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Test The Activity Of Administering Ethanol Extract Cream From Gambier Leaves (Uncaria Gambir Raxb) To Accelerate The Healing Of Incision Wounds On The Surface Of The Skin Of Male Wistar Strain Rats (Rattus Norvegicus)

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ABSTRACT

Wound healing, especially incisions, is still a problem in the health sector due to the many cases and treatment approaches used during globalization. This research tested whether ethanol extract cream from gambier leaves (Uncaria Gambir Raxb) could accelerate the healing of skin wounds in male Wistar rats. Pre-test and post-test with control group design were used in this laboratory experiment. In this study, the acceleration of healing was the dependent variable. Meanwhile, gambier leaf extract cream is an independent variable in the laboratory of the Faculty of Mathematics and Natural Sciences, University of North Sumatra. The research process has several stages: Rat acclimatization, Gambir Leaf Extract and Cream Formula, White Rat Incisions, Histopathological Observations, and Data Processing. SPSS 22 analyzes research data. Shapiro-Wilk determined data normality. One-way ANOVA calculated group mean differences for well-distributed data (P > 0.05). The Post Hockey (HSD) test detected significant treatment differences (P 0.05). The Kruskal-Walli test is used for irregular data. In white mice, 15% gambier leaf extract cream healed cuts better than 5% and 7.5%. However, gambier leaf extract cream 7.5% has a performance like 15%. At a concentration of 7.5%, secondary metabolite compounds from gambier leaf extract heal wounds, while low concentrations suppress bacteria, making them less effective. Thus, gambier leaf extract contains antioxidant phytochemicals that can be used as medicine.

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1. INTRODUCTION

Skin connects internal and exterior organs and protects against sun, fire, hot water, pressure, scrapes, and other external disturbances (IDF Committee, 2019; Jesitus, 2020). The skin is prone to cuts, boils, and burns. Wounds can happen to anyone (including animals) anytime, anywhere, even during typical home and work activities (Rodrigues, Kosaric, Bonham, & Gurtner, 2019; Röhl, Zaharia, Rudolph, & Murray, 2015).

A wound is a loss or damage to a body part that occurs on the skin in the form of tissue that is broken, torn, or damaged due to a reason such as trauma, sharp or blunt objects, changes in temperature, chemicals, or animal bites (Grey & Harding, 2009; Theoret & Schumacher, 2017). Wounds are a disorder that occurs on the skin, characterized by damage to the skin tissue units or components. Wounds can happen accidentally, such as falls, cuts, and scratches, and some are done intentionally for a specific purpose, such as incisions for surgical purposes (Asadi et al., 2013; Sorg, Tilkorn, Hager, Hauser, & Mirastschijski, 2017; Weller & Sussman, 2006). Wounds can be classified into several types and forms, such as open wounds (if there is a tear) and closed wounds (if there is no tear) (Rodrigues et al., 2019). Damages can also be divided into acute injuries (scratches, burns, trauma, needle sticks, and surgical incisions) and chronic wounds (pressure ulcers and diabetes) (Grey & Harding, 2009).

Cuts are a type of wound that can result from being scratched on a rough surface (Valizadeh et al., 2021). This type of wound is not very deep but can cause an extensive wound on the skin's surface. Characteristics of cuts include open wounds, pain, length of the wound greater than the depth of the wound, parallel wounds, and no bruising close to the edge of the skin (Tottoli et al., 2020). Cut wounds will become very susceptible to infection, especially by bacteria. Infected wounds will become slower and also often cause the formation of exudates and toxins, which are produced along with the death of regenerating cells. Therefore, there is a need to stimulate healing and restore normal function of the injured body part to prevent infection (Sorg et al., 2017; Zhang et al., 2021).

Wounds can generally heal themselves, but wounds can fail if cursors hinder them, making them difficult to heal. If wounds are not treated properly, they will result in wound-healing complications such as infection and bleeding. Proper wound healing and treatment are needed to restore the disturbed anatomy and skin function resulting from the wound (Kolimi, Narala, Nyavanandi, Youssef, & Dudhipala, 2022; Sharma, Khanna, Kaur, & Singh, 2021).

