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Incision wound healing test ethanolic extract gel from Ekor Naga (*Rhaphidophora pinnata* (L.f) Schott*)* leaves in white male rats

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ABSTRACT

Ekor naga *(Rhaphidophora pinnata* (L.f) Schott*)* leaves have been researched and tested. So, it was known that the chemical content of secondary metabolites effect wound healing. This study aimed to determine the gel effect of ekor naga leaves extracts as a wound healing medicine. The research method evaluated organoleptic, pH, spreadability, and adhesion of gel preparations which were measured every week for four weeks. The testing of gel effect on the wound healing medicine was being performed. In 5 treatment groups namely positive control: Bioplasenton, Formula 0: negative control, Formula 1: 10% extract concentration, Formula 2: 15% extract concentration, and Formula 3: 20% extract concentration. The result obtained were analyzed by one-way ANOVA and continued by the Duncan test with a level of 95% confidence. The research results showed that formula 3 has the best wound healing effect, followed by formulas 2 and 1. The statistical results have a significant difference ($p<0,05$), but the results of stability observations of the formula two preparation have a stable. Evaluation value for four weeks of observation with a care effect of 95.3%. So, formula 2 is the best formula for stability and testing wound healing effectiveness.

Keywords: Ekor Naga leaves, gel, wound healing, rats, incision

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INTRODUCTION

Traditional medicinal plants are plants used to treat various plants and have been used for a treatment known as Jammu (herbal medicine) (Pratama, 2021). Wounds are cellular disorders that can damage the skin epithelium and even extend to the subcutaneous tissue, damaging structures such as muscles, tendons, nerves, parenchymal organs, and bones. The cause of the wound comes from many things, including chemicals, microbial, physical damage, temperature, and others (Sorg et al., 2017).

Wounds are not uncommon in society, both in acute and chronic forms. Most of the causes of wounds came from trauma or surgery (48%), leg ulcers (28%), and pressure sores (21%). Incidences of wounds in Indonesia in 2018 were are being recorded by as many as 21.1% of the total population (RI Kemenkes, 2018).

Ekor naga (*Rhaphidophora pinnata* (L.f) Schott) leaves have been researched and have medicinal benefits, for example, testing for epithelialization and wound healing by extracting ekor naga leaves (Rahman & Andi, 2019; Hertian et al., 2021). The results of another study research have been conducted by Tarigan et al. (2021). They have stated that the ethanol extract of ekor naga leaves inhibits bacterial growth and is anti-inflammatory. So that the effect cold as a wound healing.

Topical preparations can provide a local effect by applying to the skin surface. If a medicine has been given topically, then the medicine can act locally, preventing the medicine from passing through first-pass metabolism and can be applied directly to the injured skin area (Oryan et al., 2016).

Based on the data above, the researcher is interested in conducting research on the effect of wound healing from variations in the gel formulation of ekor naga (*Rhaphidophora pinnata (L.f)* Schott) leaves extract.

MATERIALS AND METHOD

Materials

Fresh Ekor naga leaves were taken from Jambi City Jambi Province In Juli 2021, aqua dest, sulfuric acid 2 N, Dragendorft reagent, Mayer's reagent, Wagners reagent, bioplacenton (PT. Kalbe Farma), carbopol (PT. Brataco), glycerin (PT. Brataco), propylene glycol (PT. Brataco), Triethanolamine (PT. Brataco), methylparaben (PT. Brataco), Propylparaben (PT. Brataco) ethanol (PT. Brataco), and veet (PT. Reckitt Benckiser Indonesia).

Preparation of ekor naga (*Rhaphidophora pinnata* (L.f) Schott) leaves extract

Extraction of the Ekor Naga *(Rhaphidophora pinnata* (L.f) Schott*)* leaves was done using the 70% ethanol solvent maceration method. The container was the place to put simplicia powder. Next, a 70% ethanol solvent was added until the powder was submerged. It was covered and left three times in twenty-four hours then repaired two times to optimize the resulting extract. The next step was filtering until the solvent obtained maceration. The macerate was concentrated and evaporated to dryness in vacuum at 40^0C using a rotary evaporator to obtain a good yield.

Gel formulation

The formulation of ekor naga leaves extract gel can be seen in Table 1.

