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# KEBO LEAF ETHANOL EXTRACT (Euphorbia hirta L.) ANTI-INFLAMMATORY EFFECTS IN FEMALE WHITE RATS DETERMINED USING ARTIFICIAL UDEMA METHOD

***Mevy Trisna [1], Renatalia Fika[2], Budi Setiawan[3], Rini Wulandari [4]**
[1,2,3,4] D-III Farmasi, Akademi Farmasi Dwi Farma Bukittinggi
E-mail of Corresponding Author: *fikarenatalia@gmail.com

**ABSTRACT**

An ordinary protective reaction to tissue damage brought on by physical trauma, chemical agents, or harmful microbiological agents is inflammation. The kebo excerpt plant has significant amounts of flavonoids, which have anti-inflammatory and antioxidant properties. This study used the artificial udema method to determine the anti-inflammatory effects of Kebo Petikan leaves (Euphorbia hirta L.) ethanol extract in female white rats. This study applied a subcutaneous 1% carrageenine inducer as an anti-inflammatory drug on the soles of rats' feet. Following the injection of the test material at doses of 26 mg, 52 mg, and 104 mg, a decrease in volume was the metric that was observed. The results of the study showed the anti-inflammatory effect of ethanol extract of kebo petikan leaves at a dose of 26 mg/5ml had a strength of 32.3%, a dose of 52 mg/5ml had a strength of 78.48 %, and a dose of 104 mg/5ml had a strength of 91.46% compared to drugs.

**Keywords:** *Anti-inflammatory, Ethanol Extract. Kebo Passage Leaf (Euphorbia hirta L.).*

**ABSTRAK**

Inflamasi merupakan suatu respon protektif normal terhadap luka jaringan yang disebabkan oleh trauma fisik, zat kimia atau zat-zat mikrobiologi yang merusak. Tanaman petikan kebo memiliki kandungan flavonoid yang tinggi yang dapat digunakan sebagai agen antioksidan dan antiinflamasi. Telah dilakukan penelitian ini tentang Penentuan Efek Antiinflamasi Ekstrak Etanol Daun Petikan Kebo (*Euphorbia hirta* L.*)* Pada Tikus Putih Betina Dengan Metoda Udema Buatan. Penelitain ini digunakan penginduksi karagenin 1% sebanyak 0,2 ml sebagai agen antiinflamasi terhadap udema pada telapak kaki tikus secara subcutan. Parameter yang diamati adalah penurunannya volume udema setelah pemberian zat uji, dengan dosis 26 mg, 52 mg, dan 104 mg. Hasil penelitian yang menunjukan efek anti inflamasi ekstrak etanol daun petikan kebo pada dosis 26 mg/5ml memiliki kekuatan 32,3%, dosis 52 mg/5ml memiliki kekuatan 78,48 %, dan dosis 104 mg/5ml memiliki kekuatan 91,46% dibandingkan terhadap obat

**Kata kunci:** Antiinflamasi, Ektrak Etanol, Daun Petikan Kebo (*Euphorbia hirta* L.*)*

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## INTRODUCTION

According to data from the World Health Organization, 11.9 million people worldwide have inflammation or joint inflammation. This indicates that inflammation is a condition that affects a large number of people worldwide. Around 1.3 million people have arthritis or inflammation in high-income nations. It amounts to around 5.9 million persons in low-income nations. There are 4.4 million people in Southeast Asia who have arthritis or inflammation [1]. An ordinary protective reaction to tissue damage brought on by physical trauma, chemical agents, or harmful microbiological agents is inflammation. Many chemical-containing compounds, including anti-inflammatory medications from the steroid and non-steroidal families, are used in inflammation or inflammatory treatments. Anti-inflammatory drug use has been linked to adverse consequences that need to be taken into account, such as renal, peptic ulcer, and platelet function issues as well as diseases of the gastrointestinal tract. Anti-inflammatory medication is administered to patients to prevent or reduce the process of tissue damage that takes place in the inflammatory area [2]. To identify alternative treatments with minimal adverse effects, it is therefore vital to use medicinal herbs with anti-inflammatory qualities.

