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Analysis of the Effect of Red Betel Leaf Ointment on Incision Wound Healing In Male Wistar Rats

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Abstract
Red betel contains chemical elements that are beneficial for treatment, but the part of the red betel plant most widely used as a medicine is the leaf. This study aimed to analyze the effect of red betel leaf ointment (Piper crocatum linn.) on incision wound healing in male Wistar rats. This type of research is experimental, with a Pre-test and Post-test group-only control design approach conducted from March 2023. The research sample was 25 male white rats selected randomly and divided into five groups (4 treatment groups and one control group) so that one treatment group consisted of 5 rats. The test results obtained a Fcount value of 7.533 ≥ Ftable of 2.67, meaning that overall there is a natural effect of administering Red Betel Leaf extract (piper crocatum linn.) on wound healing with a Sig. The count value is 0.012 while the Sig (α) value is 0.05, meaning the Sig. Count value < Sig (α). This means that the administration of Red Betel Leaf extract (Piper crocatum linn.) significantly affects wound healing in rats. It is concluded that Red Betel Leaf extract (piper crocatum linn.) has several bioactive compounds such as alkaloids, flavonoids, saponins, and tannins that play a role in wound healing. Essential Oil Saleb preparation of Red Betel Leaf extract (piper crocatum linn.) can approach Bioplacenton® to recover cut wounds in rats.

Keywords: red betel, wound, healing, ointment

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I. INTRODUCTION

The red betel plant contains elements of chemical substances that are useful for treatment, but the part of the red betel plant most widely used as medicine is the leaf. The chemical content in red betel leaves phytochemical compounds, namely essential oils, alkaloids, saponins, tannins, and flavonoids. The chromatogram results show that red betel leaves contain phytochemical compounds, namely essential oils, tannins, polevenolad compounds, and flavonoids (Sudewo, 2010). Other chemical contents found in red betel leaves are hydroxycavicol, chavicol, capitol, carvacrol, eugenol, p-simen, cineol, caryophyllene, candied estragol, terpenes, and phenyl propanoids (1). Many experiences using red betel as fresh, simplified, or capsule extracts can cure diabetes, hepatitis, and kidney stones, lower cholesterol, and prevent stroke, gout, and hypertension. The effect of active substances contained in red betel can also stimulate the central nervous and thinking power. In addition, it also has the impact of premature ejaculation, anticonvulsants, antiseptics, analgesics, anti-dandruff, antidiabetes, liver protection, antidiarrheal, maintaining immunity, and swelling removal. Betel leaf is also able to overcome inflammation in the lungs, inflammation in the throat, inflammation in the gums, breast inflammation, bleeding nose, and coughing up blood (2). Essential oils act as antibacterials by interfering with forming membranes or cell walls so that they do not form or form incompletely. Essential oil is also one of the ingredients of red betel leaf (P. crocatum), which is expected to have analgesic effects. Essential oils are soluble in absolute ethanol, ether, kerosene ether, and chloroform but very little in water (3). Betel leaves contain 4.2% volatile oil, which consists mainly of betephenol, which is an isomer of Eugenol allypyrocatechine, Cineol methyl euganol, Caryophyllen (a cisquiterpene), kavikol, kavibekol, estragol and terpinene (4). This study was designed to analyze the effect of red betel leaf ointment (Piper crocatum linn.) on incision wound healing in male Wistar rats.

II. RESEARCH METHODS

This type of research is experimental, with a Pre-test and Post-test group-only control design approach conducted from March 2023. The research sample was 25 male white rats selected randomly, divided into five groups (4 treatment groups and one control group) so that one treatment group consisted of 5 rats. The materials used are alcohol, aluminum foil, distilled water, red betel, 96% ethanol, rat test animals (mus musculus), sterile gauze, Whatman filter paper, methylparaben, petroleum ether, plaster, propylene glycol, gloves, triethanolamine. The tools used included glassware (pyrex®), an autoclave, a maceration vessel, a blender (Maspion®), a porcelain

cup, a caliper (Tricle brand®), oven, tweezers, rotavapor (Heidolf®), iron spoon, analytical balance (Precisa®), and water bath.

Calculation of Red Betel Leaf Oil Yield (piper crocatum linn.)
The calculation of the yield of Red Betel Leaf Oil (piper crocatum linn.) (5).

$$\text{Yield (\%)} = \frac{\text{Red Betel Leaf Essential Oil} \times 100\%}{\text{Sample Period of Red Betel Leaf}}$$

A total of 25 rats that have been prepared, anesthetized using liquid ether, then shaved rat fur enough on the back area. Next, each rat was given an incision on its own shaved back. How to provide an incision for a rat, first put the mat under the rat's body, then wash your hands, use gloves, then disinfect the skin area to be given an incision using a sterile scalpel, make a 2 cm long incision with a depth of 1 mm from the surface of the skin of the white rat's back. Observations were made regarding changes in the wound and the size of the damage in the treated area. Data analysis using statistical data tests including normality test and ANOVA test to determine the effectiveness of ethanol extract of Red Betel Leaf (piper crocatum linn.) and Bioplacenton® on rat back incision wound healing.

III. RESULTS AND DISCUSSION

Tabel 2. Phytochemical Screening of Red Betel Leaf (piper crocatum linn.).

