




## Anti Inflammation Effectivity Gel Formulated From Ethanol Extract of Ketepeng Cina Leaves (*Cassia alata* L.) Leaves

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### ABSTRACT

Metabolites including flavonoids, tannins, saponins, alkaloids, terpenoids, anthraquinones, phenolics, glucose, and phytosterols are present in the Ketepeng Cina (*Cassia alata* L.) plant. When physical stress causes tissue injury, inflammation is the body's natural defensive reaction. This research aim to formulate gel preparation from ethanol extract of ketepeng cina leaves and determine its antiinflammatory activity on carrageenan induced mice (*Mus musculus*). This is experimental research, including collection of materials and prociessing of materials, making simplisia, making ethanol extract with a concentration of 5%, 10% and 15%, making ethanol extract gel of Ketepeng Cina leaves and testing the anti-inflammatory effect on mice. The results showed that the ethanol extract can be formulated in the form of gel dosage form with concentrations of 5%, 10% and 15% and has a qualified quality preparation evaluation. The observation results showed that the percentage of Inflammation Inhibition at the 5th hour on the gel with a concentration of 15% was 100%. Statistical Analysis of One Way Anova the percentage of inflammation at the 5th hour to the 6th hour showed a significant difference. So it can be stated that the preparation of ethanol extract gel of Ketepeng Cina leaves has the best anti-inflammatory effect at a concentration of 15%.

**Keywords:** Gel; Extract; *Cassia alata*.L; Anti-inflammation; carrageenan

### INTRODUCTION

Ketepeng (*Cassia alata* L.) is a medicinal plant that grows wild in Indonesia. The leaves contain alkaloids, saponins, flavonoids, tannins and anthraquinones. Ketepeng leaves have properties for treating skin problems such as ringworm, scabies, tinea versicolor and eczema. Apart from that, ketepeng leaves also help treat dengue fever and can help control diabetes (Fajri et al., 2023). The part of the Ketepeng Cina plant that has been widely reported is the leaves (Udin et al., 2023). Apart from the leaves, the flowers also contain secondary metabolite compounds of flavonoids, phenolics, saponins and tannins and have antioxidant activity (Safitri et al., 2020).

The Ketepeng Cina plant also has potency as a

traditional medicine for treating bacterial infections such as syphilis, bronchitis, fungal infections such as tinea versicolor, ringworm, inflammation, itching, herpes, constipation and parasitic infections such as malaria (Egra, 2019). Another name for Ketepeng Cina (*C. alata* L.), commonly known as gellinggang, has a spicy and warm taste and is believed to be anti-inflammatory (Nabil, 2023). Traditionally used as a medicine treat skin diseases and has the potential effect as anti-allergic, anti-inflammatory, antioxidant, anti-cancer, anti-diabetic, anti-fungal and has been proven to have pharmacological properties against certain diseases (Fatmawati et al., 2020).

Anti-inflammatories are drugs or classes of drugs that reduce inflammation. Inflammation is the body's

reaction to infection, irritation, or injury, characterized by redness, heat, swelling, and pain. This is a non-specific immune response and involves four microscopic pathological phenomena: swelling (tumor), increased temperature (calor), redness (ruber), and impaired organ function (Emelda et al., 2023). Gel is a semisolid preparation consisting of inorganic particles or organic molecules, and is penetrated by a liquid (Astuti & Utami, 2021). The advantages of gel preparations include that gel formulas generally provide faster drug release compared to ointments and creams. Emulgel for dermatological use has several favorable properties such as non-greasy, easy to spread, easy to remove, non-staining, water soluble, transparent and pleasant appearance (Singla et al., 2011). Researchers are interested in formulating ethanol extract of Ketepeng Cina leaves in a gel that has anti-inflammatory properties.

## METHODS

### Tools and Materials

The tools used in this research were blenders, sieves, water baths, drying cabinets, beaker glasses, jar bottles, porcelain crucibles, measuring cups, stirring rods, spatulas, dropper pipettes, filter paper, rotary evaporators, pH meters, vials, ovens, aluminum foil, medicine pot, hot plate, mortar and pestle, mice cage, analytical balance, stopwatch, plethysmometer. The ingredients used were Ketepeng Cina leaf, 1% carrageenan, 70% ethanol, the medicinal preparation used as a comparison was diclofenac sodium gel.

### Making Ketepeng Cina Leaf Extract Gel

Making ethanol extract gel from Ketepeng Cina leaves, preparing the tools and materials used, weighing the materials needed according to the formula (Table 1.). CMC-Na was developed with hot

water, stirred until completely dispersed and a gel base was formed. Add methyl paraben, glycerin, propylene glycol and then grind it homogeneously, and add the Ketepeng Cina leaf extract, grind it homogeneously until a gel forms.

