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Comparison of Healing Rates Between Giving Meniran Leaf Extract (Phyllanthus niruri) and Topical Antibiotics for Cuts on the Backs of White Wistar Rats (Rattus Norvegicus)

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ABSTRACT

Antibiotic or wound-covering gel might be used to expedite wound healing, especially incisions. The research compares healing rates of cuts on the backs of Wistar strain white rats (Rattus norvegicus) treated with meniran leaf extract (Phyllanthus niruri) and topical antibiotics. Antibiotics and meniran leaf extract (Phyllanthus niruri) are independent variables in this laboratory experiment. The dependent variable Macroscopic photographs, show the fastest wound healing without infection or allergies. The research was done in the University of North Sumatra Faculty of Mathematics and Natural Sciences lab. Rat Acclimatization, Meniran Leaf Extract and Cream Formula, White Rat Incision, Histopathological Observation, and Data Processing comprise the research method. SPSS 22 analyzes research. Shapiro-Wilk determines data normalcy. For well-distributed data, one-way ANOVA calculated group mean differences (P > 0.05). The Post Hockey test (HSD) showed treatment differences (P 0.05). The Kruskal-Walli test tests irregular data. The study indicated that the average healing rate for cuts in the negative control group (K-) was considerably different from K+, treatment groups P1, P2, and P3. This is because the negative control group (K-) lacks active chemicals that speed wound healing. The 15% meniran leaf extract gel group healed white mice and cut injuries better than the 5% and 10% green betel leaf extract gel groups. The group administered antibiotic cream (K+) was similar to that given 15% meniran leaf extract gel at 15%.

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1. INTRODUCTION

Everyone has been wounded. Wounded tissue can be damaged by blunt/sharp object trauma, temperature fluctuations, explosions, animal attacks, electric shock, or chemicals. External mechanical forces (cuts and tissue damage) can disrupt bodily tissue resistance, causing surgical wounds or injuries. Open and closed wounds have different causes. Sharp things like swords, razor blades, and glass can create cuts, which are open wounds. The wound trauma is parallel to the skin, and the damage is no more significant than the cut, painless, acute, and no tissue bridge (Biswas, 2021).

Injuries can lower a person's quality of life because they cause defective situations that lead to mental and physical problems. For example, cancer patients with unpleasant and copious exudates will influence patient interactions and client health (Price et al., 2022). Injuries affect employment and physical, social, psychological, bodily sensation, and economic quality of life. Therefore, wound care requires a holistic approach considering many different elements and circumstances.

After a physical injury like falling off a bicycle, being cut by a knife, or being hit by a complex item, a wound form. Two types of wounds exist: open and closed. However, both include additional wounds with different characteristics and origins. The wound shape depends on the cause, such as vulnus scissum or a sharp item cut (Price et al., 2022). When a surgeon makes an acute wound on a patient but soon treats it, they are intentionally produced. So a wound can heal correctly without difficulties (Theoret & Schumacher, 2017).

The 2018 North Sumatra Province Riskesdas Report found that the proportion of sliced, torn, and stabbed injuries from all characteristics (age group, education, gender, occupation, and place of residence) was 23.92 %, with 21.27% in urban areas and 26.93% in rural areas. Burn injuries from all categories were 1.04%. The number of injuries in North Sumatra Province is still high compared to the national average of 20.01% (Riskesdas, 2019). Hemostasis, inflammation, proliferation, and remodeling make up wound healing (National Wound Care Strategy Programme, 2021). This process involves neutrophils, macrophages, lymphocytes, keratinocytes, fibroblasts, and endothelial cells. Local and systemic factors can hinder wound healing by impacting one or more phases (Price et al., 2022). These elements affect each other. Some factors may affect one or more phases, affecting the healing process overall.

Phases of wound healing: Phase 1, hemostasis: the body engages its blood clotting system to prevent the drain. Platelets activate and aggregate when they touch collagen. The intermediate enzyme, thrombin, forms a fibrin mesh to reinforce the platelet cluster into a solid clot. Phase 2, inflammatory: neutrophils enter the site to kill germs and debris. These cells peak between 24 and 48 hours after damage and plummet after three days. Phase 3: Proliferation involves filling the wound, contracting the wound margins, and covering the wound. Four to 24 days are typical during the Proliferative Phase. Phase 4 is maturation, when new tissue steadily gains strength and flexibility. Collagen fibers restructure, tissue remodels and matures, and tensile strength increases (up to 80% of prepowerstrength). Maturation lasts 21 days to two years, depending on the wound (Price et al., 2022).

