

Activity Testing Of Katuk Leaf Ethyl Acetate Fraction Gel Preparation (*Sauropus Androgynus* (L.) Merr.) On Healing Wistar Strain White Rat Burns

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ABSTRACT

Burns are a condition of loss or damage to skin tissue due to contact between the skin and a heat source. The ethyl acetate fraction of katuk leaves (*Sauropus Androgynus* (L.) Merr.) is known to be able to help accelerate the healing process of burns because it contains flavonoids, alkaloids, tannins and saponins. The purpose of this study was to analyze the effect of giving the ethyl acetate fraction of katuk leaves and to find out the best concentration of the fraction in healing burns. This study was a laboratory experimental study using the Post Test Control Only Group Design approach using 25 male white rats divided into 5 groups (each group consisted of 5 rats). The treatment groups were K+ (bioplacenton), K- (base), the ethyl acetate fraction of katuk leaves which consisted of several concentrations, namely F I (5%), F II (10%), F III (20%). The parameters observed were a decrease in the diameter of the burn wound and healing of the skin of the rats. Based on the results of observations of healing of burns, statistically showed a significant difference between groups with a p value <0.05. The best concentration in healing burns on the rat's back was a concentration of 20% with a healing percentage of 83.11%, followed by a concentration of 10% (66.71%), a concentration of 5% (56.00%). The healing activity of burns in the positive control with a healing percentage of 82.35%. So the best burn healing activity was in the ethyl acetate fraction of katuk leaves with a concentration of 20% with a healing percentage of 83.11%.

Keywords: Burns, Ethyl acetate Fraction of katuk leaves (*Sauropus Androgynus* (L.) Merr.), Wistar Strain White Rat

INTRODUCTION

The burn wound healing process has a complex relationship between cellular and biochemical actions. The process begins with the restoration of structural and functional integrity, with the aim of regenerating strength in injured tissue which includes continuous cell-cell and cell-matrix interactions. These cells undergo an inflammatory process, wound contraction, re-epithelialization, tissue maturation or remodeling, and formation of granulation tissue with angiogenesis (Potter and Perry, 2015).

The progress of modern science, which is increasingly rapid and sophisticated today, cannot rule out natural medicine. This is proven by the large number of people interested in natural medicine. Apart from that, there is still a lack of knowledge and information regarding various types of plants used as natural medicines for certain treatments.

The katuk plant belongs to the Phyllanthaceae family, and has considerable potential as a raw material for natural medicine. The opportunities for medicinal plants are currently increasing, so people tend to switch to natural ingredients. Natural materials have the opportunity to become a large trade commodity. One of the medicinal plants that can be used as traditional medicine is katuk leaves (*Sauropus androgynus* (L.)). According to research

(Mukhrian, 2014) the katuk leaf fraction has antibacterial activity containing flavonoid compounds. The largest group of phenolic compounds has effective properties to inhibit the growth of viruses, bacteria and fungi. Flavonoid compounds have antioxidant properties and many have been used as components of raw materials for medicines. Flavonoids can inhibit bacterial growth by damaging the permeability of bacterial cell walls, microsomes and lysosomes and also inhibiting bacterial motility. Saponin is a compound that can stimulate the formation of collagen, a structural protein, which plays a role in the healing process of burn wounds. (I. Cikita, 2016)

The pain and tenderness that arises when a burn occurs on the skin is one of the urgency of the wound process. The main thing that makes these wounds need to be treated immediately is to reduce the pain. Therefore, the content contained in katuk leaves is a steroid which has the potential to act as an anti-inflammatory so that it can reduce pain and the compounds sulfuric acid and betulinic acid have anti-inflammatory activity which works by inhibiting the production of prostaglandin E. Prostaglandin E is a natural compound involved in increasing labor, although it is also present in inflammatory pathways. Prostaglandin E is often known by the abbreviation PGE2 and also known as dinoprostone (Jalil et al. 2015).

The flavonoid mechanism can inhibit enzymes involved in inflammation, one of which is Cyclooxygen (COX), resulting in a reduction in the number of inflammatory cells so that the process is shorter. Saponins too

has the ability to act as a cleaner and antiseptic

functions to kill or prevent the growth of microorganisms. Apart from that, saponins can also stimulate collagen growth during the healing process. Tannin functions as an astringent which can cause skin pores, harden the skin, stop exudates and cold bleeding, so that wounds close more quickly and come off more quickly (Revi, 2011). Tannins also have antibacterial properties through damage to cell walls, cell membranes, leakage of cell membranes, inactivation of enzymes and inactivation of the function of the genetic material of bacterial cells (Desiyana, 2016).