Table 1. Gel formulation design of ekor naga (*Rhaphidophora pinnata* (L.f) Schott)

Materials	Concentration (%)				Description
	F0	F1	F2	F3	
Ekor naga leaves extract	-	10	15	20	Active substance
Carbopol	1	1	1	1	Gel base
Glycerin	5	5	5	5	*Humectant*
Propylene glycol	10	10	10	10	Increased penetration
TEA	1	1	1	1	Pendapar
Methylparaben	0.18	0.18	0.18	0.18	Preservative (Antibacterial)
Propylparaben	0.02	0.02	0.02	0.02	Preservative (Antifungi)
Aquadest add	100	100	100	100	Solvent

Note:
F0 : Gel base
F1 : 10% ekor naga leaves extract
F2 : 15% ekor naga leaves extract
F3 : 20% ekor naga leaves extract

Evaluation of the gel, including organoleptic, pH, spreadability testing, and adhesion tenting, was carried out for 28 days with observation data taken every week (7 days), namely the 7th, 14th, 21th, and 28th days.

The wound healing effect test by gel extract of ekor naga leaves

The test animals were divided into five treatment groups, with each treatment consisting of five rats. The rats used were white male rats that weighed 250-300 grams. The test animals were shaved on the back and given veet cream to remove the hair on the back after 24 hours, and then the treatment was carried out by giving an incision wound on the back of 2 cm and a depth of 2 mm using a scalpel blade. The treatment group consisted of positive control (Bioplacenton), negative control (F0), 10% ekor naga leaves extract concentration (F1), 15% ekor naga leaves extract concentration (F2), and 20% ekor naga leaves extract concentration (F3). Then each treatment was given a gel preparation of 0.2 gram every two times a day for 14 days of treatment without covering the wound area. Other observations that were made for 14 days were the day of wound healing and the day of the disappearance of inflammation in test animals, namely male white rats. The degree of wound healing was calculated as percentage closure in wound area from an original wound are using the formula:

$$v\%\ W = \frac{\mathrm{Wa0} - \mathrm{WaT}}{\mathrm{Wa0}}\ X\ 100\%$$

Note :
%W : wound percentage day -x
W_{a0} : wound area on day 0
W_{aT} : wound area on day T (after induction)

Data Analysis

Research data analysis was carried out in two ways: descriptively (extract characteristic and gel valuation) and one-way ANOVA test (wound length, wound healing day, time of disappearance of inflammation) with a 95% confidence level followed by the Duncan test.

RESULT AND DISCUSSION

Ekor naga leaves extract

Plants that have been taken in this research were ekor naga plants taken from Mendalo Indah, Jambi Luar Kota subdistrict of Jambi Province. Plant determination was carried out in the plant Biosystematics Laboratory, Departement of Biology, Faculty of Mathematics and Natural Sciences, Tadulako University with number 240/UN28.1.28/BIO/2021. Stated the results of the identification of the research sample that stated it was true that it was a Ekor Naga plant form family *Araceae* and species *Rhaphidophora pinnata* (L.f) Schott in the simplicia maceration process of ekor naga leaves used as much as 700 grams using 70% ethanol solvent. The extraction results obtained as many as 61 grams of an extract with a yield value of 8.7%.

Phytochemical screening

The results of phytochemical screening showed that ekor naga leaves extract contains secondary metabolites, namely flavonoids, alkaloids, saponins, tannins, steroids, and phenols. These results were in line with research (Lestari et al., 2021).

Table 2. Phytochemical Screening

Phytochemical Test	Observation Results
Flavonoids	+
Alkaloids	+
Saponins	+
Tannins	+
Steroids	+
Triterpenoids	+
Phenols	+

