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Formulation and Effectivity of Henna Leaves (*Lawsonia inermis* L.) Extract Ointment Against Burn Healing of Rabbit (*Orctolagus cuniculus)*

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ABSTRACT

Burns are tissue injury resulting from contact with a source of heat. The henna leaves extract (Lawsonia inermis L.) contains tannin, which acts as an astringent to treat wounds. This research seeks to determine the efficacy and quality of henna leaves ointment (Lawsonia inermis L.). The extraction method for henna leaves (Lawsonia inermis L.) entailed maceration with a 96% ethanol solvent. The phytochemical analysis of the 96% ethanol extract of henna leaves revealed the presence of flavonoids, tannins, saponins, and terpenoids. Variable concentrations of henna leaves extract were used to formulate ointments: 2.5% (F1); 5% (F2); 10% (F3); negative control (C-); and bioplacenton® as the positive control. Organoleptic assays, homogeneity, pH, spreadability, and adhesion were used to evaluate the quality of the formulations. In rabbits with inflicted burns, administer ointments F1, F2, F3, C-, and C+ to determine the efficacy of burn treatment. The healing effect is evaluated based on the time it takes for the wound to close (maturation phase), which is characterised by the incision being covered with new tissue. The ointment made from 96% ethanol extract of henna leaves with various concentrations of F1, F2, and F3 met the test requirements for organoleptic, homogeneity, pH, spreadability, and adhesion, according to the results of the ointment quality test. The ANOVA analysis of the effect test revealed that F1, F2, and F3 had a healing effect on wounds. The lesion healing effect of Formula F3 (10%) was not significantly different from the positive control after 11 days.

KEYWORDS*: Burns, Henna leaves,* Ointment

INTRODUCTION

Burns are caused by direct or indirect contact with high temperatures, such as fire, hot water, electricity, chemicals, and radiation. Burns result not only in damage to the skin but also affects all body systems. Skin with burns will experience damage to the epidermis, dermis, and subcutaneously, depending on the causative factors and the

length of time the skin is in contact with the heat source (Ulviani et al., 2016).

Burns are typically described by their degree, which is determined by the burn's profundity. The severity of the laceration is dependent on its depth, size, and location. Age and previous health of the patient also influence the prognosis. The high temperature and duration of exposure to the high temperature determine the depth of the burn. There are three burn degrees. Burns of the first degree only affect the epidermis' outermost layer, causing redness, mild edema, and pain. Without treatment, recovery would take between 2 and 7 days. Burns of the second degree involve the epidermis and a portion of the dermis, blisters form, and edema causes excruciating agony. If the bulla is fractured, a red area containing a great deal of exudate will appear. Heal in 3-4 weeks. Burns of the third degree affect all layers of the epidermis and occasionally extend to the underlying tissue (Larissa et al., 2017).

Henna is one of the botanicals that can be utilized. The henna leaves plant is a form of leaf that is native to Indonesia and is used to treat inflammation of the knuckles (paniritium) and skin wounds (Fatmawati & Rustiah, 2019). In certain Indonesian rural communities, henna nail leaves are frequently used to alleviate the searing sensation of fire on the skin. Typically, henna leaves are utilized by finely grinding them and applying them directly to the affected area of scorched skin. The leaves of henna nails (*Lawsonia inermis* L.) contain tannins that can prevent bacterial infection from forming new tissue in injured skin, as well as astringents that can reduce the size of skin lesions. the ethanol extract henna leaves has inbitory power against *Pseudomonas aeruginosa.* (Devi silva & Mulyeshwari tuty, 2017). The solvent used is a polar 96% ethanol solution. Polar solvents can extract quaternary alkaloid compounds, phenolic constituents, carotenoids, tannins, carbohydrates, amino acids, and glycosides (Astriani & Wandira, 2023).

To facilitate the use of ethanol extract of henna leaves in the treatment of burns, a formulation with a high penetrating power and extended contact time is required. One of the available remedies is ointment (Voight, 1994). An ointment is a preparation easily smeared and used as an external drug. The active ingredient will be dissolved or dispersed homogeneously in a suitable ointment base. Ointments consist of an ointment base, a co-carrier of a combination of active ingredients. Ointments have the advantage of not being irritating, having adhesion, good distribution on the skin, and not inhibiting gas exchange and sweat production, so their effectiveness lasts longer (Lestari et al., 2017). The basis for taking the concentration of the ethanol extract of binahong leaves ointment was taken from Adinda Paramita's research (2016). The

henna leves extract ointment concentration was 2,.5%, 5%, and 10%.