Plant extracts and other medicines can speed up wound healing, and traditional communities have used them for a long time. Nearly 25% of developing country treatments employ trial-and-error medicinal herbs. Meniran leaf herbal plant speeds wound healing. Meniran leaves, from the Euphorbiaceae family, are a tropical Asian wild plant found throughout mainland Asia and easily found in Indonesia (Duke et al., 2022; Kemenkes RI, 2017). Meniran (Phyllanthus niruri L.), a long-lived tropical shrub plant, is used in traditional South Asian medicine to treat jaundice, diarrhea, dyspepsia, urinary tract infections, and kidney stones. Meniran contains lignans, flavonoids, alkaloids, triterpenoids, fatty acids, vitamin C, potassium, tannins, geraniin, phylantin, and hypophylantin (Eka Widiadnyani et al., 2021; Hidanah et al., 2018).

In medicine, corticosteroids are called god's medication. Steroids or corticosteroids can treat asthma, lupus, rheumatoid arthritis, and other disorders (Baeck & Goossens, 2022). The body naturally produces steroids (cortisone or corticosteroids). Steroids depress the immune system, reduce inflammation, and block DNA synthesis and histamine. Man-made steroids mimic these hormones. The disease is treated with corticosteroids. They differ from anabolic steroids used by sports and bodybuilders. Different anabolic steroids have different effects (Bond et al., 2022). Tablets, soluble tablets, liquids (solutions), lotions, ointments, inhalers, and injections include steroids. You must be know at using corticosteroids or steroids without a doctor's supervision can worsen negative effects, including wound healing (García-Arnés & García-Casares, 2022).

Several studies indicated that wound healing is faster with greater gel concentrations. Medical treatments like antibiotics or wound-covering gel can expedite wound healing (Freedman et al., 2023). Many animal and plant extract remedies were utilized to prevent inflammation and heal wounds before antiseptic liquids and wound dressing gels hit the market (Srivastava et al., 2023). For minor or medium damages, threading the edges is less cost-effective because the wound will heal if there is no infection. External and internal variables affect wound healing. External factors including cleanliness, temperature, and food affect wound healing. Internal wound healing factors include age and gender.

Topical antibiotics are used for furuncles and impetigo, localized dermal infections (Dallo et al., 2023). Consider the microorganisms' antibiotic sensitivity while picking an antibiotic. Topical antibiotics alone are insufficient for severe skin infections. Hence, systemic antibiotics are needed (AL-kahfaji, 2022). Common topical antibiotics include fusidic acid, mupirocin, bacitracine, erythromycin, and sulfonamides. The first popular topical antibiotic is mupirocin. Mupirocin treats impetigo and other bacterial skin infections. This antibiotic is ineffective against viruses and fungi. Mupirocin treats superficial skin infections like impetigo and folliculitis. It can also eradicate nasal MRSA without symptoms. Use for moretenhan 10 days is not advised due to resistance concerns.

Mupirocin is a skin lotion or ointment (Najm et al., 2022). From the problem formulation above, the research aimed to compare healing rates of cuts on the backs of Wistar strain white rats (Rattus norvegicus) with meniran (Phyllanthus niruri) leaf extract and topical antibiotics.

2. METHOD

This study is a controlled lab experiment. Laboratory experimental design is a planned or artificial research (Notoatmodjo, 2018). This laboratory experimental investigation uses a design with four essential elements: modification of independent factors, measurement of dependent variables, comparison of values between treatments, and control of additional variables. Operational variables allow researchers to carefully monitor and measure objects using observed attributes (Suwarno & Nugroho, 2023). This study uses antibiotics and meniran leaf extract (Phyllanthus niruri) as independent variables. & Dependent variable Wound healing rate is the fastest rate without infection or allergy, as measuredred by macroscopic pictures. The study compared the healing rate of cuts on the backs of Wistar strain white rats (Rattus norvegicus) with topical antibiotics and meniran leaf extract (Phyllanthus niruri) using a pre- and post-test design with a control group.

