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Dermapen Action on the Skin of White Rats Wistar Strain (*Rattus norvegicus*) to Evaluate the Efficacy of Avocado Fruit Ethanol Extract Cream (*Persea americana Mill.*) in Healing Wounds

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Abstract: Wounds disrupt anatomical and skin functions. Thus, proper treatment and healing are needed. Saponins, tannins, and flavonoids in natural medicinal extracts accelerate wound healing. Plants and natural substances are usually employed in topical therapy. This study tested the efficacy of ethanol extract cream from the avocado pulp (*Persea americana Mill.*) in treating dermapen-induced lesions on white rats (*Rattus norvegicus*) Wistar strain. This is a lab study or an experiment. Mouse samples were divided into four treatment groups of five mice each. This study also found that avocado flesh extract (*Persea americana Mill.*) significantly improved dermapen scar healing compared to base cream. The treatment groups given avocado pulp extract (*Persea americana Mill.*) exhibited higher healing percentages than the control group: 60.5, 95.7, 97.3, and 100%. Researchers found that 15% avocado flesh extract cream (*Persea americana Mill.*) healed dermapen scars best. This study found that avocado flesh extract cream (*Persea americana Mill.*) accelerates skin regeneration and increases fibroblasts more than base creams. The highest and densest number of fibroblast cells was found in treatment group 3 healing wounds. Fibroblasts indicate active dermapen wound healing.

Keywords: Avocado; Dermapen; Ethanol extract; Healing wounds; Skin

Introduction

The skin, the biggest organ in the body, encases all flesh and organs. The skin protects the body from mechanical, chemical, microbiological, and UV radiation and aids the immune system (Fam et al., 2022; Guan et al., 2021; Nilforoushzadeh et al., 2018). Everyone wants flawless, healthy, and clean skin because it boosts self-esteem (Nilforoushzadeh et al., 2018). These days, young women and men place a high value on physical attractiveness. As a result, it is not shocking that skin health and other aspects of aesthetics have received greater focus than other issues (Alster & Graham, 2018; Iriarte et al., 2017). Naturally, it would be best to have intensive and regular care to get the desired skin care outcomes of smooth and healthy skin. Rapid technological advancement and modernity have also affected health and beauty. Skin care is also popular, with many drugs, cosmetics, and therapies available.

Science and technology in health are also advancing swiftly to improve medical services, quality of life, and healing. Skin needling therapy, or microneedle therapy, is a health and beauty technology that has garnered interest. This therapy stimulates collagen and elastin formation, essential to youthful skin, and smooths and repairs damaged skin (Atiyeh et al., 2021; Schmitt et al., 2018). Dermorollers and dermapens can do microneedle therapy. Dermapen is a popular skin rejuvenation technique due to its low cost and risks. A motorized pen-shaped microneedle therapy system called Dermapen can be modified to treat skin issues. It contains 9-12 rows of needles and can alter needle depth from 0.25 to 2 mm.

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It also features a disposable needle length guide. Dermapen needles must be sterilized and used individually. Thus, one demapen serves one individual (Salman & Mohammed, 2020).

Dermapen is safer and more comfortable treating tiny areas like the nose, eyes, and lips without hurting nearby skin. The Dermapen's short, tiny needle pierces the epidermis and dermis to create micro-injuries that encourage wound healing. This procedure is called collagen induction treatment since Dermapen's results depend on each skin's natural regeneration process (Juhasz & Cohen, 2020). Dermapen therapy involves producing a wound with a needle in the pen to enter the epidermis. Dermapen treatment causes wounds, even minor ones that make the skin sensitive and lose its protective role.

Anatomical function and structure are damaged in a wound. An intentional or inadvertent wound damages the continuity of the skin, mucosa, bones, or other organs (Fam et al., 2022; Ghomi et al., 2019). Although wounds heal independently, improper treatment can lead to infection and bleeding, especially minor wounds generated by derma pen treatments. Wounds disrupt anatomical and skin functioning. Thus, proper treatment and healing are needed (Atiyeh et al., 2021; Prastika et al., 2020). To restore skin integrity quickly, wound healing is a complicated, dynamic, and predictable process. After inflammation, the proliferation phase is crucial to wound healing (Megawati et al., 2020). Optimal wound healing requires minimal tissue damage, sufficient tissue perfusion, oxygenation, and nourishment (Sonenblum et al., 2023).

