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THE EFFECT OF GIVING SWEET ORANGE PEEL ETHANOL EXTRACT LOTION (CITRUS SINENSIS) ON WOUND HEALING WISTAR WHITE RAT

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ABSTRACT

Wounds are one of the health problems that require proper treatment to speed up the healing process. Natural ingredients, such as sweet orange peel (Citrus sinensis), are known to contain flavonoid compounds, tannins, and antioxidants that have the potential to speed up the wound healing process. This study aims to determine the effect of giving sweet orange peel ethanol extract lotion (Citrus sinensis) on the wound healing process in Wistar white rats, both through macroscopic and microscopic assessments, as well as comparing the effectiveness of various doses (5%, 10%, and 15%). This study uses a true experimental post test only control group design. Wistar white rats were divided into several treatment groups with the administration of EEKNJ lotion concentrations of 5%, 10%, and 15%. Data were analyzed using ANOVA tests. The results showed that the administration of EEKNJ lotion of 5% (sig = 0.005), 10% (sig = 0.000), and 15% (sig = 0.001) had a significant effect in accelerating wound healing. However, ANOVA results on the percentage of wound healing showed a value of sig = 0.901 (> 0.05), which means that there was no significant difference between doses of EEKNJ lotion. Descriptively, the average percentage of highest wound healing was obtained in the EEKNJ group of 10% (38.72%), followed by EEKNJ 5% (35.22%), and the lowest EEKNJ 15% (26.44%). The conclusion of this study is that sweet orange peel ethanol extract lotion has the potential to accelerate wound healing in Wistar white rats, but the dose variations of 5%, 10%, and 15% did not show a significant difference in the wound healing percentage.

Keywords: *Sweet orange peel, Lotion, Wound healing, Wistar white rat*

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INTRODUCTION

The body needs a biological process known as wound healing to deal with tissue damage. Injuries can occur due to a variety of things, such as physical trauma, infection, or certain diseases, that can interfere with the integrity of the body's skin and tissues. The wound healing process involves various phases, such as inflammation, proliferation, and tissue maturation, which work together to ensure that the skin and tissues recover completely (Rosyid, 2022). Many factors, including the individual's general health condition, age, nutritional status, and medications administered to support the wound healing process, affect the speed and success of wound healing. Therefore, safe and effective wound healing drugs or drugs are constantly being sought, especially inexpensive and easy-to-use topical drugs (Floriano, 2025).

The use of natural ingredients, such as plant extracts, is one of the alternatives in wound healing therapy that is becoming increasingly popular. Plants have long been known to have many bioactive compounds that are beneficial for health, one of which is their ability to speed up wound healing. One of the plants that has this potential is the sweet orange (Citrus sinensis) (Kartikaningtyas, 2015). This frequently consumed fruit contains many active compounds, including flavonoids, alkaloids, ascorbic acid (vitamin C), and essential oils. These compounds are known to have anti-inflammatory, antibacterial, and antioxidant properties, which help speed up wound healing (Kumar, 2023).

In this case, sweet orange peels, which are usually disposed of as waste, have unrealized potential. Among the bioactive substances found in sweet orange peel are flavonoids (hesperidin, naringin), limonene, and phenolic acid, which have antibacterial and antioxidant qualities (Woraratphoka, 2024). Many studies have shown that sweet orange peel extracts, particularly those made with ethanol, may have a number of therapeutic uses, such as acting as an antibacterial, anti-inflammatory, and wound-healing agent. Ethanol extract from sweet orange peel contains bioactive compounds that can help fight infection, reduce inflammation, and speed up wound healing (Mehmood, 2015).

Along with the development of the use of natural ingredients in the health field, sweet orange peel ethanol extract lotion is becoming a form of preparation that can be developed for topical therapy (Mehmood, 2015). Lotion is a semi-solid preparation that is easy to apply to the skin, provides moisture to the wound area, and at the same time provides a therapeutic effect from the compounds contained in the ethanol extract of sweet orange peel. However, although its various potential benefits are known, there have not been many studies that have in-depth explored the effect of giving sweet orange peel ethanol extract lotion on wound healing, particularly in Wistar white rat test animals (Ansel, 2011).

