The Effect of Giving Coffee Pulp Extract Cream On The Healing of Cut Wounds In Wistar Rats

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Abstract.
Humans need skin to protect their internal organs, such as muscles, nerves, and bones, from disease. This study examines the effect of coffee grounds extract cream on wound healing in Wistar rats. This study is an experimental laboratory study. The research design used a post-test with a control group design or control on samples based on treatment groups to analyze the effect of coffee grounds extract on wound healing and skin histopathology in male Wistar white rats. According to the results of the study, coffee grounds extract accelerated wound healing in Wistar white rats, as shown by the average differences of 2.5%, 5%, and 10%. This study shows that coffee grounds extract contains saponins, alkaloids, flavonoids, and tannins. Research on skin histopathology on the best fibroblast tissue found that 10% coffee grounds extract cream was the most helpful in developing connective tissue in injured skin. The findings of this study are expected to help other researchers explore the effects of coffee grounds extract on skin collagen formation.
Keyword: *Extract Cream; Wistar Rats and Coffee Grounds Extract.*

I. INTRODUCTION

The function of the skin is very important for humans because as the outermost organ of the body, it protects the body from disease and protects internal organs such as muscles, nerves, and bones. The third layer consists of the hypodermis, a deeper subcutaneous tissue consisting of connective tissue and fat.(dr valda Gracia, 2022). As an important organ for the human body, the skin must remain healthy so that it is not damaged.Skin is also very important for us to understand our environment and to communicate through receptors in the skin.(Picture of the Skin, 2021).Based on the origin of the damage and the duration of healingBecause the skin is the largest organ covering the body, it is very susceptible to trauma and injury. (Graduation, 2015).If there is damaged or missing tissue, the body will respond and trigger the wound healing process.(Pradipta, 2010). Untreated open wounds can lead to infections such as tetanus. The infection can spread to other tissues or organs and can cause long-term infection or even death if not treated promptly.(Reddy, 2012). Chronic wounds are referred to as wounds that are difficult to heal or chronic. (Farahani, 2011).Wounds are divided into acute wounds and chronic wounds based on their healing duration. Acute wounds are wounds caused by trauma or surgical wounds, and they heal within 8–12 weeks, depending on the size and depth of the wound.(Farahani, 2011). Comprehensive treatment of chronic wounds remains a significant unmet medical need. To accelerate the healing of chronic wounds, many studies have begun using gels, including hydrogels or sol-gels, that combine a combination of antioxidant properties.(Regitha Claudia, Sri Wahyuni Et Al, 2024).External wound medications can speed up wound healing and can protect wounds from infection, relieve related symptoms, and even prevent scars. One of the external wound medications can be given in a cream preparation.(Kastika, SM, & Rahayu, 2018).

Efficient wound response and repair are essential to prevent infection. Minimizing tissue damage and providing appropriate tissue perfusion, oxygenation, and nutrition are the main principles of optimal wound healing.(Reddy, 2012).According to Clifford in his research(Wastu Ayu Diamahesa, 2023) Coffee pulp has a relatively high ANF (anti-nutrient) and crude fiber content, and has a low protein and energy content. The wound healing process consists of 3 phases, namely the inflammation phase, proliferation phase, and maturation phase..In several studies on coffee, coffee contains compounds other than caffeine, namely alkaloids, flavonoids and also tannins.(Panggabean E, 2011). Where the flavonoid content is known to help

accelerate collagen growth (synthesize collagen) through increasing fibroblasts and tissue formation.. As in the research(Yorinta Putri Kenisa, Iistiati, 2012)Robusta coffee in coffee bean extract with 45% ointment preparation can provide a good effect on the wound healing process. From the research(Ulfa Elfiah, 2023)producing robusta coffee extract gel (Coffea canephora) has been proven to have an effect on wound healing both macroscopically and microscopically, while the percentage of extract administration is 2.5%. So coffee has benefits in wound healing and researchers are interested in researching using coffee fruit but on its skin to further explore the wound healing ability of coffee pulp extract. Based on the background above, the author is interested in creating a research titleThe Effect of Giving Coffee Pulp Extract Cream on the Healing of Cut Wounds in Wistar Rats.

II. METHODS

Types of research

Laboratory experimental research is a type of research used to examine the effectiveness of administering Coffee Pulp extract cream to cut wounds in Wistar strain rats (Rattus norvegicus). The research design uses a post-test with control group design or controls samples based on treatment groups to analyze the effectiveness of Coffee Pulp extract on the wound healing process and the histopathological picture of skin tissue in the wound healing process of male Wistar strain white mice.

Research Procedures

Acclimatization of Test Animals

Acclimatization is the process of adjusting to a new environment, climate, condition, or atmosphere. Before giving treatment, all male Wistar rats went through a seven-day acclimatization process in the Laboratory of the Department of Pharmacology and Therapeutics, Faculty of Medicine, University of North Sumatra. The rats were given time to adapt to the new environment, as well as their food and drink. The provision of feed and drink to the rats was carried out according to their standard needs (ad libitum).

