Effect Of Moringa Flower Extract (Moringa Oleifera) On Collagenization And Histopathology Of Skin Tissue In The Healing Of Dermapen Scars In Obese Male Wistar White Rats

Dian Soraya Tanjung[1*], Rachmi Kurniawati[2], Tri Adi Mylano[3]

[1,2,3] Master Study Program in Biomedical Sciences, Faculty of Medicine, Dentistry and Health Sciences, Prima Indonesia University, Medan, Indonesia
[*] Corresponding Author:
Email: diansorayatanjung@yahoo.co.id

Abstract.

Injury can be accidental, intentional, or disease-related. Moringa leaves may help heal wounds. The research aims to test and assess the effects of Moringa oleifera flower extract on dermapen wound healing collagenization in male Wistar strain white rats, an obese model, and their histological findings—quantitative True Experimental Study with Post-Test Only Control Group Design. Twenty-four male Wistar white rats (Rattus norvegicus) were sampled. Accumulation of Test Animals, Moringa Flower Extract Preparation, Phytochemical Screening / Secondary Metabolite Test, Treatment Process (200, 400, and mg/kgBW of Moringa flower extract),Wound Observation, Histopathological Skin Preparations, and Histopathological Examination of Preparations were the research procedures. Window data was analyzed using SPSS 25.0 and One Way ANOVA with a 95% confidence level ($p < 0.05$). The Post Hoc Test with LSD was used for further analysis. The research results found Moringa flower extract at 200mg/Kg BW, 400mg/KgBW, and 600mg/KgBW could expedite wound healing and improve collagen density in obese mice's dermapen wounds. The 600mg dose was most beneficial. Research conclusions: Moringa flower extract aids dermapen wound healing, collagenization, and obesity weight loss, according to a study.

Keywords: *Moringa Flower, Collagenization, Wound Healing, Skin Injury and Obesity.*

I. INTRODUCTION

The skin is a protective covering for every part of the body. Like a stronghold, the skin of a person shields its internal organs from the outside world [1]. In addition to regulating temperature, shielding the body from harmful chemicals and viruses, initiating vitamin D synthesis, and controlling excretion, the skin is an important organ for many other reasons [2]. The importance of this organ makes skin damage potentially lethal [3].Wounds are one kind of skin injury. Physical contact, medical procedures, or physiological changes can all lead to wounds, disturbing the body's standard anatomical function structure. Bites, accidents, and lacerations from sharp objects are the most common causes of animal wounds [4]. Skin, mucous membranes, and organ tissues are all vulnerable to harm when they sustain wounds. To prevent infection and additional damage, it is crucial to clean and treat wounds properly after suffering trauma [5].Injuries can manifest as superficial tears in the skin's epithelial layer or as more extensive perforations that go deeper into the subcutaneous tissue, compromising underlying tissues such as muscles, tendons, blood vessels, nerves, parenchymal organs, and bones. Accidental or purposeful causes, as well as disease processes, can lead to wounds. Regardless of origin or shape, wounds harm tissues and disturb their immediate surroundings [6].Severe perforations can compromise underlying structures, including bones, muscles, tendons, blood vessels, nerves, parenchymal organs, and the epithelial layer of the skin, while more superficial rips can compromise the epithelial layer of the skin. Wounds can result from either accidental or intentional causes, as well as from the progression of diseases.

Wounds cause damage to tissues and disruption to their immediate environment, regardless of their cause or form [6].Open and closed wounds are classified according to the origin of the wound. Open wounds and closed wounds are the two primary categories of wounds. The skin is pierced, exposing the underlying tissue to the outside world; this creates an opening through which blood can drain from the body. This type of wound occurs when the outer layer of tissue, like skin, is peeled off. Invasion by microbes is possible