Wounds on the skin stimulate wound healing, involving various cell substrates and physiological processes, including the hemostasis characterized by vasoconstriction, primary hemostasis, and secondary hemostasis. Healing wounds, especially incisions, is still a challenge in the health sector, considering the large number of cases and treatment methods that have developed in the current era of globalization. Many studies on wound healing using natural ingredients such as herbal operating plants and fruit to be formulated as preparations to help heal wounds (Asadi et al., 2013; Grey & Harding, 2009; Sun et al., 2023; Tottoli et al., 2020).

According to World Health Organization (WHO) records, it is estimated that almost 80% of humanity, especially in developing countries, still uses plants as medicinal ingredients to maintain their health (Cheema & Singh, 2021; Rasool, Bhat, Sheikh, Jan, & Hassan, 2020). Plants generally produce secondary metabolite compounds, which can be used to treat various types of diseases. The secondary metabolite compounds are alkaloids, flavonoids, saponins, tannins, steroids, and triterpenoids (Mawarni et al., 2020; Syaputri, Girsang, & Chiuman, 2022; Toruntju, Banudi, Leksono, Rahmat, & Salma, 2020).

The use of plants and natural ingredients as traditional medicine has recently increased rapidly in Indonesia, and some natural ingredients have even been produced on a large scale. The use of conventional medicine is considered to have fewer side effects than medicines derived from chemicals. Traditionally, raw materials are easy to obtain and relatively cheap. Natural ingredients that are useful as traditional medicine and can be used in the wound healing process, one of which is gambier leaves.

The gambier plant (Uncaria Gambir Raxb) is an industrial plant that has high economic selling value and can be used as a medicinal mixture such as for burns, wounds, headaches, diarrhea, mouthwash, canker sores, skin aches, or to improve the digestive process, gingivitis. (sap), sore throat, dysentery, and cough (Labanni, Zulhadjri, Handayani, Ohya, & Arief, 2020). The gambier plant contains functional compounds which are included in the group of polyphenolic compounds, especially catechins. The most significant chemical compounds in gambier leaves are flavonoids, pyrocatechol, and quercetin. Traditionally, gambier is widely used as a leather tanner, dye, and mixture in betel nuts and is used as traditional medicine (Nurhayati, Susilawati, Susanto, Marthalia, & Nugroho, 2022; Winarti, Innawati, & Hemani, 2022).

Gambir (Uncaria Gambir Raxb) contains two main components: catechin and catechin tannin acid. The tannins in gambier leaves are of the proanthocyanins type (Winarti et al., 2022). Gambier leaves (Uncaria Gambir Raxb) contain catechins, which are slightly soluble in cold water but dissolve easily in hot water. This tannin has algicide, antibacterial, and antifungal properties. Young Gambier leaves have a higher catechin content compared to old leaves. In gambier plants, there is also wax located on the surface layer of gambier leaves, which is a monoester of fatty acid and alcohol (Labanni et al., 2020; Miksusanti, Fithri, Herlina, Wijaya, & Taher, 2020; Nurhayati et al., 2022).

Considering the benefits of gambier leaves in healing wounds and the results of previous research, researchers should conduct laboratory experiments on the activity test of administering gambier leaf (Uncaria Gambir Raxb) ethanol extract cream to accelerate healing incision wounds on the skin of male Wistar strain rats (Rattus norvegicus). This study tested the effectiveness of gambier

leaf ethanol extract cream (Uncaria Gambir Raxb) in speeding up skin wound healing in male Wistar strain rats (Rattus norvegicus).

2. METHOD

This laboratory experiment uses a pre-test and post-test with a control group design to test the effect of gambier leaf extract (Uncaria Gambir Raxb) on Wistar strain rats' skin wound healing (Notoatmodjo, 2018). This study included a large sample of 20 adult male white rats (Rattus norvegicus) Wistar strain weighing 160-200 grams and aged 2-3 months. The mouse samples will be separated into four groups: control (P0), treatment 1 (P1), treatment 2 (P2), and treatment 3 (P3). Everything that will be seen is a research variable. Researchers must understand their research variables because they are the phenomenon studied (Suwarno & Nugroho, 2023). The variables in this study are the independent variable, gambier leaf extract cream (0% concentration or blank without extract gambier leaves; concentrations of 5%; 7.5% and 15%), and the dependent variable, healing acceleration.