The anti-inflammatory activity of katuk leaf extract means it is necessary to develop a pharmaceutical preparation to increase its use. One pharmaceutical preparation that can make it easier to use topically is a gel preparation. Making gel preparations is one of the preparations that is often used to treat burns, namely gel preparations. Gel preparations have

the advantage of being cool, moisturizing, easy to use, easy to penetrate the skin, gel preparations also have a high water content. This preparation is preferred because when used it is transparent, elastic, has good drug release, has an attractive appearance, and does not leave a layer of oil on the skin, thereby reducing the risk of skin inflammation (Erfan Tri Prasongko, 2020). A good gel preparation can be obtained by formulating several types of gelling agents. In this research gelling

agent yang digunakan yaitu Corbopol 940, because Corbopol 940 has the advantage of being easily dispersed in water because it belongs to the hydrophilic carbomer group and in a small concentration of 0.02-2% can be used as a gel base with sufficient consistency and is easy to use when used with water. The use of Carbopol 940 base provides a fairly good appearance in each preparation formula.

Based on the description above, it is necessary to take a scientific approach to katuk leaves (*Sauropus Androgynus* (L) Merr), as a candidate for burn wound therapy. The concentration of the fraction to make a gel for healing burn wounds with the active substance of the katuk leaf fraction is 5%, 10% and 20% to find out which concentration is more effective in the process of healing and closing burn wounds in test animals of white Wistar rats.

METHODS

Research methods are the process of planning and implementing research. This research is an experimental study which includes organoleptic tests, metabolite compound content tests, pH tests, spreadability tests, adhesion tests, and gel activity tests of the ethyl acetate fraction of katuk leaves (*Sauropus androgynus*(L.) Merr) on the healing of burn wounds in white rats. Wistar strain by measuring the length of healing burn wound closure using a caliper.

The research was carried out in three stages, namely the first stage, namely preparation, the second stage, implementation and the third stage, namely testing. The preparation stage includes determining the formulation, preparing tools and materials and preparing the research flow. The implementation stage is planning which includes the process of making the ethyl acetate fraction of katuk (*Sauropus androgynus*(L.) Merr) leaves which is mixed with additional ingredients and made into a gel preparation in accordance with established procedures. The third stage is testing the preparation that has been made, the gel preparation evaluation test consists of organoleptic test, homogeneity test, spreadability test, adhesiveness test, pH test, and activity test on experimental animals.

This is done through the following stages:

1. Preparation of raw materials
2. Determination of katuk leaves (*Sauropus androgynus*(L.) Merr)
3. Formulation of katuk (*Sauropus androgynus*(L.) Merr) leaf fraction gel preparation
4. Making Simplicia
5. Making katuk leaf extract (*Sauropus androgynus*(L.) Merr)
6. Fractionation of katuk leaf extract (*Sauropus androgynus*(L.) Merr)
7. Phytochemical screening
8. Making gel preparations
9. Testing process on experimental animals
10. Data analysis

RESULT AND DISCUSSION

Research has been carried out on the activity test of the gel preparation of the ethyl acetate fraction of Katuk leaves (*Sauropus Androgynus* (L) Merr) in healing burns of Wistar white rats. This research was conducted at the Pharmacognosy, Pharmaceutics and Microbiology Laboratory at the Strada Indonesia Institute of Health Sciences, Kediri City.

The results of this research are as follows:

A. Plant Determination

The plants used for this research are determined first with the aim of knowing the correctness of the plants and avoiding errors when collecting materials and samples. The determination was carried out by the Batu Malang Herbal Materia Medica Laboratory UPT. Based on the determination results of taking materials or samples in this study, it is known that katuk leaves belong to the Euphorbiaceae family with the species *Sauropus androgynus* (L) Merr.

B. Making Katuk Leaf Simplicia Powder (*Sauropus androgynus*)

The results of making simplicia powder are obtained in table as follows:

Table Simplicia and Powder Test Results

Test Type	Weight	Standard	Picture
Fresh Leaves	2 kg	-	
Dried leaves	½ kg	-	
Drying Loss of	7,9 %	No more than	
Simplicia Powder	10%		



Fresh Leaves



Dried leaves



Powder

Image of the results of making Simplicia powder

The katuk leaves obtained are sorted with the aim of separating the dirt, separated from the stems and washed with running water to remove dirt attached to the leaves, then dried by air drying for 3 days. The drying process is carried out with the aim of preventing the growth of mold and mildew. mushrooms to obtain simplicia that is durable and can be stored for a long time. Next, grind it using a mill and blender, then sift it on mesh no. 44. The process of grinding dried simplicia into powder is carried out because the greater the surface area of the simplicia in contact with the solvent, the more optimal the process of dissolving the active compounds contained in the simplicia, then a drying shrinkage test is carried out to determine the moisture of the simplicia powder.