since the wound is open [7]. Many other types of wounds can be considered available, such as cuts, lacerations, punctures, avulsions, abrasions, penetrations, and incisions. Closed wounds do not disclose the underlying tissue to the outside world while keeping the skin intact. You won't lose the outer layer that covers the wound. There is no outward bleeding since the incision is located under the skin's surface and does not impact the skin. Rare infections of this kind often resolve independently if they do not spread. Examples of closed wounds include bruises, contusions, hematomas, and crush injuries [8].The wound-healing response is the skin's innate process of quickly and efficiently repairing itself after an injury [9]. Damage triggers the body's natural healing response. Restoration of the epithelial layer, damaged tissue healing, and missing tissue replacement co-occur. Inflammation, cell migration, and angiogenesis are supported by keratinocytes, fibroblasts, immune cells, and vascular endothelial cells [10].

The wound-healing response is the skin's innate process of quickly and efficiently repairing itself after an injury [9]. Damage triggers the body's natural healing response. Restoration of the epithelial layer, damaged tissue healing, and missing tissue replacement co-occur. Inflammation, cell migration, and angiogenesis are supported by keratinocytes, fibroblasts, immune cells, and vascular endothelial cells [10]. In perfect healing, the injured area's structure, function, and appearance all return to pre-injury levels. In less-than-ideal healing, the area's structure and function are restored, but there is no lasting improvement in function. Thus, the wound might reopen. Restoring sustained functional and anatomical continuity characterizes a healable wound that falls somewhere between these extremes [3].Impairments in the wound-healing process can occur for various reasons, including but not limited to infection, pollution, age, stress, oxygen, diet, medicine, sex hormones, obesity, diabetes, and venous or arterial disease [11]. The healing process of wounds can be slowed or even halted by obesity.When fat stores in the body become excessive, a condition known as obesity develops [12]. Excess caloric intake over energy expenditure leads to obesity [13]. Excess adipose tissue is a hallmark of obesity. Brown and white adipose tissue are the two types of adipose tissue found in humans; the former is involved in thermogenesis, while the latter stores fat. Nevertheless, there is evidence that brown adipocytes can emerge in white adipocytes in reaction to certain thermogenic stimuli. This suggests that the brown-white divide is more fluid than previously thought and casts doubt on the static categorization of adipose tissue subtypes [11].Physiologic wound healing can be significantly impaired due to the various inherent dangers associated with obesity. One example is the correlation between obesity and venous insufficiency, the leading cause of persistent ulcers. Delays in wound healing can be caused by venous stasis, which alters capillary flow due to reduced hydrostatic pressure [14].

Chronic ulcers can also be caused by peripheral vascular disease (PAD). Arterial ulcers, caused by tissue ischemia, can form in patients with peripheral artery disease because the condition reduces the flow of oxygen and nutrients necessary for tissue healing. One of the main reasons people with diabetes develop chronic wounds is neuropathy, which is also a prevalent cause of skin ulcers [15].Prevention measures should be prioritized because obesity is a risk factor for several fatal illnesses. Weight management and improving physical fitness are two of the most important preventative measures against obesity. Maintain a healthy weight by eating well and exercising regularly. Losing weight is possible with a healthy lifestyle that includes a more active lifestyle and a balanced diet. Normalizing weight and warding off metabolic diseases common among the overweight and obese are both facilitated by regular physical exercise [16].A wide variety of wound care drugs are commercially accessible. Nevertheless, there are certain drawbacks, such as the expensive price tag. While certain wound-healing medications may promote healing, most only act as anti-infective agents. Additionally, in contrast to natural remedies, the majority of these pharmaceuticals come with a laundry list of unwanted side effects. Further, the potential for natural medicinal uses and the ease of obtaining them from natural sources contribute to the widespread preference for genuine goods. For this reason, natural remedies have great promise as wound-healing agents [11].Plants and other natural resources are the basis for active pharmaceutical medications because of their abundance of bioactive components.