One of the plants is the kebo petikan plant (Euphorbia hirta L.), and several studies on kebo passages (Euphorbia hirta L.) related to the chemical compounds contained have been conducted by Karina Karim, et al. Specifically, kebo petikan leaves have been extracted, and this plant is typically used as a traditional herbal medicine because it contains active compounds [3]. The kebo-petikan plant contains a number of different chemical substances, including folifenol compounds (such as gallic acid), flavonoid quercetin, organic palmitic and oleic acids, linoleic acid, terpenoid eufosterol, tarakserol, tarakseron, tannin, mycricyl alcohol, triterpenoid eufol, friedlin, It may be used to treat laryngitis, asthma, dysentery, diarrhea, and milky lendorary inflammation [4].

The chemical compounds found in kebo passage (Euphorbia hirta L.) have pharmacological effects that include anti-inflammatory (anti-inflammatory), art deterioration, and itch elimination. Kebo passage has a bitter, sour, and cold taste. Wash 30 grams of kebo petikan leaves, then boil them in 3 cups of water (600 ml) until they are 1 1/2 cups or (300 ml) in volume to treat milk chelenjer irritation [5]. The kebo-petikan plant contains a number of different chemical substances, including folifenol compounds (such as gallic acid), flavonoid quercetin, organic palmitic and oleic acids, linoleic acid, terpenoid eufosterol, tarakserol, tarakseron, tannin, mycricyl alcohol, triterpenoid eufol, friedlin, It may be used to treat diarrhea, milky inflammatory disease, dysentery, laryngitis, and asthma. Lendable [4].

Chemical compounds contained in the kebo-petikan plant include folifenol compounds (such as gallic acid), flavonoid quercetin, organic palmitic and oleic acids, linoleic acid, terpenoid eufosterol, tarakserol, tarakseron, tannin, mycricyl alcohol, triterpenoid eufol, friedlin, β-amyrin, β-sitosterol, β-eufol, tirukalol, euphoreone, hentriacontane, and elagic acid. which has the potential to treat laryngitis, asthma, dysentery, diarrhea, inflammation of the milky lendorary. [4]. Kebo passage (Euphorbia hirta L.) has a bitter, sour, and cold taste, some of the chemicals contained in the kebo passage (Euphorbia hirta L.) can cause pharmacological effects including anti-inflammatory (anti-inflammatory), art decay and itch removal. For inflammation of the milk chelenjer, wash 30 grams of kebo petikan leaves, then boil them with 3 cups of water (600 ml) until they reach 1 ½ cups or (300 ml) [5].

**Method**

The cold maceration method, which uses 96% ethanol as a solvent, is used to create kebo petikan leaf extract. The sample is completely cleaned before being properly washed, dredged, broken into little pieces, and weighed up to 100 grams. Once the simplicia had been properly weighed, it was macerated in a 96% ethanol solvent until completely drenched. The solvent is changed every three days, corners are made once day, and the maceration results are filtered till the filtrate from the maceration process is acquired and the solution is nearly colorless. A rotary evaporator is used to concentrate the obtained phytrate till a viscous extract is produced. The viscous extract that results is then weighed and its weight is noted. Female white rats weighing 150-300 grams were the test subjects. The rats were acclimated for 7 days, divided into 5 groups, each including 3 heads, and then fasted for 18 hours while still being provided water.

Calibrate a 5 ml and a 50 ml CMC bottle. 250 mg of potassium diclofenac added to boiling water for 5 ml of let the flower, finely scour until a slurry-like mass forms in a vapor cup, then add little by little CMC suspension to the potassium diclofenac preparation up to 184 mg that has been mashed in a mortar, homogeneous scour pour into a calibration bottle add aquadest up to 50 ml shake homogeneously. As a kicking agent, 1% carrageenine solution is created by combining 0.1 grams of carrageenine with physiological NaCl of 0.9% up to a volume of 10 ml, calibrating a 10 ml bottle, and giving everything a good shake.

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**Concentration of Test Substances :**

2080 mg/100 ml is the concentration of the test substances (as a parent solution). Aquadest is created by offsetting extract ingredients up to 2080 mg of sample extract, adding a little scour water till soluble, and then increasing the amount by 100 ml. A concentration of 312 mg/30 ml (for community usage) is created by adding 15 ml of mother liquor to 30 ml of aquadest. In order to create the concentration of 156 mg/30 ml (for community use), 7.5 ml of the mother liquor are added to 30 ml of aquadest.