In this study, the administration of sweet orange peel ethanol extract lotion will be analyzed to see its effect on wound healing speed in Wistar white rats. The Wistar white rat was chosen as a test animal because it has biological characteristics that are relevant for medical tests, as well as it can be used to observe biological responses to a variety of treatments, including wound therapy. These mice are often used in various studies related to wound healing due to their physiological resemblance and the body's response to treatments applied tohumans (Festing, 2014).

Sweet orange peel ethanol extract lotion with various concentrations tested is expected to show a significant difference in terms of its effectiveness in accelerating

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wound healing. Different concentrations may give a different response to the wound healing process, both in terms of the speed of tissue regeneration, reduction of inflammation, and its ability to reduce infection (Tottoli, 2014). Thus, the study aims not only to explore the benefits of relatively safe natural ingredients, but also to find the most optimal dosage concentrations for use as wound healing therapeutic agents.

METHODS

This researcher used *a true experimental post test only control group design*. The study sample was male wistar rats (Rattus norvegicus) aged 2–3 months with a weight of 150–200 grams, as many as 30 animals divided into 5 groups (2 control and 3 treatment). The control group consisted of K+ (Hansaplast wound ointment) and K– (no treatment), while the treatment group was P1 (5% sweet orange peel extract lotion), P2 (10%), and P3 (15%). The research was conducted at the Pharmacology Laboratory, Faculty of Pharmacy and Histology Laboratory, Faculty of Medicine, University of North Sumatra in October 2024.

The extract is obtained through the maceration method with 96% ethanol, then formulated into lotion with concentrations of 5%, 10%, and 15%. A 2 cm long cut wound was made on the back of the anesthetized rat, then given treatment 2 times a day for 9 days. Evaluation was performed macroscopically (wound contraction, hyperemis, granulation, crust) on days 3, 6, and 9, as well as microscopic (cellular infiltration, collagen production, epithelial thickness, angiogenesis) on day 10 after the rats were sacrificed. Macroscopic data were analyzed descriptively, while microscopic data were tested with Shapiro-Wilk (normality), Levene's Test (homogeneity), then One-Way ANOVA followed by Duncan test if there was a significant difference ($p < 0.05$).

RESULTS

Phytochemical Screening Test Results

Table 1 Frequency Distribution Results of Research Respondent Characteristics

No.	Secondary Metabolite Compounds	Result	Picture
1.	Flavonoids	+	
2.	Alkaloids	+	

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3.	Tannins	+	
4.	Saponins	+	
5.	Glycosides	+	
6.	Steroids/Terpenoids	+	

Source : Primary Data processed (2025)

The results of phytochemical screening showed that the ethanol extract of sweet orange peel (*Citrus sinensis*) contains a variety of secondary metabolite compounds such as flavonoids, alkaloids, tannins, saponins, glycosides, and steroids/terpenoids. The presence of these compounds supports the pharmacological potential of the extract, especially in

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antioxidant, anti-inflammatory, antimicrobial, and wound healing activities, so that it is in accordance with the objectives of this study.

Organoleptic Tests

The organoleptic test aims to see the physical appearance of the lotion preparation which includes the texture and color of the lotion. It is done visually with the five senses and without the use of aids by observing colors, shapes. The following are the results of the organoleptic test which can be seen in table 3 below.

Table 2 Organoleptic Test Results

Treatment Groups	Color	Preparation Form
EEKNJ Lotion 5%	Transparent Chocolate	Semi-thick
EEKNJ Lotion 10%	Slightly more concentrated	Thick
EEKNJ Lotion 15%	Concentrated	Thicker

Source : Primary Data processed (2025)

From table 2 it is shown that from the results of organoleptic tests on EEKNJ lotion 5% has a transparent brown color and a semi-thick preparation form, for EEKNJ 10% lotion it has a slightly more concentrated color and a thick preparation form and for EEKNJ lotion 15% has a concentrated color, as well as a thicker preparation form.

pH Test

The pH test of the preparation is carried out with the aim of determining the acidity level of the lotion preparation. If the pH of the preparation is low or acidic it will cause irritation to the skin, if the pH of the preparation is high or alkaline then it will cause dry skin when applied.

Table 3 pH Test Results

Treatment Groups	Ph
EEKNJ Lotion 5%	6
EEKNJ Lotion 10%	5,6
EEKNJ Lotion 15%	5

Source : Primary Data processed (2025)

In table 3, you can see the measured pH of the three groups of treating 5% EEKNJ lotion by 6, EEKNJ 10% by 5.6, and EEKNJ 15% by 5.2. The pH value is still within the ideal pH range. According to SNI 16-4399-1996, the ideal pH is in accordance with the pH of the skin, which ranges from 4.5 - 8.0. If the pH does not match the pH of the skin, it will cause skin irritation.