Wild plants and trees have supplied the resources needed to fulfill the need, whether for food or medicinal purposes, for various illnesses, as traditional remedies are costly and accessibility is a big issue, particularly in nations with significant rural populations [17]. Because they don't have any adverse side

effects, medicinal plants in their pure chemical or extract form are likewise much sought after [10]. The Moringa tree is one example of a plant whose components have medicinal uses (Moringa oleifera).Moringa, a plant native to Africa and Asia and the most widely cultivated species in Northwest India is the only genus in the Moringaceae family. The plant consists of 13 species from tropical and subtropical climates, ranging from tiny herbs to large trees. The most widely cultivated species is the Moringa oleifera. Moringa is widely grown for its nutritious pods, edible leaves, and flowers and can be utilized as food, medicine, cosmetic oil, or animal feed [18]. When underlying chronic diseases like inflammation, infection, or diabetes are present, moringa is historically utilized to promote nutritional health [19]. The phytochemical components of the plant are responsible for the majority of its many actions and health advantages, which it exhibits via its pharmacological activities. Potassium, calcium, phosphorus, iron, vitamins A and D, vital amino acids, carbs, and powerful antioxidant chemicals like ß-carotene, vitamin C, and flavonoids are abundant in this plant, according to phytochemical research [20].Given this finding, scientists are keen to examine the effects of Moringa oleifera flower extract on dermapen scar healing in male Wistar rats, a kind of white rodent, by measuring collagenization and histological description of skin tissue.

II. METHODS

This study is an actual experiment. Genuine experiment findings are obtained by controlling all extraneous influences[21]. This study's post-intervention control group design involved watching the control and treatment groups alone [22]. This study examined how Moringa oleifera flower extract affected dermapen wound healing and histological results of obese white rat skin tissue (*Rattus norvegicus*).This study uses Moringa oleifera flower extract as the independent variable and the Dermapen wound healing process and histopathological image as the dependent factors. As a prerequisite, rats had dermapen wounds on their backs and were fed a high-fat diet to induce obesity. The term "dependent variable" describes a situation in which one variable affects or causes another to exist. An independent variable is directly or indirectly related whenever a dependent variable is studied.

Anything that may be seen to alter throughout the study topics is considered a variable [23].A three-day maceration in ethanol is performed on the Moringa flower extract (*Moringa oleifera*). Medan farmers gather Moringa oleifera blooms. For 14 days, the experimental animals were given an oral ethanol extract of Moringa oleifera flowers. Wound length, healing time, and skin tissue recovery following moringa flower extract therapy are the incision wound healing metrics used to evaluate rat skin tissue recovery. It was shown that feeding Wistar male rats (Rattus novergicus) duck egg yolk with high cholesterol caused them to gain weight [24].Subsequently, SPSS 25.0 for Windows was utilized for study analysis. We checked for data normality using the Kolmogorov-Smirnov test strategy ($p > 0.05$). A one-way analysis of variance, also known as a one-way ANOVA, was carried out at a 95 percent confidence level ($p < 0.05$) to examine the significance between the test groups. The post hoc test using the LSD approach was used for further analysis or testing [25].

III. RESULTS AND DISCUSSION

Research Result

Following a high-fat diet, rats develop obesity with a Lee index of 0.33. Rats lost weight and had decreased Lee index values after ingesting Moringa flower extract (Moringa oleifera) at 200, 400, and 600 mg/kg. The distilled water-only control group had a Lee index of 0.32. It's still obese because it's above 0.3. With a Lee index of <0.3, rats treated with Moringa flower extract (Moringa oleifera) are not considered obese. Rats fell to 0.28 in treatment groups 1 and 2, which received 200 mg/kg and 400 mg/kg dosages. With 600 mg/kg moringa flower extract (Moringa oleifera) in treatment group 3, the Lee index dropped the most, 0.27. Researchers found moringa flower extract (Moringa oleifera) influences obese mice's weight.