**Potassium Diclofenac Solution**

Set up a calibration bottle with a capacity of 5 ml, 250 mg of CMC in 50 ml of boiling water, and 5 ml of flower. Finely scour the flower until a slurry-like mass forms in a vapor cup, and then add CMC suspension, a small amount at a time, to the potassium diclofenac preparation, which has a capacity of 184 mg and has been mashed in a mortar. Pour the mixture into the calibration

**Anti-Inflammatory Testing**

Each of the left legs of the mice was marked precisely on the lateral maleus so that the intake of the foot into the mercury liquid was always the same, before the animal was given a test substance, measure the sole of the mouse's foot using a pletismometer tool as the initial volume, group 1 mice (normal control) were given aquadest, group II mice (drug control) were given potassium diclofenac solution according to the dosage and body weight of the test animal, test group mice : groups III, IV, and V extracted samples at doses of 26 mg, 52 mg, and 104 mg, one hour later the mice of all groups were injected with 1% carrageenine solution of 0.2 ml on the soles of the rat's feet subcutaneously [6], measure the volume of rat feet every 1 hour for 6 hours as the final volume (Vt), record the data of the results of measuring the volume, create an hourly udem average volume chart, calculate udema percentage and udema inhibition percentage.

Before the animal was given a test substance, measure the volume of the mouse's foot sole using a pletismometer tool as the initial volume. Group 1 mice (normal controls) were given aquadest, and group II mice (drug controls) were given potassium diclofenac solution according to the dosage and body weight of the test animal. Test group 1 mice (normal controls) received aquadest, while test group 2 mice (drug controls) received potassium diclofenac solution. Groups III, IV, and V collected samples at doses of 26 mg, 52 mg, and 104 mg; an hour later, mice from all groups were subcutaneously injected with 0.2 ml of a 1% carrageenine solution; the final

volume of the rat feet was measured every hour for the following six hours as the final volume (Vt); the data from the measurements were recorded; an hourly udem average volume chart was made; and the udema percentage and udema [7].

**Data analysis**

Rat foot soles were measured every hour for a total of six hours to determine the final volume, after which the average measurement was determined. Use the formula to determine the percentage [7] :

$$\% \text{ Udema} = \frac{(Vt - Vo)}{Vo} x100\%$$

Information:

(Vt) is the volume of the rat's foot soles at time t, and
(Vo) is the volume of the rat's foot soles at time o.

Calculate the percentage of inhibition with the formula :

$$\% \text{ Inhibisi} = \frac{(a - b)}{(a)} x100\%$$

Information:
a : % average for the group of control animals
b : % of the group of test animals' average

**Results**

The rat legs are induced with 1% caragenin as an inducer since this method is straightforward and can clearly witness the increasing profile of the rat's hind legs. This anti- inflammatory action is measured using a pletismometer. The results from the average volume of female rat soles per hour for 6 hours are shown in the table below. The initial volume shows the volume of the normal mouse soles, indicating that they have not been induced. The injection of caragenin 1 1% resulted in an increase in the volume of udem as seen on the observation of the udem volume from the first hour. The effect of potassium diclofenac medications as well as test chemicals at doses of 26 mg/ml, 52 mg/ml, and 104 mg/ml caused a drop in the soles of the rats' feet at the two-hour mark.

