH, as acidic carbopol results in low viscosity, which is increased by neutralization with TEA.

The spreadability test aims to measure the gel's ability to spread when applied to the skin. A spread diameter of less than 5 cm classifies the gel as semirigid, while a spread diameter of 5–7 cm categorizes it as semifluid[21]. A semi-solid preparation with high spreadability allows for wider distribution on the skin, ensuring the active ingredient is evenly dispersed. As viscosity increases, the gel becomes less fluid and its spreadability decreases[22]. In this study, spreadability was measured by recording the spread diameter from several angles using varying applied loads[21].

Anti-Inflammatory Test On White Rat Paws

From the average swelling diameter data, a noticeable difference can be seen between the negative control group and the four other groups induced with carrageenan. Similar to the positive control group, the 2.5%, 5%, and 10% concentration groups exhibited a continuous increase in swelling diameter from the first hour to the sixth hour after carrageenan induction. This indicates that 0.1 mL of 1% carrageenan was sufficient to induce swelling, allowing differences between the test groups to be observed. At the sixth hour, a decrease in diameter was observed in the negative control group, suggesting that carrageenan-induced swelling lasts only around 5–6 hours and gradually diminishes within 24 hours after injection[23].

Process of edema formation induced by carrageenan occurs in two phases and involves several inflammatory mediators[24]. The first phase takes place within the first 3 hours after carrageenan induction and involves the release of mediators such as histamine, serotonin, bradykinin, and increased prostaglandin synthesis around the injured tissue. The second phase occurs between the fourth and fifth hours, during which prostaglandins, proteases, and lysosomal enzymes are released. This second phase is generally more sensitive to anti-inflammatory drugs.

Table 5. Observation Results of Anti-inflammatory Test on White Rat Paws

Treatment	Rat	T0	T1	T2	T3	T4	T5	T6
Negative Control	A I	4,85	7,23	9,20	9,37	9,83	9,55	9,44
	A II	4,09	7,24	8,20	8,55	9,26	9,30	9,40
	A III	4,90	7,19	9,26	9,70	9,79	9,80	9,69
	Average	4,61	7,22	8,89	9,21	9,63	9,55	9,51
Positive Control	BI	4,45	6,68	6,67	6,86	6,20	6,89	6,88

	BII	4,98	7,11	7,22	8,08	7,74	7,13	7,85
	BIII	4,55	6,84	6,18	8,10	8,25	7,43	7,43
	Average	4,66	6,88	6,69	7,68	7,40	7,15	7,39
Concentration 2.5%	C I	4,70	7,13	9,40	9,95	9,60	9,92	8,88
	C II	5,10	7,40	7,36	7,56	8,17	8,61	8,78
	C III	5,07	5,71	8,35	9,04	8,41	7,34	7,87
	Average	4,96	6,75	8,37	8,85	8,73	8,62	8,51
Concentration 5%	D I	4,98	7,97	9,03	9,85	10,01	9,93	9,75
	D II	4,21	7,80	7,95	8,68	9,30	8,25	8,44
	D III	4,70	7,65	8,07	9,83	9,79	9,75	9,17
	average	4,63	7,81	8,35	9,45	9,70	9,31	9,12
Concentration 10%	E I	4,81	7,45	8,74	9,20	9,31	8,76	9,40
	E II	4,38	7,13	8,12	8,65	9,40	8,92	8,43
	E III	4,95	7,06	7,20	8,54	7,93	7,50	8,30
	Average	4,71	7,21	8,02	8,80	8,88	8,39	8,71

The inflammation induced by carrageenan results in acute inflammation without causing tissue damage, even though the inflammation may persist for up to 360 minutes and gradually decreases within one day. Carrageenan, as an inducer of inflammation, can be influenced by anti-inflammatory drugs. Its response to anti-inflammatory agents is more sensitive compared to other anti-irritants.

There are three phases of swelling formation induced by carrageenan. The first phase involves the release of histamine and serotonin, lasting up to 90 minutes. The second phase is characterized by the release of bradykinin, occurring between 1.5 to 2.5 hours after induction. In the third phase, prostaglandins are released approximately 3 hours post-induction. Swelling then develops rapidly and reaches its maximum diameter around 6 hours after induction.

Factors influencing the research data results may include the animal's age, body weight, and inconsistencies in postnatal developmental stages, which can lead to failures in translating animal data to humans. The age and body weight of animals can affect drug metabolism, gene expression, metabolic parameters, and other dependent variables measured in animal studies[25].

