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Effectiveness of Gedong Gincu Mango Leaf Extract Gel (*Mangifera indica* L. var. Gedong gincu) on Cut Wound Healing in Male White Rats *(Rattus norvegicus)* of the Wistar Strain

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ABSTRACT

Background: The Indonesia Basic Health Research data show the prevalence of wounds including incision/scratches/stab wounds reaches 20.1%. Natural herbal products play an important role in the wound healing process functioning as anti-inflammatories, antioxidants, antimicrobials, and collagen formation. Mango leaves are often considered waste even though they have many health benefits with the high content of coactive compounds, such as alkaloids, flavonoids, tannins, and saponins which are good for cut wound healing. The use of gel is more stable and controlled release compared to other topical preparations. Gedong Gincu mangoes originating from West Java have unique properties and they are marketed widely in some areas including Cirebon.

Aims: This study aims to identify the most effective concentration of Gedong Gincu mango leaf extract on cut wound healing in male white rats *(Rattus norvegicus)* of the Wistar Strain.

Methods: This study used a post-test-only control group design. The extract gel used three levels of concentration, namely 40%, 50%, and 60%. The positive control used 10% povidone iodine while the negative control used a gel base. The gel was applied to the cut wound twice a day for 14 days.

Results: The average length of the cut wound was 0.916 cm, 0.912 cm, and 1.050 cm for concentration levels of 40%, 50%, and 60%. For the positive and negative controls, it reached 0.996 cm and 0.702 cm respectively. This indicates no significant difference in the length of the cut wound with a p-value of 0.121 ($p>0.05$). The wound healing process was effective at a concentration level of 60% as indicated by the disappearance of erythema and edema.

Conclusion: Mango leaf extract gel (*Mangifera indica* L.var. Gedong Gincu) is effective in healing cut wounds with the disappearance of erythema and edema in male white rats (*Rattus norvegicus*) Wistar strain with a concentration of 60%.

Keywords: *Natural products, Mangifera indica, Wound healing, Povidone iodine.*

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1. Introduction

Wounds are damage or loss of part of the tissue (Sjamsuhidajat et al., 2017). The Indonesia Basic Health Research data show that in Indonesia, the prevalence of wounds including incisions/cuts/stabs reaches 20.1% (RISKESDAS, 2018). This result ranks third after abrasions/bruises/contusions and sprains. This value is based on national data, while the percentage result in West Java reaches 21.4% (RISKESDAS, 2018). Wound healing methods are varied including the use of modern products. Natural products made from herbs provide anti-inflammatories, antioxidants, antimicrobials, and collagen formation for the wound healing process with few side effects (El-Sherbeni S. A. et al., 2023; Trinh X. et al., 2022; Criollo-Mendoza M. S. et al., 2023).

Gedong gincu mangoes are exotic and have unique characteristics. These fruits are from West Java and spread across Majalengka, Indramayu, and Sumedang Districts (Ariningsih E. et al., 2021; Bangun RHB. et al., 2020; Umam K. et al., 2021; Sumantri K. et al., 2021). They have been widely distributed and marketed to various regions including Cirebon District (Awaliyah F. et al., 2020). Mango leaves are often considered waste but they have many health benefits as they contain many bioactive compounds (Kumar M. et al., 2021). Previous studies revealed that mango leaves contain alkaloids, flavonoids, tannins, and saponins. Those compounds play a role in the wound-healing process (Suhatri et al., 2022).

Previous studies focusing on the use of gedong gincu mango peel extract gel for cut wound healing showed that mango leaves contain alkaloids, flavonoids, tannins, saponins, phenols, triterpenoids, and steroids. These metabolite compounds have a mechanism of action on the assessment of wound length, erythema, edema, and wound healing time. In this study, the concentration that provides the best wound healing effect was 5% and 10% (Fathunnisa, et al., 2024).

The topical preparation formulation in the form of mango leaf extract gel with concentrations of 40%, 50%, and 60% according to previous studies with cassava leaf extract on wound healing in New Zealand white male rabbits with a good formulation with organoleptic tests, homogeneity tests, pH tests, and gel preparation spread tests, as well as final experiments for the effect on the wound healing process. The concentration of 60% provided the best wound-healing effects (Megawati S. et al., 2020). The use of topical preparations in the management of skin diseases is common. Gel formulations applied in the management of skin diseases are a safe and effective choice. Gels are more stable with more controlled release than other topical preparations. As a topical drug, gels have good absorption (Umam K. et al., 2021).

