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Effectiveness of vaseline ointment ethanol extract of moringa leaf (*moringa oleifera*) on incision wound healing

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ABSTRACT

Introduction: Wounds are damage or loss of connections between body tissues such as skin tissue which can lead to infection. Wound healing is a complex process because it goes through the phases of inflammation, proliferation, and remodeling. The purpose of this study was to determine the effectiveness of Moringa leaves (Moringa oleifera) in healing cuts by observing erythema, edema and the presence or absence of new tissue that appears for 7 days.

Methods: This study was purely experimental, using 30 male white mices (Mus Musculus) which were divided into 5 treatment groups, namely control groups of vaseline (K-), gentamicin (K+), and 3 treatment groups of Moringa leaf extract ointment with a concentration of 6% (PI), 8% (PII) and 10% (PIII).

Results: The results showed that the withdrawal of the number of mice with erythema was faster in the 10% (PIII) and 8% (PII) groups. The results of the Mann Whitney test on granulation tissue showed that the 8% (PII) and positive control groups, and the 10% (PIII) and positive control groups had no significant difference with the same p value, namely $p = 0.513$ ($p > 0.05$) The results of the Kruskal-Wallis test on the most significant edema on day 3 with $p = 0.001$ ($p \leq 0.05$).

Conclusion: The conclusion that can be drawn from this study is that the higher the concentration of vaseline ointment of the ethanol extract of Moringa oleifera leaves (Moringa oleifera) was found to have better effectiveness in accelerating wound healing, especially at concentrations of 8% and 10%.

Keywords: Incision Wound, Moringa Oleifera, Wound Healing, Erythema, Edema.
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INTRODUCTION

Wounds are damage or loss of connections between body tissues such as skin tissue, muscle tissue, soft tissue or other tissues due to physical, mechanical, chemical and thermal violence which can result in infection or complications.[1] Based on the shape of the wound, it is divided into closed and open wounds, one example of an open wound is an incision or cut.[2,3] Incision wounds often occur in everyday life. An incision wound is a trauma caused by an incision with a sharp object.[5] Wound healing is a complex process because it goes through the phases of inflammation, proliferation, and remodeling.

Treatment of inflammation generally uses Nonsteroidal Anti-Inflammatory Drugs (NSAIDS) which work by inhibiting the action of the cyclooxygenase enzyme, so that the production of inflammatory mediators such as prostaglandins decreases. However, prolonged use of NSAIDs can cause several complications such as increased blood pressure, impaired kidney function, gastrointestinal bleeding, and accumulation of fluid in a tissue.[5,6] Therefore, there is a need for alternative anti-inflammatory drugs with less side effects.

Indonesia is a country with vast tropical forests along with invaluable biodiversity. Currently around 9,600 species are known to have medicinal properties, but only 4% of this number have been cultivated and used in the traditional medicine industry. Herbal medicines are medicines made from natural ingredients which contain active substances for treatment. In general, herbal medicines do not cause serious side effects and are classified as safe for drug use. Various plants can be used as herbal medicines because they contain certain chemical compounds that have pharmacological effects to help cure a disease.[7] Moringa oleifera is one of the plants in Indonesia that can be utilized as herbal medicine. Several studies have proven the benefits of this plant, including as an anti-hypertensive, anti-oxidant, analgesic, and anti-inflammatory.[8]

Moringa oleifera contains phytochemical components including flavonoids, polyphenols, saponins, amino acids arginine, glutamine, vitamins A, C, and K which have the potential to be alternative anti-inflammatory drugs. Arginine is a semi-essential amino acid which helps the body to build protein and has the power to heal wounds by depositing collagen. Meanwhile, glutamine is the most abundant non-essential amino acid in plasma and has a role in the wound healing process by regulating leukocyte apoptosis and assisting the phagocytosis

process.[9] From the previous research, plants containing flavonoid compounds have activity in anti-inflammatory processes by inhibiting the COX-2 enzyme.[10] This study aims to find out the effectivity of vaseline ointment ethanol extract of moringa leaf (moringa oleifera) on incision wound healing.