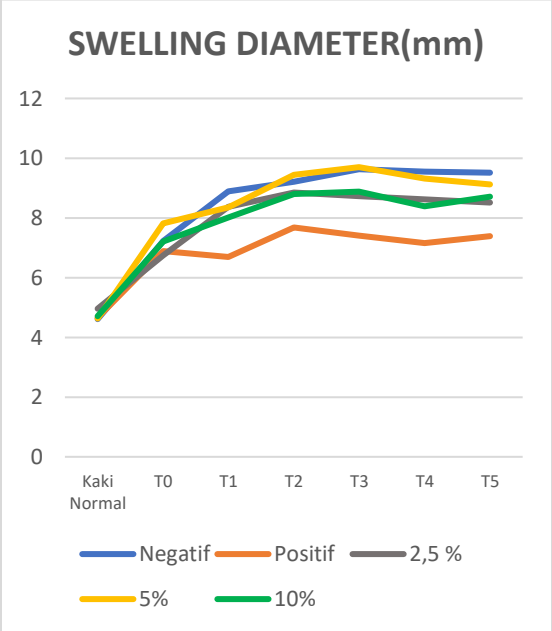

Figure 1. Swelling Diameter

Calculation of Swelling Percentage

Table 6. Swelling Percentage

Group	T0	T1	T2	T3	T4	T5	T6
Negative Control	0.00	56.50	92.63	99.57	108.67	107.01	106.14
Positive Control	0.00	47.57	43.56	64.81	58.73	53.43	58.51
2.5%	0.00	36.11	68.86	78.55	76.06	73.97	71.69
5%	0.00	68.61	80.35	104.18	109.50	101.08	96.98
10%	0.00	53.04	70.16	86.63	88.40	78.08	84.79

The swelling percentage of the experimental animals' feet, in this case white rats (*Rattus norvegicus*), can be seen more clearly in Figure 2.

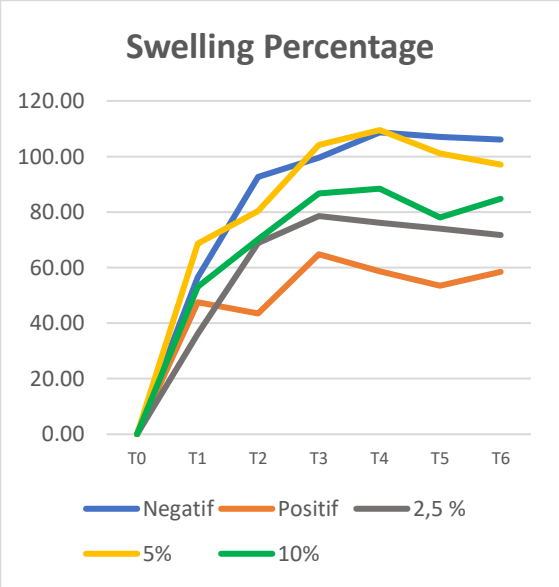

Figure 2. Swelling Percentage

Based on the swelling percentage graph data, it can be seen that 1 hour after the induction of 1% carrageenan, there was an increase in the average diameter or thickness of the rats' paw pads in each treatment group. This indicates that swelling had occurred in the paw pads of the white rats due to the induction of the irritant substance, 1% carrageenan at a dose of 0.1 ml. All treatment groups showed the presence of swelling in the rats' paw pads. The negative control group exhibited a greater swelling diameter compared to the other treatment groups, and the swelling persisted up to the 6th hour (T5). This confirms that the swelling induced by carrageenan can last for 6 hours.

Calculation of Inhibition Percentage

The calculation of the swelling inhibition percentage was carried out to determine the extent to which the ethanol extract gel of mangrove root inhibits inflammation in the paw pads of rats. The results of the swelling inhibition percentage are presented in table and graph form. Based on the findings, it was observed that the 2.5%, 5%, and 10% extract gel groups demonstrated swelling inhibition, with the positive control group showing the highest inhibition percentage.

The swelling process induced by carrageenan occurs in two phases and involves several inflammatory mediators[24]. The first phase takes place within 3 hours after carrageenan induction, during which mediators such as histamine, serotonin, bradykinin, and increased prostaglandin synthesis are released around the injured tissue. The second phase begins from the fourth to fifth hour, involving the release of prostaglandins, proteases, and lysosomes. This second phase is generally sensitive to anti-inflammatory drugs.