Based on the explanation above, this study tries to experiment with making Gedong Gincu mango leaf extract. Gedong gincu mangoes originating from West Java have unique properties as wound healers with various secondary metabolites. The determination of the sampling concentration refers to previous studies and produced significant results with different gel extracts. Therefore, this study aims to identify the use of Gedong Gincu mango leaf extract as a secondary metabolite in cut wound healing.

2. Methods

Study design/ Research procedures

This experimental laboratory study used a post-test-only control group design. This study aims to determine the effectiveness of Gedong gincu mango leaf extract gel (*Mangifera indica* L. var. gedong gincu) on cut wound healing in male white rats *(Rattus norvegicus)* of the Wistar strain. The researcher collected data on the length of the cut wound and the presence of erythema and edema for 14 days. The inclusion criteria were male white rats of the Wistar strain aged 2-3 months with a body weight of 150-250 grams and an cut wound on the back. The exclusion criteria were male white rats of the Wistar strain who got sick during treatment. The male white rats of the Wistar strain that died were dropped out. This research was conducted in the research laboratory of the Faculty of Medicine, Swadaya Gunung Jati University.

Preparation of mango gedong gincu leaf extract

The preparation of mango leaf extracts used the maceration method. The mango leaves were obtained from plantations in the Sedong area, Cirebon District. The sun-dried mango leaves were blended and sieved. The results

were added with 70% ethanol with a ratio of solute and solvent of 1:10. Thus, 1 kg of simplicia powder was added with 70% ethanol. The results were macerated for 3x24 hours and stirred twice with a rotary evaporator at a temperature of 50^{o}C. The results were weighted and put into the oven to produce a thick extract.

Phytochemistry Test Of Mango Gedong Gincu Extract Gel

For the alkaloid test, 0.5 grams of mango leaf extract extract was added with 1 mL of 2 N HCl and 9 mL of hot distilled water, then filtered. The first tube was added with bouchardat reagent with a positive result if getting black-brown sediment. Dragendorff reagent was added to the second tube with a positive result if getting a white fog sediment (Ifmaily I. et al., 2023). Hager reagent was added to the third tube with a positive result when getting a yellow sediment. Mayer reagent, methanol, and bouchardat reagent were added to the fourth tube and the result was considered positive if getting brownish-black sediment.

For the flavonoid test and phenolic test, 0.5 grams of mango leaf extract were added with 2 mL of methanol. They were then filtered and divided into two different tubes. The first tube was added with 10% NaOH and considered to have positive results if getting red hydroquinone phenol (Ifmaily I. et al., 2023; Rusnedy R. et al., 2023). Concentrated H_2SO_4 was added to the second tube with a positive indication when getting a red flavonoid compound.

For the tannin test, 1 gram of mango leaf extract was added with 10 mL of distilled water and then filtered. The results were added with $FeCl_3$ with a positive result if getting a dark blue or greenish black color. For the saponin test, 0.5 grams of mango leaf extract in the test tube was added with 10 mL of distilled water, and then shaken. It was left for 2 minutes and added with 1 drop of HCl 2 N. The results will be positive if getting foams for± 10 minutes (Ifmaily I. et al., 2023).

For the triterpenoid test, 0.5 grams of mango leaf extract was added with Bouchardat reagent. If it gets a red or purple color, it is declared positive. For the steroid test, 0.5 grams of mango leaf extract was added with ether, 3 drops of acetic acid, and 1 drop of concentrated H_2SO_4. If getting a green color, it is declared positive.

Preparation of gel mango gedong gincu leaf extract

Table 1 shows the formulation of mango leaf extract gel covering Na-CMC and hot distilled water which are homogenized, glycerin, propylene glycol, and methylparaben which are homogenized. Mango leaf extracts are added with that formulation with a certain concentration. After getting the gel, it was kept away from sunlight for one night (Hasanudin MN. et al., 2023). Then, the gel was tested using organoleptic tests, pH tests, homogeneity tests, and spreadability tests (Budi S. et al., 2020; Nurlatifah N. et al; 2022).