Table 1. Rat Body Weight

Parameter	Group	Average	
		After a high-fat diet	After 14 days of administration of Moringa Flower Extract
Body Weight (gr)	Control	318gr	309gr
	P1	320gr	262gr
	P2	321gr	259gr
	P3	318gr	247gr
Naso-anal Length (mm)	Control	204mm	209mm
	P1	201mm	226mm
	P2	203mm	227mm
	P3	203mm	225mm
Index Lee	Control	0.33	0.32
	P1	0.34	0.28
	P2	0.33	0.28
	P3	0.33	0.27

According to the findings in all groups, there appears to be a dermapen scar healing process in white rats (Rattus norvegicus) Wistar strain. The average healing % varies among all populations. The control group had a dermapen wound healing percentage of 58.4% on the last day, whereas treatment groups 1 and 2 had 83.6%, 88.6%, and 100%, respectively. Because of this, we may say that group 3's healing rate is higher than that of the control, group 1, and group 2.

Table 2. Average Wound Healing Percentage (%)

Day	Average Wound Healing Percentage (%)			
	Control	P1	P2	P3
1	0	0	0	0
2	2.5	3.6	3.4	4
3	3.8	5.5	5.7	6.5
4	6.2	8.8	9.8	11.2
5	11.6	18.3	26.1	36.6
6	17.9	29.9	38.9	43.8
7	28.4	44.5	46	52.9
8	34.2	54.4	51.8	61.7
9	39.7	59.4	62.7	72
10	44.4	66.2	68.9	78
11	49.2	72.4	72.8	82.6
12	53.2	78	82.6	89.4
13	56.3	80.8	85.7	95.7
14	58.4	83.6	88.6	100

Results from phytochemical analyses of Moringa flower extract showed the presence of steroids, alkaloids, tannins, saponins, and flavonoids [26]. The presence of flavonoids was confirmed by flavonoid testing, and the existence of a red extract was confirmed by saponin testing. Catechol tannin was detected by tannin testing, while alkaloids were detected by alkaloid testing. A positive result from the steroid test was obtained. Previous research used phytochemical analysis to corroborate the presence of flavonoids, saponins, tannins, alkaloids, and steroids in the Moringa flower extract [27]. These chemicals are also found in extracts of moringa leaves and flowers.

Table 3. Phytochemical Test

Secondary Metabolite	Color	Results
Flavonoid	Red	+
Saponin	Yellow and effervescent	+
Tannin	Blue-black	+
Alkaloid	Yellow	+
Steroid	Green	+

We found a significance level of 0.200 across the board after running the Kolmogorov-Smirnov test to ensure normalcy. A p-value greater than 0.05 indicates that the data follows a normal distribution. The data is thus assumed to follow a normal distribution. Once we know the data follows a normal distribution, we can continue checking for homogeneity by using the Levene test for each subset of our study population to see whether they're all the same.

Table 4. Normality Test Results

	Group	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Results	Control	.121	6	.200*	.983	6	.964
	P1	.202	6	.200*	.853	6	.167
	P2	.252	6	.200*	.916	6	.480
	P3	.238	6	.200*	.950	6	.737

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

The table below displays the results of the Levene test for homogeneity. There is a significance column value of 0.331 for the probability. We may conclude that the control group, treatment group-1, treatment group-2, and treatment group-3 come from populations with the same variance or that the groups are homogenous because the resulting significance probability value is more significant than 0.05.

Table 5. Homogeneity Test Results

		Levene Statistic	df1	df2	Sig.
Results	Based on Mean	1.212	3	20	.331
	Based on Median	.946	3	20	.437
	Based on the Median and with adjusted df	.946	3	16.609	.441
	Based on trimmed mean	1.196	3	20	.337

The significant value of the one-way ANOVA test is 0.000, which is less than 0.05, as seen in the table above. These results suggest that the treatment group differs significantly from the control group. On average, the difference in LDL levels between the groups was examined using a post hoc LSD further test. See the following table for the post-hoc LSD additional test results: table 6.Finding out if groups are significantly different from each other is done using the post hoc LSD test. In this study, the post hoc LSD test analysis revealed a significance value of 0.000, which is less than 0.05. This indicates that the group in question differs significantly from the other groups.