Since ancient times, people have used plants and natural compounds to treat pain and prevent disease (Depkes, 1995; Duke et al., 2022). Avocado can aid in wound healing. Avocado pulp extract cream can heal dermapen-related skin damage. Avocado (*Persea americana Mill*.) is easy to find and has various health benefits, including antihyperlipidemia, analgesia, anti-inflammatory, anticonvulsant, hypoglycemia, hypercholesterolemia, wound healing, and cancer prevention (Pamungkas & Wahyuningsih, 2022). Saponins, alkaloids, and flavonoids in avocado fruit, seeds, and leaves make it an antibacterial medicinal plant. Additionally, avocado leaves contain polyphenols, and the fruit includes tannins.

Saponins, tannins, and flavonoids in natural medicinal extracts accelerate wound healing. Saponin, tannin, and polyphenols heal wounds. Saponin cleanses and heals open wounds, while tannin's antibacterial and wound-healing qualities prevent infections. Flavonoids, saponins, and tannins are antioxidants, proangiogenesis, and oxygen-rich for wounded skin (Bu et al., 2020; Hoseinkhani et al., 2020). Published avocado plant search results in general, avocado plants have been studied as antibacterials against *Staphylococcus aureus* and *Escherichia coli* bacteria (Hoseinkhani et al., 2020; Kupnik et al., 2023; Trujillo-Mayol et al., 2021), skin moisturizers (Fares et al., 2023; Ferreira et al., 2022; Lister et al., 2021) and Malondialdehyde (Vincent et al., 2020) and blood triglycerides (Hannon et al., 2020).

Research on using plants, especially avocados, to treat wounds, especially Dermapen, is unusual and never done. Kaban found that a 5% avocado seed methanol extract gel healed cut wounds in male mice (Kaban et al., 2022). Pamungkas et al. (2022) found that avocado leaf ethanol extract (5, 10, and 20%) can treat rabbit burn lesions. Medication can be applied topically, orally, or both to treat wounds. Plants and natural substances are usually employed in topical therapy. Topically given drugs are easier to use and have fewer dangers, which increases patient compliance (AL-kahfaji, 2022).

Creams, lotions, ointments, and gels are topicals. Cream is a W/O or O/W semi-solid emulsion. Creams are more accessible to apply uniformly than other topicals. Avocado fruit extract can be made into cream (Ferreira et al., 2022). The organismal evaluation showed that the 6% cream had a darker color and odor, and the pH measurement showed that it was around 5.0, or within the normal skin pH range of 4.5-6.5 (Marini et al., 2020). According to the problem statement, this study tested the efficacy of ethanol extract cream from the avocado pulp (*Persea americana Mill*) in treating derma pen-induced wounds on white rats (*Rattus norvegicus*) Wistar strain. The outcomes of this research can help biomedical researchers use and prepare avocado flesh as a natural medicine, notably for wound healing.

Method

This is a lab study or an experiment (Notoatmodjo, 2018). The post-test with the control group design tested the wound healing efficacy of ethanol extract cream from the avocado pulp (*Persea americana Mill*) on wistar strain white rats (*Rattus norvegicus*) due to dermapen action. This study used wistar strain adult male white rats (*Rattus norvegicus*) weighing 160-200 grams and 2-3 months old, identified as healthy by vigorous movement and no physical abnormalities. Twenty white rat samples, a substantial sample, were used. For the number of experimental animals, employ the 3R principle: Replacement, Reduction, and Refinement (Russell, 1995). Rat samples were sorted into four groups of five animals each: The control group (P0) received basic cream without avocado flesh ethanol extract, while Treatment group 1 (P1) received fruit flesh extraction cream avocado with a concentration or cream

formulation of 7.5%, Treatment group 2 (P2) received 10%, and Treatment group 3 (P3) received 15%.