**Table 1. Average Rat Female Foot Volume Per Hour For Six Hours**

| Group | Animal Number | Volume Beginning | Volume 1 | Palm 2 | Feet 3 | Rats' 4 | (Hour 5 | To) 6 |
|---|---|---|---|---|---|---|---|---|
| **Negative control** | **1** | 0,8 | 1,2 | 1,3 | 1,1 | 1,1 | 1,0 | 0,9 |
| | **2** | 0,6 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,7 |
| | **3** | 0,7 | 1,1 | 1,2 | 1,2 | 1,2 | 1,0 | 1,0 |
| **Average** | | **0,7** | **1,13** | **1,03** | **1,1** | **1,1** | **0,93** | **0,87** |
| **Potassium Diclofenac** | **1** | 0,6 | 0,9 | 0,9 | 0,9 | 0,7 | 0,7 | 0,6 |
| | **2** | 0,7 | 0,9 | 0,9 | 0,8 | 0,7 | 0,7 | 0,7 |
| | **3** | 0,6 | 1,0 | 0,9 | 0,9 | 0,8 | 0,7 | 0,8 |
| **Average** | | **0,63** | **0,93** | **0,9** | **0,87** | **0,77** | **0,7** | **0,7** |
| **Test substances Dosage 26 mg/5ml** | **1** | 0,7 | 1,1 | 1,1 | 0,8 | 0,8 | 0,8 | 0,7 |
| | **2** | 0,7 | 1,1 | 1,0 | 0,9 | 0,8 | 0,8 | 0,7 |
| | **3** | 0,7 | 1,1 | 0,9 | 0.8 | 0,8 | 0,7 | 0,8 |
| **Average** | | **0,7** | **1,1** | **1,0** | **0,83** | **0,8** | **0,77** | **0,73** |
| **Test substances Dosage 52 mg/5ml** | **1** | 0,6 | 0,9 | 0,9 | 0,8 | 0,8 | 0,7 | 0,6 |
| | **2** | 0,7 | 0,9 | 0,8 | 0,8 | 0,7 | 0,7 | 0,8 |
| | **3** | 0,7 | 1 | 0,9 | 0,8 | 0,8 | 0,7 | 0,7 |
| **Average** | | **0,67** | **0,93** | **0,87** | **0,8** | **0,77** | **0,7** | **0,7** |
| **Test substances Dosage 104 mg/5ml** | **1** | 0,6 | 0,9 | 0,8 | 0,8 | 0,8 | 0,7 | 0,7 |
| | **2** | 0,7 | 0,8 | 0,8 | 0,8 | 0,8 | 0,8 | 0,8 |
| | **3** | 0,8 | 0,9 | 0,8 | 0,8 | 0,7 | 0,7 | 0,7 |
| **Average** | | **0,7** | **0,87** | **0,8** | **0,8** | **0,77** | **0,73** | **0,73** |

## Discussion

In this study, the phalanx was lowered using kebo excerpt leaves. Kebo passage leaves contain flavonoids, which have been shown in in vitro research [8], to have the ability to stabilize or repair cells harmed by inflammation and can reduce prostaglandins in inflammatory areas and be used as an anti-inflammatory [9]. Lipoxygenase, an enzyme involved in the formation of leukotriene, is inhibited by flavonoids in the body. Arachidonic acid metabolism is also inhibited to lessen the generation of prostaglandins. The release of lysosome enzymes, which are inflammatory mediators, is likewise inhibited by flavonoids. The polyfurcation of the inflammatory process may be prevented by inhibiting these inflammatory mediators A solvent consisting of 96% ethanol was used for extraction [10,11,12]. Maceration of 96% ethanol extract has the ability to draw flavonoid molecules. The sample was macerated for 9 days in the study to form a thick extract while being cornered once every 24 hours. The sample was then filtered every 3 days, and the pulp was macerated once more for 3 days. Following the mixing of the

maceration products from steps 1, 2, and 3, the extract is condensed using a water bath tool, and finally it is weighed [13].

The procedure utilized to assess the anti-inflammatory activity involved injecting male white rats' legs subcutaneously with up to 0.2 ml of a 1% caragenin solution to generate artificial formation[14]. Caragenin is derived from the Irish red seaweed variety Chonrus crispus extraction findings. A mucopolysaccharide called caraggenin contributes to the development of the acute inflammatory model. When a foreign substance or antigen, such as carragenin, enters the body, it triggers the release of inflammatory mediators like histamine, which causes inflammation as a result of the body's immune system responding to the antigen to counteract its effects.

The ability of a pharmaceutical substance to lessen or inhibit the degree of inflammation induced in test animals is known as its anti-inflammatory activity. Using a pletismometer, anti-inflammatory benefits are tested. Archimedes' law, which asserts that if an object is introduced into a liquid material, it will generate a force or pressure above the amount of the dipped object, serves as the foundation for measurement[15].