Test of Caffeine Content and Secondary Metabolites in Coffee Pulp Extract

This caffeine test refers to HPLC analysis of bioactive compounds in coffee plants.HPLC(High Performance Liquid Chromatography)ais an analytical technique used to separate, identify or measure each component in a mixture. The mixture is separated using the basic principles of column chromatography and then identified and measured by spectroscopy.(FR, 2022). This test uses coffee pulp samples. Phytochemical testing is an initial testing method to determine the content of active compounds contained in plants so that they can be used as medicine. Phytochemical testing is carried out to determine whether there are active compounds in coffee extract in the coffee pulp section. Phytochemical testing includes flavonoid, saponin, tannin, alkaloid and steroid/triterpenoid tests.

Scoring System

The parameters observed in this study were the distribution of collagen tissue formed in wound healing. Histopathology scoring parameters for collagen tissue distribution density were carried out based on the calculation of 1 field of view, on a 400 x magnification object.

0= No collagen fibers were found in the wound area.

+1= Collagen fiber density in the wound area is low (less than 10%)

+2= Collagen fiber density in the wound area is moderate (10-50%)

+3= Collagen fiber density in the wound area is tight (50-90%)

+4= The density of collagen fibers in the wound area is very dense (90-100%)

(Rizka, A., 2013).

Data analysis

The results of histopathological observations of skin tissue were then scored. The research data were then tabulated and the data were presented descriptively. The data from observations of wound healing were analyzed using SPSS (Statistic of Package for Social Science) 25.0. for windows. For the normality test using the Shapiro Wilk test with $p > 0.05$, testing the significance between trial groups was carried out using the one sample t test at a 95% confidence level ($p < 0.05$).

III. RESULTS AND DISCUSSION

Description of Research Results

This study was conducted to analyze the effectiveness of Coffee Pulp extract on the healing process of cuts and histopathological features of skin tissue in the healing process of cuts in male white Wistar rats. Before further analyzing the test animals, the researchers first measured the caffeine content in coffee pulp using the HPLC method.Low caffeine coffee not only has a good taste and aroma, but is also better to consume because it can stimulate the nervous system, which can improve mood and prolong concentration.(Dewi Septiningtyas Hastuti, 2018). After knowing the caffeine content, the researchers then examined the secondary metabolite content in Coffee Pulp extract through phytochemical testing and made an extraction which was then given to experimental animals that received cut wound treatment and observed the healing of the cut wounds.

In Vitro Penetration Testing of Coffee Pulp Extract Cream

Preparation of Phosphate Buffer Solution (LDF). Potassium dihydrogen phosphate 0.2 M 50.0 mL was mixed with 0.2 N sodium hydroxide 39.1 mL, then diluted with carbon dioxide-free water to 200.0 mL. In this study, researchers wanted to see different concentrations in each treatment group that would be given extract cream, namely 2.5%, 5%, and 10%. In the Organoleptic test (blank, F1, F2, F3) with the test results on the cream preparation, it was known that the Coffee Pulp extract was odorless, white, light brown, brown and its homogeneity was homogeneous, solid structure with an average Ph F1 of 6.46, an average F2 of 6.24 and an average F3 of 6.15 so that the pH level is still in accordance with human skin. While the results of the cream spreadability test were in diameter ranging from 4.2 -5.2 cm in 0 to 125 gr packaging. So the cream is safe to use for the experiment.

Coffee Pulp Secondary Metabolite Test

Coffee has many antioxidants, especially polyphenols, which have anti-inflammatory properties. This content helps reduce redness and irritation on the skin and speeds the healing of minor wounds and acne.On the article page(Dwi Ratih Ramadhany, 2023)Coffee is not only useful for eliminating drowsiness but also has health benefits such as maintaining heart health. If you drink coffee regularly, it can reduce the risk of heart disease and stroke. Coffee can also maintain ideal body weight because its caffeine content can support weight loss. Coffee can also reduce the risk of type 2 diabetes. Secondary metabolite testing was conducted to determine the content of organic compounds found in coffee pulp. The results of the saponin test of 0.5 mL sample extract + 5 mL of distilled water, then shaken for 30 seconds showed that there was foam in the test results so that it was positive for containing saponins.

In the alkaloid test with 0.5 mL sample + 5 drops of chloroform + 5 drops of Mayer's reagent, the color changed to brownish white so that it was positive for alkaloids. In the flavonoid test with 0.5 mL sample + 0.5 gr Mg powder + 5 mL concentrated HCl heated for 15 minutes, the color turned yellow and there was foam so that it was positive for containing flavonoids. In the tannin test with 1 mL sample + 3 drops of 10% FeCl3 solution, the color turned bluish black so that it was positive for containing tannins.With the tests that have been carried out, the conclusion is that the coffee pulp extract positively contains secondary metabolite compounds, namely saponins, alkaloids, flavonoids and also tannins. Where these compounds are antioxidants that are good for body health. Compounds that play a role in the wound healing process in this fraction are alkaloids, flavonoids, saponins, phenols, and triterpenflavonoids and saponins. The content of flavonoids and saponins has anti-inflammatory properties so that it can reduce inflammation and accelerate wound healing(Sukmawati, SS, Siwi, H., 2021).