## Anti-inflammatory Testing of Gel Preparations

### Making Carrageenan and Preparation of Test

#### Animals

A total of 1 gram of carrageenan powder is dissolved in 30 mL of 0.9 % NaCl solution (Astika et al., 2022). The anti-inflammatory effect was tested using 25 healthy male white mice, 20-40 grams, aged 2-3 months. The mice that will be used in research need to be quarantined and acclimatized for one week, to reduce stress during transportation (Noor et al., 2022). Each treatment group used 5 mice which were calculated using the Federer formula (Nindya RA., 2021) shown in equation 1.

$$(n-1)(t-1) \geq 15 \quad (1)$$

Note n : sample of each group

t : number of groups

### Anti-Inflammatory Gel Test on Male White Mice (*Mus musculus*)

Prepare all test animals, then weigh and mark the tail and left leg. All mice used had leg volume measured using a plethysmometer (Vo). 0.1 mL of carrageenan was injected into the soles of the mice's feet. Then the mice were waited for 1 hour and the volume of the mice's legs that had been induced was measured to confirm that edema had occurred in the legs. Gel was applied to the legs of mice that had developed edema and after 1 hour, it was measured as the volume of the first hour (V1) after treatment.

**Table 1.** Ketepeng Cina Leaf Gel Formula 5%, 10%, 15% (Hamzah et al., 2006)

Component	Concentration 5% (F3) (g)	Concentration 10%(F4) (g)	Concentration 15%(F5) (g)
Crude extract	0.75	1.5	2.25
CMC-Na	0.75	0.75	0.75
Glycerin	1.5	1.5	1.5
Propylene glycol	0.75	0.75	0.75
Methyl paraben	0.3	0.3	0.3
Aquadest	ad.15	ad.15	ad.15

F1 = control negative (without extract)

F2 = control positive (Diclofenac Sodium Gel 1% Voltaren)

F3 = Gel Formula 5%

F4 = Gel Formula 10%

F5 = Gel Formula 15%

Prepare all test animals, then weigh them and mark their tails and left legs. All mice used had their leg volume measured using a plethysmometer 0.1 mL of carrageenan was injected into the soles of the mice's feet. After 1 hour, the foot volume of mice that had been induced with carrageenan was measured as the initial volume ( $V_0$ ) before treatment. Then the gel was applied to the feet of mice that had been induced by carrageenan (F1, F2, F3, F4 and F5) in each group of mice. After 60 minutes of treatment, the volume of the mice's left leg was measured again using a plethysmometer. Measurements were carried out every 60 minutes for 360 minutes. Changes in the level of swelling that occurred were recorded as the volume of the mice soles ( $V_t$ ). The volume of inflammation (inflammation) is the difference in the volume of the soles of the mice's feet after and before the injection of 1 % carrageenan (Apridamayanti et al., 2018).

Calculation of percent inflammation and percent inflammation inhibition using equation (1) and (2).

$$\% \text{ Inflammation} = \frac{V_t - V_0}{V_0} \times 100\% \quad (1)$$

$V_t$ : volume of mice's feet after was induced by carrageenan

$V_0$ : volume of mice's feet before was induced by carrageenan

$$\% \text{ Inflammation inhibition} = \frac{a-b}{a} \times 100\% \quad (2)$$

a: Control group mean inflammation percent

b: Average percent inflammation of the test treatment group and Diclofenac Sodium Gel 1% Voltaren

### Data Analysis

Data obtained from the research results were analyzed using Oneway Analysis of Variance (ANOVA).

**Table 2.** Measurement of Mice Foot Edema Volume

Group	Foot Volume at the hour - (mL) $\pm$ SD						
	0	1	2	3	4	5	6
F1	0.3 $\pm$ 0.00	0.5 $\pm$ 0.00	0.5 $\pm$ 0.00	0.5 $\pm$ 0.00	0.48 $\pm$ 0.03	0.48 $\pm$ 0.03	0.53 $\pm$ 0.03
F2	0.33 $\pm$ 0.06	0.43 $\pm$ 0.06	0.5 $\pm$ 0.09	0.5 $\pm$ 0.00	0.46 $\pm$ 0.12	0.33 $\pm$ 0.06	0.33 $\pm$ 0.058
F3	0.23 $\pm$ 0.06	0.28 $\pm$ 0.06	0.35 $\pm$ 0.09	0.38 $\pm$ 0.06	0.36 $\pm$ 0.12	0.35 $\pm$ 0.03	0.33 $\pm$ 0.05
F4	0.27 $\pm$ 0.06	0.37 $\pm$ 0.06	0.43 $\pm$ 0.08	0.43 $\pm$ 0.12	0.38 $\pm$ 0.03	0.35 $\pm$ 0.03	0.26 $\pm$ 0.058
F5	0.27 $\pm$ 0.12	0.35 $\pm$ 0.12	0.38 $\pm$ 0.14	0.38 $\pm$ 0.14	0.38 $\pm$ 0.03	0.26 $\pm$ 0.12	0.26 $\pm$ 0.116
Sig Anova	0.485	0.89	0.380	0.467	0.232	0.024	0.04