Homogeneity Test

Table 4 Homogeneity Test

Treatment Groups	Homogeneous	
	Yes	Not
EEKNJ Lotion 5%	✓	-
EEKNJ Lotion 10%	✓	-
EEKNJ Lotion 15%	✓	-

Source : Primary Data processed (2025)

The homogeneity check at all three concentrations aims to observe the presence of coarse particles in the glass of the object. The observation results showed that the three formulas were physically homogeneous, this showed that the ingredients used in making sweet orange peel ethanol extract lotion (*Citrus Sinensis*) were perfectly mixed.

Dispersion Test

A dispersion test is carried out to determine the ability of the base to spread on the surface of the skin when the lotion is applied. The results of the dispersion test can be seen in Table 6 below.

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Table 5 Dispersion Test Results

Treatment Groups	Spreadability	
	Horizontal	Vertical
EEKNJ Lotion 5%	8.2 cm	8.4 cm
EEKNJ Lotion 10%	7.5 cm	7.1 cm
EEKNJ Lotion 15%	6.4 cm	6.2 cm

Source : Primary Data processed (2025)

The observation results showed that EEKNJ Lotion 5% had a horizontal dispersion of 8.2 cm vertically, 8.4 cm vertically, EEKNJ Lotion 10% had a horizontal dispersion of 7.5 cm and a vertical dispersion of 7.1 cm, and EEKNJ Lotion 15% had a horizontal dispersion of 6.4 cm and a vertical dispersion of 6.2 cm. From these results, it shows that in EEKNJ Lotion 5% has a greater horizontal and vertical dispersion value, which shows that the lower the concentration of ethanol extract of sweet orange peel, the wider the distribution area produced.

Normality Test Results

Table 6 Normality Test Results

Treatment Groups	Sig
Untreated	0,869
Hansaplast ointment	0,978
EEKNJ Lotion 5%	0,885
EEKNJ Lotion 10%	0,798
EEKNJ Lotion 15%	0,846

Source : Primary Data processed (2025)

The normality test was carried out to find out whether the data in each treatment group were distributed normally. The results of the normality test in table 6 showed that the entire group, namely the untreated group (Sig. = 0.869), the Hansaplast ointment group (Sig. = 0.978), the EEKNJ lotion group 5% (Sig. = 0.885), the EEKNJ lotion group 10% (Sig. = 0.798), and the EEKNJ lotion group 15% (Sig. = 0.846) had a significance value greater than 0.05. This means that the data in each group is normally distributed. Thus, it can be concluded that statistical analysis can be continued using a parametric test, i.e. ANOVA, to compare differences between treatment groups.

Effect of Applying Sweet Orange Peel Ethanol Extract Lotion (*Citrus Sinensis*) on Wound Healing Speed in Wistar White Rats

The following are the results of a study on the effect of giving sweet orange peel ethanol extract lotion (*Citrus sinensis*) on wound healing speed in Wistar white rats.

Table 7 Results of Research on the Effect of Applying Sweet Orange Peel Ethanol Extract Lotion (*Citrus Sinensis*) on Wound Healing Speed in Wistar White Rats

Treatment Groups	Day 0-3	Days 3-6	Days 6-9	Days 0-9
Untreated	5.43%	4.05%	5.14%	4.87%
Hansaplast ointment	4.75%	8.83%	8.48%	7.35%
EEKNJ Lotion 5%	5.71%	5.60%	6.90%	6.07%
EEKNJ Lotion 10%	5.18%	6.72%	9.74%	7.21%
EEKNJ Lotion 15%	3.66%	4.65%	6.16%	4.82%

Source : Primary Data processed (2025)

Table 7 shows the effect of giving sweet orange peel ethanol extract lotion (*Citrus sinensis*) on wound healing speed in Wistar white rats observed from day 0 to day 9. In the untreated group, the average wound healing rate was relatively low, at 5.43% on days 0 to 3, decreased to 4.05% on days 3 to 6, and increased slightly to 5.14% on days 6 to 9, with a total healing rate of 4.87% until day 9. In the comparison group using Hansaplast ointment, a higher

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healing speed was seen than the untreated group, which was 4.75% on days 0 to 3, increased sharply to 8.83% on days 3 to 6, and remained high at 8.48% on days 6 to 9, with a total cure of 7.35%.