Coffee Pulp Caffeine Testing Using HPLC Method

This test aims to determine the caffeine content in coffee drinks made from coffee pulp.Pulping aims to separate the seeds from the fruit skin so that coffee beans are obtained that are still wrapped in their horn skin. To achieve this goal, caffeine samples are extracted from the coffee skin using boiled distilled water before being partitioned with chloroform. ThenWith respect to the standard caffeine solution, the extracted caffeine samples were analyzed at concentrations of 5-25 g/mL.In this test the materials used are black coffee, Chloroform, NH4OH, CaCO3, Mayer's reagent, Wagner's reagent, Dragendorf's reagent, Parry's reagent and Mureksid reagent. Methanol for HPLC, aquades.Caffeine is found in common foods and

beverages that we consume every day, such as coffee and tea. Coffee and tea leaves contain a maximum of 5% caffeine in them. In a chemistry lab, caffeine is made by the reaction between dimethylurea and malanic acid. In this short article, let us learn more about the chemical formula of caffeine, its chemical and physical properties along with its chemical structure.

1) Types of HPLC Testing

Qualitative test by comparing the standard tR of caffeine with the sample and comparing the spectra of the sample with the spectra of the standard caffeine on a UV spectrophotometer. One gram of coffee powder is put into a glass, and while stirring, 150 milliliters of hot aquadest are added. The hot coffee solution is put into an Erlenmeyer through a funnel with filter paper, and then 1.5 grams

2) Sample Preparation:

CaCO3 and coffee solutions were added to the separator and extracted four times, adding 25 ml of chloroform each time. The bottom layer was removed, and the extract, which was the chloroform phase, was evaporated with a rotary evaporator until the chloroform was completely evaporated. After adding the solvent-free caffeine extract into a 100 mL volumetric flask, distilled water was used to dilute it until the mark line appeared. Then, the caffeine extract was homogenized. Furthermore, the solution content was determined using ultraviolet spectrophotometry and HPLC.

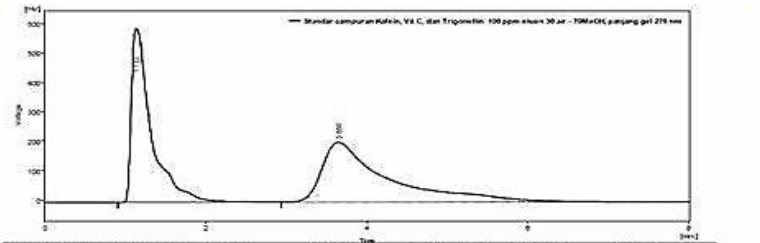
3) Results of Determination of Caffeine Levels:

Extraction of caffeine in the sample was carried out before the determination of caffeine in the sample. The purpose of extraction is to convert caffeine in coffee, which is usually in the form of salt, into a base by creating an alkaline environment in the sample suspension in water. To extract caffeine, which is a base, which is chloroform soluble, chloroform solvent is used next. The table shows the results of determining caffeine levels in samples using HPLC and ultraviolet spectrophotometry methods. The comparison is between coffee pulp and black coffee in preparation. Here is the table

Table 1. Results of caffeine content determination

Sample	Caffeine Content (%)*	
	HPLC	**UV Spectrophotometry**
Coffee Pulp	0.224	0.257
Coffee Leaves	0.113	0.171

From the data above, it can be seen that the caffeine content in coffee pulp is higher than in coffee leaves using HPLC andultraviolet spectrophotometry.Caffeine concentration was determined using high performance liquid chromatography equipped with a UV detector (HPLC-UV) set at 272 nm and a run time of 6 minutes at a flow rate of 1 mL/min at room temperature. Isocratic solution was used using HPLC grade methanol (100%) with a total run time of 6 minutes. And can be seen from the graph below.



No	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	1.133	10339.214	592.737	46.8	74.3	0.22
2	3.650	11760.031	204.977	53.2	25.7	0.68
	Total	22099.245	797.714	100.0	100.0	

Fig 1. HPLC chromatogram of Caffeine

Wound Healing Observation Results

All research samples, namely 24 male rats, were divided into 5 groups, namely the control group without P- extract given base cream, P+ given betadine and treatment groups P1, P2 and P3.which was given Coffee Pulp extract cream with 3 different concentrations, namely 2.5%, 5%, and 10%. Researchers conducted macroscopic observations of the healing of rat wounds by measuring the length of the wound using a caliper. The wound healing process produces scars that can be seen without the aid of a microscope, making it possible to observe through macroscopic observation or with the naked eye. This observation was

carried out with the aim of comparing wound healing between the group given the base cream and the group given Coffee Pulp extract cream with 3 different concentrations, namely 2.5%, 5%, and 10%. This observation was carried out every day for 14 days. The results of observations of cuts on the backs of rats are presented in the following figure:

Table 2. Average Wound Healing (cm)