The animal is acclimated for seven days before to testing so that it can acclimate and become accustomed to its surroundings. The goal of the 18-hour fast is to fully remove all food ingredients from the test animal's body so that the medication will be more readily absorbed into the blood and have an immediate effect. Measurements of the volume of the rat legs were made every hour during the 6-hour observation period. The initial volume of the mice's legs was measured before the animals were tested, and then the normal control group received aquadest, the drug control group received a suspension of potassium diclofenac, and the group received the test substance solution in accordance with the dosage that had been predetermined. [16].

A maximum of 0.2 ml of caragenin was administered into the rat's left foot sole an hour later. Using a plestimometer, measure the mice's leg volume every hour for six hours. Because the regular group just received aquadest and not a caragenin inducer, there was an increase in volume in the normal group from the first to the fourth hours, no medicine was administered. Because diclofenac sodium has been clinically shown to have anti-inflammatory characteristics, the potassium diclofenac medication group has the highest average percentage of inhibition. Kebo, on the other hand, has an average percentage of inhibition that is lower than potassium diclofenac in the test substance solution of ethanol extract. Diclofenac potassium is used to control drug consumption. A non-steroidal anti-inflammatory drug, potassium diclofenac. [17].

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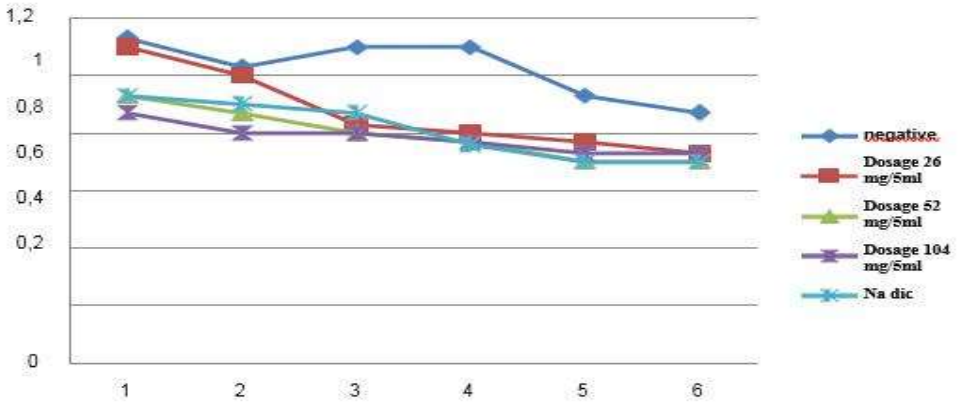


**Figure 1. shows the average volume of white female rats' soles throughout a six-hour period.**

It is evident from table 1 and figure 1 that the average volume of rats' soles was measured every hour for a period of six hours. Due to the drug impact lasting only until the fifth hour, it declined in the drug group from one to four o'clock while experiencing an increase in the fifth and sixth hours. The normal group, however, observed an increase in volume from the second to the sixth hour because they received a carrageen induction but no medication; instead, they received aquadest, which caused the volume to rise from the second to the fifth hour[18].

Anti-inflammatory medications may have an impact on caragenin as an inflammatory factor. Compared to other anti-inflammatories, its reaction to anti-inflammatory medications is more sensitive. Caragenin causes three steps of formation to occur. Serotonin and histamine are released during the first phase, which can last up to 90 minutes. The release of bradykinin, which happens 1.5 to 2.5 hours after induction, is the second phase. Three hours after induction, prostaglandins are released during the third phase. Then, shortly after induction, udem develops quickly and lasts for a maximum of around 5 hours [6].

The analysis of the data revealed that kebo passage leaf extract is effective as an anti-inflammatory. Data with homogeneous variances and a normal distribution are acquired by statistical methods. It is clear from F count (2.4140) and F table (4.07) that there were no appreciable differences among the three concentrations of the test material.