Meanwhile, in the treatment group with various doses of sweet orange peel ethanol extract lotion (EEKNJ), the speed of wound healing varied. The EEKNJ 5% lotion group showed a moderate increase with a speed of 5.71% on days 0 to 3, 5.60% on days 3 to 6, and 6.90% on days 6 to 9, for a total of 6.07%. In the intermediate dose EEKNJ group, a higher increase was observed, namely 5.18% on days 0 to 3, increased to 6.72% on days 3 to 6, and reached 9.74% on days 6 to 9, for a total of 7.21%. As for the highest dose of EEKNJ, the cure tended to be lower than the intermediate dose, which was 3.66% on days 0 to 3, 4.65% on days 3 to 6, and 6.16% on days 6 to 9, for a total of 4.82%. In general, these results suggest that the administration of EEKNJ lotion was able to speed up the wound healing process compared to the untreated group, although the best effect was seen at medium doses that were close to the effectiveness of Hansaplast ointment.

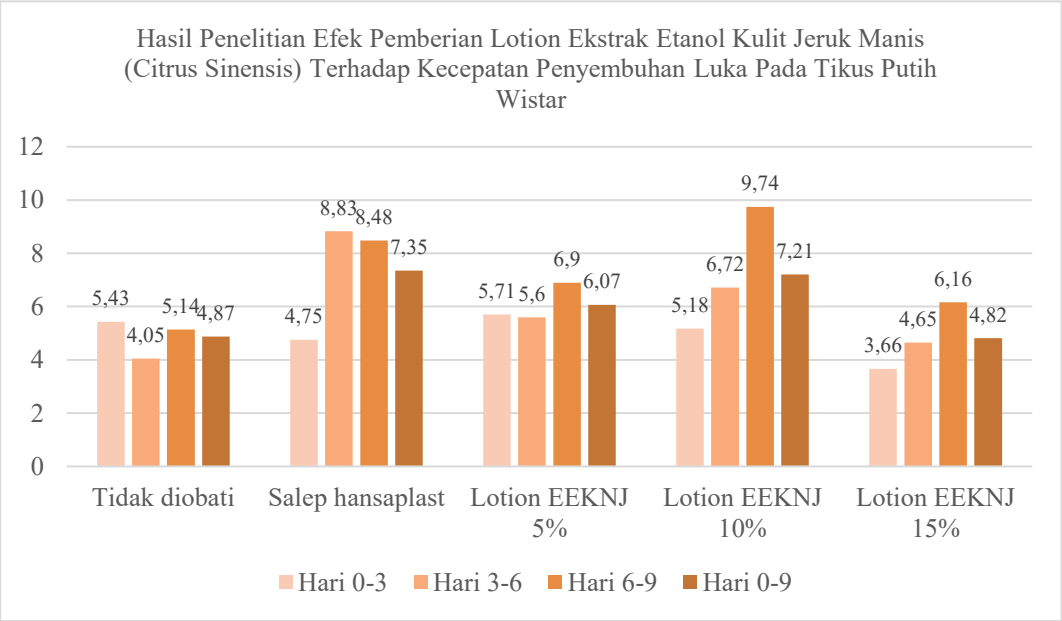

Figure 1 Percentage of wound healing speed in wistar white rats

Effect of Sweet Orange Peel Extract Lotion (*Citrus Sinensis*) on the Healing Process with Macroscopic Assessment

The following are the results of the study on the effect of giving sweet orange peel extract lotion (*citrus sinensis*) on the healing process with macroscopic assessment.

Table 8 Effect of Sweet Orange Peel Extract Lotion (*Citrus Sinensis*) on the Healing Process with Macroscopic Assessment

Treatment Groups	Momogenity	Sig
Untreated	0,859	0,112
Hansaplast ointment		0,000
EEKNJ Lotion 5%		0,005
EEKNJ Lotion 10%		0,000
EEKNJ Lotion 15%		0,001

Source : Primary Data processed (2025)

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Table 8 shows the results of the homogeneity test and the significance of the effect of applying sweet orange peel ethanol extract lotion (*Citrus sinensis*) on the healing process of wounds of white wistar rats with macroscopic assessment. The results of the homogeneity test showed a value of sig = 0.859, which means > 0.05 so that it can be concluded that the data from all groups have homogeneous or equal variance, so they are eligible to continue with the ANOVA test.