Day	P-	P+	P1	P2	P3
1	2	2	2	2	2
2	1.97	1.97	1.94	1.91	1.89
3	1.92	1.90	1.83	1.71	1.72
4	1.87	1.83	1.72	1.50	1.46
5	1.76	1.72	1.61	1.28	1.20
6	1.65	1.63	1.37	1.06	1
7	1.46	1.42	1.13	0.85	0.75
8	1.35	1.25	1.09	0.63	0.56
9	1.23	1.18	0.92	0.48	0.34
10	1.11	1.09	0.73	0.37	0.19
11	0.93	0.87	0.54	0.21	0
12	0.87	0.79	0.36	0.11	0
13	0.75	0.65	0.26	0	0
14	0.57	0.48	0.12	0	0

The following are the average results of the comparison of the length of the rat wounds in each group. From the data, it can be seen that those who experienced perfect wound closure were in treatment groups 2 and 3, namely 0cm. On the 14th day, the control group P- which was given base cream and P+ which was given betadine and the treatment group P1 which was given 2.5% coffee pulp extract cream did not experience perfect wound closure, namely 0.57c, 0.48 cm and 0.12 cm on the 14th day of observation. The following is an explanation in the graph

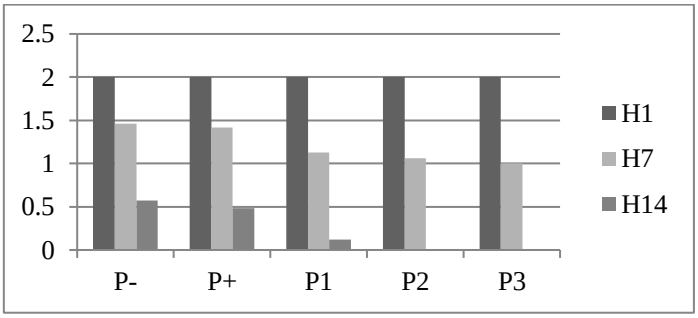


Fig 2. Graph of Incision Wound Healing

From the graphic image above, it can be seen that groups P2 and P3 have experienced wound healing on the 14th day at zero. While group P0 which was given base cream still experienced wounds on the 14th day. Furthermore, the researcher showed the process of measuring wound healing in mice. The following is the process of measuring wound healing in mice:

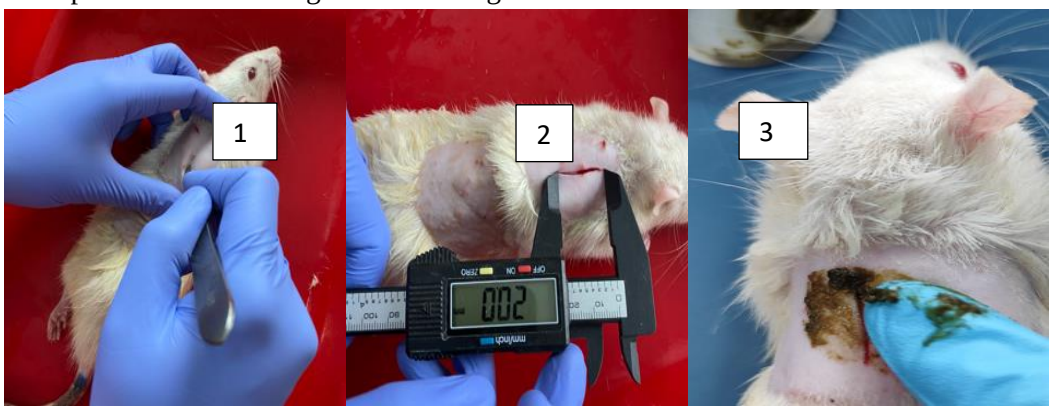


Fig 3. Incision Wound Observation Process

From the image above, it can be seen that image 1 shows the wound being applied to the mouse, image 2 shows the measurement of the length of the cut wound on the mouse and image 3 shows the

administration of the extract.*coffee pulp*in mice. Next, we look at the skin collabilization of mice that were given incision wounds and extracts through mouse skin histopathology.

Histopathology of Mouse Skin

The compounds contained in coffee pulp extract (CPE) are known to have the potential to heal injured skin. For this reason, it is necessary to conduct histopathological observations of mouse skin tissue after 14 days of observation. Here are the results:

In this study, researchers also compared wound healing with the control group P- (base cream) and P+ (betadine) with the results of wound healing looking better in the administration of betadine compared to only being given base cream, better collagen density and tighter skin tissue formation. However, if we look at the administration of Coffee Pulp extract cream, the results of this study indicate that the administration of Coffee Pulp extract cream can affect cells that play a role in the formation of connective tissue (fibroblasts) dermal fibroblasts found in the skin are very important in their function in wound healing. The following are the results of the percentage graph of differences in fibroblasts produced by each group:

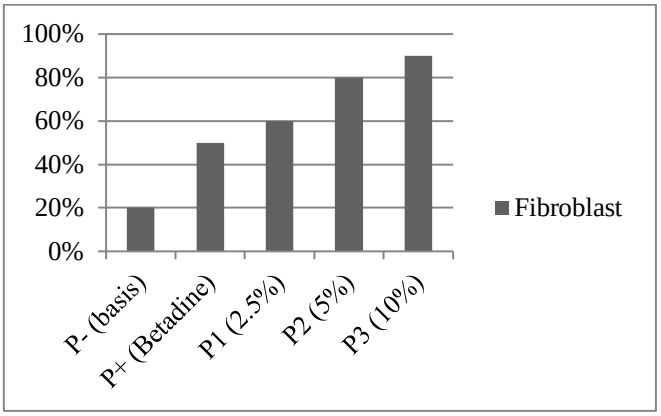


Fig 4. Percentage of Fibroblast Network

From the picture above, it can be seen that the best fibroblast network is in group P3 with a dose of 10% more effective in forming connective tissue on skin that has experienced cuts. While the administration of betadine is not better than the administration of coffee pulp extract cream with a dose of 2.3%. This is also seen in skin collagulation where there is a difference in collagen density between the control group and the treatment group. The following is a graph presented in the difference in skin collagulation of each group:

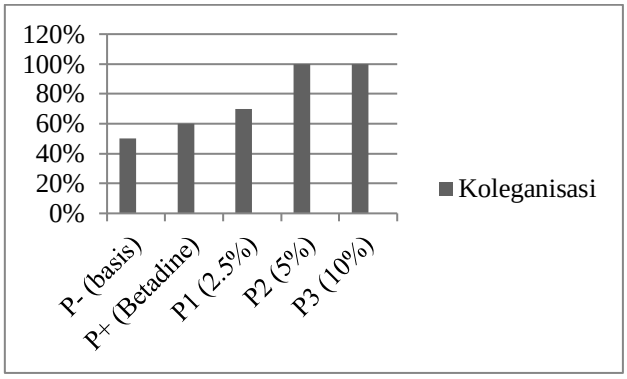


Fig 5. Collagen Density Percentage

The results showed that the control group (P0) which was only smeared with base cream and given distilled water produced very little collagen growth, but there were still several points of needle puncture scars that had not completely closed in the mouse skin tissue, so it received a score of 1 (less than 10%). However, in the group of miceP+ (betadine)showed slightly better results in terms of collagen density in mouse skin, which appeared denser compared to the application of base cream in the P- control group.Meanwhile, treatment group 1 (P1) with the administration of Coffee Pulp extract cream with a concentration of 2.5% showed that collagen and fiber growth was visible and scattered, although not yet dense and thick, the score given was 2, namely (10-50%). And treatment groups 2 and 3 (P2, P3) with the

administration of Coffee Pulp extract cream with a concentration of 5% and 10% obtained an increase in dense collagen fibers so that it was seen to dominate the results and the scoring was 4.

Collagen fibers in the wound area are very dense (90-100%).So thatCoffee Pulp extract is effective in healing cuts in mice with the secondary metabolite content of this extract being useful for skin collagenization that has been cut by sharp objects. This is in line with research(Ulfa Elfiah, 2023)which proves the efficacy of robusta coffee extract on healing burns in mice. In his research, the calculation of wound healing on days 2, 4, 6, 8, 10, 12, and 14. In the sample of mice that had burns and were given robusta coffee extract, the average wound length was 0.889 cm at an initial wound condition of 2 cm x 2.25 cm. The following is a comparison table between rosbuta coffee gel extract and coffee pulp extract cream in healing wounds in mice:

Table 3. Comparison of Rat Wound Healing
In Previous Research

Coffee Pulp Extract Cream		**Robusta Coffee Extract Gel**	
H0	H14	H0	H14
2 cm	0 cm	2 cm	0.889

Judging from the final results of wound healing, coffee pulp extract cream is more effective in accelerating wound healing on mouse skin compared to gel extract. So coffee extract can help the wound healing process on mouse skin. However, this study needs to be further studied by comparing cases and methods of administering similar wounds.

Data analysis

Normality Test

The normality test aims to determine whether the data is normally distributed or not. The normality test in this study uses the Kolmogorov-Smirnov test. The data normality test is important because with normally distributed data, the data is considered to be able to represent the population. If the p value> 0.05 then the data is declared normally distributed and vice versa if the p value <0.05 then the data is declared not normally distributed. The results of the data normality test in this study can be seen in the following table:

Table 4. Normality Test Results

Group	df	*Asymp Sig (2-Tailed)*
P-	14	.964
P+	14	.944
P1	14	.962
P2	14	.965
P3	14	.886

Based on the results of the normality test that has been carried out using the Kolmogorov-Smirnov Test where all test groups that have been measured in 14 days obtained significant results of the control group P- = 0.964, P + = 0.944, Treatment group P1 = 0.962, P2 = 0.965 and P3 = 0.886, the p value> 0.05 is seen. Therefore, it can be concluded that all test groups have normally distributed data.