C. Extraction of Katuk (*Sauropus androgynus*) Leaf Powder**Table Yield of katuk (*Sauropus androgynus*) leaf extract**

Powder weight	Thick extract weight	% Yield
465,53 g	103,98 g	26 %

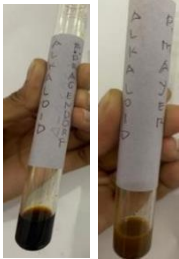
To obtain a thick extract, katuk leaf simplicia powder is previously extracted using the maceration method with the aim of extracting the nutritious substances that are not heat resistant contained in the extract. The solvent used in the extraction process is 70% ethanol which can attract the active substances in katuk leaves which are polar. This is because ethanol has two groups with different polarities, namely the hydroxyl group which is polar and the alkyl group which is nonpolar so it can lift compounds which are non-polar. polar or nonpolar (Lestari, 2017). 70% ethanol solvent can also provide protection against contamination from microbes during the extract manufacturing process because it contains little water. After maceration for 5 days with 10 liters of ethanol solvent used, it was filtered using a Bouchard funnel and covered with flannel cloth. The filtrate obtained is then concentrated to determine the percent yield while preventing the possibility of damage to the components contained in the extract and making it easier to store when compared to the condition of the extract which still contains solvent.

D. Identification of the Chemical Compound Content of Katuk Leaf Ethanol Extract

Phytochemical testing in this research is qualitative, namely by looking at the presence of precipitates or color changes that form after the addition of several reagents for testing the alkaloids, saponins, flavonoids and tannins.

The results obtained were that katuk leaf extract positively contained flavonoids, alkaloids, saponins and tannins. This is the same as previous research which proved that katuk plants contain alkaloid, saponin, tannin and flavonoid compounds (Susanti, et al. 2014). The content of these compounds can strengthen the antibacterial activity of katuk leaf extract. Results of phytochemical screening of ethanol extract of katuk leaves. in table below:

Table Phytochemical Screening Results

Metabolite Compounds	Reactor	Standard/Reference	Results Observation	Conclusion
Flavonoid	Mg powder, HCl 5 ml	Dark red solution, orange or yellow (Soediono et al, 2019)	Yellow	 (+)
Alkaloid	HCl 2N, Dragendrof and Mayer	Red/orange precipitate, white, brown precipitate (Tatang Shabur Julianto, 2019)	Red precipitate and brown precipitate	 (+)
Saponin	Aquadest, HCl 2N	Terbentuk buih tinggi 1-10 cm (Susanti dkk, 2012)	Busa dengan tinggi 2 cm	 (+)

Tanin	FeCl ₃ 1%	Green or bluish black color (Soediono et al, 2019)	Bluish black	 (+)
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Information: (+) Positive extract contains metabolite compounds

(-) there are no metabolite compounds

E. Evaluation Results of Katuk Leaf Fraction Gel Preparation

The thick fraction obtained was made into a gel preparation formulation. The katuk leaf fraction is the active substance and the water-soluble base carrier is Propylene glycol (PEG). Apart from that, the additional ingredient nipagin is used as a preservative to maintain the durability of the preparation. The gel making process begins with weighing the katuk leaf fraction according to the concentration, TEA, Carbopol 940, propylene glycol, methylparaben, glycerin and distilled water. Then put carbopol 940 into a porcelain cup and melt it in a water bath. After that, TEA, propylene glycol, methylparaben, glycerin and distilled water were added and stirred until a gel mass was formed. The katuk leaf fraction is added little by little, then stirred until homogeneous. Finally, put it in a gel pot and evaluate it. Addition of fractions to the formula with different concentrations, namely 5% formula, 10% formula and 20% formula. Variations in fraction concentration affect the physical properties of the preparation so that physical quality evaluations are carried out for organoleptic testing, homogeneity, pH, stickiness, spreadability and viscosity.

F. Organoleptic Test Results

Table Organoleptic Test Results

Observation	Formulas				
	K +	K -	F I	F II	F III
Colour	Clear white	Clear white	Deep green	Dark green, slightly black	Blackish dark green
Form	Thick	Thick	Thick	Thick	Thick
Smell	Gel fragrance Bioplacenton	Gel scent	The distinctive aroma of katuk leaf fraction	The distinctive aroma of katuk leaf fraction	The distinctive aroma of katuk leaf fraction

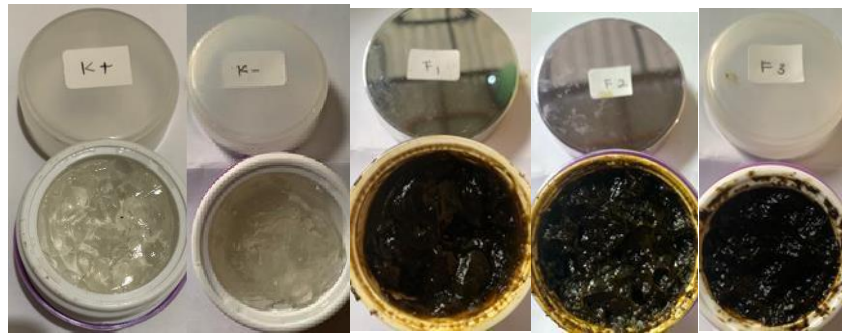


Image of Organoleptic Test Results of Katuk Leaf Fraction Gel Preparation

G. Homogeneity Test Results

Table of Homogeneity Observation Results

Formulas	Observation
K +	Homogeneous
K -	Homogeneous
F I	Homogeneous
F II	Homogeneous
F III	Homogeneous