Furthermore, the test results showed a significance value in each group of EEKNJ lotion 5% of 0.005, EEKNJ lotion of 0.000 and EEKNJ lotion of 15% of 0.001. Because all these significance values < 0.05. Thus, the administration of sweet orange peel ethanol extract lotion at various doses had a significant effect on the healing process of Wistar white rat wounds based on macroscopic assessment.

Effect of Various Doses of Sweet Orange Peel Ethanol Extract Lotion (*Citrus Sinensis*) on Wound Healing Rate in White Wistar Rats

The following are the results of research on effect of various doses of sweet orange peel ethanol extract lotion (*Citrus sinensis*) on wound healing rates in Wistar white rats.

Table 9 Effect of Various Doses of Sweet Orange Peel Ethanol Extract Lotion (*Citrus Sinensis*) on Wound Healing Rate in Wistar White Rats

Treatment Groups	Healing Percent Score			P value
	Median	Min	Max	
Untreated	30,07	16,29	43,85	
Hansaplast ointment	40,21	14,24	66,17	
EEKNJ Lotion 5%	35,87	17,13	54,61	0,901
EEKNJ Lotion 10%	40,23	15,54	64,92	
EEKNJ Lotion 15%	27,20	10,98	43,42	

Source : Primary Data processed (2025)

The results of the one-way ANOVA test on the variable percent wound healing showed that the significance (Sig. = 0.901). Because the Sig. value is greater than 0.05, it can be concluded that there is no significant difference in the percentage of wound healing between the groups given sweet orange peel ethanol extract lotion (EEKNJ) with different doses (5%, 10%, and 15%), hansaplast ointment and untreated.

Although descriptively there is a variation in the average percentage of cure (EEKNJ is 10% higher than 5% and 15%), statistically the difference is not significant.

Table 10 Comparison of Wound Healing Percentage in Wistar White Rats After Being Given Sweet Orange Peel Ethanol Extract Lotion (EEKNJ) with different concentrations (5%, 10%, and 15%)

Treatment Groups	Subset for alpha = 0.05
EEKNJ Lotion 5%	35,22
EEKNJ Lotion 10%	38,72
EEKNJ Lotion 15%	26,44
Sig.	0,750

Source : Primary Data processed (2025)

Table 10 shows the comparison of wound healing percentages in Wistar white rats after being given sweet orange peel ethanol extract lotion (EEKNJ) with different concentrations (5%, 10%, and 15%).

The average percentage of healing obtained was: EEKNJ 15% = 26.44%, EEKNJ 5% = 35.22%, and EEKNJ 10% = 38.72%. These results showed that the 10% EEKNJ lotion group had the highest average wound healing compared to the other groups, followed by the EEKNJ 5%, while the lowest was EEKNJ 15%.

However, the significance value between groups was 0.750 (> 0.05), which means that there was no significant difference between EEKNJ doses in accelerating wound healing. In

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other words, although descriptively 10% EEKNJ lotion shows the average best cure percentage, the difference between doses of 5%, 10%, and 15% is not statistically strong enough to be declared meaningful

DISCUSSION

Effect of Giving Sweet Orange Peel Ethanol Extract Lotion (*Citrus Sinensis*) on Wound Healing of White Rats Wistar

The results of this study show that the administration of sweet orange peel ethanol extract lotion (*Citrus sinensis*) can accelerate the wound healing process in Wistar white rats compared to the control group without treatment. This is in line with research on the skin of sweet citrus fruits (*Citrus sinensis*) which has revealed the presence of other bioactive compounds besides flavonoids, namely tannins, saponins, and steroids/triterpenoids. Tannins are known for their astringent properties that can help reduce inflammation and have potential as an antimicrobial agent. Saponins, another compound found in sweet orange peel, have natural surfactant activity that can increase cell membrane permeability and play a role in increasing the absorption of other active compounds, in addition to having anticancer, antimicrobial, and antioxidant activities. In addition, the presence of steroids and triterpenoids in sweet orange peel shows significant pharmacological potential, especially in terms of anti-inflammatory, anticancer, and inhibiting microbial growth activities. The combination of these compounds makes the peel of sweet citrus fruits a rich source of bioactive ingredients with various therapeutic potentials. (April 2024)