The Animal House, Faculty of Mathematics and Natural Sciences, Medan State University, conducted this research. This study used Wistar strain adult male white rats (Rattus norvegicus) weighing 150-300 grams, 2-3 months old, and healthy, as shown by active mobility and no physical deformities. This study used experimental observation to divide samples into five groups and watch them daily for macroscopic healing indications. From treatment start to finish, this observation is done to detect changes.

The antibiotic cream was mupirocin with varied stearyl alcohol and cera delanol concentrations compared to the market leader. The formulation for 1 gram of cream comprises 20 mg of mupirocin calcium. Maceration 70% ethanol filter fluid extracted Meniran (Phyllanthus niruri) leaves. This study will create a gel formulation with three extract concentrations: F1 (Formula 1) 5%, F2 10%, and F3 15%. HPMC was used to make a gel base in this study. Meniran (Phyllanthus niruri) leaf extract was tested for components that might cure rat back cuts. Data from each observation parameter (variable) is tabulated. SPSS was used to examine the importance of quantitative data (independent variables) on the treatment group (dependent variable).

3. RESULTS AND DISCUSSION

Table 1. Phytochemical Test Results of Meniran Leaf Extract

Phytochemistry	Reactor	Result	Note
Flavonoid	Mg, Concentrated HCL	Yellow	+
Saponin	Aquades	Foamy	+
Tanin	FeCl3 5%	Blackish Green	+
Alkaloid	Wagner Reagent	Brown Precipitate	+

Table 1 shows that meniran leaf extract (Phyllanthus niruri) contained flavonoids, saponins, tannins, and alkaloids. Therefore, meniran leaf extract contains phytochemicals with potent antioxidant properties that can be used as medicines.

Table 2. Cut Wound Healing Length (cm)

Days to -	C-	C+	P1	P2	P3
2	1.96	1.78	1.94	1.80	1.78
4	1.68	1.51	1.71	1.68	1.51
6	1.55	1.30	1.50	1.46	1.30
8	1.31	1.15	1.21	1.15	1.15
10	1.11	0.76	0.76	0.76	0.76
12	0.87	0.35	0.47	0.34	0.34
14	0.64	0.00	0.11	0.10	0.00
Mean	1.30	0.98	1.10	1.04	0.98
SD	0.47	0.64	0.68	0.66	0.64

Note: C- = Negative Control, Group without any treatment, C+ = Positive Control, Group given antibiotic cream, P1 = Treatment group given a 5% dose of extract gel, P2 = Treatment group given a 10% dose of extract gel, P3 = Treatment group given a 15% dose of extract gel

The negative control group (C-), those without treatment, the antibiotic cream group (C+), and the group given 5% meniran leaf extract gel (P1), 10% (P2), and 15% (P3). Wound healing was observed every 2 days for 14 days. The P3 therapy group had a better average wound healing area of 0.98 ± 0.64 cm, measured from the first to the 14th day. Next was the K+ group, with similar results (0.98 ± 0.64 cm). The average wound healing rate in the K-, P1-, and P2 groups was 1.30 ± 0.47 cm, 1.10 ± 0.68 cm, and 1.04 ± 0.66 cm, respectively.

Table 3. Percentage of Cut Wound Healing (%)

Days to -	C-	C+	P1	P2	P3
2	2.00	11.10	3.10	9.80	11.10
4	15.80	24.40	14.40	16.00	24.40
6	22.40	34.90	24.90	27.00	34.90
8	34.50	42.30	39.70	42.30	42.30
10	44.70	62.00	62.20	62.20	62.00
12	56.30	82.60	76.60	82.80	82.80
14	67.90	99.80	94.70	94.90	100.00
Mean	34.80	51.01	45.09	47.86	51.07
SD	23.26	31.98	33.88	33.09	32.06

Note: C- = Negative Control, Group without any treatment, C+ = Positive Control, Group given antibiotic cream, P1 = Treatment group given a 5% dose of extract gel, P2 = Treatment group given a 10% dose of extract gel, P3 = Treatment group given a 15% dose of extract gel

Table 3 shows that the P3 treatment group had a more significant average wound healing % (51.07 ± 32.06 cm) from the the first to 14th day. Next, the K+ group had similar results (51.01 ± 31.98 cm). The C-, P1-, and P2 groups had average wound healing rates of 34.80 ± 23.26 cm, 45.09 ± 33.88 cm, and 47.86 ± 33.09 cm, respectively.