Tabel 1. Gedong gincu mango leaf extract gel formulation

Ingredient	Formulations group (grams)			
	K1 (40%)	K2 (50%)	K3 (60%)	KN
Mango gedong gincu leaf extract	20	25	30	-
Na-CMC	0,5	0,5	0,5	0,5
Metyl paraben	0,25	0,25	0,25	0,25
Glyserin	5	5	5	5
Propylene glycol	2,5	2,5	2,5	2,5
Aquadest ad	50	50	50	50

Evaluation of mango gedong gincu leaf extract gel preparation results

1. Organoleptic test
   The results of the organoleptic test for gedong gincu mango leaf extract covered the physical form, smell, and color of the gel preparation (Budi S. et al., 2020).

2. pH test
   The pH test aims to assess the acidity level of the gedong gincu mango leaf extract gel preparation. The test used a pH meter (Budi S. et al., 2020). A good gel preparation has a value of 4.5-6.5 (Nurlatifah N. et al; 2022).
3. Homogeneity test
   The homogeneity test aims to assess the distribution of the gedong gincu mango leaf extract gel content evenly (Budi S. et al., 2020). This test was conducted by applying the gel to clear glass and looking at whether coarse grains appear or not. The result of the test is considered good if all groups based on extract concentration do not contain coarse grains (Nurlatifah N. et al; 2022).
4. Spreadability test
   This test aims to assess the spreadability of the gedong gincu mango leaf extract gel preparation. A value of 5-7 cm is considered good. This test was carried out by dropping 0.5 grams of gel on an object glass and then covering the top with another object glass. The results were in the form of spreadability value (Nurlatifah N. et al; 2022).

Making cut wounds on male white rats

The researcher used white male rats of the Wistar strain with cut treatment. Before getting the cut, the rats were given 2% lidocaine subcutaneously and got their back fur shaved. The cut area was cleaned with alcohol cotton. The cut was made using a scalpel with a length of ± 2 cm and a depth of ± 0.3 cm. The cut wound healing was based on 3 criteria, namely the length of the cut, erythema stopped, and edema stopped. The Gedong gincu mango leaf extract gel was applied twice a day for 14 days.

Measurements

In this research, the independent variable was Gedong gincu mango leaf extract gel (*Mangifera indica* L. var. gedong gincu). Then, the dependent variable was the cut wound healing in male white rats of the Wistar strain. The sample size was based on the *Federer* formula and the determination of the sample used a simple random sampling technique.

Statistical analysis

The cut wound healing was seen from 3 criteria, namely the length of the cut, erythema elliminated, and edema disappeared. The treatment was performed by applying mango leaf extract gel twice a day for 14 days. Statistical analysis used SPSS (Statistical Package for the Social Sciences). The data obtained were analyzed using the following steps. The length of the cut was assessed first with a normality test using the Shapiro-Wilk test because the sample was less than 50, namely only 25 male white rats. Second, the homogeneity test used the Levene Test. Third, the comparison test used the One-Way Annova test when the requirements for normality and homogeneity are met or (p (Sig.) > 0.05). Then the assessment of erythema and edema was based on direct observation to determine whether the erythema and edema have disappeared or not.

Ethical clearance

This study has received approval from the Ethics Commission of the Faculty of Medicine, Swadaya Gunung Jati University, Cirebon Number 8/EC/FKUGJ/IV/2024, dated April 8, 2024. The mango plants used in this study have been tested at the UNNES Biology Laboratory with the number 54/UN.37/SHP/Lab. Plant Taxonomy/III /2024. Male white rats of the Wistar strain have an animal identity certificate number 09.141/RTP/VI/2024 which comes from Pahlevi's house rats.

3. Results

The researcher obtained 311 grams of thick mango leaf extract. The characteristics of this mango leaf extract gel were thick with a blackish-brown color and had a distinctive mango leaf odor and a bitter taste. Table 2 shows that the Gedong gincu mango leaf extract (*Mangifera indica* L. var. Gedong gincu) contains secondary metabolite compounds such as phenolics, flavonoids, tannins, saponins, triterpenoids and steroids.

