

COMPARISON OF THE EFFECTIVENESS OF GIVING BINAHONG LEAF (*Anredera cordifolia* (Ten) Steenis) AND PAPAYA LEAF (*Carica papaya*) ON SKIN WOUND HEALING IN WHITE RAT (*Rattus novergicus*)

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ABSTRACT

Introduction: The incidence of acute and chronic injuries increases every year. Most injuries in the world population, as many as 48%, are caused by trauma or surgery. the highest incidence of wounds in the world based on the etiology was from surgery, which was 110.30 million cases. One of the handlings of wounds on the skin can be done by giving herbal medicines, which can be easily accessed by the public, such as binahong leaves and papaya leaves.

Purpose: To analyze the effectiveness of giving 40% binahong leaf extract cream and 40% papaya leaf extract cream on the wound distance in the white rat wound healing process.

Method: this study is an experimental study with post-test only control group design approach. The sampling technique used in this study was a random sampling method where the number of samples was calculated using the Federer formula, with a total sample of 28 white rats. The distance of the wound was measured using a micrometer.

Results: Twenty-eight wound distance on rats were measured as subjects of the study and then treated with binahong leaf extract cream and papaya leaf extract cream, then the wound distance of each treatment was measured using a micrometer. According to the results, 40% binahong leaf extract cream and 40% papaya leaf extract cream showed better effectiveness in reducing the wound distance of white rat incision than the negative control group (cream base) and positive control group (gentamicin ointment). According to the Mann Whitney test comparing the P1 group (40% binahong leaf extract cream) and P2 (40% papaya leaf extract cream), p-value >0.05, which is 0.543, which means that P1 has no significant mean difference with P2.

Conclusion: There was no significant difference in effectiveness between the treatment of 40% binahong leaf extract cream and 40% papaya leaf extract cream.

Keyword: Wounds incision, wound distance, cream, 40% binahong leaf extract, 40% papaya leaf extract cream.

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INTRODUCTION

Injury is a condition of damaged body tissue, which can occur due to surgery, trauma, gunfire, chemicals, sharp or blunt objects, electric shock, etc¹. Every year, there is an increase in the incidence of acute and chronic wounds. Most of the injuries that occur in the world population are caused by surgery or trauma (as much as 48.00%)². All people can experience injuries. Injuries to the skin can cause discomfort such as pain, if the wound is left and not treated, it can interfere with phase of wound healing and cause inhibition of wound healing, and complications such as infection, emergence of hypertrophic scarring, brush matrix, and keloid.^{3,4}

Wound healing is an attempt to repair damaged skin. Physiologically, there are four phases in wound healing: hemostasis, inflammation, proliferation, and maturation³. Standard treatment of skin lesions includes primary and secondary wound healing. In secondary wound healing, usually, no treatment was given to the wound. The wound heals by itself or is given anti-inflammatory, antiseptic antibiotics (such as bacitracin, fusidic acid, mupirocin, and gentamicin) with topical herbal medicines. While in primary wound healing, the edges of the wound can be met by stitching, but for

small or medium cuts, wound suturing is considered less economical because the wound can heal by itself without stitching if there is no infection.

People tend to prefer herbal medicines to other treatments because treatment with herbal medicines is more accessible, cheaper, less toxic, less side effects, and easier to use⁶. Binahong leaves contain bioactive compounds such as flavonoids and saponins. Saponin compounds are antiseptic. Saponins are also known to have the ability to increase the number of fibroblast cells and also stimulate the formation of type I collagen, which is helpful in wound healing⁷. Flavonoid compounds found in binahong leaves are capable of being anti-inflammatory. In addition, the content of vitamin C in the leaves of binahong is useful as an antioxidant. It can influence the formation of collagen, which is useful in wound healing⁸.

One of the plants containing saponins, flavonoids, alkaloids, and polyphenols is papaya leaves (*Carica papaya* L). papain enzyme in the papaya leaves can increase granulation tissue formation in the proliferation phase of the wound healing process and reduce bacterial infections. Besides, the beta carotene content in papaya leaves is useful as an antioxidant that acts to neutralize

free radicals and neutralize the results of neutrophil phagocytosis in bacteria^{9,10}.

Previous studies have shown that binahong leaf extract at a concentration of 40% is beneficial for wound healing. In contrast, in other studies, papaya leaf extract with a concentration of 100% has been shown to accelerate wound healing. Still, the difference in the effectiveness of giving binahong leaf extract (*Anredera cordifolia*) and papaya leaf extract (*Carica papaya* L.) on wound length in wound healing of white rats (*Rattus norvegicus*) is not certainly known, therefore, this research is focused on comparing the effectiveness of giving binahong leaf extract cream (*Anredera cordifolia*), and papaya leaves extract cream (*Carica papaya* L.) at concentrations 40%, which one is the most useful for topical wound healing through measurement of wound length in healing white rats (*Rattus norvegicus*)^{5,11}.

METHOD

This research was conducted experimentally using post-test-only control group design method. This study used white rats (*Rattus norvegicus*) male wistar strain and grouped into four groups, two control groups, and two treatment groups. The sampling technique in this study was by simple random sampling.

The population of this research was white rats (*Rattus norvegicus*) male wistar strain. The number of samples from this study was calculated using the Federer formula.¹² Based on the results of these calculations, each group was obtained as many as six rats. It is possible that the experimental animals died during the study, so each group was added 10% of the amount, which is one experimental animal in each group. So each group consists of 7 white rats. Total sample size = 4 groups x 7 white rats = 28 white rats.