Based on the average percentage of cuts healed and the length of cuts healed in each group, the P3 group or the group given 15% meniran leaf extract gel healed cut faster, followed by the C+ group with similar results. Incision wounds healed slowly in the negative control group (C-) or untreated group.

Normality test

This research used the Shapiro-Wilk SPSS normality test. This strategy was employed because each group had fewer than 50 data samples. Thus, the Shapiro-Wilk Technique was best for data normality detection in this investigation. This test determined if study data was regularly distributed. According to Ghozali (2018), regularly distributed data represents the population. A p-value>0.05 indicates regularly distributed data, while p <0.05 indicates non-normal distribution (Ghozali, 2018).

Table 4. Normality Test Results

Group Extract Dose	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Negative Control (C-)	.194	5	.200*	.964	5	.706
Positive Control (C+)	.210	5	.200*	.976	5	.913
Treatment 5% (P1)	.259	5	.200*	.910	5	.467
Treatment 10% (P2)	.271	5	.200*	.897	5	.395
Treatment 15% (P3)	.188	5	.200*	.986	5	.965

*. This is a lower bound of the true significance

a. Lilliefors Significance Correction

Table 4 demonstrates that the control and treatment groups have the same average cut wound healing percentage from day 1 to day 14 after SPSS testing for normalcy. The significance value (p) in the Shapiro-Wilk Test is the value that exceeds the standard margin of p>0.05, which is 0.706 for the negative control group (C-), 0.913 for the positive control group (C+), 0.467 for the 5% extract dose group (P1), 0.395 for the 10% extract dose group (P2), and 0.965 for the 15% extract dose group Shapiro-Wilk normality test shows that wound healing average % data is regularly distributed.

Data Homogeneity Test Between Groups

Table 5. Results of the ANOVA Test of Homogeneity of Variances

	Levene Statistical	df1	df2	Sig.
Base on Mean	.875	4	20	.497
Base on Median	.610	4	20	.660
Based on Median and with the adjusted df	.610	4	18.791	.660
Based on trimmed mean	.842	4	20	.515

In Table 5, Group C-, group C+, group P1, group P2, and group P3 have homogeneous research data variances of 0.497 (p>0.05). An experiment was conducted to compare the average healing of cut wounds between the four research or observation groups (Table 6), according to the table's "Sig" column. The p-value is 0.000. At the actual level = 0.05, Ho is rejected. Hence, the five groups have significantly different mean wound healing times.

Table 6. Results of the ANOVA

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	691.438	4	172.859	161.561	.000
Within Groups	21.399	20	1.070		
Total	712.836	24			

Table 7. Post Hoc Bonferroni Test Results

Test	Experimental Group (I)	Experimental Group (J)	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Bonferroni	Negative Control (C-)	Positive Control (C+)	-14.19000*	.65420	.000	-16.259	-12.1271
		Extract Dosage 5% (P1)	-9.00000*	.65420	.000	-11.0629	-6.9371
		Extract Dosage 10% (P2)	-11.42600*	.65420	.000	-13.4889	-9.3631
		Extract Dosage 15% (P3)	-14.23800*	.65420	.000	-16.3009	-12.1751
	Positive Control (C-)	Negative Control (C-)	14.19000*	.65420	.000	12.1271	16.2529
		Extract Dosage 5% (P1)	5.19000*	.65420	.000	3.1271	7.2529
		Extract Dosage 10% (P2)	2.76400*	.65420	.004	.7011	4.8269
		Extract Dosage 15% (P3)	-.04800	.654201	.000	-2.1109	2.0149
	Extract Dosage 5% (P1)	Negative Control (C-)	9.0000*	.65420	.000	6.9371	11.0629
		Positive Control (C+)	-5.19000*	.65420	.000	-7.2529	-3.1271
		Extract Dosage 10% (P2)	-2.42600*	.65420	.014	-4.4889	-.3631
		Extract Dosage 15% (P3)	-5.23800*	.65420	.000	-7.3009	-3.1751
	Extract Dosage 10% (P2)	Negative Control (C-)	11.42600*	.65420	.000	9.3631	13.4889
		Positive Control (C+)	-2.76400*	.65420	.004	-4.8269	-.7011
		Extract Dosage 5% (P1)	2.42600*	.65420	.014	.3631	4.4889
		Extract Dosage 15% (P3)	-2.81200*	.65420	.004	-4.8749	-.7491
	Extract Dosage 15%	Negative Control (C-)	14.238000*	.65420	.000	12.1751	16.3009
		Positive Control (C+)	.048000*	.654201	.000	-2.0149	2.2209