Tabel 2. Results phytochemistry test

Phytochemicals	Reagent	Results	Depiction
Alkaloids	Bouchardat	-	Photo 1
	Dragendroff	-	Photo 2
	Hager	-	Photo 3
	Mayer+methanol+bauchardat	-	Photo 4
Fenolics	NaOH 10%	++	Photo 5
Flavonoids	H_2SO_4 concentration	+	Photo 6
Tannins	$FeCl_3$	+++	Photo 7
Saponins	HCl 2 N	+++	Photo 8
Triterpenoids	Bouchardat	+	Photo 9
Steroids	Eter+3 drops anhydrous+1 drop of H_2SO_4 concentration	+	Photo 10

Description:

1. Negative results = (-)
2. Positive results:
   a. Weak = (+)
   b. Strong = (++)
   c. Very strong = (+++)
   d. Extremely strong = (++++)

Table 3 shows that the physical form, odor, and color of gel are in accordance with the extracts used. The physical form of the gel should be semi-solid, have a mango leaf extract odor, and a blackish brown color. The results of the organoleptic test showed that the mango leaf extract gel preparation is as expected.

Tabel 3. Results organoleptic test

Groups	Results		
	Physical form	Odor	Colour
40% concentration	Semi-solid/viscous	Mango leaf extract	Brown-black
50% concentration	Semi-solid/viscous	Mango leaf extract	Brown-black
60% concentration	Semi-solid/viscous	Mango leaf extract	Brown-black
Gel base	Semi-solid/viscous	Don't have odor	Pellucid

Table 4 shows that the concentrations of 40%, 50%, and 60% have good standard normal pH values. The negative control, namely the gel base preparation, did not show a normal pH value. So, concentrations of 40%, 50%, and 60% show good pH results.

Tabel 4. pH test (Photo 11)

Groups	Normal value	Results
40% concentration	4,5-6,5	6
50% concentration	4,5-6,5	6
60% conecntartion	4,5-6,5	6
Gel base	4,5-6,5	7

Photo 1. Bouchardat alkaloids (-)

Photo 2. Dragendroff alkaloids (-)

Photo 3. Hager alkaloids (-)

Photo 4. Mayer alkaloids (-)

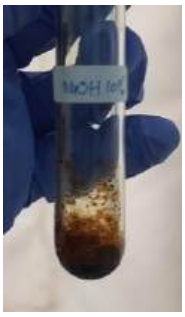

Photo 5. Phenolics (++)

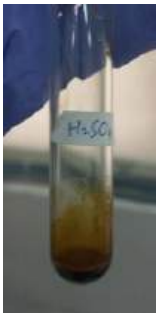

Photo 6. Flavonoids (+)

Photo 7. Tannins (+++)

Photo 8. Saponins (+++)

Photo 9. Triterpenoids (+)

Photo 10. Steroids (+)

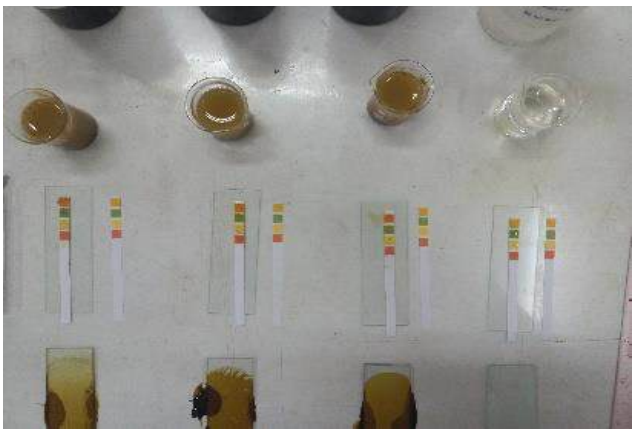

Photo 11. Results of pH test of mango leaf extract gel

Table 5 shows that the spreadability at concentrations of 40%, 60%, and the negative control obtained good spreadability. The 50% concentration had poor spreadability as indicated by a value of lower than 5-7 cm.

Tabel 5. Spread test

Groups	Normal value	Results	Depiction
40% concentration	5-7 cm	5,1 cm	Photo 12
50% concentration	5-7 cm	4,9 cm	Photo 13
60% concentration	5-7 cm	5,2 cm	Photo 14
Gel base	5-7 cm	5,3 cm	Photo 15

Photo 12. 40% consentation

Photo 13. 50% concentration

Photo 14. 60% concentration

Photo 15. Gel base

Table 6 shows that the gel preparations with concentrations of 40%, 50%, 60% and negative control obtained good results that the gel was homogeneous and did not clot.

