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The Effect of Guava Leaf Extract (Psidium Guajava Linn) on Wound Healing Time in Mice Induced with Cut Wounds

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Guava leaves (Psidium guajava Linn) contain flavonoids, tannins, saponins, and polyphenols that have antioxidant, anti-inflammatory, and antibacterial activities, thus potentially accelerating the wound healing process. This study aims to evaluate the topical effects of guava leaf extract on the healing time of incision wounds in Rattus norvegicus rats. The research method used a laboratory experimental design by administering guava leaf extract to the treatment group and a comparison control. Parameters observed included wound closure time, fibroblast proliferation, collagen deposition, re-epithelialization, neovascularization, and the level of inflammation through histological examination. The results showed that administration of guava leaf extract was able to accelerate wound healing compared to the control group, characterized by faster wound closure, increased fibroblast numbers, better collagen formation, and reduced inflammation. In conclusion, guava leaf extract has the potential to be an effective natural therapy in accelerating the wound healing process, although further research regarding optimal dosage and clinical trials are still needed.

Keywords: guava leaf extract; Psidium guajava Linn; incision; wound healing; fibroblasts; neovascularization; antioxidant capacity; IL6.

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1. Introduction

A wound is a condition where tissue continuity is disrupted due to damage to the anatomical structure of the skin, disrupting its integrity and physiological function as the body's primary protective layer. The skin plays a crucial role in maintaining bodily balance, preventing the entry of microorganisms, and protecting underlying tissues from environmental exposure. When tissue damage occurs, the body engages in a series of biological mechanisms to repair the injured area through a wound healing process involving the phases of hemostasis, inflammation, proliferation, and tissue remodeling [1].

In general, wounds can be classified into two main groups: open wounds and closed wounds. An open wound occurs when damage occurs to the surface of the skin, allowing the underlying tissue to come into direct contact with the external environment. One common type of open wound is an incised wound, which is trauma caused by a sharp object that causes a break in the skin tissue with relatively regular wound edges. Based on their depth, skin wounds can be categorized into four stages, ranging from minor damage to damage involving deeper tissue [2].

In stage I, the skin remains intact, but physiological changes may be observed in the area surrounding the wound, such as changes in color, temperature, tissue consistency, and local sensation. Stage II is characterized by partial loss of the epidermis and dermis, resulting in a wound on the skin's surface. Stage III indicates more extensive damage, involving the entire epidermis and dermis without affecting the fascia.

Stage IV, on the other hand, is the most severe, with damage involving all layers of the skin and subcutaneous tissue, leading to tissue necrosis [2,3].

Based on the 2018 Basic Health Research (Riskesdas) data, the prevalence of injuries in Indonesia reached 9.2%. The highest number of injuries was found in Central Sulawesi Province with a prevalence of 13.8%, while the lowest number was in Jambi Province at 5.6%. Based on the type of injury that occurred, abrasions and bruises were the most common type of injury found at 64.1%, while lacerations or cuts were next in line at 20.1% [4].

The increasing number of injury incidents from year to year indicates that wound problems remain a concern in the health sector. Data shows that the national injury prevalence has increased from 8.4% in 2013 to 9.2% in 2018. This condition indicates the need to develop wound care methods that are effective, safe, easily accessible, and able to accelerate the process of tissue regeneration to reduce the risk of complications due to wounds that are not optimally treated [4].

In modern medicine, wound care generally utilizes pharmacological agents such as povidone iodine, which has antiseptic activity against various microorganisms, including gram-positive and gram-negative bacteria, fungi, spores, and protozoa. Povidone iodine is widely used due to its effectiveness in preventing wound infections. However, long-term use or in certain individuals can cause local side effects such as skin irritation, redness, edema, and itching due to sensitivity reactions to the substance [5,6].