METHODS

This study was a pure experimental, using a one way completely randomized design (CRD) using 30 male white mices (Mus Musculus) BALB/c strain aged 10 weeks, weighing 20-25 grams. The treatments can be seen in Table 1 below.

Animal Study Model

The animal models used in this study were 30 mice with a body weight of 20-25 grams. Prior to the intervention, the mice were acclimatized for 7 days to adapt to the new environment. According to the number of sample groups, there are 5 cages measuring 50x40 cm made of plastic, the mice will be placed separately based on each treatment. Mice were maintained with the same humidity, the same temperature, and did not change. All test animals kept were given ad libitum mice feed and water. After the experiment, the mice will be destroyed by incineration.

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Moringa Leaf Ointment

This study used the maceration method. This method is carried out by immersing crushed dry samples in a solvent at room temperature. Moringa leaves (*Moringa oleifera*) are dried without direct sunlight. Dried Moringa leaves are blended to make it easier to extract. After that, the extract powder was macerated using 70% alcohol as a solvent and left for the first 6 hours, shaken occasionally, then left for 18 hours. The remaining dregs then going through the 2nd maceration for 1x24 hours. After 2 days, the results of the first and second maceration were collected and then processed using a vacuum rotary evaporator at 40°C to obtain a thick extract of Moringa leaves.

The extract is mixed with heated Vaseline. The composition of the vaseline ointment of Moringa leaf extract can be seen in Table 2 below.

Table 1. Kinds of treatment

Treatment	Description	Number of repetitions
K- (Negative control)	Mice were incised and treated with Vaseline ointment	5
K+ (Positive Control)	Mice were incised and treated with gentamicin	5
PI (Treatment I)	Mice were incised and treated with moringa leaf extract with a concentration of 6%	5
PII (Treatment II)	Mice were incised and treated with moringa leaf extract with a concentration of 8%	5
PIII (Treatment III)	Mice were incised and treated with moringa leaf extract with a concentration of 10%	5

Table 2. Moringa (*Moringa oleifera*) leaf extract Vaseline ointment formula

Material	Ingridient (gram)		
	6%	8%	10%
Moringa leaf extract	1,2	1,6	2
Vaselin	18,8	18,4	18

Table 3. Organoleptic test, homogenity test, pH analysis, spreadability test, and stickiness test of moringa leaf extract ointment

Indicator	PI	PII	PIII
Form	Semi-solid		
Color	Brownish yellow		
Smell	Typical smell of Moringa leaf extract		
Homogeneity	Homogenous		
pH	6		
Spreadability			
The glass lid (51.5 g) stands for 1 minute	3,2 cm	2,9 cm	3 cm
+100 g stands for 1 minute	3,7 cm	3,7 cm	4 cm
Stickiness	5,71 s	2,80 s	2,63 s

The quality of the ointment that has been made then being analyzed. Examination of the physical properties of the ointment was carried out including organoleptic tests, homogeneity tests, pH analysis, spreadability tests.[11]

Expertimental Phase

30 mice were divided into 5 groups, each group consisting of 6 mice. Each group is called the K-, K+, PI, PII, PIII group according to the research matrix. Mice are placed in individual cages measuring 50x40 cm and given ad libitum mice feed. The back region of the mice was incised with a scalpel, 1 cm long and a depth of up to the dermis which was marked by bleeding. The incision wound on the back of the mice was smeared with Vaseline ointment, gentamicin ointment and Moringa leaf extract ointment, according to the study matrix. The treatment is given twice a day in the morning and evening at 08.00 WITA and 17.00 WITA. Observation of the injury degree was carried out for 7 days by documenting it using a digital camera. The indicators of healed wound are dry wound, covered with new tissue, no erythema, and swelling.

Data Analysis

Data analysis would be performed using the SPSS (Statistical Package for the Social Science) digital data processing program version 26, and will be analyzed descriptively in tabular form.