Tabel 6. Homogeneous test

Groups	Results	Depiction
40% concentration	Homogeneous, don't have lumps	Photo 16
50% consentration	Homogeneous, don't have lumps	Photo 17
60% concentration	Homogeneous, don't have lumps	Photo 18
Gel base	Homogeneous, don't have lumps	Photo 19

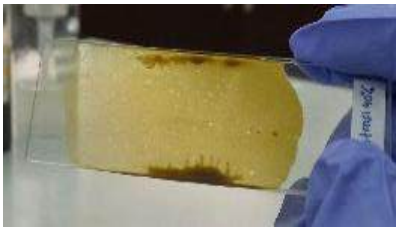

Photo 16. 40% concentation

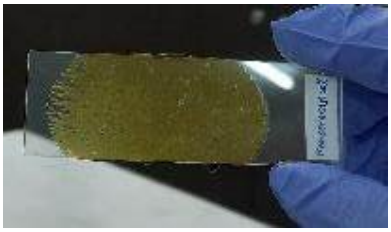

Photo 17. 50% concentration

Photo 18. 60% Concentration

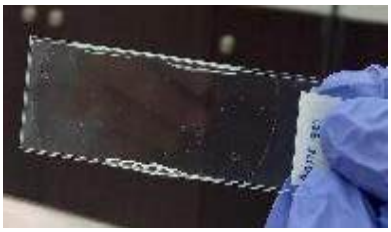

Photo 19. Gel base

Table 7 shows that the average length of the cut wound in each treatment group did not differ significantly.

Tabel 7. Measurement results of the length of the cut wound

Concentration	Average length of cut wound (cm)				
	1	**2**	**3**	**4**	**5**
40%	1,81	1,83	2,29	1,73	1,63
50%	1,67	1,48	1,86	1,41	2,03
60%	1,71	1,60	1,98	1,68	1,98
(+)	1,46	1,23	1,67	1,50	1,99
(-)	1,68	1,52	1,90	1,93	1,81

Table 8 shows that 3 rats did not experience healing of erythema. In the group with a concentration of 60% and positive control, all rats experienced healing of erythema.

Tabel 8. Results of erythema observation

Group	Rat	Erythema disappeared	The day the erythema disappeared
40% concentration	1	Yes	Day 14
	2	No	-
	3	Yes	Day 11
	4	Yes	Day 11
	5	Yes	Day 11
50% concentration	1	Yes	Day 13
	2	Yes	Day 12
	3	No	-
	4	Yes	Day 12
	5	Yes	Day 14
60% concentration	1	Yes	Day 12
	2	Yes	Day 12
	3	Yes	Day 11
	4	Yes	Day 11
	5	Yes	Day 13
Positive control (+)	1	Yes	Day 7
	2	Yes	Day 13
	3	Yes	Day 11
	4	Yes	Day 9
	5	Yes	Day 13
Negative control (-)	1	Yes	Day 11
	2	No	-
	3	Yes	Day 11
	4	Yes	Day 12
	5	Yes	Day 14

Table 9 shows that only group 3 with a concentration of 60% experienced edema healing. At a concentration of 40% and positive control, edema did not disappear in one rat. At a concentration of 50%, two rats whose edema did not disappear. In the negative control with a gel base, edema was difficult to assess in one rat because it was covered by scabs.

Tabel 9. Results of edema observation

Group	Rat	Edema disappeared	The day the edema disappeared
40% concentration	1	Yes	Day 8
	2	No	-
	3	Yes	Day 13
	4	Yes	Day 11
	5	Yes	Day 10
50% concentration	1	No	-
	2	Yes	Day 14
	3	Yes	Day 11
	4	Yes	Day 12
	5	No	-
60% concentration	1	Yes	Day 11
	2	Yes	Day 13
	3	Yes	Day 10
	4	Yes	Day 13
	5	Yes	Day 10
Positive control (+)	1	Yes	Day 6
	2	No	-
	3	Yes	Day 11
	4	Yes	Day 10
	5	Yes	Day 12
Negative control (-)	1	Yes	Day 7
	2	It's hard to judge	-
	3	Yes	Day 9
	4	Yes	Day 11
	5	Yes	Day 14