This study uses independent and dependent variables (Suwarno & Nugroho, 2023). This study used avocado pulp ethanol extract cream at 7.5, 10, and 15% concentrations as independent variables. This study's dependent variable is dermapen's effect on wistar white rats' skin wound healing. The research lasted one week in the Animal House laboratory, Faculty of Mathematics and Natural Sciences, University of North Sumatra. This investigation has multiple steps, from preparation to testing. This research began with acclimatizing test animals, creating ethanol extract from avocado flesh, and making a cream formula. Then, Dermapen Wound Creation, Management, Observation, and Histopathological Evaluation were tested. The research data was evaluated using SPSS at a 95% significance level ($\alpha = 0.05$). Data normality was tested using Kolmogorov-Smirnov ($p > 0.05$). A One-way ANOVA was performed to test significant differences between test groups. If the One-way ANOVA test findings were significant ($p < 0.05$), a Post Hoc Test using LSD was conducted to determine the most successful treatment group (Ghozali, 2018).

Result and Discussion

Result

According to Table 1, the mice were healthy before and after therapy. Before treatment, mice weighed 200 grams in the control group, 201 grams in treatment groups 1 and 2, and 202 grams in treatment group 3. After therapy, the mice lost only a little weight. As long as the investigation lasted, the mice were healthy. Next, the researcher started treatment.

Table 1. Characteristics of Test Animals

Component	Group K	Group P1	Group P2	Group P3
Types of Rats	*Rattus norvegicus*			
Gender	Male			
Condition	White fur, healthy and active			
Initial B/W	200gr	201gr	201gr	202gr
Final B/W	198gr	199gr	199gr	197gr

Mice receive Dermapen wounds to start treatment. Begin by shaving the back area to provide a clean, bald appearance for the desired wound area (2 cm x 2 cm). After shaving, the rats were deprived of consciousness with ketamine (80 ml/kg BW) and xylazine (5 ml/kg BW) to prevent pain and excessive movement. Puncture of the dermapen needle causes wounds. After the wound occurred, mice received ethanol extract of avocado flesh (*Persea americana Mill.*) thrice a day in four dosages. The control group received basic cream without avocado pulp extract (0%), treatment group 1 received 7.5% avocado pulp extract cream (*Persea americana Mill.*), treatment group 2 received 10%, and treatment group 3 received 15%—one-morning cream application.

Table 2. Results of Mean Wound Healing

Day	Size (cm)				Percentage (%)			
	C	P1	P2	P3	C	P1	P2	P3
1	2.00	2.00	2.00	2.00	0	0	0	0
2	1.97	1.93	1.91	1.89	1.5	3.6	4.6	5.7
3	1.94	1.86	1.76	1.71	3.5	7.0	12.5	14.5
4	1.89	1.79	1.63	1.50	5.5	10.6	18.3	25.2
5	1.84	1.66	1.41	1.23	9.0	16.6	30.0	38.7
6	1.79	1.56	1.2	1.07	10.6	17.2	40.0	46.9
7	1.75	1.25	1.05	0.94	12.7	37.4	48.0	52.9
8	1.64	1.15	0.88	0.75	18.2	42.5	56.0	62.3
9	1.55	0.90	0.70	0.58	22.5	55.2	65.0	71.1
10	1.46	0.72	0.53	0.36	27.5	63.8	73.3	82.1
11	1.17	0.57	0.42	0.22	41.4	71.4	78.9	89.1
12	0.94	0.36	0.28	0.08	53.1	81.9	86.2	95.9
13	0.87	0.22	0.16	0	56.5	88.8	92.2	100
14	0.79	0.09	0.05	0	60.5	95.7	97.3	100

Table 2 compares mice's average wound lengths by group. In treatment group 3, 0 cm, perfect wound closure was achieved, and the control group had the most extended wound length, 0.79 cm. Table 2 shows that dermapen wounds in white wistar rats (*Rattus norvegicus*) heal in all groups. Average healing percentages differed between groups. Control group Dermapen wound healing on the last day averaged 60.5%, treatment group 1 (95.7%), treatment group 2 (97.3%), and treatment group 3 (100%). Thus, treatment group 3 healed faster than the control, treatment 1, and treatment 2.