RESULTS

The results of this study use vaseline ointment of the ethanol extract of Moringa leaves. The physical quality test of the ointment includes organoleptic test, homogeneity test, pH analysis,

Table 4. Observation results of the average wound length, the number of mice experiencing edema, erythema, and formation of granulation tissue of the control and treatment groups

Group	Day							
	0	1	2	3	4	5	6	7
Wound length								
Negative Control	1,00	0,90	0,66	0,56	0,46	0,38	0,24	0,20
Positive Control	1,00	0,74	0,50	0,34	0,30	0,18	0,10	0,02
PI	1,00	0,80	0,58	0,50	0,44	0,38	0,22	0,14
PII	1,00	0,70	0,42	0,38	0,28	0,22	0,12	0,04
PIII	1,00	0,66	0,50	0,44	0,36	0,32	0,16	0,04
Sig.	1,000	0,024	0,012	0,029	0,052	0,067	0,101	0,025
Experiencing Edema								
Negative Control	0	5	5	5	3	1	0	0
Positive Control	0	3	1	0	0	0	0	0
PI	0	5	4	1	0	0	0	0
PII	0	4	2	0	0	0	0	0
PIII	0	3	2	0	0	0	0	0
Sig.	1,000	0,308	0,077	0,001	0,011	0,406	1,000	1,000
Experiencing Erythema								
Negative Control	5	5	5	5	3	0	0	0
Positive Control	5	5	5	2	0	0	0	0
PI	5	5	5	4	2	1	0	0
PII	5	5	3	0	0	0	0	0
PIII	5	5	3	0	0	0	0	0
Formation of Granulation Tissue								
Negative Control								
Part of the wound	0	0	1	3	4	3	2	0
All wound	0	0	0	0	1	2	3	5
Positive Control								
Part of the wound	0	3	4	5	1	0	0	0
All wound	0	0	0	0	4	5	5	5
PI								
Part of the wound	0	1	3	5	4	3	2	0
All Wound	0	0	0	0	1	2	3	5
PII								
Part of the wound	0	4	4	5	2	0	0	0
All Wound	0	0	0	0	3	5	5	5
PIII								
Part of the wound	0	3	5	3	1	0	0	0
All Wound	0	0	0	2	4	5	5	5

spreadability test.

Organoleptic tests were carried out to visually observe the shape, smell and color of the preparation. The parameters of a good quality ointment are semi-solid form, the ointment smells, and the color similar to the extract used. pH measurement aims to determine the pH value of a preparation that is acceptable to the skin and does not cause irritation. The recommended pH value for a topical preparation is in the range of 4.5-6.5. Other than that, ointment preparations must be homogeneous so that it would not cause irritation to the sample and can be distributed evenly. The three ointment preparations showed homogeneous results because there were no lumps that reduces their homogeneity.

Impact on Wound Healing

The length of the wound in mice was measured every day before giving treatment with a ruler which can be seen in table 4, it was found that the fastest reduction in wound length was found in the positive control group, followed by the Moringa leaf extract treatment group with concentrations of 8%, 10%, 6%, and finally the negative control group. Data on wound length reduction were not normally distributed and were not homogeneous because the Kolmogorov-Smirnov test obtained $p \leq 0.05$ accompanied by differences in the mean and median and mode results, so the researchers used non-parametric tests, namely the Kruskal-Wallis and Mann Whitney tests. Especially on the second day of the study, the Kruskal-Wallis test showed the most significant results which can be seen in table 4, $P = 0.0012$ ($p \leq 0.05$). The results of the Mann Whitney test for reducing wound length in the 6% ointment group and the negative control showed no significant difference with a p value > 0.05 on each

Table 5. Results of the wound length test for the control and treatment groups (mann-whitney test)