4.2.2 t Test

The t-test was conducted using one sample t-test, this test was conducted to test the significant effectiveness between the trial groups. The following data was produced:

Table 5. T test

Group	**t**	**df**	**Sig**
P-	10,642	13	.000
P+	9,734	13	.000
P1	6,442	13	.000
P2	4.525	13	.001
P3	3.959	13	.002

From the results of the t-test above, it can be seen that the sig value (2 tailed) for all groups is <0.05, so it is concluded that there is a significant (real) difference between each group.

Discussion

Cuts are a type of wound that occurs due to friction of the skin with a sharp object. These wounds are divided into shallow and deep based on the severity of the wound. Minimizing tissue damage and

providing proper perfusion, oxygenation, and nutrition to the tissue are the main principles of optimal wound healing.(Reddy, 2012). Coffee has many antioxidants, especially polyphenols, which have anti-inflammatory properties. This content helps reduce redness and irritation on the skin and speeds up the healing of minor wounds and acne.However, not only the seeds have benefits, even coffee pulp waste also has good benefits for the skin because it helps exfoliate the skin by cleaning dead skin cells, removing cellulite, reducing dark circles, reducing inflammation, reducing the risk of skin cancer and some studies also discuss the process of healing wounds on the skin. According to Clifford in the study(Wastu Ayu Diamahesa, 2023) Coffee pulp has a relatively high ANF (anti-nutrient) and crude fiber content, and has a low protein and energy content.The phytochemical results in this study prove thatcoffee pulp extract positively contains secondary metabolite compounds, namely saponins, alkaloids, flavonoids and also tannins. Where this compound is a good antioxidant for body health. And also the results of caffeine testing with the HPLC method with the results of caffeine levels in coffee pulp, namely 0.224% and higher than coffee leaves by HPLC andultraviolet spectrophotometry.

Testing withCaffeine concentration was determined using high performance liquid chromatography equipped with a UV detector (HPLC-UV) set at 272 nm and a run time of 6 minutes at a flow rate of 1 mL/min at room temperature. Isocratic solution was used using HPLC grade methanol (100%) with a total run time of 6 minutes. However, caffeine levels are still in the safe category if consumed in moderation.Then the study was continued to compare wound healing between the groups given base cream and betadine with the group given Coffee Pulp extract cream with 3 different concentrations, namely 2.5%, 5%, and 10%. All research samples, namely 20 male rats, were divided into 5 groups, namely the control group P- (base cream) and P + (betadine) and the treatment groups P1, P2 and P3 which were given Coffee Pulp extract cream with 3 different concentrations, namely 10%, 20%, and 30%. This observation was carried out every day for 14 days. All groups (P-, P +, P1, P2 and P3) were given cut wound treatment with an incision of ± 2 cm with a wound depth of up to 0.5 cm in the subcutaneous or hypodermis area. From the results of observations of wound healing that experienced perfect wound closure were in treatment groups 2 and 3, namely 0cm. On the 14th day, groups P0 and P1 did not experience perfect wound closure, namely 0.57 cm and 0.12 cm on the 14th day of observation.In the histopathology results of the skin, the best fibroblast tissue was seen in group P3 with the administration of a 10% coffee pulp extract cream dose which was more effective in forming connective tissue on skin that had experienced cuts.

This was also seen in skin collagenization where there was a difference in collagen density between the control group and the treatment group. It was seen that the control group (P-) which was only smeared with base cream and distilled water produced very little collagen growth, there were still several points of needle puncture wounds that had not closed completely in the rat's skin tissue, so it got a score of 1 (less than 10%). In the control group (P+) which was given betadinewith wound healing results seen to be better with betadine administration compared to just being given a base cream, collagen density is seen to be better and skin tissue formation is tighter. The administration of betadine was seen to be better in the formation of fibroblast tissue and collagen in mouse skin, although not as good as the administration of coffee pulp extract.Meanwhile, treatment group 1 (P1) with the administration of Coffee Pulp extract cream with a concentration of 2.5% showed that collagen and fiber growth was visible and scattered, although not yet dense and thick, and the score given was 2, namely (10-50%). And treatment groups 2 and 3 (P2, P3) with the administration of Coffee Pulp extract cream with a concentration of 5% and 10% obtained an increase in dense collagen fibers so that it was seen to dominate the results and the scoring was 4.Collagen fibers in the wound area are very dense (90-100%).So thatCoffee Pulp extract is effective in healing cuts in mice with the secondary metabolite content of this extract being useful for skin collagenization that has been cut by sharp objects. This is in line with research(Ulfa Elfiah, 2023)which proves the efficacy of robusta coffee extract in opening burn wounds in mice.