The limitations in the use of these chemical agents have encouraged increased research into natural ingredients that have potential as alternatives for wound healing. Traditional plant-based medicine has become one approach that is widely developed due to its advantages in terms of readily available materials, lower costs, and the content of bioactive compounds that can support tissue repair. One plant known to have wound healing activity is guava (Psidium guajava Linn.), which contains various secondary metabolites such as flavonoids, tannins, saponins, and alkaloids [5].

Guava leaves (Psidium guajava Linn.) are known to contain various bioactive compounds that play a role in wound healing. Flavonoids have antioxidant and anti-inflammatory activity that can help reduce tissue damage caused by free radicals and inhibit excessive inflammation. Furthermore, flavonoids also play a role in hemostasis by helping to stop bleeding by increasing platelet activity and forming fibrin in the wound area [8,9].

In addition to flavonoids, the saponin content in guava leaves plays a crucial role in the proliferation and remodeling phases of tissue. Saponins are known to stimulate fibroblast activity, which plays a role in the formation of collagen, the main component of connective tissue. Increased collagen synthesis strengthens new tissue structures, accelerates skin regeneration, and helps restore the integrity of tissue damaged by wounds [8,9,11].

The tannin content in guava leaves also has activity in supporting the wound healing process through antibacterial and antiseptic mechanisms. Tannins can inhibit the growth of microorganisms by damaging bacterial cell walls, altering cell membrane permeability, and inhibiting enzyme activity and microbial protein synthesis. Through these activities, tannins can help prevent infection, allowing for optimal tissue regeneration [8,9,11].

In addition to flavonoids, saponins, and tannins, the alkaloids found in guava leaves also play a role in wound healing through their antimicrobial activity. Alkaloids work by inhibiting the formation of peptidoglycan in bacterial cell walls, disrupting the stability of the cell structure and ultimately killing the microorganism. This activity makes alkaloids play a role in controlling infection during the inflammatory phase and supporting new tissue formation during the proliferative phase [8,9,11].

Based on its various bioactive contents, guava leaf extract (Psidium guajava Linn) has the potential as a natural agent in accelerating wound healing. Therefore, this study was conducted to evaluate the effect of guava leaf extract on the wound healing process of incisions in rats (Rattus norvegicus) by assessing its effectiveness in accelerating wound closure time and improving tissue regeneration processes. Based on this background, the formulation of the research problem is how the effect of Psidium guajava Linn leaf extract on the wound healing process of incisions in rats (Rattus norvegicus) as an experimental animal model. The general objective of this study is to determine the effectiveness of guava leaf extract (Psidium guajava Linn) in accelerating wound healing time in rats induced by incisions..

2. Method

This study used a post-test only experimental design with a control group design which aimed to determine the effect of guava leaf extract (Psidium guajava Linn) on wound healing time in white rats (Rattus norvegicus) induced by incisions. This study was conducted from June 2024 to August 2025, including the stages of literature study, proposal preparation, proposal seminar, processing of research ethics permits, research implementation, data processing, data analysis, and results seminar. The location of the study was at the Integrated Laboratory Animal Management Unit, Faculty of Medicine, University of Muhammadiyah North Sumatra. The study population was adult white rats (Rattus norvegicus) of the Wistar strain aged more than two months obtained from the Integrated Laboratory Animal Management Unit, Faculty of Medicine, University of Muhammadiyah North Sumatra. The study sample was selected based on predetermined inclusion and exclusion criteria to ensure that the experimental animals had conditions appropriate to the research objectives.

The inclusion criteria for this study included male Wistar rats, aged 8–12 weeks, weighing 200–250 grams, and in good health without any disease or medical disorder that could affect the results of the study. The exclusion criteria included rats showing signs of disease or infection before the study, female rats, rats that had received other treatments or drugs that could affect the wound healing process, rats with stress or abnormal behavior, and rats with wound induction that did not meet research standards. The sample size was determined using the Federer formula, namely $(n-1) \times (t-1) \geq 15$. Based on this calculation, the minimum sample size was 6 rats in each group. This study consisted of four treatment groups, resulting in a total of 24 rats. To anticipate the possibility of losing subjects during the study (loss to follow-up), a 10% increase in the sample size was made, thus adding 4 rats as reserves.