At the University of North Sumatra Faculty of Mathematics and Natural Sciences, gambier leaf extract (Uncaria Gambir Raxb) content and phytochemical tests were studied. Farmers in Gurusinga Village grew gambier leaves (Uncaria Gambir Raxb) from Berastagi, Karo Regency. This research uses minor surgical equipment (stainless steel tray, scalpel, blade, scissors, and tweezers), scales, sterile gloves, cotton swab, gauze, rat cage, food container, stationery, marker, and calipers. Gambier leaves (Uncaria Gambir Raxb), glycerin, triethanolamine (TEA), ethyl alcohol, acetic acid, methyl and propylparaben, distilled water, sterile tampons, ketamine, xylazine, white rat strain wistar, rat chow, and drink are utilized.

The research procedure was carried out in several stages: Acclimatization of Rats, Making Gambir Leaf Extract, Making Gambir Leaf Extract Cream Formula, Making and Handling Cut Wounds on White Rats, Histopathological Observations, and data processing. Research data was analyzed using SPSS 22. For data normality, the Shapiro-Wilk method was used. If data are normally distributed (P > 0.05), use One-Way ANOVA to calculate group mean differences. The Post Hockey test (HSD) determines if treatments differ significantly (P 0.05). If data are irregular, the Kruskal-Walli's test is used.

3. RESULTS AND DISCUSSION

Phytochemical Test Results of Gambir Leaf Extract

Table 1. Phytochemical Test Results of Gambir Leaf Extract

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

According to phytochemical testing, Gambier leaf extract (Uncaria Gambir Raxb) contained flavonoids, saponins, tannins, and alkaloids. Therefore, gambier leaf extract contains phytochemicals with potent antioxidant properties that can be employed as medicines.

Table 2. Average Healing of Cut Wounds (cm)

Days to -	P0	P1	P2	P3
2	1.96	1.94	1.86	1.78
4	1.70	1.75	1.71	1.51
6	1.57	1.49	1.48	1.30
8	1.34	1.21	1.20	1.15
10	1.13	0.99	0.76	0.76
12	0.88	0.71	0.47	0.34
14	0.64	0.37	0.11	0.07
Mean	1.32	1.21	1.08	0.99

The healing of cut wounds was observed every two days for 14 days in four treatment groups: 5% gambir leaf extract ointment (P1), 7.5% (P2), 15% (P3), and control (P0). From the first to the

14th day, the P3 therapy group had a 0.99 cm average wound healing rate. The average wound healing rate for groups P0, P1, and P3 was 1.32 cm, 1.21 cm, and 1.08 cm. On the 14th day, the average incision wound length in the P3 group was 1.1 cm (figure 8), down 0.10 cm from the original 2 cm. For groups P0, P1, and P3, the average wound length reduction from the starting condition was 1.36 cm, 1.63 cm, and 1.89 cm. Based on the average healing of cut wounds in each group, group P3 or the group given 15% gambier leaf extract cream healed faster, followed by group P2 and then group P1. Incision wound healing was slowest in the control group (P0) or base cream group (0% extract).

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, regularly distributed data represents the population. Data is normally distributed if the p-value is > 0.05 and not generally distributed if p < 0.05 (Ghozali, 2018).

Table 3. Normality Test Results

Group Extract Dose	Statistical	Significance
Control (P0)	0,974	0,899
Treatment 2,5% (P1)	0,979	0,928
Treatment 7,5% (P2)	0,894	0,377
Treatment 15% (P3)	0,990	0,980

Table 3, assessed for normality using SPSS, indicates that the control and treatment groups have significant values for the average cut wound healing variable from day 1 to day 14. The Shapiro-Wilk Test significance value (p) exceeds the average margin of p>0.05, 0.899 for Group P0, 0.928 for Group P1, 0.377 for Group P2, and 0.980 for Group P3. Shapiro-Wilk normality test shows data is usually distributed.

Data Homogeneity Test Between Groups

Table 4. Results of the ANOVA Test of Homogeneity of Variances

Results Category	Levene Statistical	Significance
Mean	0,393	0,760
Median	0,286	0,835
Trimmed Mean	0,394	0,759

The control group (P0), group P1, group P2, and group P3 have uniform data variance from study variables, 0.760 (p>0.05). Table 4's "Sig." yields 0.000. At the fundamental level = 0.05, Ho is rejected. Hence, the four groups have significantly different wound healing times.