Based on the description above, the formulation of the problem in this study was whether the 96% ethanol extract ointment of henna leaves had effectivity on the healing of rabbit (*Oryctolagus cuniculus*) burns. This study aimed to determine the efficacy and quality of henna leaves ointment ethanol extract from henna leaves as a burn healing in rabbit.

MATERIAL AND METHODS

Chemicals and Instrument

The chemicals used in this study were aquadest, adeps lanae, ethanol 70%, ethanol 96%, feri(III) chloride, chloride acid, chloroform, anhydrous acetic acid, henna leaves, hypoallergenic plaster, lidocaine injection, mayor reagent, sodium chloride 0,9%, rabbit (*Oryctolagus cuniculus*), sterile gauze.

The instrument used in this study were animal scale, glassware (Pyrex®), induction metal, pH meter (Milwaukee MW151 Max®), maceration container.

Sampling samples

Henna leaves were taken from Mandate Village, South Wangi-Wangi District, Wakatobi Regency, Southeast Sulawesi, South Latitude 5°20'4.5672" and East Longitude 123°32'21.9732". The samples were aerated in the absence of direct sunlight until they were completely desiccated, after which they were ground in a blender.

Extraction

The dried henna leaves simplicia was weighed as much as 500 grams and then put into the maceration container. The sample was first moistened with 96% ethanol solvent, then 5000 mL of 96% ethanol was added again until the simplicia was submerged. Left for three days with occasional stirring in a closed vessel and protected from light. After the liquid is filtered, the dregs are re-massaged with the same filter liquid. The filtrate was evaporated with aerated until a thick extract was obtained. Then it was weighed to determine the rendemen.

Active phytochemical compounds screening

Alkaloid compound test, 1 mL extract into a test tube, then add 0.1 mL of 2 N hydrochloric acids, and then test it with alkaloid reagents, namely Mayer and Dragendorff reagents. Positive test results are obtained when a yellow precipitate is formed with Mayer's reagent and a red precipitate with Dragendorff's reagent (Endarini, 2016).

Flavanoid compound test, 1 mL extract, add six drops of concentrated HCl and 0.1 g of Mg powder, and then shake gently. If red, orange, and green colors occur, it indicates the presence of flavonoid compounds (Harborne, 1996).

Saponin compound test, 1 mL extract was added with 0.1 mL of hot water, then shaken for 1 minute, and 0.1 mL of HCl 2 N. If a stable foam is formed for 7 minutes, it indicates a positive for saponin compounds (Harborne, 1996)

Tanin compound test, 1 mL extract, add 0.1 mL of 1% FeCl3 solution. If green and blue colors are formed, it indicates a positive for tannins (Harborne, 1996).

Terpenoids compound test, 1 mL, and add 0.1 mL of chloroform, anhydrous acetic acid, and concentrated sulfuric acid. A positive reaction occurs when a brown ring is formed at the solution boundary (Shabur Julianto, 2019.)

Manufacturing Ointment of Henna Leaves

It made ointments with an ointment base: adeps lanae album and vaseline. Adeps lanae is first put into the mortar, then stir it slowly until it is blended using a stamper. Vaseline album is put into the mortar and stirred slowly at a constant speed so that the mixture of adeps lanae and album vaseline is mixed evenly. The ethanol extract of henna leaves was added (2,5%) according to the required concentration and stirred until homogeneous. It lacks clumping particles and has colors that are uniformly mixed. The finished ointment is then put into a container. The henna leaves extract ointment formulation was remade with 5% and 10% concentrations (Table 1).

Characteriazation of Ointment

Organoleptic test

Observation appearance physically observed through the test of organoleptic covers smell, color, and smell on preparations ointment.

Homogeneity test

Ointment takes in the part top, middle, and bottom. Each ointment was smeared in a manner evenly on the glass transparent. Homogeneity was observed based on there being nope details rough on ointments.

pH test

As much as 0.5 g ointment diluted with 5 ml of distilled water, then stirred until homogeneous. The solution has then measured the pH with a pH meter (Rachmalia et al., 2016).

Spreadability test

As much as 0.5 gram sample was placed on a glass plate, then given a 100-gram load for 1 minute ago, measuring the diameter of the spread ointment (Rachmalia et al., 2016).