The research sample was then divided into four groups, namely a negative control group that was not given any intervention, a positive control group that was given standard therapy in the form of 10% povidone-iodine, treatment group I that was given Psidium guajava Linn leaf extract at a dose of 100 grams, and treatment group II that was given Psidium guajava Linn leaf extract at a dose of 150 grams. All treatments were administered topically using sterile cotton buds. The research data used were primary data obtained directly from the results of treatment on experimental animals. Observations were made by measuring the length of the incision wound using a wound ruler and digital measuring tape, and documenting the progress of the wound every day until it reached a perfect epithelialization process. The tools used in the research included a blender, Pasteur pipette, scalpel, scissors, tweezers, sterile marker, wound ruler, wound plaster, cotton buds, digital measurement application, refrigerator, digital scale, camera, measuring cup, sterile gloves, and mouse cage. The research materials consisted of guava leaves, white Wistar rats, distilled water, vaseline (petroleum jelly), 10% povidone-iodine, 70% ethanol, lidocaine HCL monohydrate, and rat food and drink.

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The preparation of guava leaf extract begins with a plant identification process carried out at the Biology Laboratory of the University of North Sumatra. After the identification is complete, the extract preparation process is carried out at the Biochemistry Laboratory of the Faculty of Medicine, Muhammadiyah University of North Sumatra [25]. Guava leaves were obtained from the Melati Abadi flower shop in the Medan area, then fresh leaves were selected for processing into an extract [25]. The leaves were washed until clean, then weighed as much as 100 grams and 150 grams using a digital scale. Next, each weight of guava leaves was blended with the addition of 200 ml of distilled water to produce an extract. After the crushing process, the extract was filtered and stored in the refrigerator for one day for the sedimentation process. The final stage was the separation of the liquid and the resulting extract sediment to obtain a guava leaf extract preparation that was ready for use in research.

3. Results and Discussion

Research result

This research was conducted in the Experimental Animal Laboratory, Integrated Laboratory of the Faculty of Medicine, Muhammadiyah University of North Sumatra; the Biochemistry Laboratory, Faculty of Medicine, Muhammadiyah University of North Sumatra; and the Plant Systematics Laboratory, Herbarium Medanense, University of North Sumatra. The entire research series was carried out based on the approval of the Health Research Ethics Committee of the Faculty of Medicine, Muhammadiyah University of North Sumatra, with the number 1357/KEPK/FKUMSU/2024.

Plant Identification Results

The botanical identification process was carried out to ensure the suitability of the plant specimens used in the research, thereby minimizing the possibility of specimen errors. The identification was conducted at the Plant Systematics Laboratory, Herbarium Medanense, University of North Sumatra. Based on the taxonomic verification results, the research specimen was confirmed to be the species Psidium guajava Linn.

Univariate Analysis

Data on the Results of Measuring the Length of the Rat Incision Wound on Day 1

Table 1 Results of Measurement of the Length of the Rat Incision Wound After Treatment on Day 1

	N	cm
K-	6	1.99 cm
K+	6	1.99 cm
P1	6	1.97 cm
P2	6	1.97 cm

From table 1. above, it is known that the statistical results of incision wounds in mice on day 1 show an average value of k- 1.99, K+ 1.99, P1 1.97, and P2 1.97. This shows that there is variation in incision wounds between various types of treatments, because the treatment has been carried out on each mouse.