Group	Day							
	0	1	2	3	4	5	6	7
Wound Length								
Positive and Negative Control	1.000	.050	.094	.039	.133	.041	.033	.009
PI and Negative Control	1.000	.131	.443	.324	.746	.913	.910	.501
PI and Positive Control	1.000	.166	.065	.058	.197	.083	.156	.125
PI and PII	1.000	.116	.007	.018	.019	.068	.193	.217
PI and PIII	1.000	.037	.065	.288	.214	.389	.314	.217
PII and Negative Control	1.000	.034	.012	.019	.019	.041	.033	.013
PII and Positive Control	1.000	.502	.065	.700	.410	.911	.740	.513
PII and PIII	1.000	.496	.065	.174	.042	.100	.419	1.000
PIII and Negative Control	1.000	.019	.094	.104	.125	.262	.058	.013
PIII and Positive Control	1.000	.121	1.000	.316	.656	.145	.307	.513
Experiencing Edema								
Positive and Negative Control	1.000	.134	.014	.003	.050	.317	1.000	1.000
PI and Negative Control	1.000	1.000	.317	.014	.050	.317	1.000	1.000
PI and Positive Control	1.000	.134	.072	.317	1.000	1.000	1.000	1.000
PI and PII	1.000	.317	.221	.317	1.000	1.000	1.000	1.000
PI and PIII	1.000	.134	.221	.317	1.000	1.000	1.000	1.000
PII and Negative Control	1.000	.317	.050	.003	.050	.317	1.000	1.000
PII and Positive Control	1.000	.513	.513	1.000	1.000	1.000	1.000	1.000
PII and PIII	1.000	.513	1.000	1.000	1.000	1.000	1.000	1.000
PIII and Negative Control	1.000	.134	.050	.003	.050	.317	1.000	1.000
PIII and Positive Control	1.000	1.000	.513	1.000	1.000	1.000	1.000	1.000
Experiencing Erythema								
Positive and Negative Control	1.000	1.000	1.000	.050	.050	1.000	1.000	1.000
PI and Negative Control	1.000	1.000	1.000	.317	.549	.317	1.000	1.000
PI and Positive Control	1.000	1.000	1.000	.221	.134	.317	1.000	1.000
PI and PII	1.000	1.000	.134	.014	.134	.317	1.000	1.000
PI and PIII	1.000	1.000	.134	.014	.134	.317	1.000	1.000
PII and Negative Control	1.000	1.000	.134	.003	.050	1.000	1.000	1.000
PII and Positive Control	1.000	1.000	.134	.134	1.000	1.000	1.000	1.000
PII and PIII	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
PIII and Negative Control	1.000	1.000	.134	.003	.050	1.000	1.000	1.000
PIII and Positive Control	1.000	1.000	.134	.134	1.000	1.000	1.000	1.000
Formation of Granulation Tissue								
Positive and Negative Control	1.000	.050	.072	.134	.072	.050	.134	1.000
PI and Negative Control	1.000	.317	.221	.134	1.000	1.000	1.000	1.000
PI and Positive Control	1.000	.221	.513	1.000	.072	.050	.134	1.000
PI and PII	1.000	.072	.513	1.000	.221	.050	.134	1.000
PI and PIII	1.000	.221	.134	.134	.072	.050	.134	1.000
PII and Negative Control	1.000	.014	.072	.134	.221	.050	.134	1.000
PII and Positive Control	1.000	.513	1.000	1.000	.513	1.000	1.000	1.000
PII and PIII	1.000	.513	.317	.134	.513	1.000	1.000	1.000
PIII and Negative Control	1.000	.050	.014	.058	.072	.050	.134	1.000
PIII and Positive Control	1.000	1.000	.317	.134	1.000	1.000	1.000	1.000

study day. In the treatment of Moringa leaf extract ointment at a concentration of 6% and the positive control also showed no significant difference. Comparison of the 6% and 8% concentration ointment treatments showed significant results on days 2, 3, and 4. The treatment of the 6% and 10% moringa leaf extract ointment groups showed significant differences on the first day. Comparison of the 8% and 10% ointment groups showed a significant difference on the 4th day. Table 4 shows the results of the Kruskal-Wallis test for the most significant edema on day 3 with $p = 0.001$ ($p \leq 0.05$) and also the data on observation of edema in the control group and the treatment group that experienced the least edema, namely the positive control group, followed by the 10%, 8%, 6% moringa leaf extract ointment treatment, and finally the negative control