Test	Experimental Group (I)	Experimental Group (J)	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
	(P3)	Extract Dosage 5% (P1)	5.23800*	.65420	.000	3.1751	7.3009
		Extract Dosage 10% (P2)	2.81200*	.65420	.004	.7491	4.8749

Further Post Hoc Bonferroni Test results are in Table 7. Most comparisons between groups I and J demonstrate a difference in the average percentage of wound healing in the Wistar strain of white rats (Rattus norvegicus), denoted by "*." The K+ and P3 groups were not different, and no "*" stars were detected. Bonferroni Post Hoc Test group testing was done in SPSS for Windows.

Physiological Observations on Cut Wound Healing

The cut wound healing process was observed by measuring how long each control and treatment group took to recover. The healing of a cut wound is measured by erythema, swelling, and closure. Table 6 shows the presence or absence of redness (erythema), swelling, and closure of healed cut wounds in 4 groups for 14 days.

Table 8 shows that the negative control group (C-) lost erythema (redness) on days 9–11, while experimental animals 1, 4, and 5 lost it faster. The positive control group (C+) occurred on days 6–7, while experimental mice 2 occurred fastest. The fastest happened in experimental mice 1, 2, and 3 in treatment group 1 (P1) on days 8–9. Treatment group 2 (P2) had it on days 6–8, faster than experimental mice 1. Day 6–7 in treatment group 3 (P3), fastest in experimental mice 5.

Table 8 shows experimental mice 1, 4 and ,5 had the fastest swelling elimination in the negative control group (C-) on day 7. Positive control mice (C+) had it on day 4, but experimental animals 2 had it faster. Day 6 was the fastest for experimental mice 1, 2, and 3 in treatment group 1 (P1). For experimental mice 1, the fastquickest was the 4th in treatment group 2 (P2). In treatment group 3 (P3), experimental mice 5 experienced the fasmost rapid day 4.

Table 8. Description of Physiological Observations of Cut Wounds

Rat Group		Observation Day													
		1	2	3	4	5	6	7	8	9	10	11	12	13	14
Control Negative (C-)	1st	Mb	Mb	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Kt
	2nd	Mb	Mb	Mb	Mb	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt
	3rd	Mb	Mb	Mb	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt
	4th	Mb	Mb	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Kt
	5th	Mb	Mb	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Km
Control Positive (C-)	1st	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Kt	Km	-
	2nd	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Kt	Kt	Km	-
	3rd	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Km	Km	-
	4th	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Km	Km	Km
	5th	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Km	Km	Km	Km
5% dose (P1)	1st	Mb	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Km	Km
	2nd	Mb	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Km	Km
	3rd	Mb	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Kt	Km
	4th	Mb	Mb	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Km
	5th	Mb	Mb	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Km
10% dose (P2)	1st	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Km	Km	-	-
	2nd	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Kt	Km	Km
	3rd	Mb	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Km	Km
	4th	Mb	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Kt	Km
	5th	Mb	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Km	Km
15% dose (P3)	1st	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Kt	Km	-
	2nd	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Kt	Km	-
	3rd	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Km	Km	-

Rat Group	Observation Day													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
4th	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Km	Km	-
5th	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Km	Km	-	-