Table 10 shows that this research involved 25 sample rats. So, the normality test used was the Shapiro-Wilk Test. Data are considered normally distributed if the significance value is higher than 0.05 ($p>0.05$). The data are the result of dividing Day 14 by Day 1. In group 1 with a concentration of 40%, the Sig. value was 0.611. In group 2 with a concentration of 50%, the Sig. value was 0.232. In group 3 with a concentration of 60%, the Sig value was 0.555. In group 4 with the administration of 10% povidone-iodine as a positive control, the Sig value was 0.994. Group 5 with gel base as a negative control obtained a Sig. Value of 0.206. So, the results of the normality test presented in table 10 show that the data are normally distributed because the p-value is higher than 0.05.

Tabel 10. Normality test for the cut wound length

Groups	Amount	Sig.	Description
40% concentration	5	0,611	Normal
50% concentration	5	0,232	Normal
60% concentration	5	0,555	Normal
Positive control (+)	5	0,994	Normal
Negative control (-)	5	0,206	Normal

*Shapiro-Wilk test

Table 11 shows the results of the homogeneity test using the Levene test. The data are homogeneous with a significance value of 0.232 meaning that the p-value is higher than 0.05.

Tabel 11. Results of homogeneous cut wounds

Variable	Sig.	Description
Length of cut wound	0,232	Homogeneous

*Levene test

Table 12 shows that the data are normally distributed so it is continued with a one-way ANOVA test to see the effect of treatment on the length of the cut wound based on the group in the sample of male white rats of the Wistar strain. A p-value lower than 0.05 (p <0.05) is considered significant.

Tabel 12. Results of One-way Annova Test

Kelompok	Mean±SD	Sig.
40% concentration	0,916±0,171	
50% consentration	0,912±0,107	
60% concentration	1,050±0,251	0,121
Positive control (+)	0,996±0,309	
Negative control (-)	0,702±0,101	

*One Way Annova Test

The treatment group 1 with a concentration of 40% obtained a mean value of 0.916 (Photo 20). The treatment group 2 with a concentration of 50% obtained a mean value of 0.912 (Photo 21). The treatment group 3 with a concentration of 60% obtained a mean value is 1.050 (Photo 22). The treatment group 4 with 10% povidone iodine as a positive control obtained a mean value of 0.996 (Photo 23). The treatment group 5 with the administration of gel base as a negative control obtained a mean value of 0.702 (Photo 24). The analysis using One-Way ANOVA obtained a p-value of 0.121 which is lower than 0.05. Thus, there is no significant difference in all treatment groups for cut wounds.

Photo 20. 40% concentration

Photo 21. 50% concentration

Photo 22. 60% concentration

Photo 23. Positive control (+)

Photo 24. Negative control (-)

4. Discussion

Mechanism of secondary metabolite compounds in wound healing process

Wound healing processes cover 3 important stages, namely the inflammation, proliferation, and remodeling phases. The inflammation phase is characterized by the appearance of erythema and edema (Sjamsuhidajat, et al., 2017). Previous studies examining cut wounds with gedong gincu mango leaf extract showed that mango leaves contain flavonoids, tannins, phenols, triterpenoids, steroids, alkaloids, and saponins. The optimum concentrations were 5% and 10% which provided the best wound healing effect (Fathunnisa, et al., 2024).

Gedong gincu mango leaves have various secondary metabolite compounds that can help the wound healing process. Phytochemical tests show that mango leaves contain phenolic compounds, flavonoids, tannins, saponins, triterpenoids, and steroids. However, they do not contain alkaloids. Generally, plants that have close taxonomic classifications will have secondary metabolite compounds that are not much different (Julianto TS, et al., 2019). Secondary metabolites are the result of biosynthesis metabolism that passes through 3 pathways and the results of this metabolism can be influenced by some factors (Anggraito YU, et al., 2018). Secondary metabolite compounds in plants depend on plant growth conditions, such as season, year, and environment. Plant growth is influenced by genetic factors in the biosynthesis metabolism pathway for the formation of secondary metabolite compounds (Li Y, et al., 2020). This contradicts the results of a previous study that obtained positive alkaloid results (Suhatri, et al., 2022).