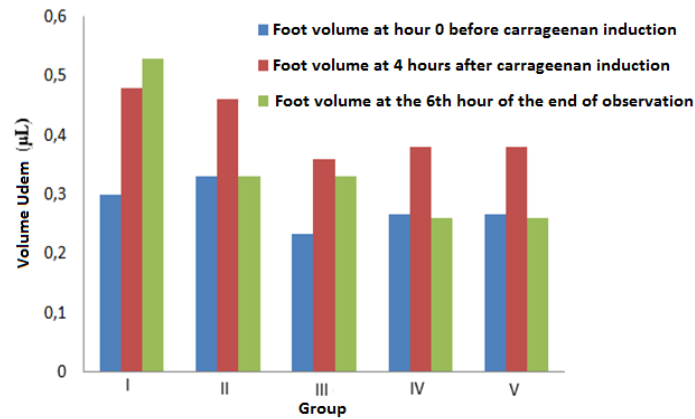
## RESULTS AND DISCUSSION

### Results of Inflammation Volume in Mice Feet

Changes that occur in the volume of the mice's feet are expressed as the volume of mice inflammation. The group that experiences a decrease closer to the initial volume can be interpreted as having the effect of reducing the volume of mice's foot inflammation caused by carrageenan. Volume measurements are taken every hour for 6 hours, and starting from the initial foot volume before inflammation occurs (Table 2). Figure 1 showed changes in the volume of the mouse paw before inflammation ( $V_0$ ), during inflammation at 4 hours and at the end of observation (6 hours).

The results showed a decrease in the volume of inflammation at the concentration (5%) by 0.33 mL at the 6th hour, approaching the initial volume of 0.23 mL. The concentration (10%) showed a good decrease at the 6th hour of 0.27 mL, in accordance with the initial volume. The concentration of (15%) showed a decrease at the 6th hour of 0.27 mL, returning to the initial volume. All concentrations showed the effect of reducing the volume of inflammation in the feet of mice.

Based on the statistical results of the edema volume values above at the 1st hour to the 4th hour there were no differences between groups with respective significance values of 0.485, 0.089, 0.380, 0.467 ( $p > 0.05$ ), and at the 5th hour Until the 6th hour, there was a significant difference of 0.024 and 0.004 respectively ( $p < 0.05$ ). Observations from the statistical test results from the time before inflammation to the 4th hour showed a decrease and at the 5th and 6th hours it could be stated that there was a difference from the previous time.



**Figure 1.** Graph of edema volume at the 0th, 1st and 6th hours

### Percentage of Inflammation in Mice's Feet

Based on the results obtained, the smaller the inflammation produced, the better the anti-inflammatory activity of the Ketepeng Cina leaf extract gel preparation is in reducing inflammation. This is thought to be due to the activity of the active compounds contained in Ketepeng Cina leaves. Based on the results of phytochemical screening, overall Ketepeng Cina leaves contain bioactive contents such as flavonoids, alkaloids, tannins and others. Compounds that play an active role in reducing edema are flavonoid compounds in the body that act to inhibit lipooxygenase and cyclooxygenase which play a role in inhibiting the accumulation of leukoside in inflammatory areas.

The percentage of inflammation at the concentration 10% at the 6th hour was 0.0%, and at the concentration 15% at the 5th to 6th hour was also 0.0%. Inhibition of inflammation at concentrations of 10% and 15% reached 100% at the 5th and 6th hours. Concentration 15% provided the most effective anti-

inflammatory activity.

Based on the statistical results of the edema volume value above at the 1st hour there was no difference between groups with a significance value of 0.416 ( $p > 0.05$ ), and at the 2nd and 3rd hours there was a significant difference of 0.008 each. and 0.035 ( $p < 0.05$ ), and at the 4th hour there was no difference between groups with a significance value of 0.919 ( $p > 0.05$ ), and at the 5th to 6th hour it was seen there is a significant difference of 0.000 and 0.000 respectively ( $p < 0.05$ ).

Observations for the percentage of inflammation that researchers had previously carried out, for the hourly observation process for 6 hours, the differences between groups, were significantly different from several studies on anti-inflammation. (Wima et al., 2023) Researchers found that there were differences in the 5th and 6th hours. The healing process for edema caused by carrageenan induction lasted for 6 hours and gradually reduced within 24 hours (Taufiq et al., 2008; Utami et al., 2011).