Note: Mb (red swelling), M (red), Kt (dry open), Km (dry closed), - (wound healed/clean)

Observation of Histopathological Preparations

Image J can be used to view histological collagen density preparations in mice from each group's skin. Figure 1 shows that the 5% meniran leaf extract gel (P1) group had more fibroblasts and denser cells than the K-, K+, 10%, and 15% groups. The positive control group and the treatment with 10% and 15% meniran leaf extract had few and sparse fibroblast cells, while the negative control group had many dense ones. This phase involves fibroblast cell growth. The repair process relies heavily on fibroblasts, which prepare protein structural components for tissue regeneration. Research shows that flavonoids stimulate fibroblasts (Everts et al., 2006; Guan et al., 2021; Mohd Yusof et al., 2021).

In Figure 2, the histopathological observation of the cut wound on the 14th day after giving 15% meniran leaf extract gel showed denser collagen fibers than in the negative control group, the 5% group, and the extract gel group. Meniran departs 10%. However, the positive control group administered antibiotic cream had virtually as many collagen fibers as the P3 group. Myofibroblasts, contractile fibroblasts, pull and come closer to the wound margins to cling together at the start of healing. Growth of fibroblasts occurs during recovery. Collagen production by these cells allows granulation tissue to gather connective tissue matrix and become thick fibrosis (Aziz et al., 2018; Guan et al., 2021; Kang & Lu, 2022).

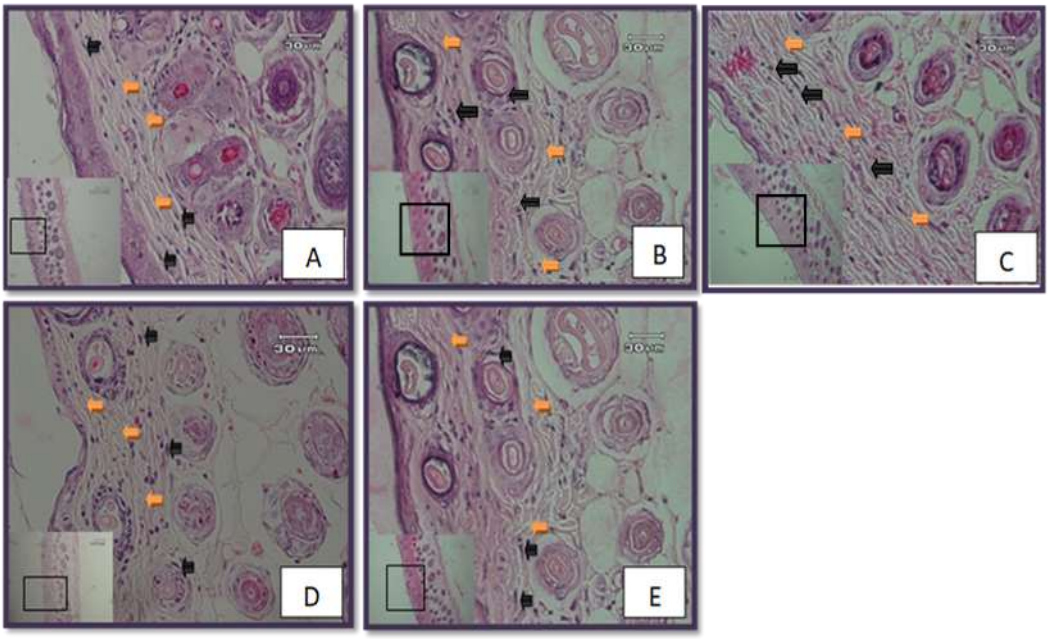

Figure 1. Fibroblast Cell Proliferation 400x Magnification (Day 14)
Note: A: Group C-, B: Group C+, C: Group P1, D: Group P2, E: Group P3, Black →: fibroblast cells and orange →: collagen.