IV. CONCLUSION AND SUGGESTIONS

Conclusion

The conclusion of this study is:

1. The caffeine content in coffee pulp using the HPLC method is 0.224% and the secondary metabolite content in the phytochemical test of coffee pulp extract is positive for saponins, alkaloids, flavonoids and tannins.
2. Looking at the comparison of the incision wounds on the 14th day in the control group P- mice that were given base cream and P+ mice that were given betadine and the treatment group P1 that was given 2.5% coffee pulp extract cream did not experience perfect wound closure, namely 0.57c, 0.48 cm and 0.12 cm while the treatment groups P2 and P3 had closed perfectly.
3. A concentration of 10% Coffee Pulp extract was more effective in healing cut wounds in mice with the wound closing completely on the 11th day of observation, followed by a concentration of 5% with the wound closing completely on the 13th day.
4. The administration of Coffee Pulp extract cream with a concentration of 10% and 5% with the best results with a score of 4, namely the collagen fibers in the wound area are very dense (90-100%), while the P0 group scored 1 (less than 10%) with the wound point still visible.

Suggestion

What can be recommended as suggestions from this research are:

1. Further research is needed with concentration levels or extract doses.*coffee pulp* which is higher and better to be used as a treatment preparation material.
2. The research results need to be compared with other research, so that they can become suggestions and references for other researchers who want to research the provision of coffee pulp extractespecially in an effort to accelerate the growth of skin collagen.

REFERENCES

[1] Abdo, JM, Sopko, NA, & Milner, SM (2020) 'The applied anatomy of human skin: ***A model for regeneration', Wound Medicine*** [Preprint].

[2] Alice Erza (2023) Benefits of Coffee Skin: Enjoy the Magic Behind Your Coffee, ***Biotifor***.

[3] Amirlak, B. (2015) 'Skin Anatomy: Overview, Epidermis, Dermis.', ***Medscape***, 7.

[4] Akiria Santi, A., & Sukarni, S. (2023). The Effectiveness Of Using Corsets On Reducing Pain Scale In Post SC Patients At Eka Hospital, South Tangerang In 2022. ***International Journal of Health and Pharmaceutical (IJHP),*** 3(4), 677–682.https://doi.org/10.51601/ijhp.v3i4.225

[5] Laia, O. ., Lestari Nasution, S. ., & Ginting, . J. . (2023). Evaluation Of The Implementation Of Primary Care (P-Care) Application At Puskesmas Onolalu Nias Selatan In 2022. ***International Journal of Health and Pharmaceutical (IJHP)***, 3(4), 629–636.https://doi.org/10.51601/ijhp.v3i4.224

[6] Duha, KB, Lestari Ramadhani Nasution, S. ., Girsang, E. ., & Suyono, T. . (2022). Analysis of Efficiency of KDT-OAT and Removal Preparations on the Recovery of Pulmonary Tuberculosis. ***International Journal of Health and Pharmaceuticals (IJHP)***, 2(2), 284–289.https://doi.org/10.51601/ijhp.v2i2.43

[7] Puspitaloka Mahadewi, E. ., Reza Hilmy, M., Chairun Nisa, P. ., Pamungkas, A. ., Purnama, S. ., Harahap, A. ., & Pantja Djati, S. . (2025). Inequality of Thought (IOT) on HIV-Aids and LGBT Through Social Media: A Case Study of Gen Z in JPC Foundation. ***International Journal of Health and Pharmaceutical (IJHP)***, 5(1), 26–30.https://doi.org/10.51601/ijhp.v5i1.401

[8] Rachmi Yuana, S., Girsang, E., & Ginting, . L. . (2023). Analysis Of The Influence Of Leader Behavior And Public Health Center Management Processes On Immunization Program Performance At Kuala Bali Public Health Center, Serdang Bedagai. ***International Journal of Health and Pharmacy (IJHP)***, 3(4), 594–601.https://doi.org/10.51601/ijhp.v3i4.211

[9] Noni Rokaya Pasaribu, Ermi Girsang, Sri Lestari Ramadhani Nasution, & Chrismis Novalinda Ginting. (2022). Evaluation of Planning and Implementation of Occupational Safety and Health in Embung Fatimah Hospital, Batam in 2021. ***International Journal of Health and Pharmaceutical (IJHP),*** 2(2), 225–232.https://doi.org/10.51601/ijhp.v2i2.34

[10] Dewi Septiningtyas Hastuti (2018) 'Caffeine Content in Coffee and Its Effects on the Body', Chemistry, Faculty of Administrative Sciences, Sepuluh Nopember Institute of Technology [Preprint].

[11] dr valda Gracia (2022) Skin Function, ***Klikdokter.***

[12] Dwi Ratih Ramadhany (2023) Not Only Eliminates Sleepiness, Here Are 7 Other Benefits of Coffee for the Body, Hallosehat. Available at: https://hellosehat.com/nutrisi/fakta-gizi/manfaat-kopi/.

[13] Harahap, et, all, Macrozoobenthos diversity as an bioindicator of the water quality in the Sungai Kualuh

Labuhanbatu Utara, ***AACL Bioflux***, 2022, Vol 15, Issue 6.

[14] Harahap, A. 2020. Species Composition & Ecology Index Of The Family Gobiidae At The Mangrove Belawan Of Sicanang Island ***International Journal of Scientific & Technology Research*** Volume 9, Issue 04, April 2020.