Based on Table 3, erythema (redness), edema (swelling), and crusting (scab) have different healing rates. Treatment groups P2 and P3 have a shorter average healing time for erythema, followed by P1 and the control group. Edema healing in this trial was slower in the control group than in the avocado flesh extract group. The greatest concentration for long-term healing of dermapen wounds in white wistar rats is Group P3, followed by Groups P2 and P1. Next, check the treatment group's wounds for crusts or scabs. Group P3 vanished faster than P2 and P1. In contrast, the control group lost the longest.

Table 3. Wound Healing Physiological Results

Group	Erythema (Redness)	Edema (Swelling)	Crusts (Scabs)
Control	0.48	0.40	0.42
P1	0.45	0.21	0.28
P2	0.42	0.19	0.36
P3	0.34	0.12	0.21

The secondary metabolite components of avocado pulp extract (*Persea americana Mill.*) were tested phytochemically. Flavonoid, saponin, tannin, alkaloid, and steroid phytochemical assays. Flavonoid testing began. In a test tube, 1 gram of avocado flesh extract (*Persea americana Mill.*) was added to concentrated HCl and cooked for 15 minutes in a water bath. Red or yellow indicates flavonoids (flavone, chalcone, and aurone). A yellow extract indicates the presence of flavonoids.

Second is the saponin test, which involves adding 1 gram of avocado flesh extract to a test tube, 10 ml of boiling water, cooling, and shaking rapidly for 10 seconds. Saponin is present if the foam is 1-10 cm high in 10 minutes and does not dissolve after adding one drop of 2 N HCl. This study revealed froth in avocado (*Persea americana Mill.*) pulp extract, indicating saponin. In the third tannin test, 1 gram of avocado flesh extract (*Persea americana Mill.*) is placed in a test tube, 10 mL of hot water is added, boiled for 5 minutes, and 3-4 drops of $FeCl_3$ are added to the filtrate Blue-green (green-black) is good. Catechol tannin, while blue and black indicate tannin. A yellow liquid in tannin test results means no tannin.

Two grams of avocado flesh extract (*Persea americana Mill.*) was placed in a test tube, dripped with 5 mL of 2 N HCl, heated, cooled, and divided into three 1 ml test tubes for the fourth alkaloid test. Reagents are added to each tube. If Mayer's reagent precipitates white or yellow, alkaloids are present. In this study, the alkaloid test showed yellow, indicating alkaloids. A test tube with 2 grams of avocado pulp extract (*Persea americana Mill.*) and 2 mL of ethyl acetate was shaken for the fifth steroid test. The ethyl acetate layer was dropped onto a drop plate to dry. After drying, two drops of acetic acid and one drop of concentrated sulfuric acid were added. Terpenoids are present if they become red or yellow. Steroids are present if they turn green. If the steroid test turns red, triterpenoids are present.

Table 4. Phytochemical Test

Metabolites	Color	Result
Flavonoids	Yellow	+
Saponins	Yellow and foamy	+
Tannin	Yellow	-
Alkaloids	Yellow	+
Triterpenoids	Red	+

Table 5. One-Sample Kolmogorov-Smirnov Test Normality Results

Group	Statistic	df	Sig.
Control	.175	5	.200*
Treatment P1	.244	5	.200*
Treatment P2	.167	5	.200*
Treatment P3	.220	5	.200*

Table 5 shows the One-Sample Kolmogorov-Smirnov Test normality results. The results were significant at 0.200 for each group. A p-value > 0.05 indicates regularly distributed data. This implies that the data is regularly distributed.

Table 6. Result of Homogeneity Test of Variances

	Levene Statistic	df1	df2	Sig.
Based on Mean	.854	3	16	.485
Based on Median	.648	3	16	.596
Median adjusted df	.648	3	12.845	.598
Base trimmed Mean	.840	3	16	.492

Table 6 shows that the significance column probability value for the Levene homogeneity test is 0.854. Since p > 0.05, the control group, treatment 1, treatment 2, and treatment 3, come from populations with the same variance or are homogeneous. The One-Way ANOVA test in Table 7 yields a significance value of 0.000 or < 0.05. These statistics show significant treatment group differences. The post-hoc LSD follow-up test compared group average LDL values. Table 8 shows LSD post-hoc follow-up results.