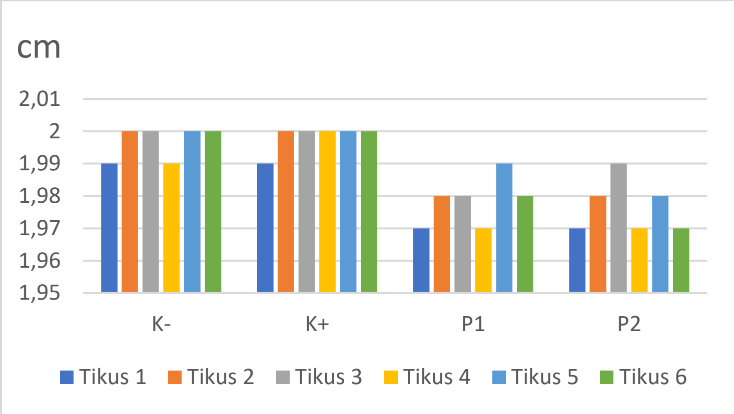

Figure 1. Graph of Rat Incision Wounds on Day 1

The data analysis showed that the average incision length across all treatment groups was 1.98 cm. This finding indicates variation in incision wound size between groups, which occurred as a consequence of the intervention administered to each experimental animal.

Data on the Results of Measuring the Length of the Rat Incision Wound on Day 6

Table 2 Results of Measurement of the Length of the Rat Incision Wound After Treatment on Day 6

	N	cm
K-	6	1.86 cm
K+	6	1.41 cm
P1	6	1.44 cm
P2	6	1.34 cm

From table 2 above, it is known that the statistical results of incision wounds in mice on the 6th day showed an average value of k- 1.86, K+ 1.41, P1 1.44, and P2 1.34. This shows that there is variation in incision wounds between various types of treatments, because the treatment has been carried out on each mouse.

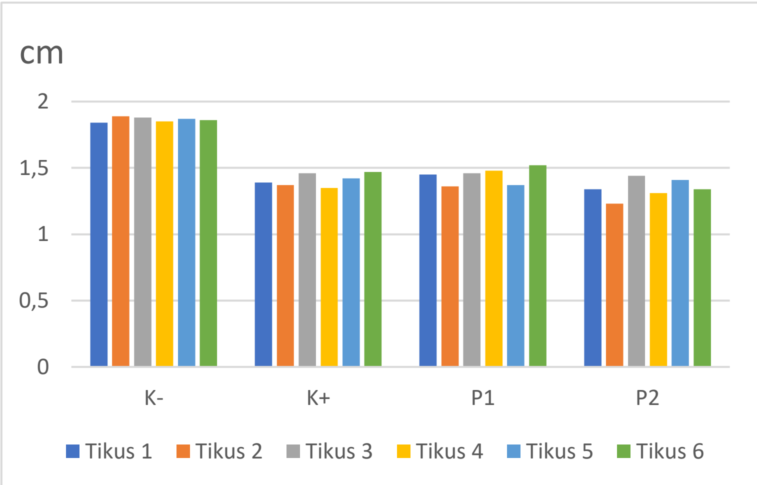

Figure 2. Graph of Mouse Incision Wounds on Day 6

Based on the data above, it can be seen that the average length of the incision wound in each treatment group was 1.51 cm, indicating that there was variation in incision wounds between the various types of treatments, due to the treatment carried out on each mouse.

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Data on the Results of Measuring the Length of the Incision Wound in Mice After Treatment on the 8th Day

Table 3 Results of Measurement of the Length of the Rat Incision Wound After Treatment on Day 8

	N	cm
K-	6	1.75 cm
K+	6	1.05 cm
P1	6	1.05 cm
P2	6	1.01 cm

From table 3. above, it is known that the statistical results of incision wounds in mice on the 8th day show variations in incision wounds among various types of treatments. The treatment that is fastest in reducing the length of the wound is treatment P2, which is by providing 150 grams of guava leaf extract induction and the treatment that takes the longest in reducing the length of the wound is K-, which is by not providing any induction.