**Table II. Average volume of the foot of white female rats, as a percentage**

| Hour | Negative control | Potassium Diclofenac | average volume % for udem | | |
|---|---|---|---|---|---|
| | | | Dosage 26 mg/5ml | Dosage 52 mg/5ml | Dosage 104 mg/5ml |
| 1 | 61,43 | 47,62 | 57,14 | 38,81 | 24,29 |
| 2 | 47,14 | 42,86 | 42,86 | 29,85 | 14,29 |
| 3 | 57,14 | 38,10 | 18,57 | 19,40 | 14,29 |
| 4 | 57,14 | 22,22 | 14,29 | 14,93 | 10 |
| 5 | 32,86 | 11,11 | 10 | 4,48 | 4,29 |
| 6 | 24,29 | 11,11 | 4,29 | 4,48 | 4,29 |

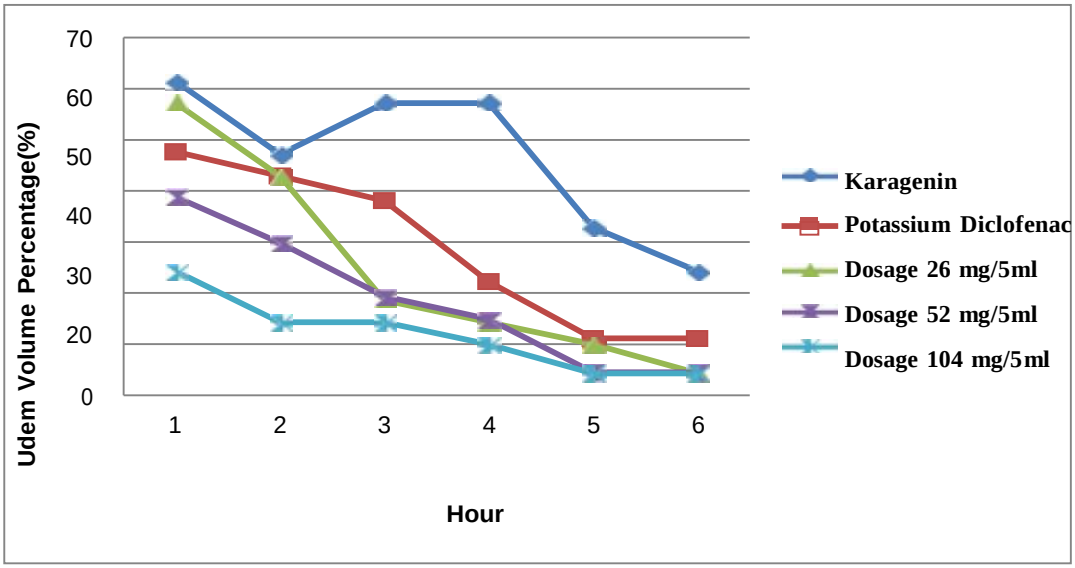


**Figure 2 shows a graph of the typical volume percentage of the white female rats' foot.**

Based on the analysis's findings, it can be seen in figure 2 and table II that the ethanol extract of kebo petikan leaves has a dose-dependent anti-inflammatory effect. It will be stronger the higher the dose of ethanol extract of kebo petikan leaves used to inhibit therapy in rat legs. This is a result of the doisis's increasingly high flavonoid content.

**Table III. Potassium diclofenac and ethanol extract of kebo treatment time (hours)-dependent percentage of inhibition of the average foot of female rats**

| Hour | | Inhibition percentage | | |
|---|---|---|---|---|
| | Potassium Diclofenac | Dosage 26 mg/5ml | Dosage 52 mg/5ml | Dosage 104 mg/5ml |
| 1 | | 6,98 | 36,82 | 60,46 |
| 2 | 9,08 | 9,08 | 36,68 | 69,69 |
| 3 | 33,32 | 67,50 | 66,05 | 74,99 |
| 4 | 61,11 | 74,99 | 73,87 | 82,50 |
| 5 | 66,19 | 69,57 | 86,37 | 86,94 |
| 6 | 54,26 | 82,34 | 81,56 | 82,34 |