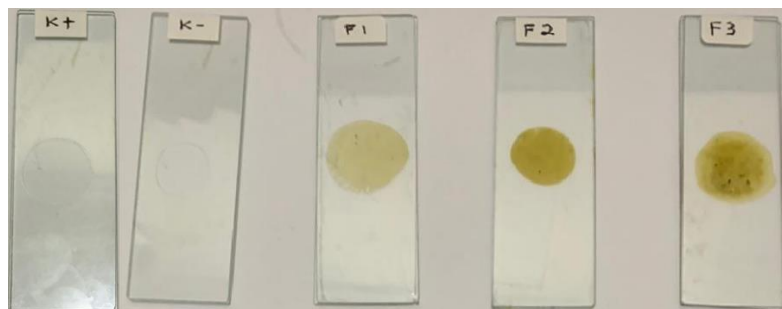


Image of Homogeneity Test Results

Testing the homogeneity of the Bioplacenton K + and K - gel preparations, as well as the katuk leaf fraction gel preparations of formula I, formula II, formula III, did not show any coarse particles, resulting in a homogeneous gel preparation. This shows that all additional ingredients and fractions as active substances used in making gel preparations are mixed evenly.

H. Recapitulation of Physical Quality Evaluation Results

RECAPITULATION TABLE OF PHYSICAL QUALITY EVALUATION RESULTS

Physical Evaluation	Quality	Formulas	Replication				Average	Range	Description Qualify/Not
Test pH		K +	6,98	6,93	6,92	6,94		pH 4,5-7	Qualify
		K -	8,01	7,95	8	7,99			Not
		F I (5%)	6,09	6,1	6,08	6,09			Qualify
		F II (10%)	6,81	6,77	6,76	6,78			Qualify
		F III (20%)	6,46	6,45	6,46	6,45			Qualify
Spreadability Test (weight 100 g)		K +	5,3	5,7	5,6	5,5		5-7 Cm	Qualify
		K -	4,5	4,3	4,4	4,4			Not
		F I (5%)	4,5	4,8	4,9	4,7			Not
		F II (10%)	6,6	6,8	6,6	6,7			Qualify
		F III (20%)	6,5	6,9	7	6,8			Qualify
Adhesion Test		K +	3,8	3,7	3,9	3,8		Kurang dari 4 detik	Qualify
		K -	10,2	10,7	10,5	10,5			Not
		F I (5%)	4,5	3,7	4,1	4,1			Not
		F II (10%)	4	4,1	3,8	3,9			Not
		F III (20%)	3,8	3,6	3,9	3,8			Qualify
Viscosity Test		K +	2.506	2.508	2.503	2.505		2.000-50.000 cP	Qualify
		K -	607.282	607.303	607.295	607.293			Not
		F I (5%)	312.433	312.450	312.502	312.462			Not
		F II (10%)	668.702	668.715	668.712	668.710			Not
		F III (20%)	10.307	10.315	10.310	10.311			Qualify

I. Thin Layer Chromatography (TLC) Test Results

Retardation factor (Retardation factor=Rf) is a factor used to describe the migration of compounds in TLC. Meanwhile, the Rf value is a parameter that states the position of the stain in the stationary phase after elution. The Rf value can be calculated using the following formula:

$$Rf = \text{Distance traveled by compound} / \text{Distance traveled by solvent}$$

The greater the Rf value of the sample, the greater the distance the compound moves on the thin layer chromatography plate. The Rf value meets the requirements for a good Rf value, namely between 0.2-0.8 (Rohman, 2009). The materials used for the TLC test were butanol, alcohol, chloroform, methanol and ethyl acetate using a chamber, silica plate.