Table 5. Post Hoc Bonferroni Test Results

Test	Percentage Healed Wounds (I)	Percentage Extract Dosage (J)	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Bonferroni	Control (P0)	2,5% (P1)	.09400*	.01411	.000	.0516	.1364
		7,5% (P2)	.20400*	.01411	.000	.1616	.2464
		15% (P3)	.28600*	.01411	.000	.2436	.3284
	Extract Dosage 2,5% (P1)	Control (P0)	-.09400*	.01411	.000	-.1364	-.0516
		7,5% (P2)	.11000*	.01411	.000	.0676	.1524
		15% (P3)	.19200*	.01411	.000	.1496	.2344
	Extract Dosage 7,5% (P2)	Control (P0)	-.20400*	.01411	.000	-.2464	-.1616
		2,5% (P1)	-.11000*	.01411	.000	-.1524	-.0676
		15% (P3)	.08200*	.01411	.000	.0396	.1244
	Extract Dosage 15% (P3)	Control (P0)	-.28600*	.01411	.000	-.3284	-.2436
		2,5% (P1)	-.19200*	.01411	.000	-.2344	-.1496
		7,5% (P2)	-.08200*	.01411	.000	-.1244	-.0396

Check the Test of Homogeneity of Variances table to decide what to test next. This test shows the same variance; hence, the Bonferroni Test is applied. Based on Table 5 and further tests using the Post Hoc Bonferroni Test, the comparison of group I and group J shows that the average length of healing of cuts in white rats (Rattus norvegicus) of the Wistar strain is different, marked with an asterisk "*." Group Bonferroni Post Hoc Testing was done using 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 6 shows that the Control Group (P0) lost erythema (redness) on days 9–11, but experimental animals 1, 4, and 5 lost it faster. The fastest was 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, and experimental mice 1 had it fastest. Treatment Group 3 (P3) occurred on days 6–7, fastest in mice 5. Table 6 shows experimental mice 1, 4, and 5 had the quickest swelling removal in the Control Group (P0) on the 7th day. Experimental mice 1, 2, and 3 experienced the fastest on day 6 in Treatment Group 1 (P1). In Treatment Group 2 (P2), experimental mice 1 ran quickest on day 4. In Treatment Group 3 (P3), experimental mice 5 experienced the fastest on day 4.

Table7. 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 group (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
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
7,5% 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	Km
	2nd	Mb	Mb	Mb	Mb	M	M	Kt	Kt	Kt	Kt	Kt	Kt	Km	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	-
	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

Cut wounds heal by inflammation, proliferation, and maturation. Fibroblasts produce collagen and other wound-healing proteins during proliferation. Vascular and cellular responses to skin tissue injury define inflammation. Collagen scar tissue reorganizes and strengthens over months. This maturation phase perfects new tissue creation into muscular, high-quality healing tissue. This study found fibroblast cell proliferation and collagen density.