Table 7. ANOVA Test

Result Group	Sum of Squares	df	Mean Square	F	Sig.
Between	1.231	3	.410	273.104	.000
Within	.024	16	.002		
Total	1.255	19			

Table 8. LSD Post Hoc Test Results

Group (I)	Group (J)	Mean Difference	Std. Error	Sig
Control	Treatment 2	.39200*	.02452	.000
	Treatment 3	.54000*	.02452	.000
	Treatment 4	.65800*	.02452	.000
P1	Control	-.39200*	.02452	.000
	Treatment 3	.14800*	.02452	.000
	Treatment 4	.26600*	.02452	.000
P2	Control	-.54000*	.02452	.000
	Treatment 2	-.14800*	.02452	.000
	Treatment 4	.11800*	.02452	.000
P3	Control	-.65800*	.02452	.000
	Treatment 2	-.26600*	.02452	.000
	Treatment 3	-.11800*	.02452	.000

*. The mean difference is significant at the 0.05 level.

Table 8 shows if groups differ significantly using LSD Post Hoc Test Results. The Post Hoc LSD test analysis in this study shows a significance value of 0.000 or less than 0.05, indicating significant differences between groups.

Histopathological investigations were made with a 400x light microscope. This observation examined the structure and morphology of cells, particularly fibroblast cells, in each dermapen wound specimen in the treatment group with base cream (0) and avocado

flesh extract cream at 7.5, 10, and 15%. Daily cream application occurs in the morning. Wound healing involves inflammation, proliferation, and maturation. Wound healing has four stages: hemostasis (seconds to minutes), inflammation (3–5 days), proliferation (4–14 days), and remodeling. The proliferation phase is called fibroplasia because fibroblast cell proliferation is prevalent. The proliferation phase lasts 3–14 days following damage. Fibroblasts produce mucopolysaccharides, glycine, and proline from undifferentiated mesenchymal cells, which form collagen fibers that link wounds.

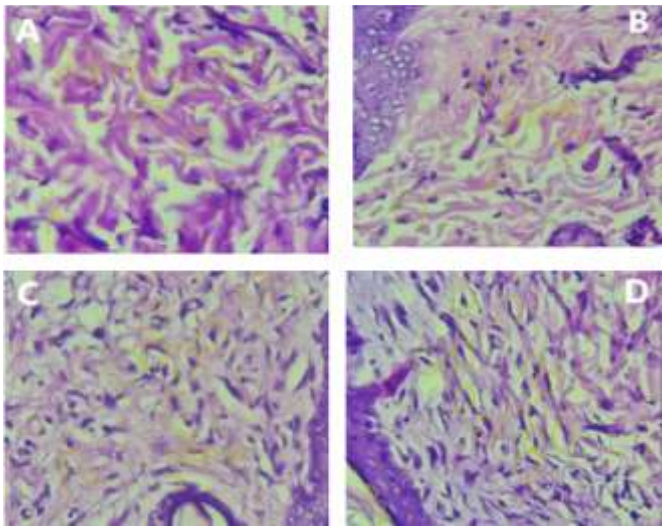

Figure 1. Histopathological findings

Fibroblasts produce collagen and other wound-healing proteins during proliferation. Histopathological study of dermapen wound healing treatment with base cream and avocado flesh extract indicated variations in fibroblast quantity and density (Figure 1). Fibroblasts indicate active Dermapen wound healing. The control group (Figure A) administered base extract cream had fewer and rarer fibroblast cells. Treatment group 1 (Figure B) with avocado flesh extract cream had more fibroblasts. Treatment group 2 (Figure C), given avocado pulp extract cream, had more fibroblast cells and were closer together. Number and density were higher in 15% of treatment group 3 (Figure D). Histopathological investigations showed that the 15% avocado flesh extract cream group had the most numerous and dense fibroblasts.

Discussion

This study confirms that topical avocado pulp extract cream accelerates dermapen scar healing on rat skin. Twenty Wistar white rats (*Rattus norvegicus*) were separated into four groups for this study. Weighting the mice preceded the study. Mouse weight averaged 201 grams before the test. To conclude the study, the mice were weighed again and averaged 198.25 grams per test group. These data show that the mice's body weight did not vary considerably before and after the trial.