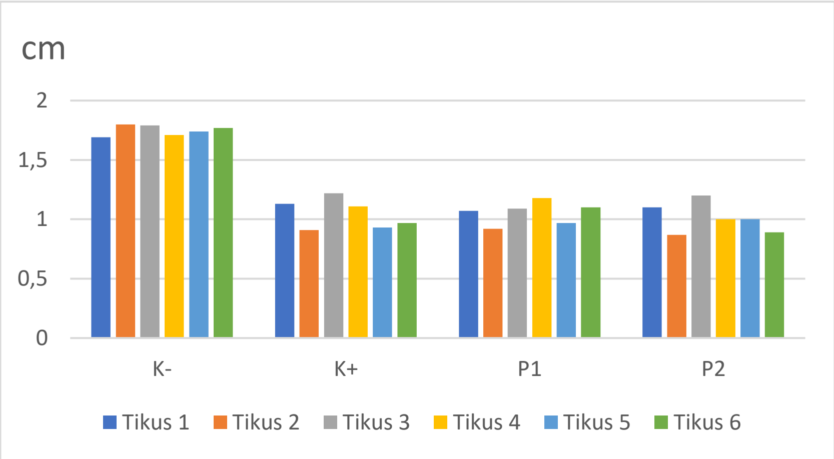

Figure 3. Table Graph of Rat Incision Wounds on Day 8

The analysis results showed that the P2 treatment group had the shortest average incision length, with a wound healing rate approximately 21% faster than the other groups. This finding indicates that the P2 group experienced a more optimal tissue repair process compared to the negative control (K-), positive control (K+), and P1 treatment groups. Conversely, the negative control (K-) group showed the longest average incision length, which was approximately 36%, indicating that the wound healing phase in this group was the slowest compared to the other groups.

Data on the Results of Measuring the Length of the Rat Incision Wound on Day 14

Table 4. Results of Measurement of the Length of the Rat Incision Wound After Treatment on Day 14

	N	cm
K-	6	1.19 cm
K+	6	0.00 cm
P1	6	0.23 cm
P2	6	0.00 cm

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From table 4. above, it is known that the statistical results of incision wounds in mice on the 14th day showed an average value of k- 1.19, K+ 0.00, P1 0.23, and P2 0.00. This shows that there is variation in incision wounds between various types of treatments, because the treatment has been carried out on each mouse.

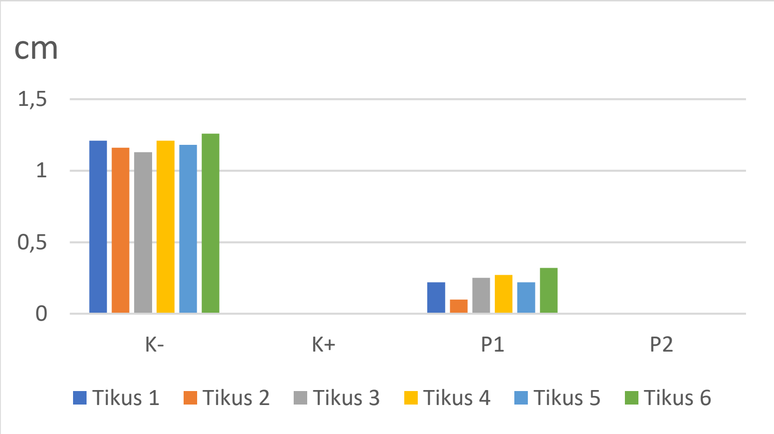

Figure 4. Table Graph of Rat Incision Wounds on Day 14

Data analysis showed that the average incision length across all treatment groups was 0.35 cm, indicating variations in wound size between treatment groups due to the interventions given to each test animal. On day 14, the positive control group (K+) and the P2 treatment group did not display measurement graphs, because during that period the wounds had completely healed so that no open incisions were found.

Bivariate Analysis

Normality Test

TestNormality in this study used Shapiro-Wilk because the sample used was ≤ 50.