**Table 3.** Inflammation from the first hour to the sixth hour

Group	Average percentage of inflammation hour to - ± SD (%)					
	1	2	3	4	5	6
F1	66.67 ± 0.0	66.67 ± 0.0	66.67 ± 0.0	60.00 ± 0.09	60.00 ± 0.09	76.67 ± 0.09
F2	30.0 ± 0.05	50.0 ± 0.0	52.78 ± 0.24	38.00 ± 0.09	0.00 ± 0.00	0.00 ± 0.00
F3	21.42 ± 0.05	50.0 ± 0.0	62.85 ± 0.14	54.29 ± 0.09	50.00 ± 0.24	8.28 ± 0.03
F4	33.333 ± 0.09	63.89 ± 0.13	61.25 ± 0.09	42.25 ± 0.241	23.75 ± 0.19	41.43 ± 0.42
F5	31.25 ± 0.21	45.85 ± 0.07	42.5 ± 0.07	35.00 ± 0.433	0.00 ± 0.00	0.00 ± 0.00
Sig Anova	0.416	0.008	0.035	0.919	0.000	0.000

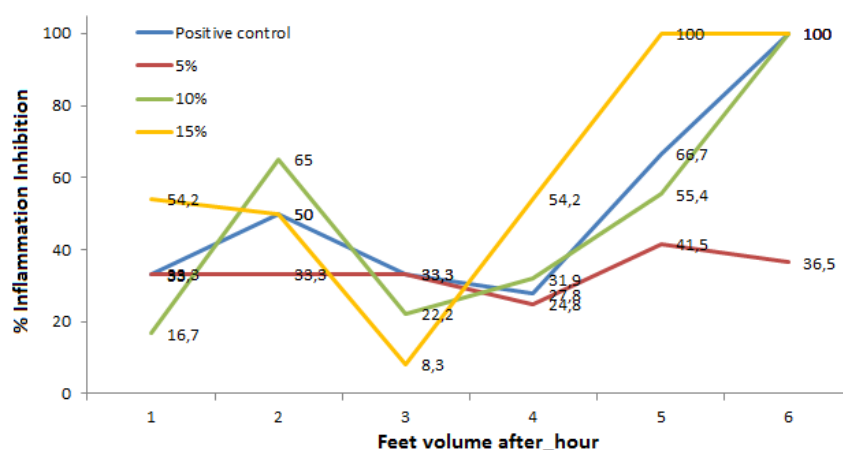


Figure 2. Inflammation Inhibition Graph

Table 4. One Way ANOVA Statistical Analysis of Inflammation Inhibition

hour	1st	2nd	3rd	4th	5th	6th
Sig Anova	.029	.331	.371	.633	.235	0.04

#### Inhibition of Inflammation in Mice' Feet

Based on the research results, looking at the percentage of inflammation inhibition in the 6th hour positive control, the results of inflammation inhibition were 100%, which was the result of the highest inhibition. In the Ketepeng Cina leaf extract gel preparation, the percentage of inflammation inhibition decreased at the concentration 5%, which can be seen at the 6th hour, namely 36.5%, at the concentration 10% there was a good reduction in inflammation, namely 100% and at concentration 15% decreased inflammation inhibition in mice's feet at the 5th and 6th hours with a value of 100%. So it can be concluded that the higher the percentage of inhibition produced, the better the inhibitory power provided as an anti-inflammatory to the feet of mice.

Based on the statistical results of the edema volume value above, at the 1st hour there was a difference between groups with a significance value of 0.029 ( $p < 0.05$ ), and at the 2nd to 5th hour there was no significant difference between each group. 0.331, 0.371, 0.633, 0.235 ( $p > 0.05$ ). And at the 6th hour there was a significant difference of 0.004 ( $p < 0.05$ ). The reduction in edema is caused by flavonoids in the gel which inhibit COX and LOX enzymes, reduce the biosynthesis of eicosanoids and leukotrienes, and act as antioxidants that capture free radicals. The arabinogalactan compound in the gel also has antinociceptor activity in mice by blocking the cyclooxygenase pathway, thereby reducing carrageenan-induced edema in the feet of mice

(Priamsari et al., 2020; Honmore et al., 2016).

#### CONCLUSION

Based on the results of the research, it can be concluded that the preparation of ethanol extract gel of ketepeng Cina leaves shows effectiveness as an anti-inflammatory, with the best effect at a concentration of 15%. The percentage of inhibition of 100% was obtained at the 5th hour of observation when compared to other concentrations (5% and 10%).

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#### CONFLICT OF INTEREST

Author hereby declares that there is no conflict of interest in the writing and publication of this article

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