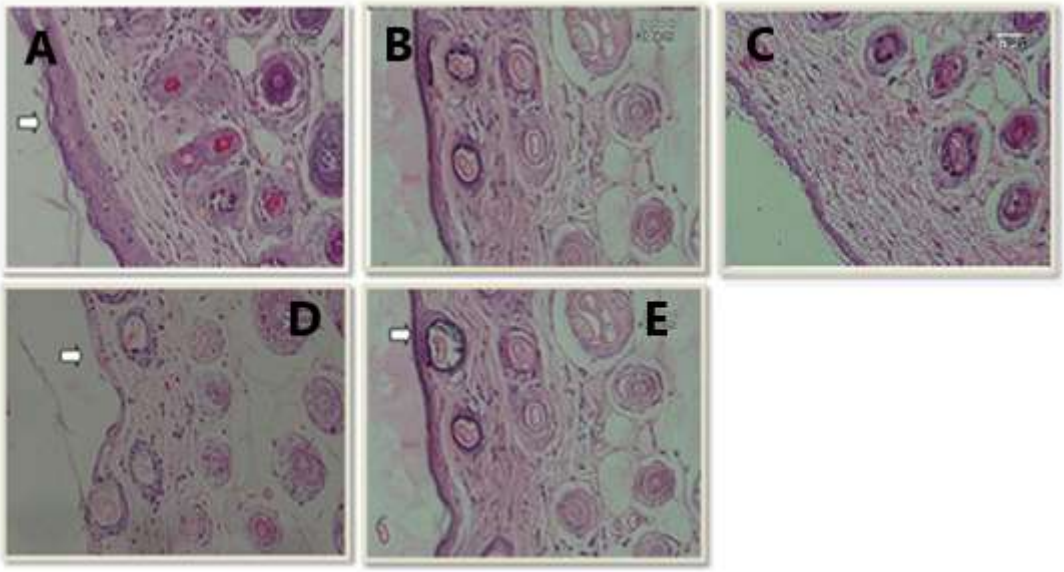

Figure 2. Collagen Density on the 14th Day
Note: A: Group C-, B: Group C+, C: Group P1, D: Group P2, E: Group P3, White →: Epithelial formation at the wound's edges.

Discussion

This study tested incision wound healing by reducing wound length and healing %. Phyllanthus niruri leaves were employed in this study's extract—air-dry 1500 grams of meniran leaves after washing them with running water. After drying, meniran leaves were broken into powder, weighed 500 grams, and macerated for five days in a 90% ethanol solvent that had been distilled. A thick meniran leaf extract is obtained by vacuuming the maceration results with a rotary evaporator. Ethanol meets extracting requirements. Ethanol dissolves most polar and non-polar compounds (Ginting et al., 2020; Guan et al., 2021; Jesitus, 2020; Mohd Yusof et al., 2021). The meniran extract is then verified using HPMC. The more solvents utilized, the higher the yield.

Male white rats were utilized in this study because they are easy to handle and have human-like physiology and anatomy. We used 25 2-3-month-old mice. To adapt, mice were acclimatized for one week before treatment. Each mouse was grouped into five groups: group I was the negative control (C-) and received no treatment; group II was the positive control (C+) and received antibiotic cream; group III (P1) received 5% topical meniran leaf extract gel, group IV (P2) received 10% topically, and group V (P3) received 15% topical. Two mice were placed in a cage with a divider to minimize movement so as not to impact the healing of the cut wounds or cause issues between the animals. This study recommends plaster and gauze for cut wounds to prevent infection. Treatment of cuts was complex since the application could not attach to the rat's skin. Thus, it came off, and the rat nibbled the plaster and gauze. This researcher treated cuts without bandage and gauze. The incision wound was 2 cm long and 0.1 cm deep but widened more than 0.2 cm. Despite chloroform anesthesia, the mice moved throughout induction. During 14 days of healing, wounds were treated and measured daily using calipers. This study estimates erythema, edema, and wound closure. Redness (erythema) is the first sign of inflammation. Rat wounds turn red due to inflammation (Alster & Graham, 2018; Bielach-Bazyluk et al., 2021; Chilicka, 2021; Eve Sonenblum et al., 2023; Jesitus, 2020; Vanthitha et al., 2018). Significant blood vessel releases of fibrinogen protein and activated platelets cause blood clots.