Table 5. Results of the Shapiro-Wilk Normality Test

Inspection	Group	Sigma Value (P)	Information
Length of Wound Day 1	Control -	0.001	Abnormal
	Control +	0.001	Abnormal
	Treatment 1	0.212	Normal
	Treatment 2	0.212	Normal
Length of Wound Day 6	Control -	0.961	Normal
	Control +	0.623	Normal
	Treatment 1	0.474	Normal
	Treatment 2	0.809	Normal
Length of Wound Day 8	Control -	0.636	Normal
	Control +	0.412	Normal
	Treatment 1	0.718	Normal
	Treatment 2	0.640	Normal
Length of Wound Day 14	Control -	0.940	Normal
	Control +	-	-
	Treatment 1	0.501	Normal
	Treatment 2	-	-
Length of Wound Day 28	Control -	-	-
	Control +	-	-
	Treatment 1	-	-

Inspection	Group	Sigma Value (P)	Information
	Treatment 2	-	-
Length of Wound on the 30th day	Control -	-	-
	Control +	-	-
	Treatment 1	-	-
	Treatment 2	-	-

Based on the results of the normality test above, it was found that on days 1, 6 and 8 the p value was > 0.05, which indicates that the data was normally distributed.

Homogeneity Test

This test was conducted to determine whether there were equal variances in each group. Levene's Test was used as a homogeneity test.

Table 6. Levene's Test of Homogeneity

Wound Length Check Day Rat Fasting	**Sigma P Value**	**Information**
Day 1	0.491	Homogeneous
Day 6	0.147	Homogeneous
Day 8	0.102	Homogeneous
Day 14	0.009	Not Homogeneous

Based on the table above, it is stated that days 1, 6 and 8 meet the homogeneity requirements, so it is continued using the Post Hoc Test using Bonferroni.

One Way Anova Test

Table 7. One Way Anova Test

Group Treatment	Sigma P Value	Information
Length of Wound Day 1	<0.001	There is a difference in the average

Group Treatment	Sigma P Value	Information
Length of Wound Day 6	<0.001	There is a difference in the average

Group Treatment	Sigma P Value	Information
Length of Wound Day 8	<0.001	There is a difference in the average

Group Treatment	Sigma P Value	Information
Length of Wound Day 14	<0.001	There is a difference in the average

Based on the table above, a P value of <0.05 indicates a significant difference in the average effect of each group. Data analysis will continue using the Bonferroni post hoc test to determine which groups have different data.

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Table 8. Bonferroni Post Hoc Test on Day 1

Group		Difference in average wound length	Sigma P Value
K-	K+	-0.00167	1,000
	P1	0.01833	<0.001
	P2	0.01833	<0.001
K+	K-	0.00167	1,000
	P1	0.02000	<0.001
	P2	0.02000	<0.001
P1	K-	-0.01833	<0.001
	K+	-0.02000	<0.001
	P2	0.00000	1,000
P2	K-	-0.01833	<0.001
	K+	-0.02000	<0.001
	P1	0.00000	1,000

Table 9. Bonferroni Post Hoc Test on Day 6

Group		Difference in average wound length	Sigma P Value
K-	K+	0.45500	<0.001
	P1	0.42500	<0.001
	P2	0.52000	<0.001
K+	K-	-0.45500	<0.001
	P1	-0.03000	1,000
	P2	0.6500	0.331
P1	K-	-0.42500	<0.001
	K+	0.03000	1,000
	P2	0.09500	0.045
P2	K-	-0.52000	<0.001
	K+	-0.06500	0.331
	P1	-0.09500	0.045

Table 10. Bonferroni Post Hoc Test on Day 8

Group		Difference in average wound length	Sigma P Value
K-	K+	0.70500	<0.001
	P1	0.69500	<0.001
	P2	0.74000	<0.001
K+	K-	-0.70500	<0.001
	P1	-0.01000	1,000
	P2	0.03500	1,000
P1	K-	-0.69500	<0.001
	K+	0.01000	1,000
	P2	0.04500	1,000
P2	K-	-0.74000	<0.001
	K+	-0.03500	1,000
	P1	-0.04500	1,000