Adhesion test

Table 1. Formulation Ointment of Henna Leaves

Materials	Formulation (g)			
	F1	F2	F3	C-
Henna leaves extract	0,75	1,5	3	-
Adeps Lanae	4.5	4.5	4.5	4.5
Vaseline album	ad 25	ad 25	ad 25	ad 25

As much as 0.25 grams of ointment is placed on both glass objects and then on a 1 kg load for 5 minutes. After that, a glass object was installed on the test equipment. Then the time was recorded until the two

glass objects were released (Rachmalia et al., 2016).

Animals Treatment

Preparation of test animals

There were 3 test animals. The test subject was an rabbit (*Oryctolagus cuniculus)*. For one week, rabbits become accustomed to their surroundings.The backs of the rabbits were shaved in 5 parts with a diameter of ± 2 cm and then anaesthetized.

Induction of the wound

The male sex is 1.5-2.0 kg/BB, and the rabbits were chosen because they were healthy and free of skin flaws. Rabbit fur was shaved on the back to be induced, smeared with 70% alcohol, and then anesthetized with 2% lidocaine. Each test animal was anesthetized with 0.09 mL of lidocaine into the rabbit's back. Rabbits were induced with heated metal for 10 minutes. Then the metal was attached to each shaved back for 10 seconds, after which the burn was rinsed with 0.9% NaCl. Wounds that occur are measured, then given appropriate treatment.

Provision of ethanol extract from henna leaves

This test used three rabbits (A, B, and C), each of which had been burnt into a wound area on the rabbit's back. Each rabbit was divided into five treatment sites; namely, on side, It was given base (negative control), side II was given ethanol extract 96% henna leaves 2.5% (F1), side III was given ethanol extract henna leaves nails 5% (F2) , side IV side given ethanol extract of henna leaves 10% (F3), and for the V side given Bioplacenton®.

The burn wound that has been made is smeared with an ointment preparation and covered with sterile gauze and hypoallergenic plaster so that there is no irritation, then wrapped again with a bandage. The same treatment was for rabbits 2 and 3 as triplicate. The frequency of treatment of test animals was each given thrice a day every 8 hours, thinly and evenly on each side. The burn area of each test animal was observed on the second day. Then the burn area was measured using a ruler. Observations were made on the first day until the wound was 100% closed (completely healed).

RESULTS AND DISCUSSION

The level of burns in this study used second-degree (superficial) burns because superficial second-degree burns often occur in the community, especially in households characterized by reddish, wet blisters, erythema blanching due to pressure, and severe pain (Warby et al., 2020). The ethanol extract of henna leaves is made as an ointment. The ointment was chosen because the ointment form is easier to use, spreads evenly, does not irritate, and has good adhesion and distribution on the skin (Voigt, 1984).

Phytochemical screening of active compounds from secondary metabolites that

have been carried out has resulted in several classes of compounds in the extract shown in Table 2. Henna leaves extract contains flavonoids, saponin, tannin, and terpenoids. Results of clinical studies and experiments on flavonoids can increase vascularization and reduce edema. Research, the latest, proves that flavonoids have anti-inflammatory and antioxidant effects. The content of flavonoids is also believed to have benefits in wound healing. Henna leaves also contain saponin from foam formation as high as 1-10 cm, which is stable for 10 minutes. Saponins as antiseptic and stimulates cell formation new cells. Saponin is one of the compounds stimulating collagen formation in the wound-healing process. Tannin compound support wound healing with their astringent and antimicrobial (Nuralifah et al., 2022).

In this study, ointment preparation was made using various concentrations of extract henna leaves, namely 2,5% (F1), 5% (F2), and 10% (F3). Physical evaluation of ointment preparation, namely organoleptic, homogeneity, pH test, adhesion test, and spreadability test.

The organoleptic test included observing the color and smell. The organoleptic test of henna leaves extract ointment showed consistent color and smell. The results of organoleptic observations can be seen in Table 2. Odor examination showed that the odor observed in each ointment preparation was the same, namely the characteristic odor of henna leaves. The ointment base is yellow because it does not contain extracts. While the color of the F1 is brownish green, F2 is brown, and F3 is dark brown. The higher concentration of the extract can cause the color intensity to increase. Good ointments should not include rancid ingredients and should have a soft consistency (Rachmalia, 2016).

Table 2. Screening active phytochemical compounds of the extract results

Compound	Results
Alkaloid	-
Flavonoid	+
Saponin	+
Tannin	+

The homogeneity test was carried out to determine whether the ointment preparation had been made homogeneous. The results of the observations can be seen in Table 3. The henna leaves extract ointment preparation has good homogeneity. It can be concluded that it is homogeneous because there are no lumps that reduce its homogeneity. Homogeneous ointment preparations indicate that mixing the ingredients of the ointment and henna leaves extract is good so that lumps or coarse grains are not found in the preparation. An ointment preparation must be homogeneous and even so as not to cause irritation and be distributed evenly when used.