TLC Test Results Table (RF Value)

Replication	Rf Calculation (Cm)			
	Alkaloid	Tanin	Saponin	Flavonoid
1	3,5	4,2	1	4
2	-	4,2	1,2	4,1
3	-	4,3	1,3	4,2
Average	3,5	4,2	1,2	4,1
Rf value	0,7	0,8	0,2	0,8

Information :

Silica plate length: 5 cm, bottom side distance: 2 cm, top side distance: 1 cm

Alkaloid

Tanin

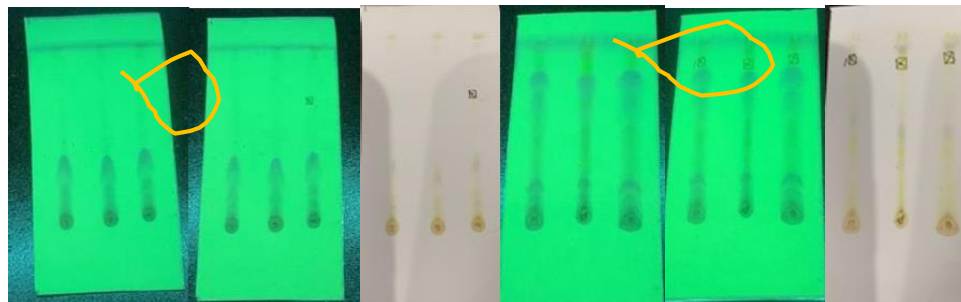


Image of UV TLC results for alkaloids and tannins

Saponin

Flavonoid

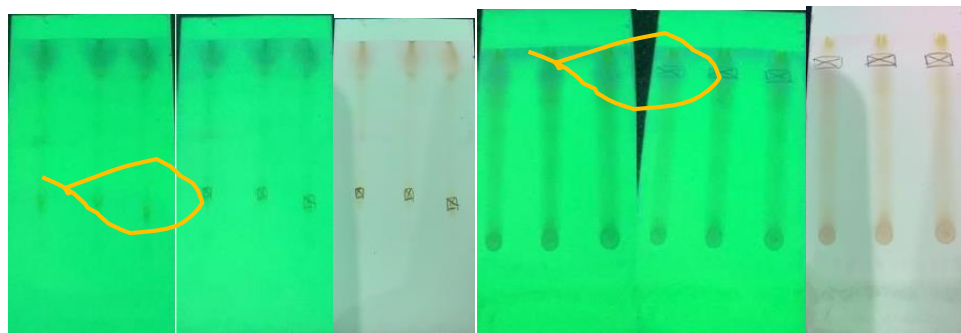


Image of UV TLC results for saponins and flavonoids

Activity of Katuk Leaf Ethyl Acetate Fraction Gel Preparation to Accelerate

Burn Wound Healing in Rats

The activity test of the katuk leaf ethyl acetate fraction gel preparation on burn wound healing aims to determine the activity or effect on reducing the diameter of the burn wound, the percentage of burn wound healing. This test was carried out experimentally against Wistar strain white mice as test animals.

The results of observations and data analysis show that the ethyl acetate gel fraction of katuk leaves has an influence on the healing process of burn wounds in Wistar rats. This effect is due to the compounds contained in it, namely tannins and flavonoids. This is shown in the results of data analysis according to parameters in burn wound healing which include measuring the diameter of the burn wound and the percentage of burn healing. Observations of burn wounds can be seen in the picture.

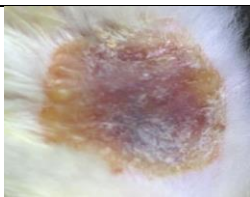
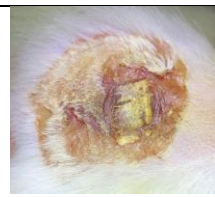
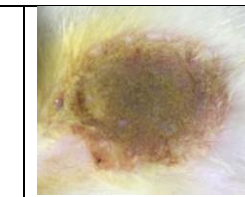
Day 0 Burns				
				
Control +	Control -	Formulation 5%	Formulation 10%	Formulation 20%
Burns Day 15				
				
Control +	Control -	Formulation 5%	Formulation 10%	Formulation 20%

Image Comparison of Burns on Day 0 and Day 15

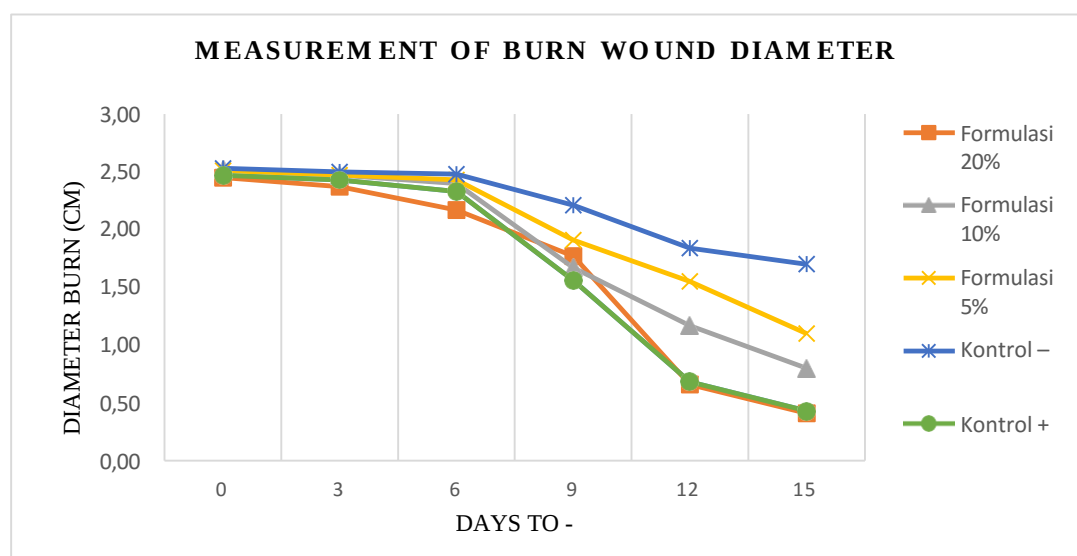
Average results data Average results of burn wound diameter measurements are shown in the figure in the form of descriptive data. The results obtained from measuring the diameter of the burn wound can be shown in the picture which shows that there is a decrease in the diameter of the burn wound on the rat's back.