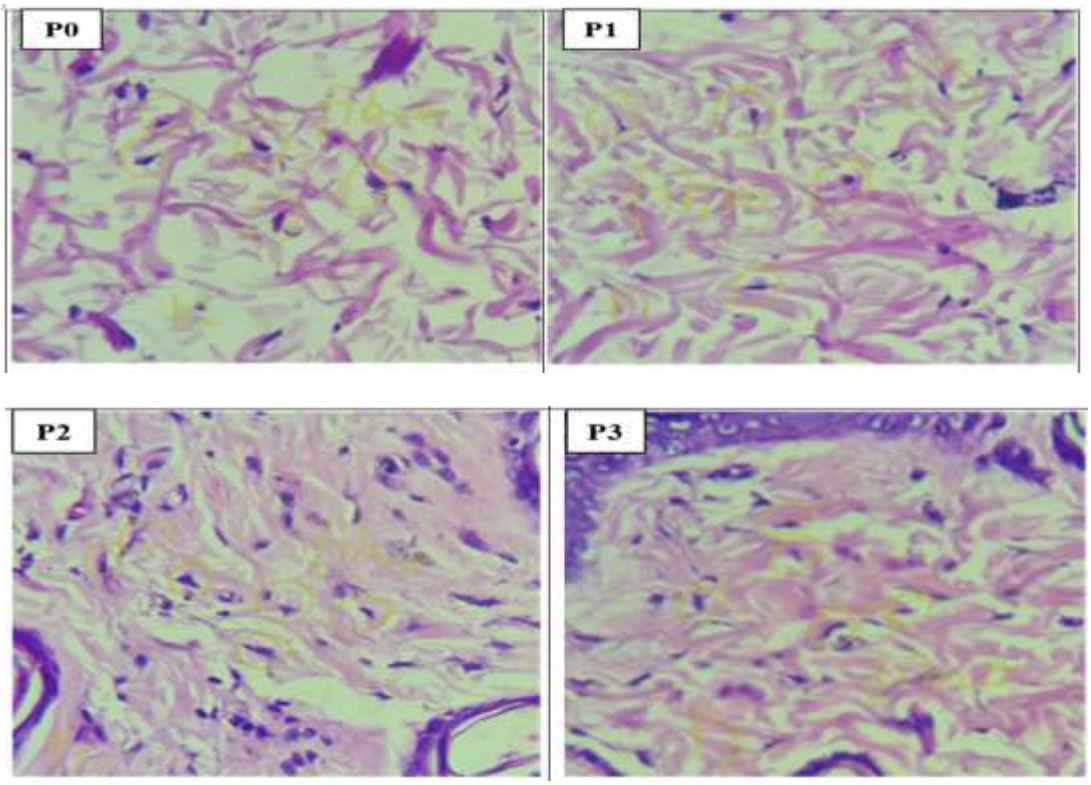

Figure 1. Fibroblast Cell Proliferation 400x Magnification (Day 14)

Figure 1 shows that the treatment groups given 7.5% gambier leaf extract cream (P2) and 15% (P3) had more fibroblast cells and denser cells than the control group (P0) and the cream group (P1). However, histological findings showed thicker collagen fibers in the P3 group compared to the P2 group. The P0 control group had more fibroblast cells and were more densely packed, while the P1 group given 5% gambier leaf extract had fewer sparser cells. However, group P1 collagen fibers were thicker and denser than P0. 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.

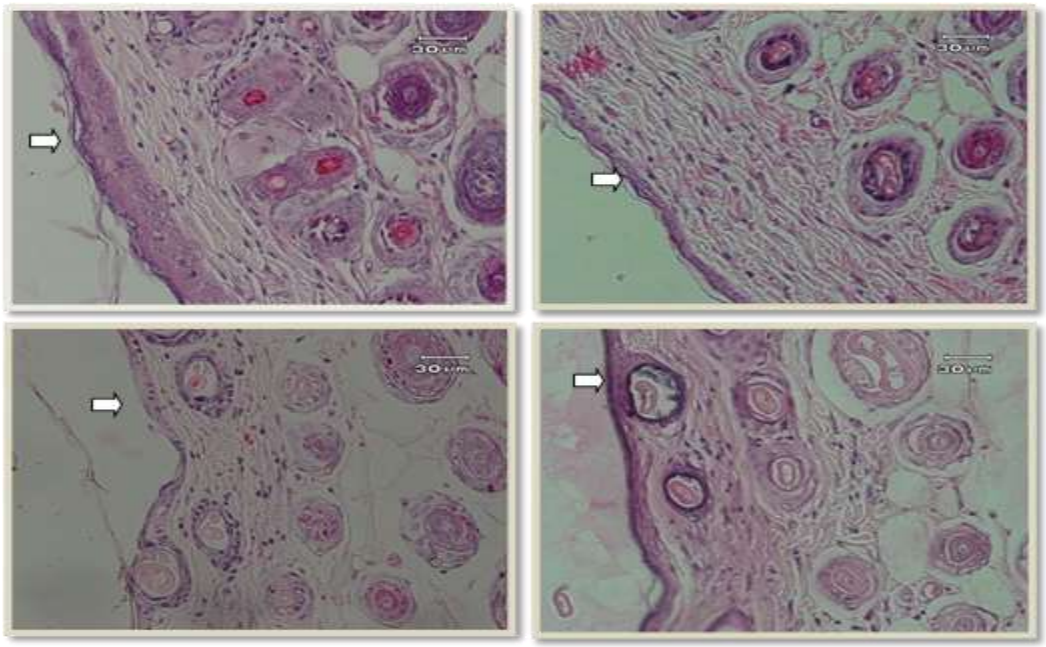

Figure 2. Collagen Density on the 14th Day

Note: A (Control Group P0), B (Group P1), C (Group P2), D (Group P3) and → Epithelial formation at the edge of the wound

From Figure 2, the histopathology of the cut wound on the 14th day after administering 15% gambier leaf extract cream (P3) showed denser and better epithelial formation than in the control group, the 5% group, and the 7.5% 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.