group. The Mann Whitney test on edema showed that the comparison in the group with 6% Moringa leaf extract ointment and the negative control was most significant on the third day with p = 0.014 (p ≤ 0.05), whereas in the comparison of the 6% Moringa leaf extract ointment treatment and the positive control it was not there is a significant difference. In the treatment group, the concentration of 6% and 8% Moringa leaf extract ointment showed no significant difference, as well as the treatment group with 6% and 10% Moringa leaf extract ointment. Comparison of the concentration of 8% and 10% ointment treatment showed no significant difference. The results of observations of erythema in the control and treatment groups in table 4 show that the treatment group with the least number of mice experiencing erythema was shown in the 8% and 10% ointment groups, followed by the positive control group, 6% ointment, and finally the negative control. The Kruskal-Wallis test for erythema in the control and treatment groups showed the most significant results on the third day with p = 0.003 (p ≤ 0.05). The results of the Mann-Whitney erythema test for the control and treatment groups in table 5 show that comparisons in the treatment group with 6% concentration of Moringa leaf extract and negative control and 6% ointment and positive control did not show a significant difference, whereas in the treatment group with leaf extract ointment Moringa concentrations of 6% and 8% and the 6% and 10% treatment groups showed the same results, that is, there was a significant difference on the third day with a value of p = 0.014 (p ≤ 0.05). Comparison of the 8% and 10% ointment groups showed no significant results. In table 4 regarding the results of granulation tissue observations of the control and treatment groups, it shows that the number of mice that experienced the most formation of granulation tissue occurred in the 10% concentration of Moringa leaf extract ointment group, followed by the positive control group, the 8% ointment group, the 6% ointment group and negative control. The Kruskal-Wallis test for granulation tissue formation showed the most significant difference in results on the fifth day with p = 0.023 (p ≤ 0.05). In table 5 for the results of the Mann Whitney granulation tissue test for the control and treatment groups, there was no significant difference in the 6% ointment group and the negative control, while in the 6% ointment group and positive control, the 6% and 8% ointment group, and the 6% and 10% ointment groups had a significant difference on the fifth day with a value of p = 0.05 (p ≤ 0.05). Comparison of the 8% and 10% ointment groups showed no significant difference.

The results of observations after 24 hours after the mice's backs were incised, the five groups showed an inflammatory phase marked by erythema (redness) and edema (swelling) in the wound. On the 4th day it can be seen that the five groups experienced wound contractions, but there was still edema. It can be seen that in the PI treatment group there was new tissue but the wound was still wide. On day 5, the positive control group, PII, and PIII ointment treatment group showed visible wound contraction from the previous day. Meanwhile, the negative control and 6% ointment treatment (PI) did not experience a significant change in wound contraction. On the 5th day, the positive control wound was covered with a scar. In the sample given Moringa leaf extract at a concentration of 6%, the wound looked dry and covered with new tissue, but the wound was still wide. In the 10% ointment treatment (PIII) a scab was seen. On the 6th day, all groups experienced wound closure, except for the negative control group, which was only given Vaseline, the wound was still open. On the 7th day, wound closure in the negative group was not perfect, while in the other groups it was perfect.

DISCUSSION

The development of erythema and edema is a common sign of an inflammatory response. When experiencing a wound, vasodilation will occur which causes symptoms of redness and swelling.[12] Based on the results of the study, the administration of vaseline ointment of ethanol extract of Moringa leaves was given treatment by applying twice a day at 08.00 WITA and 17.00 WITA on the back region of mice with concentrations of 6%, 8%, 10%, vaseline as a negative control, and gentamicin as a positive control, showed that with a concentration of 8% and 10% vaseline ointment ethanol extract of Moringa leaves had better effectiveness in accelerating wound healing.