Flavonoids are compounds with a chemical formula of C6C3C6 whose fifteen-carbon basic framework consists of two benzene rings (A and B) and is connected by a heterocyclic pyran ring (C) (Julianto TS, 2019). Flavonoids are secondary metabolite compounds that work by inhibiting the migration of leukocyte cells that appear after getting wound, encouraging the formation of apoptosis, and maintaining cell survival (Anisa N, et al., 2019; Al-Khayri JM, et al., 2022). In this study, erythema and edema did not disappear in the concentrations of 40% and 50%.

The inflammatory phase is influenced by other secondary metabolic compounds, namely phenolics and tannins. In the wound healing process, phenolics work by counteracting free radicals to prevent tissue damage and inhibiting the formation of enzymes that work in the inflammatory phase, namely the cyclooxygenase enzyme (Anisa N, et al., 2019). Tannins are natural compounds contained in various plants (Das AK, et al., 2020). The molecular weight of tannins ranges from 500-3000 (gallic acid ester) and higher than 20,000 (proanthocyanidins) (Julianto TS, 2019; Anisa N, et al., 2019). Tannins function to prevent free radicals, reduce edema, and prevent pus in wounds (Suhatri, et al., 2022; Anggraito YU, et al., 2018). In the negative control with a gel base, rats discharged pus from their wounds indicating that the mango leaf extracts prevent the formation of pus because the negative control was not provided with the mango leaf extract. Tannins act as anti-inflammatories and antibacterials by reducing mucosal permeability and strengthening mucosal bonds causing difficulties for bacteria to penetrate wounds and inhibit bacterial proliferation. Therefore, the cut wound heals faster without being worsened by a bacterial infection (Mustika S.Y., et al., 2020).

Saponins have properties like soap and detergent because they contain a fat-soluble group (sugar) in one molecule (Das AK, et al., 2020). Shaking saponin can produce foam on the surface of the water because saponin has the property of reducing the tension on the surface of the water (Mustikasari SY, et al., 2020). Saponins can strengthen the edges of open wounds to close faster. Saponin plays a role in the formation of collagen and tissue epithelialization in the proliferation phase. Besides, saponin encourages the formation of type 1 collagen which helps wound healing process (Sjamsuhidajat, et al., 2017; Mustikasari SY, et al., 2020; Anggraeni PP, et al., 2023). Most of the rats in each treatment group closed their wounds on day 4.

Gedong gincu mango leaves contain other secondary metabolite compounds, namely steroids. Ki et al (2011) revealed that steroids play a role in the epithelialization mechanism, where the epithelium will be formed faster enabling faster closure of epithelialization (Dewi A.A., et al., 2020).

Based on the phytochemical tests, Gedong gincu mango leaves contain secondary metabolite compounds, namely triterpenoids. Triterpenoids inhibit ROS (Reactive oxygen species) interference in the wound-healing process. Thus, the presence of triterpenoids can reduce interference with the healing process. Besides, triterpenoids act as compounds that increase antioxidant activity (Vitale S, et al., 2022). This compound helps the wound healing process.

Cut wound healing process in different concentration levels

Treatment groups with 40% concentration levels show that the average length of the cut wound is not significantly different as the cut line does not disappear until the last day of the treatment. Erythema and edema disappeared and almost all rats experienced wound healing. However, the 2nd rat did not experience healing indicated by the presence of erythema, edema, and abscesses. A total of 4 treatment rats experienced healing until the last day of treatment. Negative alkaloids in Gedong gincu mango leaves affect the wound healing process. The 2nd rat did not experience the wound-healing process.

The treatment groups with 50% concentration levels show a difference in the average length of the cut wound. Erythema and edema did not completely disappear in all rats. Only 2 rats in this group experienced the wound-healing process. This shows that this concentration level is not as good as the 40% concentration level. Based on the spreadability test of the mango leaf extract, the 50% concentration showed poor spreadability, namely less than 5 cm.

The group with 60% concentration level shows a difference in the average length of the cut wound. In all rats, erythema and edema disappeared with wound healing until the last day of treatment. In this group, the day of wound healing did not differ much among rats. This shows that the 60% concentration is good for the wound-healing process.