Note:
+ : Detected

Table 3. Evaluation results of gel preparations of ekor naga leaves

Formulas	Observation	Result				
		Week 0th	Week 7th	Week 14th	Week 21th	Week 28th
F0	Organoleptic					
	a. Color	Clear	Clear	Clear	Clear	Clear
	b. Odor	Unique	Unique	Unique	Unique	Unique
	c. Form	Viscous	Viscous	Viscous	Viscous	Viscous
	Homogeneity	Homogeneous	Homogeneous	Homogeneous	Homogeneous	Homogeneous
	pH	6.41 ± 0.05*	6.83 ± 0.03*	6.25 ± 0.02*	6.46 ± 0.08*	6.70 ± 0.02*
	Spreadability	3.45 ± 0.74*	3.69 ± 0.69*	4.12 ± 0.48*	3.91 ± 2.26*	4.36 ± 1.44*
	Adhesion	5.00 ± 5.29*	5.20 ± 7.63*	5.70 ± 4.07*	9.58 ± 4.05*	5.71 ± 2.55*
F1	Organoleptic					
	a. Color	Blackish Green	Blackish Green	Blackish Green	Blackish Green	Blackish Green
	b. Odor					Unique
	c. Form	Unique	Unique	Unique	Unique	Viscous
	Homogeneity	Viscous	Viscous	Viscous	Viscous	Homogeneous
	pH	Homogeneous	Homogeneous	Homogeneous	Homogeneous	6.49 ± 0.01*
	Spreadability	6.62 ± 0.18*	6.16 ± 0.04*	6.32 ± 0.02*	6.53 ± 0.02*	3.88 ± 0.90*
	Adhesion	4.18 ± 0.68*	4.17 ± 1.43*	4.19 ± 0.74*	4.23 ± 3.41*	1.81 ± 0.06*
		1.19 ± 0.35*	1.12 ± 0.19*	1.07 ± 0.08*	1.04 ± 0.80*	
F2	Organoleptic					
	a. Color	Blackish Green	Blackish Green	Blackish Green	Blackish Green	Blackish Green
	b. Odor					Unique
	c. Form	Unique	Unique	Unique	Unique	Viscous
	Homogeneity	Viscous	Viscous	Viscous	Viscous	Homogeneous
	pH	Homogeneous	Homogeneous	Homogeneous	Homogeneous	6.51 ± 0.06*
	Spreadability	6.62 ± 0.09*	6.20 ± 0.26*	6.67 ± 0.02*	6.43 ± 0.03*	4.24 ± 2.46*
	Adhesion	4.18 ± 0.68*	3.93 ± 0.81*	4.04 ± 0.22*	3.58 ± 4.46*	1.04 ± 0.40*
		1.19 ± 0.64*	1.11 ± 0.20*	1.03 ± 0.05*	1.02 ± 0.29*	
F3	Organoleptic					
	a. Color	Blackish Green	Blackish Green	Blackish Green	Blackish Green	Blackish Green
	b. Odor					Unique
	c. Form	Unique	Unique	Unique	Unique	Watery
	Homogeneity	Watery	Watery	Watery	Watery	Homogeneous
	pH	Homogeneous	Homogeneous	Homogeneous	Homogeneous	6.70 ± 0.01*
	Spreadability	6.84 ± 0.06*	6.30 ± 0.30*	7.00 ± 0.20*	6.83 ± 0.15*	4.03 ± 1.72*
	Adhesion	4.16 ± 0.65*	4.24 ± 0.62*	4.09 ± 0.44*	4.05 ± 1.42*	0.68 ± 0.04
		0.91 ± 0.16	0.86 ± 0.10	0.86 ± 0.10	0.89 ± 0.03	

Note:
1. The sign (*) indicates the data meets the requirements for evaluating topical preparations.
2. F0: Gel Base, F1:10% ekor naga leaves extract, F2: 15% ekor naga leaves extract, and F3: 20% ekor naga leaves extract.

Evaluation results of gel preparations of ekor naga leaves

The evaluation results of gel preparations of ekor naga leaves extract can be seen in table three. The evaluation observed was organoleptic, pH, spreadability, and adhesion for four weeks, namely the 0th, 7th, 14th, 21th, and 28th.

Results of the evaluation of the gel preparation of ekor naga leaves extract can be seen in table three where all of the extracts are showed no organoleptic changes from the preparation during four weeks of observation of the gel evaluation. At a pH value of 6 to 8 and a spreadability of 3 to 5, it falls within the range of gel preparation requirements, but the adhesion in formula 3 does not qualify for the adhesion test because it is greater than 1 second. This is because the higher the concentration of the extract, the lower the cohesion force so that the bonds between carbopol molecules are also reduced, and the gel becomes more watery (Suhail et al., 2020).

Formula 0	Formula 1	Formula 2	Formula 3
			

Figure 1. The gel of Ekor Naga leaves extract

The effectiveness test of wound healing by gel extract Ekor Naga Leaves

The result of measuring the length of the wound and the percentage of the wound healing on the 14th day can be seen in Table 4. This research has an ethical clearance number 3096/UN28.1.20/KL/2021, which was carried out by the ethics committee of the Faculty of Medicine, Tadulako University.

Table 4. Average wound healing length and wound healing percentage 14th day ± SD

Group	Average wound length (cm) ±SD	Percentage wound length (%)
Positive Control	0.812 ± 0.698^{a}	$100\%^{a}$
F0 (Gel Base)	1.568 ± 0.332^{e}	$50.4\%^{e}$
F1(10% of Extract)	1.135 ± 0.581^{d}	$88.8\%^{d}$
F2 (15% of Extract)	1.098 ± 0.610^{c}	$95.3\%^{c}$
F3(20% of Extract)	0.981 ± 0.676^{b}	$100\%^{b}$

Note:
Different lowercase superscripts on the same column indicated a significant difference ($p<0,05$)

Wound length measurements were carried out every day for 14 days. The results of one-way ANOVA analysis showed that there was a significant difference between the treatment group ($p<0,05$) during the wound healing process on the rat's back. The best formula in wound healing is formula 3 because on the 14th day the wound has up to 100%. The greater the amount of extract, the more it will affect wound. The results of the observation can be seen in Figure 2.