Table of Average Results of Diameter Measurements on Rat Backs (Cm)

Days To -	Control + (Mean±SD)	Control - (mean±SD)	Formulation 5% (mean±SD)	Formulation 10% (mean±SD)	Formulation 20% (mean±SD)
0	2.47±0.05	2.53±0.06	2.51±0.08	2.52±0.09	2.45±0.15
3	2.43±0.05	2.5±0.07	2.47±0.07	2.47±0.08	2.37±0.15
6	2.33±0.05	2.48±0.07	2.43±0.09	2.4±0.07	2.17±0.34
9	1.56±0.25	2.21±0.16	1.91±0.16	1.67±0.24	1.77±0.13
12	0.68±0.19	1.84±0.08	1.55±0.18	1.17±0.24	0.66±0.19
15	0.43±0.17	1.7±0.11	1.1±0.22	0.8±0.26	0.41±0.12

Information :

Number of samples (n) = 5 mice per treatment group Total sample = 25 mice



Graphic image of burn diameter measurement

Measurement data. The data obtained from measuring the diameter of the burn wound were then processed statistically using SPSS 25.0. Statistical analysis of burn wound diameter measurement data includes normality test, homogeneity test, one way ANOVA test and if there is a significant difference then a further test is carried out using the LSD (Least Significance Different) test.

The burn wound diameter measurement data obtained was tested for normality using the Kolmogorov – Smirnov test. It was found that the burn wound measurement results were normally distributed for all treatment groups with ($p > 0.05$), namely $p = 0.200$. The data were normally distributed and then tested for homogeneity using the Levene test. It was found that the results of measuring the diameter of the burn wound were homogeneous data with a value of ($p > 0.05$), namely $p = 0.563$.

The results of analysis of wound diameter measurement data obtained from the ANOVA test showed a significance value of $p < 0.05$, namely $p = 0.001$, which means there were significant differences in each treatment group. To find out what it is

Significant differences in each treatment group were continued with the LSD (Least Significance Difference) test.

Table of Statistical Analysis Results of the LSD Test on Day 15

GROUP	Control +	Control -	Concentratio n 5%	Concentratio n 10%	Concentratio n 20%
Control +		0,000**	0,000**	0,002**	0,839*
Control -	0,000**		0,000**	0,000**	0,000**
Concentratio n 5%	0,000**	0,000**		0,032**	0,000**
Concentration 10%	0,002**	0,000**	0,032**		0,001**
Concentration 20%	0,838*	0,000**	0,000**	0,001**	

Information :

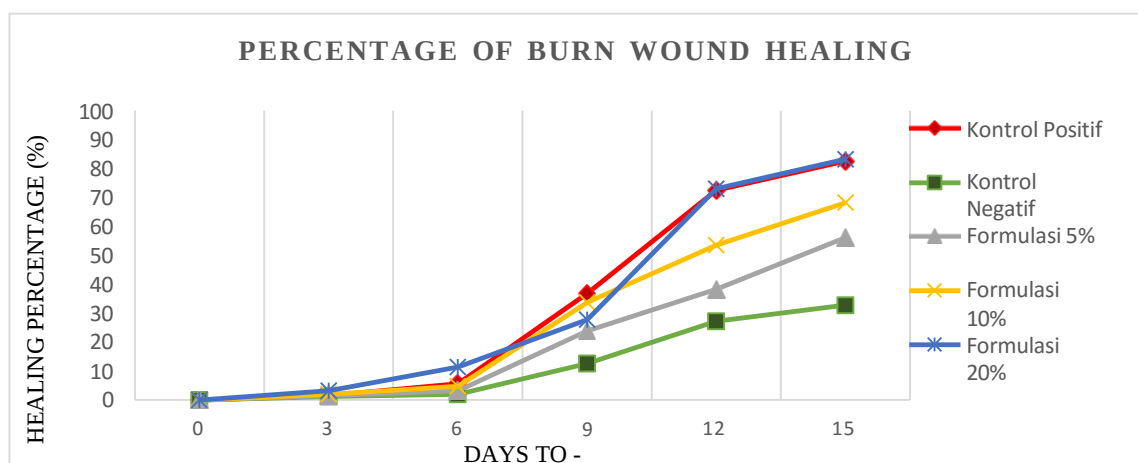
(*) = not significantly different (**) = significantly different