Wounds heal independently (Amer et al., 2018), but improper treatment can cause infection and bleeding, incredibly minor dermapen-caused wounds (Juhasz & Cohen, 2020). Wounds disrupt anatomical and skin functioning. Thus, proper treatment and healing are needed (Juhasz & Cohen, 2020). Avocados (*Persea americana Mill.*) are easy to find and provide various health benefits, including antihyperlipidemia, analgesia, anti-inflammatory, anticonvulsant, hypoglycemia, hypercholesterolemia, and wound healing (Fares et al., 2023; Ferreira et al., 2022; Kupnik et al., 2023; Lister et al., 2021). Avocados include saponins, alkaloids, steroids, and flavonoids with antimicrobial characteristics (Fares et al., 2023; Ferreira et al., 2022; Kupnik et al., 2023). Researchers also screened avocado pulp extract phytochemicals. Positive results showed that avocado flesh extract contained saponins, alkaloids, steroids, and flavonoids that aid wound healing. Researchers have also begun testing avocado pulp extract creams to see if they improve dermapen wound healing in white wistar mice.

Data from treatment procedures was collected for the study. The collected data is processed to test its normalcy. The researcher tested normalcy first. The data normality test showed a significance value of 0.200 > 0.05, indicating that the data was normally distributed and typical of the population. A Levene homogeneity test was then performed to determine subject variance. The significance level is 0.485. Since the significance probability value is more significant than 0.05, all treatment groups come from a population with the same variance. Finally, a one-way ANOVA test determined significance. If the significance value is 0.000 or less than 0.05, H0 is rejected, Ha is approved, or Post Hoc LSD is needed since the test group heals differently. The Post Hoc LSD test analysis in this study shows a significance value of 0.000 or less than 0.05, indicating significant differences between groups.

Histopathological investigation of treated skin tissue fibroblast cells was also done. In treatment group 3, which received 15% avocado pulp extract cream, fibroblast cells were more numerous and denser than in the control group, which received base cream without extract, treatment group 1, which received 7.5%, and group 2, which received 10%. The highest and densest number of fibroblast cells was found in treatment group 3 healing wounds. Fibroblasts indicate active dermapen wound healing. Avocado pulp extract cream heals dermapen scars because it includes secondary metabolites such as saponins, tannins, alkaloids, and flavonoids, which may function as anti-inflammatories

and antioxidants. This study confirms Pamungkas et al. (2022) research that ethanol from avocado leaves (5, 10, and 20%) can treat rabbit wounds.

Conclusion

According to observations and data analysis, avocado flesh extract cream (*Persea americana Mill.*) accelerates dermapen scar healing in wistar white rats (*Rattus norvegicus*). This study also found that avocado flesh extract significantly improved dermapen scar healing compared to base cream. The One-Way ANOVA test revealed a significant difference in dermapen scar healing between the base cream treatment group and avocado flesh leaf extract cream (p-value < 0.05). The treatment groups given avocado pulp extract exhibited higher healing percentages than the control group: 60.5, 95.7, 97.3, and 100%. Researchers found that 15% avocado flesh extract cream healed dermapen scars best. Avocado flesh extract cream accelerates skin regeneration and increases fibroblasts better than base creams. The avocado pulp extract cream group healed dermapen scars faster than the base cream group. Avocado flesh extract cream was also found to produce more wound-healing fibroblasts than base cream. Avocado flesh extract contains saponins, alkaloids, steroids, and flavonoids that may be anti-inflammatory and antioxidants to inhibit free radicals and speed wound healing. According to the research results, avocado fruit extract cream may accelerate the healing of dermapen scars in people. More research is needed. Other microscopic metrics and wound healing factors should be studied for further investigation. This research should show how avocado flesh extract cream speeds dermapen scar repair and skin regeneration.

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Author Contributions
Tan Suyono conceptualized the research idea, designed of methodology, management and coordination responsibility; Rica Mucmaini analyzed data, conducted a research and investigation process; Chrismis Novalinda Ginting and Irza Haicha Pratama conducted literature review and provided critical feedback on the manuscript.

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The authors declared no conflict of interest.

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