The efficacy of topical therapy highly depends on the patient spreading the formulation in an even layer on the skin to deliver a standard drug dose. That is why spreadability is one of the essential

Table 3. The average results of physical tests

Test	K (-)	F1	F2	F3
Organoleptic Color Smell Shape	Yellow Odorless ointment	Green brown Extract odor Ointment	Brown Extract odor ointment	Dark brown Extract odor ointment
Homogeneity	Homogenous	Homogeneous	Homogeneous	Homogeneous
pH	7,6	5,23	4,77	4,54
Spreadability (cm)	5,9	5,9	5,7	5,2
Adhesion test (s)	4,18	4,3	4,38	4,50

characteristics of a semi-solid dosage form. The difference in spreading power greatly affects the diffusion speed of the active substance in the membrane. The good spreading power range is 5 - 7 cm (Bakhrushina et al., 2022).

Observations can be seen in Table 3. The results obtained show that henna leaves extract ointment F1, F2, F3, and negative control have appropriate spreading power because the spreading power is included in. the more wide skin surface spot preparations spread so absorption of the material drug which contained will increase (Naibaho et al., 2013) .

Testing the adhesion of the ointment was carried out to determine the ability of the ointment to stick to the skin surface. The greater the adhesive power of the ointment, the greater the drug's absorption because the bond between the ointment and the skin is getting longer. The requirement for adhesion to topical preparations is not less than 4 seconds (Ulaen et al., 2012) .

The results of the adhesion test can be seen in Table 3. The results obtained by henna leaves extract ointment at each concentration had good spreading power because the observations were not less than 4 seconds.

The pH test on the ointment is a test to determine the acidity-base level of the ointment preparation. Ointment preparations must match the skin's pH, 4.5 – 6.5 (Azkiya et al., 2017). The results of testing the pH of the ointment can be seen in Table 2. The henna leaves extract ointment results fall within the ideal normal skin pH range. The increase in pH in each ointment preparation is affected by the addition of the active substance.

Bioplacenton was selected as a positive control because it's one of the most commonly prescribed topical medications for treating burns and wounds in gel form. Burns or other infected injuries are treated with gel bioplacenton. 10% bovine placenta extract and 0.5 percent neomycin sulfate make up the bioplacenton gel's active ingredients. Three phases comprise the wound healing process: the inflammatory, proliferative, and remodelling phases. The inflammatory phase, characterized by swelling, the proliferative phase, characterized by exudate and fibroblast formation that resembles a crust on the wound, and the healing phase,

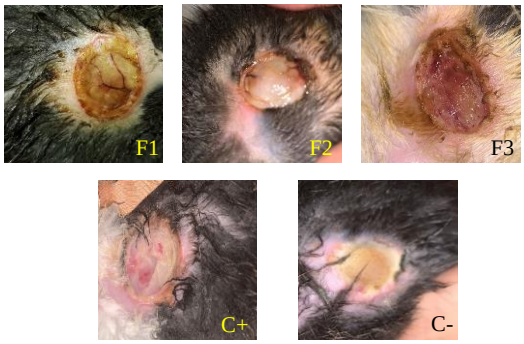

Figure 1. Comparing rabbit burns from the first day

characterized by the formation of a new network, indicate that the wound has diminished or healed (Izzati, 2015).

Figure 1, level wound burn in this study used wound burn degree II (superficial) because wound burns shallow II degree with reddish skin blister wet, erythema pale because of pressure and painful great (Rachael, 2021). Up to three days after an injury, an inflammatory process develops. Without inflammation, the wound healing process will not occur. Wounds will continue to be a source of pain due to inflammatory processes, and wound healing will often be accompanied by pain (Izzati, 2015).

In Figure 2, it can be seen that the rabbits have already reached the stage of proliferative damage. Granulation tissue is a collection of cells, including fibroblasts and inflammatory cells, which coexist with new capillaries. On average, fibroblasts appeared on day 3 and attained their peak on day 7.