Table 6. One-Way ANOVA Test Results

	Total	df	Mean square	F	Sig
Between Groups	.721	3	.240	828.716	.000
In Group	.006	20	.000		
Total	.727	23			

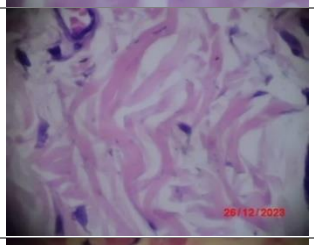
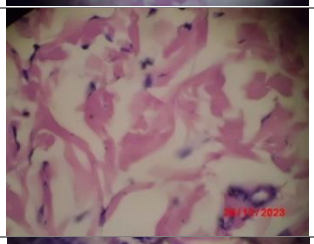
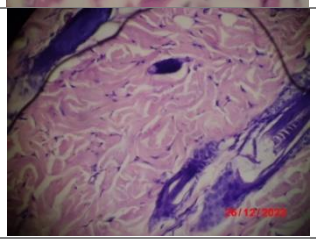
Table 7. LSD Post-Hoc Test Results

(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Control	P1	.28333*	.00983	.000	.2628	.3038
	P2	.33667*	.00983	.000	.3162	.3572
	P3	.47667*	.00983	.000	.4562	.4972
P1	Control	-.28333*	.00983	.000	-.3038	-.2628
	P2	.05333*	.00983	.000	.0328	.0738
	P3	.19333*	.00983	.000	.1728	.2138
P2	Control	-.33667*	.00983	.000	-.3572	-.3162
	P1	-.05333*	.00983	.000	-.0738	-.0328
	P3	.14000*	.00983	.000	.1195	.1605
P3	Control	-.47667*	.00983	.000	-.4972	-.4562
	P1	-.19333*	.00983	.000	-.2138	-.1728
	P2	-.14000*	.00983	.000	-.1605	-.1195

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

The experiment used dermapen wound samples treated with distilled water and Moringa flower extract at 200 mg/kg, 400 mg/kg, and 600 mg/kg to analyze cell shape and structure, specifically collagen density. Because it gives tissues their structure and strength, collagen is essential for wound healing [28]. If it can control collagen production, extract from moringa flowers might be a substitute for anti-inflammatory, antioxidant, and antibacterial activities [29]. Complete collagen filling in tissues of varying densities was observed in the treatment group, according to the data. In contrast, the histology of fat white rats revealed a density of collagen produced.

Fig 1. Histopathology Results

No	Group	Histopathologic features of skin tissue	
1	Control (Aquades)		
2	Treatment 1 (200mg/KgBW)		
3	Treatment 2 (400mg/KgBW)		
4	Treatment 3 (600mg/KgBW)		

Research Discussion

In this experiment, researchers used a male Wistar strain obesity model to examine how well an extract from moringa flowers accelerated the healing of dermapen wounds in white rats. Each of the four rats received a different dosage of moringa flower extract; the fourth group served as a control and received distilled water.As said before, the skin acts as a protective barrier, isolating the body from the elements. Skin injury can be fatal because this organ is vital [3]. Wounds are one kind of skin injury. Damage to the body's anatomical function structure can occur due to physical contact, medicinal operations, or physiological changes, known as a wound [4]. Reducing the risk of infection and further harm requires careful attention to wound care [5].As part of its normal wound healing response, the skin creates new, more effective mechanisms to seal off any spaces between its protective outer layer and the wound [9]-[30]. The keratinocytes, fibroblasts, vascular endothelial cells, and immune cells that make up the healing process begin to work once damage has occurred. This process includes repairing and replacing damaged tissue and restoring the epithelial layer [10].Chronic wounds that don't heal can be caused by several causes, including infection, age, stress, diet, drugs, sex hormones, obesity, diabetes, and venous or arterial disease [11]. When a person's caloric intake is higher than their energy expenditure, a condition known as obesity can impede wound healing [13]. Natural items can treat wound issues caused by obesity with few adverse effects.Wound healing in obese people is best accomplished with natural ingredients due to their ease of extraction and great potential as natural remedies [11].