Discussion

This study tested the healing impact of incision wounds by shortening them. This study extracted gambier leaves (Uncaria Gambir Raxb). Wash 1500 grams of gambier leaves under running water and air-dry. After drying, the gambier leaves were crushed into powder, weighed 500 grams, and macerated for five days in a 90% ethanol solvent that had been distilled. A thick gambier leaf extract was obtained by vacuuming the maceration results with a rotary evaporator. Ethanol meets extracting requirements. Ethanol dissolves most polar and non-polar compounds (Latcuba, Chiuman, Nasution, & Ginting, 2022; Li & Li, 2020; Mawarni et al., 2020). Then, gambier leaf extract is made into cream. 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. The average weight of the 20 mice was 108.87 grams. To adapt, mice were acclimatized for one week before treatment. Each rat was grouped into four groups: group I (P0) received base cream (0% extract), group II (P1) received 5% topically applied gambier leaf extract cream, group III (P2) received 7.5% topically and group IV (P3) received 15% topically. 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 0.2 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.

Mouse wounds are red due to inflammation. Large blood vessel releases of fibrinogen protein and activated platelets cause blood clots (Dong et al., 2019; Sahu, Jeon, Lee, Yang, & Tae, 2021). According to visual observations of 20 white mice, the cuts showed erythema and swelling on the 1st to 3rd day after treatment with 5%, 7.5%, 10%, and base cream. This is the inflammatory phase where blood clots and bleeding stops. On the fourth day, group P2 and P3 had a proliferative phase where tissue creation resumed and did not experience erythema, while group P1 and the control group (P0) did. Cut wounds matured fastest in the 7.5% extract concentration treatment group (P2) and the 15% group (P3), where the five mice on the 10th day had closed and merely scars. Some cut wounds in group P1 and control group P0 had partially closed, forming a scab during proliferation. 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 (Čoma et al., 2021; Wynn, 2021). Groups P2 (7.5%) and P3 (15%), given gambier leaf extract cream, had a faster wound length reduction in the inflammatory phase from the first to the fourth day than groups P1 (5%) and K, which had the inflammatory phase until day 6. 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. Gambier's phenolic acid prevents free radical-induced cell damage and inflammation.

This study found that 15% gambier leaf extract cream (P3) was the most effective. After the P3 treatment group, the 7.5% gambier leaf extract cream (P2) group also healed cut wounds in white mice better than the 5% and base cream (P0) groups. At 15% concentration, gambier leaf extract's secondary metabolite chemicals benefit wounds, but at low concentrations, they merely inhibit

microbes, making them less effective. Antibacterials are bacteriostatic at low concentrations but destroy microbes at high concentrations (Baquero & Levin, 2021; Zhang et al., 2021). This research found that gambier leaf cream has good physical stability when stored at room temperature for 14 days, with no changes in organoleptic, pH, adhesive power, spreadability, or viscosity, and meets cream dosage form requirements. Additionally, cream preparations are more accessible and more desirable.

4. CONCLUSION

Conclusions The phytochemical test of ethanol extract cream from gambier leaves (Uncaria Gambir Raxb) found flavonoids, saponins, tannins, and alkaloids, which accelerated the healing of cuts on the skin of male Wistar strain rats (Rattus norvegicus). Therefore, gambier leaf extract contains phytochemicals with potent antioxidant properties that can be employed as medicines. Compared to the treatment groups P1, P2, and P3, the control group (P0) had a considerably different average cut healing rate. Because the control group (P0) lacks active compounds that speed wound healing, this study found that 15% gambier leaf extract cream healed cut wounds in white mice better than 5% and 7.5%. However, 7.5% gambier leaf extract cream had results similar to 15%. At 7.5%, gambier leaf extract's secondary metabolite chemicals start to treat wounds, but at low concentrations, they inhibit microbes, making them less effective. For future research, higher concentrations of gambier leaf extract (Uncaria Gambir Raxb) should be used and compared to the positive control group (bioplacenton). Gambier leaf extract (Uncaria Gambir Raxb) may help heal cut wounds safely, but more research is needed. Further research is required on various forms/preparations of gambier leaf extract (Uncaria Gambir Raxb) that are more helpful and easier to manufacture on a big scale, especially in North Sumatra and other farmed areas. The research results should be compared to other studies to help other researchers study gambier leaf extract (Uncaria Gambir Raxb) for cut wounds.

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