On day 10, the F3 and C+ fibroblasts began to detach from the epidermis, indicating that this group had reached the peak phase of proliferation and entered the

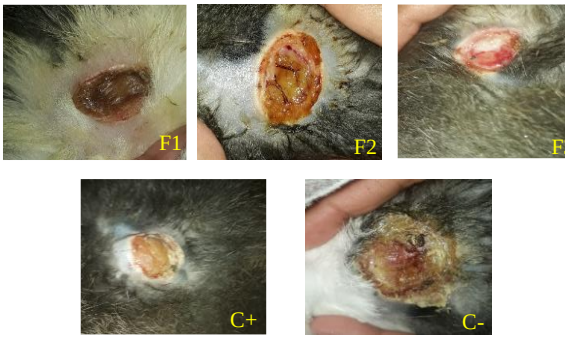

Figure 2. Comparing rabbit burns from the fifth day

remodeling phase, which was characterized by tissue formation (figure 3). Meanwhile, groups F1 and F2 were still in the phase of proliferation. This indicates that F1 and F2 have a delayed rate of healing. Because C- does not contain an active ingredient, the lesion diameter in group C- remains large.

Based on the results of observations on burn activity can be seen in figure 3. From the graph, it was found that each treatment group showed a decrease in burn diameter. The negative control group (the ointment base without extracts) showed a slower decline than sample. At the same time, the 10% extract ointment group showed a decrease in burn healing days, almost the same as the positive control group. In contrast to the 2.5% and 5% ointment extract groups, it was

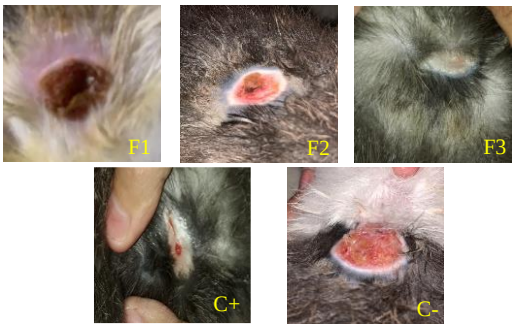

Figure 3. Comparing rabbit burns from the tenth day

slower than the 10% ointment because the henna leaves extract contained less.

Due to the presence of several compounds in the ethanol extract of the leaves, this substance is capable of accelerating tissue regeneration, re-epithelialization, stimulating fibroblasts and collagen formation on burn skin, and inhibiting microorganisms that slow wound healing (Izzati, 2015). There are also tannins, flavonoids, and saponins.

Tannins are astringents that can reduce the diameter of skin pores, harden the skin, stop mild exudation and bleeding, and cover wounds to prevent normal bleeding. Saponins have the ability as a cleanser and antiseptic to kill or prevent the development of microorganisms that commonly develop in wounds, thereby preventing infection. Flavonoids possess anti-inflammatory, hypoallergenic, anti-oxidant, and other functions (Izzati, 2015).

Based on the visual observations (Table 4), burn healing can be concluded that the higher concentration of henna leaves extract will accelerate the healing process and reduce the diameter of burns in rabbits. Ointment F3 (10%) indicates time almost healing, same with Bioplacenton®.

Large absorption drugs in preparation ointment (absorption percutaneous) not only depend on the nature physics chemical from the ingredient drug but also depends on the nature career and conditions skin. Absorption percutaneous something drugs are influenced

Table 4. Healing periode

Formula	Time (Days)
F1	15
F2	13
F3	11
C+	9
C-	18

F1 contain 2,5%; F2 contain 5%; and F3 contain 10% henna leaves extract; C- without extract; and C+ is Bioplacenton®

by several matters that, as concentration medicine, broad membrane the place preparations spread, degrees solubility ingredient drug good in oil nor water, effect hydration skin, time drug attached to the skin (Ansel, 1989).

Analysis of variance for variations in burn diameter was used to see whether there were differences in the effect of ointment concentrations of 2.5% (F1), 5% (F2), 10% (F3), negative control and positive control statistically using the One Way ANOVA test version 26.0 which has a p value <0.05. To see which treatment groups had the same or distinct effects from one another, a Tukey analysis was carried out.

All treatment groups had significant differences, according to data analysis results (p 0.05). Tukey's post hoc analysis revealed that, when compared to F1, F2, and F3, the positive control had the highest impact. F3 exhibited the same healing effect as the positive control, nevertheless, since the positive control did not significantly differ from F3. F2 and F1 are barely different from one another.

CONCLUSION

According to the research's findings, henna leaf ethanol extract (Lawsonia inermis L.) ointment with a 10% concentration has a healing effect on burns in rabbits (Oryctulagus cuniculus), which is not significantly different from Bioplacenton® as a positive control with physical properties of dark brown color, spreadability of 5.2 cm, adhesion of 4.50 seconds, and pH of 4.54.

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