The absence of side effects makes processed medicinal plants highly sought after, whether pure components or extracts [31]. The diverse characteristics of the moringa tree make it a popular plant for both culinary and medicinal purposes; the tree's pods, leaves, and flowers are all edible [18]. The possible wound-healing effects of moringa flower extract were studied in experiments using obese white rats. According to the Lee index, the research proved that the animals were made obese by feeding them a high-fat diet. Ketamine and xylazine were used to execute dermapen wounding after the diet to numb the patient and stop

any excessive movement. All scars were compressed using the dermapen instrument, which had a bleeding tip at its end [32].Data collected over 14 days necessitated testing for homogeneity, relevance, and normalcy. With a significance level of 0.200 across all test groups, the data followed a normal distribution, suggesting that it accurately represents the population. The Levene test was used to test the homogeneity of the normally distributed data, revealing that the control group, treatment group 1, and treatment group 3 are homogeneous or from the same population, and their effectiveness and significance were also assessed.The significance value of 0.000, which is more than 0.05, is shown by the results of the one-way ANOVA test. These results suggest a statistically significant difference between the three groups (control, treatment 1, and treatment 2), necessitating further post hoc LSD testing. To examine the average difference in total cholesterol levels across groups, a post hoc LSD test was used. The significance value of the Post Hoc LSD test analysis in this study was 0.000, which is smaller than 0.05.

This indicates that there are significant differences between all of the groups.To determine if the rats were obese, the researchers used data on their body weight and nasal length to establish the Lee index value. We may conclude that rats are obese because after being fed a high-fat diet, every single one of the test animals had a Lee Index score of 0.33 or higher than 0.3. On the final day of the experiment, researchers recalculated the rats' Lee Index values and discovered that they had lost weight. The result for the control group was 0.32, which is still higher than 0.3. This Lee index score confirms that the control group of test animals is still classified as obese.Treatment groups 1, 2, and 3 show decreased body weight in test animals, attributed to flavonoid content in Moringa flower extract, reducing obesity, as indicated by Lee Index values below 0.3 [33]. The study found that treatment group 3 had a higher rate of dermapen wound healing than the control group, treatment 1, and treatment 2. Collagen retention in treated skin tissue, crucial in wound healing, proliferation, remodeling, and intracellular matrix formation, was also observed [34]. The study reveals differences in collagen density between the control group and those treated with Moringa oleifera flower extract. The control group had thin collagen growth due to inflammatory skin tissue. Treatment groups 1, 2, and 3 showed higher collagen density, with treatment group 3 having the highest density.Moringa flower extract contains secondary metabolites such as tannins, alkaloids, saponins, and flavonoids, which transport free radicals from dermapen wounds and obesity-related disorders [35]. These metabolites speed up the healing process, collagenization, and weight reduction. [36], who found that tannins, saponins, alkaloids, and flavonoids can hinder oxidative stress and boost antioxidant activity, which speeds up wound healing and aids weight loss.

IV. CONCLUSION

In obese Wistar rats (Rattus norvegicus), the healing process of dermapen wounds may be seen for 14 days after administration of moringa flower extract (Moringa oleifera) at dosages of 200 mg/kg, 400 mg/kg, and 600 mg/kg, respectively.Compared to the group that received moringa flower extract, the control group exhibited the most extended wound length (Moringa oleifera). According to the results of the histological examination of skin tissue, collagen density was different in the treatment group compared to the control group. The collagen density was most significant in the third treatment group, which received 600 mg/kg BB of moringa flower extract. Obese rats' dermapen wounds can heal faster and have more collagen density when given Moringa flower extract at 200, 400, and 600 mg/kg BB, with 600 mg/kg BB showing the most significant improvement.Flavonoids, saponins, tannins, alkaloids, and steroids are some secondary metabolite compounds in moringa flower extract. These compounds have anti-inflammatory, antioxidant, and antimicrobial properties; they also aid in the healing of dermal wounds, the formation of collagen, and the reduction of obesity in mice.

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