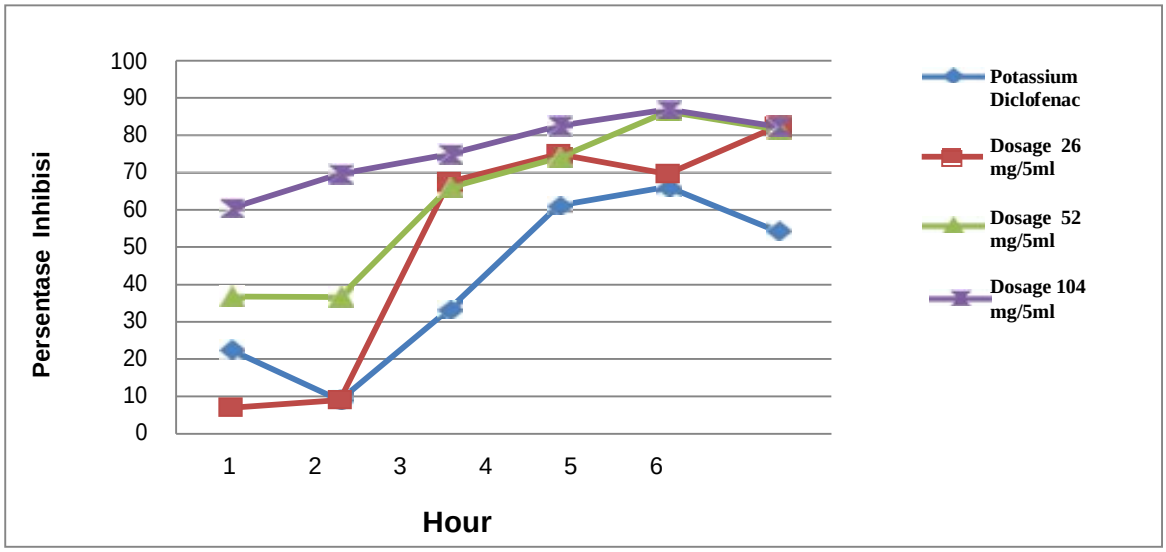


**Image 3. (Graph of the inhibition percentage of the soles of the feet of female white rats)**

The volume of the soles of the feet of the rats in the treatment group as compared to the volume of the feet in the negative control group was used to compute the percentage of drug inhibition shown in Figure 3 and Table 3. According to table 3, the first dose of 26 mg/5 ml inhibited the occurrence by 6.98% in the first hour and continued to grow in the fourth hour, preventing it from occurring by 74.99%. In the first hour, there was a difference between dosage I and dose II or dose 52mg/5 ml. This difference shows that dose 2 has a faster start of action because the flavonoid content of 2 is higher than dose I. This discrepancy demonstrates that

dosage 2 has a quicker onset of action due to dose 2's higher flavonoid concentration than dose I.

When compared to other treatments, the results at dose III of the kebo petikan leaf extract indicated a higher percentage of resistance. The first hour's inhibition was 60.46%, and it increased until the fifth hour, when it reached 86.94%. At the fifth hour, dose III revealed a difference in magnitude compared to the negative control. This indicates that it has anti- inflammatory effect at 5 o'clock. According to the percentage of inhibition data, the anti- inflammatory potential of dosage III is greater than that of dose II in terms of percentage of inhibition. However, statistically speaking, there is no difference in magnitude ($p > 0.01$) between dosage I and dose II. This demonstrates that dosages II and III have the same anti- inflammatory potential, but dose III has a distinct potency. With dose I in the first hour, third dank, and hour four, (p 0.01). Dosage III therefore has a different potential than dose I.

In this investigation, phenyl acetate derifate, which has a pharmacological impact suppressing the formation of prostaglandins, was treated with potassium diclofenac, a nonsteroidal anti-inflammatory. Diclofenac potassium was chosen because, potassium diclofenac and its metabolite products can reach quite significant concentrations on the soles of the feet that are suffering inflammation. The outcomes of the statistical test revealed that positive control and negative control had different magnitudes (p 0.01) from each other. Potassium dichlorophenac displayed the highest activity in the fifth hour of 66.19% at a percentage of inhibition of the formation of 200%. because prostaglandin production was prevented by diclofenac potassium before the third phase.

## CONCLUSION

The results of the study, which lasted for around two days of testing, seven days of acclimation, and roughly 18 hours, show that the kebo leaf extract at doses of 26 mg/ml, 52 mg/ml, and 104 mg/ml is effective as an anti-inflammatory. According to the third statistical calculation, the concentration of the test solution for kebo leaf extract had no appreciable impact.

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