Table 11 Bonferroni Post Hoc Test on Day 14

Group	Difference in average wound length	Sigma P Value
K- K+	1.19167	<0.001
P1	0.96167	<0.001
P2	1.19167	<0.001
K+ K-	-1.19167	<0.001
P1	-0.23000	<0.001
P2	0.00000	1,000
P1 K-	-0.96167	<0.001
K+	0.23000	<0.001
P2	0.23000	<0.001
P2 K-	-0.96167	<0.001
K+	0.00000	1,000
P1	-0.23000	<0.001

Based on the Bonferroni Post Hoc test results table on days 1, 6, 8, and 14, it shows that all comparisons between groups showed a significant difference in wound length ($p < 0.001$), where the P2 treatment group had the shortest wound length compared to all other groups, followed by P1, while the K+ and especially K- groups showed a much larger wound length, which confirms that the administration of guava leaf extract, especially the 150 gram dose, provided the most optimal wound healing effect compared to other treatments after eight days of observation.

Discussion

This study shows that administration of guava leaf extract (Psidium guajava Linn) has a significant effect on accelerating wound healing in male white Wistar rats. The effectiveness of wound healing was evaluated based on changes in wound length during the observation period. The results of the analysis using the One Way ANOVA test showed a significant difference between treatment groups on day 6 and day 8 ($p<0.05$). The group that received guava leaf extract, especially the 150 gram dose, showed a faster reduction in wound length compared to the negative control group and the positive control group that received povidone-iodine. These findings indicate that guava leaf extract is able to accelerate the tissue regeneration process so that wound healing time is shorter. [15]

The results of the univariate analysis showed that the 150 gram dose treatment group (P2) had the smallest average wound length compared to the negative control group (K-), the positive control group (K+), and the 100 gram dose treatment group (P1). Conversely, the negative control group showed the largest average wound length, thus depicting a slower healing process. This condition indicates that the administration of guava leaf extract is able to accelerate wound contraction compared to the natural healing process without intervention. The results of this study are in line with Asyifa's research which reported that the administration of herbal plant extracts made a significant difference in the speed of wound healing in experimental animals. [16]

Observations on day 6 showed that group P2 had the shortest average wound length compared to all study groups. This difference indicates that administering high doses of guava leaf extract was able to accelerate the tissue proliferation phase more effectively than povidone-iodine or the untreated group. These results are in accordance with Panjaitan's research which stated that increasing the dose of guava leaf extract is associated with increased effectiveness of wound healing due to the higher flavonoid, saponin, and tannin content. Harsa's research also reported that bioactive compounds from herbal plants are able to increase the formation of granulation tissue and collagen synthesis, thereby accelerating the wound healing process. [17]

On the 8th day, the group receiving 150 grams of guava leaf extract again showed the smallest wound size compared to the other groups. These results indicate that the effectiveness of guava leaf extract becomes more apparent as the observation time increases. This finding is in line with Agustina's research which reported that plant extracts can accelerate wound healing by reducing the inflammatory response, increasing collagen formation, and accelerating the re-epithelialization process. Sutrisna's research also stated that plant extract-based therapy provides better wound healing results than conventional therapy. [18]

Before conducting a comparative analysis, the research data were first tested for normality using the Shapiro-Wilk test because the sample size was less than 50. The test results showed that all data had a normal distribution, thus fulfilling the assumptions of using parametric tests. In addition, a homogeneity test using Levene's Test showed that the data variance between groups was homogeneous. With these two assumptions met, analysis using One Way ANOVA was deemed appropriate for comparing the effectiveness of treatments in each research group. [19]