Therefore, the use of EEKNJ lotion can have a positive effect on the wound healing phases. Interestingly, the study found that the intermediate dose (10%) gave the most optimal results and was almost comparable to the effectiveness of Hansaplast ointment used as a positive control. This can be explained by the phenomenon of *dose-dependent response*, where the active compounds of plants have a certain optimal point to work optimally. At low doses (5%), although the healing effect is already visible, the concentration of the active substance may not be strong enough to produce the full effect of accelerating tissue regeneration. On the other hand, high doses (15%) actually showed less than optimal results compared to the 10% dose. This condition may be caused by several factors, such as tissue saturation of active substances, potential local irritation due to too high levels of compounds, or interactions between bioactive components that cause their pharmacological effects to decrease. Similar phenomena have also been reported in other drug plant studies, where medium doses are more effective than high doses.

Based on statistical tests, the administration of EEKNJ lotion with different doses was proven to have a significant effect on wound healing based on macroscopic and microscopic assessments ($p < 0.05$). This shows that in general, EEKNJ lotion is indeed effective in accelerating wound tissue repair. Macroscopically, the difference can be seen from the shrinking size of the wound, the formation of granulated tissue, and faster epithelialization compared to the control group. Meanwhile, microscopically, tissue observation showed improvements in histological structures such as increased fibroblasts, collagen deposition, and new epithelial growth. These results strengthen the evidence that the active content in sweet orange peel works not only on the wound surface, but also improves the healing process at the cellular level.

However, the results of ANOVA's analysis of the wound healing percentage showed that there was no significant difference between doses of EEKNJ lotion ($p = 0.901$). This means that although descriptively the 10% dose provides the highest average wound healing (38.72%), followed by the 5% dose (35.22%), and the lowest dose of 15% (26.44%), the difference is not strong enough to be statistically significant. This can be influenced by the limited sample size so that the variation in data between groups is quite large. Another factor that may play a role is the different biological responses of individual mice to the bioactive

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compounds in the extract. Thus, although the descriptive results support the 10% dose as the best dose, follow-up studies with larger sample numbers are needed to confirm the significance of the results.

The finding that high doses (15%) did not result in better wound healing actually opened up opportunities for further discussion. Pharmacologically, the high concentration of active compounds is not always directly proportional to effectiveness. At certain concentrations, polyphenol compounds in sweet orange peel can have pro-oxidant effects, which actually inhibit the process of tissue regeneration. In addition, high concentrations can also cause local pH changes in the wound or cause mild irritation that interferes with the formation of new tissue. This explains why in this study the 15% group did not show better results than the 10% or 5% groups.

Overall, this study supports the potential use of sweet orange peel as a basic ingredient for making herbal lotions to accelerate wound healing. The results obtained are also consistent with previous studies that confirm the role of flavonoids and tannins in the wound healing process. However, the finding that there was no significant difference between doses underscores the need for concentration optimization as well as advanced preclinical testing to ensure the most effective and safe dose to use. In addition, clinical trials in humans are also needed to strengthen scientific evidence so that lotions made from sweet orange peel extract can be developed as a natural, affordable, and high-potential wound therapy alternative for mass production.

CONCLUSION

Based on the results of the study, the administration of sweet orange peel ethanol extract lotion (*Citrus sinensis*) was shown to speed up the wound healing process in Wistar white mice compared to the untreated group. The effect is best seen in medium doses, which are almost comparable to Hansaplast ointments, while low doses show moderate improvement and high doses are less than optimal. Administration of sweet orange peel ethanol extract lotion (*Citrus sinensis*) at various doses had a significant effect on the wound healing process of Wistar white rats based on macroscopic and microscopic assessments with significance values of the entire group of sweet orange peel ethanol extract lotion (*Citrus sinensis*) < 0.05. Administration of sweet orange peel ethanol extract lotion (*Citrus sinensis*) with different doses (5%, 10%, and 15%) showed no significant difference in wound healing percentage in Wistar white rats (Sig. = 0.901). Although descriptively the EEKNJ 10% group showed the highest average wound healing (38.72%), followed by EEKNJ 5% (35.22%) and EEKNJ 15% (26.44%), the difference was not statistically significant.

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