According to visual observations of 25 white mice, the cuts showed erythema and swelling on the 1st to 3rd day after treatment with meniran extract gel at 5%, 10%, and 15%, without treatment and antibiotic cream. This is the inflammatory phase where blood clots and bleeding stops. On day 4, the C+, P2, and P3 groups underwent a proliferative phase where tissue creation continued without erythema, while the P1 and no treatment (C-) groups still had erythema. Cut wounds matured fastest in the positive control group (C+), 10% extract dosage treatment group (P2), and 15% extract dose

treatment group (P3), where five animals had closed and only a trace on the 10th day. In the P1 group and the group without K-treatment, some cut wounds had partially closed and formed a scab in the proliferation phase. This shows fresh cell development by bringing the wound edges together. Scabs mark the end of the inflammatory phase and the start of the proliferation and maturation phases.

The wound-healing phase includes inflammation, proliferation, and maturation (Price et al., 2022). The control group given antibiotics (K+), the group given meniran leaf extract gel, group P2 (10%), and group P3 (15%) experienced an inflammatory phase that reduced wound length faster than the P1 group (10%) and the negative control group (K-) which shared the inflammatory stage until the 6th day. Lemongrass contains flavonoids that inhibit wound bleeding and impact inflammatory cell formation during wound healing. As an astringent, tannin reduces mucosal permeability and strengthens mucosal connections, avoiding irritants. It also shrinks and kills germs by affecting their permeability. Lemongrass' phenolic acid prevents free radical-induced cell damage and inflammation.

This study found that 15% meniran leaf extract gel (P3) was the most effective. The positive control group with antibiotic cream (K+) also had a good healing effect after the P3 treatment group on cut wounds in white mice compared to the 5%, 10%, and untreated groups. The secondary metabolite chemicals in meniran leaf extract heal wounds better at more significant concentrations or doses, whereas they inhibit microbes at low quantities. According to researchers, antibacterials are bacteriostatic at low concentrations but destroy microbes at high concentrations (Adha et al., 2022; Aldulaimi, 2018; Dallo et al., 2023).

As an extract formulation, green betel leaf cream had good physical stability when stored at room temperature for 14 days, with no organoleptic, pH, stickiness, spreadability, or viscosity changes, and met the requirements. Additionally, cream preparations are more accessible and more desirable (Dallo et al., 2023; Najm et al., 2022). It's also worth noting that the study relied on a somewhat small sample size, with only 25 male white rats total and five rats per group, which could affect the reliability of the results. If many samples are employed, there will be less room for error in any generalizations made from a study. Stress, which can affect the rat's wound-healing process, is one possible internal element that cannot be disregarded and may influence the outcomes. According to the cited source many researchers, chronic stress can elevate cortisol, which in turn suppresses cellular immunity and slows wound healing (Cusack & Buggy, 2020; Decker et al., 2021; Theoret & Schumacher, 2017; Wynn, 2021).

4. CONCLUSION

The conclusion was drawn from a study that compared the effectiveness of treating cuts on the backs of white rats (Rattus norvegicus) of the Wistar strain with either meniran leaf extract (Phyllanthus niruri) or topical antibiotics for 14 days. The phytochemical test of meniran leaf extract (Phyllanthus niruri) revealed the presence of flavonoids, saponins, tannins, and anthraquinones. Therefore, it is reasonable to assume that the phytochemicals found in meniran leaf extract have therapeutic potential. The average rate at which cuts healed varied significantly between the negative control group (C-) and the positive control group (C+) and between the treatment groups P1, P2, and P3. This is because no active chemicals in the C-negative group promote quick healing of cut wounds. Results demonstrated that white mice given 15% meniran leaf extract gel had faster wound healing than those shown 5% and 10% green betel leaf extract gel. The antibiotic cream (C+) group, on the other hand, experienced similar results to the meniran leaf extract gel (15%) group. This is because the processed branches contain chemicals from the C+ group secondary metabolite that impact wounds even at a concentration of 15%. Future studies should use greater concentrations of meniran leaf extract (Phyllanthus niruri) and compare them with other variables. Our research on cutting wound healing should be safer for humans. Future research should also focus on various forms/preparations of meniran leaf extract (Phyllanthus niruri) that are easier to manufacture and use regionally for producing this plant variety.

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