Additional observations to confirm the effectiveness of ekor naga leaves extract gel on wound healing in white male rats were observations of wound healing days and days of loss of inflammation due to wounds on the backs of rats. For all data can be seen in Table 5. Statistically, one way ANOVA showed a significant difference for each treatment group ($p<0,05$). Where formula 3 product was the posttest average wound healing time on the 14th day. The length wound was 11.6, and the average loss of inflammation was the 3.60th day. Then followed by Formula 2 days of disappearance of inflammation 4.40th day and for formula I healing day on 4.80th day.

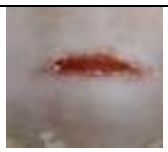
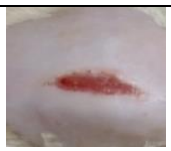
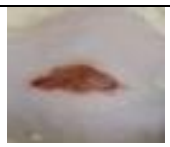
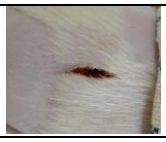
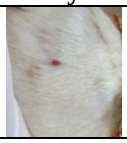
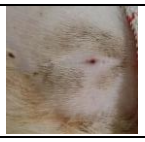
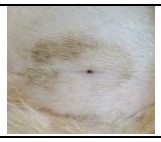
Formula 0	Positive Control	Formula 1	Formula 2	Formula 3
0th days				
				
14th days				
				

Figure 2. a picture of the change in the length of wound area on 0th and 14th days

Table 5. Average wound healing and inflammation disappear

Group	Average Wound Healing Days ± SD	Average Days of Inflammation Loss ±SD
Positive Control	10.40 ± 0.548[a]	3.00 ± 0.000[a]
F0 (Gel Base)	14.00 ± 0.000[d]	6.80 ± 0.447[d]
F1(10% of Extract)	14.00 ± 0.000[d]	4.80 ± 0.447[c]
F2 (15% of Extract)	13.40 ± 0.548[c]	4.40 ± 0.548[c]
F3(20% of Extract)	11.60 ±0.548[b]	3.60 ± 0.548[b]

Note:
Different lowercase superscripts on the same column indicated a significant difference (p<0,05).

The wound healing effect that has been given by ekor naga leaves extract gel was obtained from the chemical content of secondary metabolites, namely alkaloids, flavonoids, saponins, triterpenoids, tannins, and phenols. The function of alkaloids is to inhibit inflammation by reducing the number of cytokines after injury to the skin (Mahibalan et al., 2016; Tyavambiza et al., 2021). Flavonoids can inhibit the activity of cyclooxygenase and lipoxygenase enzymes. The inhibition of these enzymes can inhibit the metabolism of the biosynthesis of the formation of prostaglandins and leukotrienes which are products of the cyclooxygenase enzymes. So that the number of accumulated leucocytes in the inflamed area can be reduced, flavonoids can also inhibit lysosomal secretion, causing proliferation and exudation (Muralidhar et al., 2013; Chaniad et al., 2020; Carvalho et al., 2021).

Saponin compounds can inhibit the release of LPS stimulated pro-inflammatory substances such as iNOS, IL, and TNF-α so that they can inhibit the formation of exudate fluid and inhibit the permeability of the vascular system (Masfria et al., 2017; Abdulkhaleq et al., 2018). Saponins act as antibacterial and antiinflamatory support (Tagousop et al., 2018; Umami & Malika, 2020). Tannins help the process of wound healing speed, this is because tannins act as astringents that can precipitate proteins on the surface of cells with low permeability so that it can cause closure of skin pores, hardening of the skin, stopping exudates, and light bleeding (Kumari et al., 2018; Ma et al., 2020; Kom et al., 2021).

The function of steroids and terpenoids are to inhibit the enzyme phospholipase A2 which plays a role in the arachidonic synthesis, and produces inflammatory mediators and ate able to dissolve lipids and agglomerate proteins in the bacterial cell wall so that the integrity of the bacterial cell wall is disrupted and will reduce the permeability of the bacterial cell wall, resulting in disrupted bacterial metabolism and cause bacterial death (Barreto et al., 2014). The working mechanism must support each other to eliminate inflammation and prevent.

CONCLUSION

Gel extract of ekor naga *(Rhaphidophora pinnata* (L.f) Schott*)* leaves has a wound healing effect which statistically has a significant difference for each treatment group (p<0,05). Formula 2 which has 15% concentration of ekor naga leaves extract is the best formula in terms of stability of the preparation and test of the wound healing effect. Evaluation value for 4 weeks of observation with a care effect 95.3%.

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