Based on the results of the LSD test, it can be concluded that there was 1 treatment group that showed no significant difference, namely the positive control group versus the 20% contrast group with a p value = 0.838. This shows that a concentration of 20% has a recovery effect on burn wounds in mice that is the same as the recovery level of the positive control group. And had a better recovery rate than the 5% concentration, 10% concentration, and negative control groups.

The data from measuring the diameter of the burn wound was then converted into a percentage to see the percentage of burn wound healing produced by the ethyl acetate fraction gel of katuk leaf extract. Based on the results table, the average percentage of burn wound healing shows that the 20% concentration group has a higher percentage than the other groups.

Table of Results - Average Percentage of Burn Wound Healing

Mouse	Control +	Control -	Formulation 5%	Formulation 10%	Formulation 20%
	%	%	%	%	%
1	74.38	34.98	60.62	49.60	77.87
2	91.93	36.29	47.96	70.76	90.31
3	83.13	32.81	52.34	74.01	82.68
4	85.18	24.89	70.15	66.15	86.33
5	77.14	34.80	48.97	73.04	78.35
Mean ± SD	82.35±6.91	32.75±4.57	56.01±9.37	66.71±10.04	83.11±5.30



Graph of Burn Wound Healing Percentage

Data on the percentage of burn wound healing were then analyzed using the normality test and homogeneity test. The results of the normality test using Kolmogorov-SmirnovZ with a value ($p > 0.05$), namely 0.200, which means that the data on the percentage of burn wound healing is normally distributed. The results of the homogeneity test using the Levene test with a value ($p > 0.05$) namely 0.412, this shows that the data on the percentage of burn wound healing is homogeneously distributed. The next data analysis was carried out by carrying out the One-Way Anova test with a value ($p < 0.05$), namely 0.000, which means that the data on the percentage of burn wound healing was significantly different.

Statistical analysis was then continued with the LSD (Least Significant Difference) test, which is to determine whether there are significant differences between one group and another group.

Table of Statistical Analysis Results of LSD Test Percentage of Wound Healing

GROUP	Control +	Control -	Concentratio n 5%	Concentratio n 10%	Concentratio n 20%
Control +		0,000**	0,000**	0,004**	0,876*
Control -	0,000**		0,000**	0,000**	0,000**
Concentration 5%	0,000**	0,000**		0,036**	0,000**
Concentration 10%	0,004**	0,000**	0,036**		0,003**
Concentration 20%	0,876*	0,000**	0,000**	0,003**	

Information :

(*) = not significantly different (**) = significantly different

Based on the LSD test results in the table, it shows that there is no significant difference in the positive control group versus the 20% concentration group with a p value = 0.876. This shows that a concentration of 20% has an effect on the percentage of recovery from burn wounds in mice that is the same as the percentage of recovery from the positive control group. And had a better recovery rate than the 5% concentration, 10% concentration, and negative control groups.

The activity test of the katuk leaf ethyl acetate fraction gel preparation on burn wound healing aims to determine the activity or effect on reducing the diameter of the burn wound, the

percentage of burn wound healing. This test was carried out experimentally on Wistar strain white mice.

The research design was carried out by dividing 25 white male Wistar rats into 5 treatment groups, namely a positive control given bioplacenton gel, a negative group with a gel base, and three groups treated with the ethyl acetate fraction of katuk leaves with varying concentrations of 5%, 10% and 20%. This study used Bioplacenton gel as a positive control containing 10% placenta extract and 0.5% neomycin sulfate. Placenta extract in Bioplacenton is known to have the effect of triggering the formation of new tissue and helping in the wound healing process. (Nur, 2017).

Burns were made by using money or iron coins with a diameter of 2 cm which were heated over a gas stove for 30 seconds and then placed on the rat's back for 5 seconds. Before the burn wounds were made, the mice were anesthetized using the anesthetic Lidocain 0.3cc for weights under 200g and 0.4cc for weights above 200g. According to Erlinda et al (2019), choosing the right anesthetic drug and the correct method of administration will minimize unwanted side effects on the body's systems, especially on the cardiovascular system, respiratory system and body temperature.

The burns that have been created are then treated using the katuk leaf ethyl acetate fraction gel preparation according to the treatment groups, namely the positive control group (Bioplacenton), negative control (gel base), 5% concentration group, 10% concentration, and 20% concentration gel fraction preparation. katuk leaf ethyl acetate. Measurement of burn wound diameter in all treatment groups was carried out on days 0, 3, 6, 9, 12, and 15.