Table 7. Inhibition Percentage

Group	T1	T2	T3	T4	T5	T6	Average
Negative Control	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Positive Control	15.81	52.97	34.91	45.96	50.07	44.87	40.77
2.5%	36.09	25.66	21.11	30.01	30.87	32.46	29.37
5%	-21.43	13.26	-4.63	-0.77	5.54	8.64	0.10
10%	6.13	24.26	12.99	18.65	27.04	20.11	18.20

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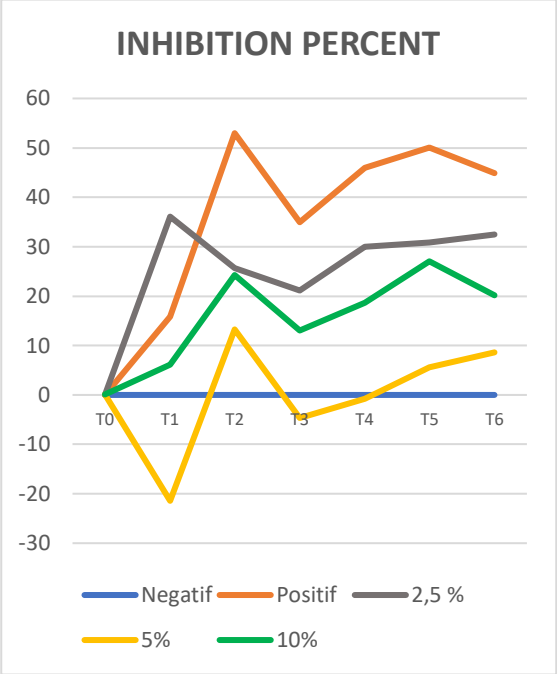

Figure 3. Inhibition Percentage

Based on the table and graph of inhibition percentages, it can be seen that the positive control group, as well as the groups treated with 2.5%, 5%, and 10% concentrations of the mangrove root extract gel, exhibited anti-inflammatory activity against inflammation (swelling) in the feet of white rats (*Rattus norvegicus*). The inhibition percentage indicates that the positive control group had the highest inhibition rate.

In the results for the 5% extract gel concentration, the inhibition percentage was lower than that of the negative control group during the first 1–2 hours after treatment. This may be due to differences in the animals' physiological responses during the release of inflammatory mediators after carrageenan induction, which led to a higher swelling percentage compared to the negative control group. These variations could be influenced by the test animals' conditions, such as body weight and age.

The anti-inflammatory activity of the mangrove root extract gel can also be seen in the average inhibition percentage of inflammation. The negative control group did not exhibit any inhibition percentage because it only contained the gel base without any active anti-inflammatory compound (placebo). The positive control group showed the highest inhibition percentage within 1–5 hours after treatment. The 2.5%, 5%, and 10% extract gel concentrations also demonstrated inflammation inhibition, indicating that the mangrove extract gel began to show activity as early as the 2nd time point (T1), or 1 hour after treatment, with its activity gradually declining over time.

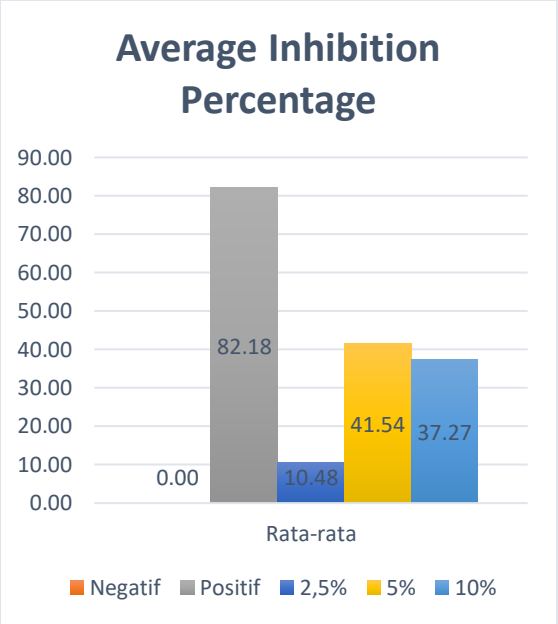

Figure 4. Average Inhibition Percentage

The results of the anti-inflammatory activity test based on the measurement of swelling diameter in the rats' paw pads using a caliper may be influenced by several factors. These include the difficulty of handling the test animals and their positioning during scale reading, as well as the presence of impurities in the 0.9% NaCl solution, which could affect the accuracy of the measurements.

4. CONCLUSION

The results of the study indicate that the ethanol extract of *Sonneratia alba* mangrove root can be formulated into a gel preparation, and in in vivo testing, the ethanol extract gel of *Sonneratia alba* mangrove root demonstrated anti-inflammatory activity. Based on the observations, the positive control group showed the highest percentage of inhibition compared to other control groups. The gel preparation groups containing ethanol extract of *Sonneratia alba* mangrove root at concentrations of 2.5%, 5%, and 10% exhibited edema inhibition, which indicates that the gel formulations at these concentrations possess anti-inflammatory activity.

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