The results of the One Way ANOVA analysis showed a significant difference between groups after treatment. Further analysis using Post Hoc Bonferroni showed that the treatment group with a 150 gram dose of guava leaf extract had the highest wound healing effectiveness compared to the control group and the 100 gram dose group. These results indicate that increasing the dose of guava leaf extract has an effect on increasing the effectiveness of wound healing. Research by Putry and Olatunde also reported that flavonoids and tannins play an important role in supporting the inflammatory, proliferation, and tissue remodeling phases, thereby accelerating wound healing. [20]

The effectiveness of guava leaf extract in this study is thought to be related to the content of flavonoids, tannins, saponins, and alkaloids that work synergistically during the wound healing process. Flavonoids have antioxidant and anti-inflammatory activities, thus being able to inhibit the formation of free radicals and reduce the production of inflammatory mediators. Tannins act as antibacterials that can prevent the colonization of microorganisms on the wound surface, while saponins stimulate fibroblast proliferation and collagen synthesis which are essential for the formation of granulation tissue. The combination of these biological activities causes the wound contraction process to occur more quickly compared to the control group. [21]

In addition to accelerating wound contraction, guava leaf extract is also thought to work through molecular mechanisms by suppressing the expression of inflammatory mediators such as TNF-α, IL-6, and nitric oxide (NO) through inhibition of the NF-κB and MAPK pathways. The reduction in inflammatory mediators causes the inflammatory phase to last shorter so that the fibroblast proliferation process can begin earlier. The increase in the number of fibroblasts then stimulates collagen deposition which plays an important role in strengthening new tissue and accelerating the re-epithelialization process until the remodeling phase. [22]

The results of this study also showed that the effectiveness of guava leaf extract was better than the administration of povidone-iodine as a positive control. Although povidone-iodine is effective as an antiseptic to prevent infection, this agent does not have bioactive activity that directly stimulates tissue regeneration. In contrast, guava leaf extract not only provides antimicrobial effects, but also has anti-inflammatory and antioxidant activities, as well as the ability to increase fibroblast proliferation and collagen synthesis. Therefore, the wound healing process in the treatment group took place faster than the positive control group. [22]

Overall, the results of this study demonstrate that administration of guava leaf extract (Psidium guajava Linn.), especially at a dose of 150 grams, significantly accelerated wound healing in Wistar white rats. This accelerated healing was demonstrated by a more rapid reduction in wound length, improved wound contraction, and optimal tissue proliferation and remodeling. These findings strengthen the evidence that guava leaf extract has the potential to be developed as an effective alternative herbal therapy in accelerating wound healing, although further research is needed to determine the optimal dosage, long-term safety, and efficacy in humans.

4. Conclusion

Based on the results of the research that has been conducted, it can be concluded that the administration of guava leaf extract (Psidium guajava Linn) has an effect on accelerating the healing of cuts in white rats (Rattus norvegicus). This is indicated by a more significant reduction in wound length in the treatment group compared to the control group. In addition, the administration of guava leaf extract at a dose of 150 grams provides higher effectiveness than a dose of 100 grams, characterized by faster healing time and a shorter average wound length during the observation period. In fact, the effectiveness of guava leaf extract at a dose of 150 grams was proven to be better than the administration of povidone-iodine as a positive control and a negative control group, thus demonstrating the potential of guava leaf extract as an effective natural therapy alternative in accelerating the wound healing process.

Based on the results of this study, it is recommended that further research use more accurate wound healing evaluation methods, such as digital measurements and tissue histopathology examination, to obtain more comprehensive data on the tissue regeneration process. Furthermore, research with a wider variety of doses is needed to determine the optimal dose, accompanied by further phytochemical testing to identify bioactive compounds that play a role in wound healing. Future research is also expected to evaluate the long-term effects and safety of guava leaf extract use, while developing various topical dosage forms such as gels or ointments and comparing them with other standard drugs used in wound therapy, so that the clinical benefits of guava leaf extract can be demonstrated more widely.

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