[15] Harahap, A., et all (2021), Monitoring Of Macroinvertebrates Along Streams Of Bilah River International ***Journal of Conservation Science this link is disabled***, 12(1), pp. 247–258.

[16] Fadhilah, H., Sari, FP, & Febriza, S. (2022) 'Literature Study of the Effectiveness of Plants in Healing Cut Wounds', ***Edu Masda Journal,*** 6(1), pp. 1–9.

[17] Farahani, M., & Shafiee, A. (2011) 'Wound Healing: From Passive to Smart Dressings', Advanced Healthcare Materials, 10(6).

[18] FR (2022) HPLC – Definition, Function, Principles and Uses, analisa.co.id. Available at: https://analitika.co.id/hplc/.

[19] Girsang, LC, Fachrial, E. and Lister, INE (2020) 'Effectiveness Test of Robusta Coffee (Coffea cenephora) Extract from North Sumatra in Collagen and Hydration Skin Level of Female Wistar Rattus norvegicus', ***American Scientific Research Journal for Engineering Technology and Sciences (ASRJETS),*** 65,pp.108–115.

[20] Kartika, RW (2015) 'Chronic Wound Care with Modern Dressings', Mirror of the World of Medicine - ***Kalbe Farma***, 42(7), pp. 546–550.

[21] Kastika, SM, & Rahayu, R. (2018) 'Bioprospects', 13(1), pp. 26-32.

[22] Kawulusan, FR, Sonny, JRK, Martha, M.. (2015) 'Description of Antemortem Wound Inflammation Reaction Examined 1 Hour Postmortem in Experimental Animals. Faculty of Medicine. ***Manado', J. E-Biomed,*** 2(1), pp. 393–397.

[23] Kevin Adrian (2021) 6 Functions of Skin and How to Maintain Its Health, Alodokter. Available at: https://www.alodokter.com/5-fungsi-kulit-dan-cara-menjaga-kesehatannya.

[24] Marks, James G; Miller, J. (2006) 'Lookingbill and Marks' Principles of Dermatology.', Elsevier Inc, 4.

[25] Panggabean E (2011) ***Smart coffee book***. Jakarta: Agromedia Pustaka.

[26] Paramita, A. (2016) The Effect of Breadfruit Leaf Extract (Artocarpus altilis) on Collagen Density.

[27] *Picture of the Skin*(2021) WebMD.

[28] Pradipta, I.. (2010) The Effect of Topical Propolis Administration on Polymorphonuclear Cell Migration in Rat Cut Wounds, Faculty of Medicine. University of Jember.

[29] Reddy, GAK, Priyanka, B., S., Ch.S. and Kumar, C.K. (2012) 'Wound Healing Potential Of Indian Medicinal Plants', ***International Journal Of Pharmacy Reviews & Research***, 2, pp. 75–78.

[30] regitha claudia, sri wahyuni, ali napiah, wahyu widowati, faradhina, H. (2024) 'Antioxidant Potential Of Temulawak (Curcuma Xanthorrhiza) Extract Gel As A Candidate For Wound Healing', J***ournal Of Vocational Health Studies,*** 7(3), pp. 166–174.

[31] Rita Elfianis SP M.Sc (2022) Classification and Morphology of Coffee Plants, Agrotek.id.

[32] Rizka, A., and SBV (2013) 'Density of type 1 collagen in surgical wounds of Wistar rats experiencing anemia due to acute bleeding. .', ***Media Journal Of Emergency,*** 1(2), pp. 1–12.

[33] Schweinfurth, MK (2020) 'The social life of Norway rats (Rattus norvegicus).', eLife. 9, 4.

[34] Staff, MC (2014) Diabetes tests and diagnosis, mayoclinic.org.

[35] Sukmawati, SS, Siwi, H., & SR (2021) 'Activity Test of Ethanol Extract of Cassava Leaves (Manihot esculenta Crantz) on Wound Healing in Rabbits', ***IJMS***, 8(2).

[36] Ulfa Elfiah, Maidy Frista Rosanti, Fatimatuzzahra Fatimatuzzahra, MAH (2023) 'The Effect of Giving Robusta Coffee Extract Gel (Coffea canephora) on Macroscopic and Microscopic Images of Second Degree Burns in Long Evans Rats', ***JPSCR-Journal of Pharmaceutical Science and Clinical Research***, 8(2).

[37] Wastu Ayu Diamahesa, NM (2023) 'Utilization of Coffee Pulp Waste in Fisheries Cultivation (Review)', ***Journal Of Fish Nutrition,*** 3(1).

[38] Wintoko, R., & Yadika, AD. (2020) Current Management of Wound Care. ***JK Unila.***

[39] Y, N. (2017) Coffee: Cultivation and Handling After Harvest. Jakarta: ***Penebar Swadaya***.

[40] Yorinta Putri Kenisa, Iistiati, and WSJ (2012) 'Effect of Robusta coffee beans ointment on full thickness wound healing', ***Dental Journal***, 45(1).

[41] Yousef H, Alhajj M, SSA (2023) Skin (Integument), Epidermis, StatPearls Publishing. ***Treasure Island (FL).***