In this research, a gelling agent was used in the gel preparation of the ethyl acetate fraction of katuk leaves, namely Carbopol 940, the gel preparation can increase adhesion, consistency, spreadability, stickiness and viscosity. This can help increase the effectiveness and quality of pharmaceutical preparations that use Carbopol 940 as a gelling agent (Yusuf, 2020). Burns are one of them incidents that often occur in society, especially households.

The results of observations and data analysis show that the ethyl acetate gel fraction of katuk leaves has an influence on the healing process of burn wounds in Wistar rats. This effect is due to the compounds contained in it, namely tannins and flavonoids. This is shown in the results of data analysis according to parameters in burn wound healing which include measuring the diameter of the burn wound and the percentage of burn healing.

In the inflammatory phase, the tissue repair process occurs through hemostasis, namely the temporary constriction of blood vessels to send blood and cells to the wound area. Next, a soft tissue response occurs, namely damaged tissue and mast cells release histamine and other mediators, causing vasodilation in the blood vessels around the undamaged wound and increasing blood flow to the wound area, resulting in a feeling of warmth and redness in the wound area. The inflammatory process is the body's response to tissue injury caused by physical trauma, dangerous chemicals, or microbiological agents. The goal of the inflammatory process is to repair tissue that has been damaged. In the inflammatory phase, various vascular and cellular responses occur which are caused by injury to the soft tissue. The wound healing process also involves polymorphonuclear cells (PMN) which play an important role in the inflammatory phase (Rinawati et al, 2015). The content of flavonoid compounds in the ethyl acetate gel fraction of katuk leaves helps in the healing process of burn wounds.

Flavonoid compounds have anti-inflammatory activity which functions as an anti-inflammatory and can prevent stiffness and pain. Flavonoids are anti-inflammatory so they can reduce inflammation and help reduce pain when bleeding or swelling occurs in wounds (Sendi, 2023). Flavonoids have strong antioxidant properties. Protects body cells from oxidative damage caused by free radicals. In burns, flavonoids can help reduce oxidative stress and relieve inflammation. inhibits the activity of the enzyme cyclooxygenase-2 (COX-2), which is

responsible for the production of prostaglandins that cause inflammation. By inhibiting COX-2, flavonoids help reduce inflammation in burn wounds. inhibits the release of histamine, which is one of the mediators of inflammation. By inhibiting the release of histamine, flavonoids help reduce inflammation in burn wounds. The active compounds contained in katuk leaves are thought to be able to help in the healing process of burn wounds in mice.

The process of healing burns using the ethyl acetate fraction gel preparation of katuk leaves also occurs because of the tannin compound content . Its anti-inflammatory function can inhibit the production of inflammatory mediators and reduce the inflammatory response. The astringent effect of tannin compounds can shrink tissue and reduce bleeding in burn wounds. This helps reduce inflammation and speed up the healing process (Rokhmah, 2021). helps increase the formation of new tissue in burn wounds by stimulating collagen production. Collagen is a protein that forms connective tissue and helps speed up the healing process (Komang, 2021). Tannin compounds also have a synergistic effect similar to flavonoid compounds, namely inhibiting the activity of the cyclooxygenase-2 (COX-2) enzyme, which is responsible for the production of prostaglandins which cause inflammation. By inhibiting COX-2, tannins help reduce inflammation in burn wounds. The flavonoid compounds and tannin compounds in the ethyl acetate gel fraction of katuk leaves are thought to be able to assist in the healing process of burn wounds in Wistar white rats.

CONCLUSION

Based on the results of research testing the activity of the ethyl acetate fraction gel preparation of katuk leaves (*Sauropus Andragynus* (L.) Mer) on the healing of burns in Wistar white rats, the following conclusions were obtained:

The gel preparation of the ethyl acetate fraction of katuk leaves (*Sauropus Andragynus* (L.) Mer) at a concentration of FI 5%, F II 15%, FIII 20% has activity to heal burn wounds in white Wistar rats which is characterized by an increase in the healing percentage , reducing the diameter of the burn wound and providing effectiveness in healing burn wounds of the Wistar strain of white rats which provided the fastest effectiveness was at an FIII concentration of 20% on the 15th day. This is caused by the chemical content of katuk (*Sauropus Andragynus* (L.) Mer) leaves, namely Flavonoids, Tannins, Alkaloids and Saponins which can help accelerate the healing of shallow second degree burns on the skin of Wistar white rats. (Mosque and Muchardi, 2018).

Formulation with a concentration of katuk leaf ethyl acetate gel fraction (*Sauropus Andragynus* (L.) Mer) which provides the most effective burn wound healing effect on Wistar white rats is at a concentration of 20%.

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