Reduction in the number of mice experiencing erythema was faster in the 10% and 8% ointment group, compared to all groups. In another study, it was stated that the ethanol extract gel preparation of Moringa leaves at a concentration of 40% had the same speed of wound healing as the positive group. The difference in the results of this study is probably caused by the type of wound studied, namely burns, whereas in this study examined cuts.

It can be seen in table 4 that the observed results on reducing the number of mice with edema in the 10% concentration ointment group were not much different from the positive control group. This is in accordance with a study which stated that the greater the concentration of Moringa leaf extract, the effect on wound healing. The 20% concentration in the topical preparation of Moringa leaf extract experienced more wound contraction than the 10% concentration.[13] Other research states that a concentration of 5% has the greatest effect on reducing edema compared to the 1%, 3% group. The decrease in edema can be caused by a flavonoid compound found in Moringa leaf extract, namely quercetin. A study conducted by Sulistyawati and Pratiwi in 2016 stated that quercetin works by inhibiting the COX-2 enzyme, so that arachidonic acid cannot turn into prostaglandins. Inhibition of cyclooxygenase enzyme activity will reduce edema volume caused by increased blood vessel permeability by prostaglandins and COX-2 expression by neutrophils.[10]

In this study, the results of the Mann Whitney test for reducing wound length for the 8% concentration of Moringa leaf extract ointment group and the negative control indicated that there was a significant difference. This can happen because the negative control group only used Vaseline, without being given additional interventions that could accelerate wound healing, whereas in the ethanol extract ointment group Moringa leaves contain complex phytochemicals

that can accelerate wound healing. The results of the Kruskal-Wallis test for reducing wound length in table 4 showed the most significant results on the second day p = 0.012 (p <0.05). This is consistent with other studies which state that the results of the Kruskal-Wallis test on macroscopic wound healing obtained a significant value, namely p = 0.007 (p <0.05). The results of the Mann Whitney test for reducing wound length shows that the comparison of the 8% ointment group and the positive control, and the 10% ointment group and the positive control did not have a significant difference with the same p value, namely p = 0.513 (p > 0.05). Saponins found in Moringa leaves have the ability to act as an antiseptic which prevents wounds from experiencing severe infections, by blocking the growth of microorganisms that usually occur in wounds.[14]

In table 4 regarding the results of observations of granulation tissue in the control and treatment groups, it shows that the 10% ointment group and the positive control group got the most granulation tissue formation results compared to the other groups, this is different from the study conducted by Poernomo and Setiawan (2019) which stated that extract There was a significant difference in the formation of new tissue in the 15% moringa leaf concentration and the control group, because the 15% moringa leaf extract group was more effective in increasing collagen density and shortening bleeding time compared to the control group. The difference in the results of this study was probably caused by a different control group, namely using 2% CMC-Na. CMC-Na is a solvent that does not have effectiveness on wound healing.[14] Moringa leaves contain antioxidant properties that come from the content of flavonoids. The study conducted by Berkovich, et al. (2013) stated that flavonoids significantly accelerate wound healing by shortening the epithelialization period, increasing collagen deposition, and causing tissue granulation.[15]

CONCLUSION

The conclusion that can be drawn from this study is that the higher the concentration of vaseline ointment of the ethanol extract of Moringa oleifera leaves (Moringa oleifera) was found to have better effectiveness in accelerating wound healing, especially at concentrations of 8% and 10%, compared to concentrations of 6%, positive control, and negative control.

Based on the research that has been done, the following suggestions can be given. There are limitations in this study, namely that observations were only carried out macroscopically, thus allowing for differences in perceptions in determining the development of wound healing. Conduct further research development regarding the uses and benefits of Moringa leaves. Finally, future research is expected to determine the effective dose in humans so that it can be widely used in society.

ETHICS APPROVAL

This study has been ethically approved by Ethics Committee of Faculty of Medicine Udayana University with Ethical Clearance Number: 02/UN.14.2.2.VII.14/LT/2023.

CONFLICT OF INTEREST

None to be declared.

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AUTHORS CONTRIBUTION

All authors contributed equally in the writing of this article

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