Test	Result	Description
Alkaloid	Red-brown precipitate	(+)
	White precipitate	(+)
	Brown precipitate	(+)
Flavonoid	The red color in the amyl alcohol layer	(+)
Saponin	Permanent foam	(+)
Tanin	Blackish green color	(+)

Table 2 shows that the Red Betel Leaf extract (piper crocatum linn.) contains alkaloid, flavonoid, saponin, and tannin chemical compounds. In the alkaloid test, a red-brown precipitate was found to form for the Dragendorff reagent, a white deposit resulting from adding the Mayer reagent, and a brown precipitate for the Bouchardt test (6); (7).

Table 3. Inhibition percentage data of Red Betel Leaf extract (piper crocatum linn.) against DPPH.

Extract Concentration (ppm)	Absorbance Extract	Absorbance Control	Inhibisi (%)
3	0.221	0,524	57.73
6	0.218	0,524	58.48
9	0.213	0,524	58.86
12	0.162	0,524	66.19

Based on the table above, it can be seen that the absorbance of DPPH by the extract of Red Betel Leaf extract (piper crocatum linn.) shows a decrease along with the increase in extract concentration. The inhibition value of the section also increases as the concentration of the section increases, with the most significant inhibition value being 66.19% at a concentration of 9 ppm. The essential oil of Red Betel Leaf (Piper crocatum linn.) has antimicrobial activity against Escherichia coli, Staphylococcus aureus, Bacillus subtilisin, and Streptococcus sp. Still, the extract of Red Betel Leaf (Piper crocatum linn.) is more active against S. aureus, giving a more expansive inhibition zone.

Table 4. Changes in wound length with various concentrations of Red Betel Leaf extract (piper crocatum linn.)

Days	Perubahan Panjang Luka (cm)				
	Concentration 3%	Concentration 6%	Concentration 9%	Concentration 12%	Bioplacenton
1	2	2	2	2	2
3	1.7	1.5	1.5	1.4	1.6
5	1.6	1.4	1.4	1.3	1.3
7	1.4	1.1	1.1	1.2	0.9
9	1.2	0.8	0.8	1	0.6
11	1	0.5	0.5	0.7	0.4
14	0.9	0.5	0.3	0.4	0.2

Based on the table above, it can be seen that Bioplacenton®, as the positive control, experienced faster wound healing. On day 3, the wound length was already reduced, and on day 14, the incision wound treated with Bioplacenton® had the highest percentage of recovery. When viewed from the wound healing rate per day, from day 1 to day seven, the wound healing rate was still linear, but from day 9 to day 14, there was a decrease in the healing rate at 9% concentration compared to the treatment at 6% concentration and far behind when compared to those treated with Bioplacenton®.

Antioxidant content also plays a role in accelerating wound healing (8). The antioxidant content in the form of alkaloids and flavonoids in Red Betel Leaf plays a role in maintaining cellular redox balance (9). Based on Rosidah's research, the alkaloid content in Red Betel Leaf acts as a lipid-soluble antioxidant that protects cellular membranes from free radical attack. Betel Leaf is also antibacterial to help wound healing and prevent secondary infections. The flavonoids, alkaloids, and tannins in Red Betel Leaf can prevent the growth of pathogenic microorganisms such as Escherichia coli, Staphylococcus aureus, and Pseudomonas aeruginosa (10). Red Betel Leaf extract can cause bacterial cells to undergo lysis by damaging the bacterial cell wall and increasing the permeability of the cell wall so that the leakage of intracellular metabolites of bacteria occurs (11).

Table 5. Test Results of the Effect of Red Betel Leaf Extract (Piper crocatum linn.) on Wound Healing

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
Red Betel Leaf Extract	Between Groups	6.814	3	2.276	7.533	.012
	Within Groups	38.314	136	.286		
	Total	45.151	139			

The table above shows the Fcount value of 7.533. To find the value in the F Value Table for df = 3/136 with a probability (α) of 0.05, the Ftable value is 2.67. So the importance of Fcount> Ftable means that overall, there is a natural effect on the administration of Red Betel Leaf extract (piper crocatum linn.) on wound healing. To emphasize this hypothesis test, it can be seen in the Sig. The count value is 0.012 while the Sig (α) value is 0.05, meaning the Sig. Count value < Sig (α). This means that administering Red Betel Leaf extract (Piper crocatum linn.) significantly affects wound healing in rats.

Table 6 Test Results of the Effect of Bioplacenton® (positive control) on Wound Length

ANOVA

	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	11.224	6	1.786	36.178	.006
Within Groups	1.632	28	.083		
Total	12.632	34			

Based on the table above, it can be seen that the Fcount value is 36.178 while the Ftable value is 2.45, which means Fcount> Ftable. When viewed from the significance value, the calculated significance value is 0.006, smaller than the alpha value of 0.05 or $p < 0.05$. From this data, it can be concluded that there is a real influence in the administration of Bioplacenton® on wound healing.

IV. CONCLUSION

Based on the results of research and data analysis on the effectiveness of Essential Oil Saleb administration of Red Betel Leaf extract (piper crocatum linn.) and Bioplacenton® on wound healing in white rats, it can be concluded that:

1. Essential Oil Saleb of Red Betel Leaf extract (piper crocatum linn.) has several bioactive compounds such as alkaloids, flavonoids, saponins, and tannins that play a role in wound healing.
2. The optimum concentration of Essential Oil Saleb of Red Betel Leaf extract (piper crocatum linn.) that can heal cut wounds in white rats is 9%.
3. The highest percentage of healing on day k-14 was in the positive control (Bioplacenton®), which was 95% fol, lowed by 9% v/v extract with a 90% healing percentage.
4. Essential Oil Saleb preparation of Red Betel Leaf extract (piper crocatum linn.) can approach Bioplacenton® in healing cut wounds in rats.

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