The positive control used 10% povidone iodine. Previous studies revealed that the use of 10% povidone-iodine does not have an anti-inflammatory and antiseptic effect and can interfere with collagen synthesis because it can attack healthy cells (Mustikasari SY, et al., 2020). In this group, erythema disappeared in all treated rats, but the edema did not disappear in the 2nd rat.

The negative control uses a gel base to ensure whether the mango extract plays a role in the wound healing process. Based on the result of the study, the negative control showed wound healing in four rats only. However, in the second rat, there is no healing process, erythema does not disappear, and edema is difficult to assess due to being covered by scars. This means that the gel base gel does not contain mango leaf extract so it does not contain secondary metabolite compounds. Tannin affects the discharge of pus. The gel base does not contain this compound, so pus comes out of the wound.

Previous studies with the same concentration of 40%, 50%, and 60% with topical extract gel preparations from cassava leaves. This study assessed the percentage of cut wound length on wound healing. The highest concentration of 60% provided the best effect in accelerating the wound healing process (Megawati S. et al., 2020). The same concentration of 40%, 50%, and 60% in this study showed insignificant results on the length of the cut wound. However, for other wound healing criteria, namely erythema and edema, a concentration of 60% is the best concentration for eliminating erythema and edema.

Another study with concentrations of 5%, 10%, and 15% of gedong gincu mango extract showed the best cut wound healing at the concentrations of 5% and 10%. The best healing of erythema and edema was at a concentration of 5% and 10% respectively on the same day (Fathunnisa. et al., 2024). In this research, based on the length of the cut wound, the wound healing criteria were not significant in all treatment groups. However, at a concentration of 40%, 4 out of 5 rats experienced healing until the end of the study. At a concentration of 50%, 3 out of 5 rats experienced healing. At a concentration of 60%, all rats experienced a healing process for both erythema and edema. In the positive control group, the use of 10% povidone-iodine indicated that all rats experienced healing with the disappeared erythema. However, only 4 rats experienced healing with the disappeared edema with no influence on the length of the cut wound between the positive control and other treatment groups. Moreover, in this study, the best concentration to eliminate erythema and edema in all rats was 60%.

The group with 50% concentration has good quality in terms of shape, smell, color, and pH with poor spreadability. The 60% concentration was able to eliminate erythema and edema. The 60% concentration was the best concentration in eliminating erythema and edema until the last day of treatment in five rats compared to the other groups.

Results of Statistical Testing and Wound Healing

The significance of the length of the cut wound was tested using one-way ANOVA test. It obtained a p-value of 0.121 which is higher than 0.05. The statistical test showed that the length of the cut wound was not significant among all treatment groups. The intervention group with 60% concentration level experienced healing with erythema and edema disappearing in all treated rats.

5. Conclusion

Mango leaf extract (*Mangifera indica L.var. Gedong Gincu*) contains secondary metabolite compounds such as flavonoids, phenolics, tannins, saponins, triterpenoids, and steroids. This extract has good quality in terms of shape, smell, color, pH, and poor spreadability at a concentration of 50%. Mango leaf extract gel has no effect on the length of the cut wound in male white rats of the Wistar strain. The group with a concentration of 60% can make erythema and edema disappear in male white rats of the Wistar strain. Mango leaf extract gel (*Mangifera indica L.var. Gedong gincu*) managed to help heal cut wounds in male white rats (*Rattus norvegicus*) of the Wistar strain.

6. Limitations

This study has two limitations. First, the levels of active substances in mango leaf extract that affect the wound healing process have not been tested. Therefore, the extent to which the active substance influences the wound-healing process cannot be identified. Second, the levels of toxicity and toxic substances contained in Gedong Gincu mangoes are not known yet. Gedong gincu mango leaves have not been tested. Thus, which substances that have side effects on wound healing cannot be identified.

7. Clinical and Future Studies

Further studies are expected to prepare extracts with different treatments, and leaf extract gels with dependent variables of burns or cuts. Further studies can examine different topical preparations, creams, ointments or gel fractions, not only on the length of the wound, but also the width and area of the wound to assess its effectiveness.

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Conflict of Interest

The authors declare no conflict of interest for the results.

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