Inclusion criteria in this study are white rats (*Rattus norvegicus*) male, Wistar strain, 1.5-3 months, weighing 200-250 grams, no anatomical abnormalities, active activity, and no injuries or infections, for exclusion criteria: there are skin abnormalities or injuries before the treatment, and the drop out criteria are the rats appearing sick (mice movement appears less active), there is an infection in the wound, or die during the process of adaptation or treatment.

In this study, the data collection procedure was the preparation of experimental animals, which are white rats (*Rattus norvegicus*) held in cages with a size of 17.5x23.75x17.5cm made of plastic tubs and given a cage cover made of wire. Rats were kept and adapted for a week in a cage and given the same pellet food and

drink. After being adapted for one week, rats are ready to be treated. Binahong leaves and papaya leaves were purchased and determined at Materia Medica Batu, Lahor street no.87, Pesanggrahan, Batu sub-district, Batu city of East Java Indonesia 65313. The making of 40% Binahong Leaf Extract Cream and 40% Papaya Leaf Extract Cream was carried out at the Natural Materials Laboratory of the Faculty of Pharmacy, Widya Mandala University, Surabaya.

Incision wounds on white rats were made at the Educational Animal Hospital Airlangga University.

Before being given treatment, a sedative action was carried out on rats with a mixture of 1:1 xylazine and ketamine, with a dose of 10 mg xylazine and 50 mg of ketamine (0.1 cc/g body weight of rats). After that, the fur on the backs of rats was shaved 3x3cm, and that area disinfected using 10% poodone iodine. Then an incision wound is made with a scalpel, which is two centimeters long with a wound depth of 0.2cm.¹³

After the incision, group 1 rats (P1), as many as seven rats, were given binahong leaf extract, which was smeared on the wound using cotton buds. Then group 2 mice, P2, and seven rats were given papaya leaf extract by applying it to the wound using cotton buds. Group 3 rats,

KK1, consisting of seven mice, were given a cream base by laying it on the wound using cotton buds. Whereas group 4 rats, KK2, composed of seven mice, were assigned gentamicin ointment. Treatment on rats was carried out for fourteen days with two treatments each day, in the morning and evening, then incision wounds in all four groups were bandaged so that the wound was not contaminated. Measurement of the wound length (macroscopic) was done with a micrometer before giving treatment to the groups.

RESULTS

The comparison result of wound length between groups is P2 group, the group given papaya leaf extract cream 40% had the highest reduction in wound length. Then the second highest wound length reduction was group P1 by giving binahong leaf extract cream 40%, then in the third position was P3 group given a cream base and the fourth is group P4 given gentamicin.

The results of the calculation of the average length of incision wounds obtained: the average value of wound length from the group that was given 40% binahong leaf extract cream was 1.195 cm, then the wound length of the treatment group with papaya leaf extract cream 40% was 1.145 cm, the wound length of the

negative control group treated with a cream base was 1,485 cm, then the length of the wound of the positive control group that was treated with gentamicin was 1,670 cm.

In this study, the hypothesis test was carried out using Kruskal Wallis test, followed by a post hoc test. After the Kruskal-Wallis test was carried out, the Mann-Whitney test continued to find significant differences between the two variables. It can be seen that P1 and P2 do not have a significant mean difference because the value of $p > 0.05$ is equal to 0.543. Comparison between P2 and P3 also does not have a significant mean difference because of the p-value of 0.147. In comparison, P1 and P4 have a significant mean difference because the value of $p < 0.05$ is equal to 0.012, P2 and P4 have a significant mean difference because of the p-value of 0.024. Then for P2 and P4, the mean difference is also significant because it has a p-value of 0,000. Then, P3 and P4 has a significant mean difference because the p-value is 0.037, which means $p < 0.05$.

DISCUSSION

The results and analysis of incision wound distance data in the 4 groups stated that the average length of incision wounds in group P1 (treatment group with

binahong leaf extract cream 40%) was 1.1954 ± 1.222928 , group P2 (treatment group with papaya leaf extract cream 40%) was 1.1452 ± 1.09528 , group P3 (negative control group with cream base) was 1.4854 ± 0.98399 , and group P4 (positive control group with gentamicin ointment) 1.6701 ± 1.06456 . This shows that papaya leaf extract cream 40% has the highest reduction in wound length. The second-highest reduction in wound length is in the group given binahong leaf extract cream 40%. The third is the negative control group with a cream base, and the fourth is the positive control group with gentamicin ointment.

Active ingredients such as saponins, flavonoids, and alkaloids found in papaya leaves and binahong leaves can assist the wound healing phases. In addition to its role in the inflammatory phase as an antiseptic, in the proliferation phase, saponins can increase the process of angiogenesis, increase the number of fibroblast cells and stimulate the formation of type I collagen. The flavonoid content also plays a role in the wound healing phase as an antiseptic, anti-inflammatory, and antioxidant. In addition to the proliferation phase, the flavonoid content can help increase vascularity.^{11,14,15} Alkaloid content plays a role in the inflammatory phase as an antiseptic.¹⁵ The

reduction in wound length of the group given papaya leaf extract cream 40% is higher than the treatment group with binahong leaf extract cream 40%. This is possibly due to the content of the papain enzyme in papaya leaves which is not possessed by extracts of other ingredients. The papain enzyme acts as an anti-inflammatory, accelerating the work of macrophages in the inflammatory phase. Besides that, in the proliferation phase, the enzyme papain also plays a role in the formation of granulation tissue, increasing the contraction of the wound edges and bringing the wound edges together.^{16,17}

In this study, the Mann-Whitney test results comparing the treatment group with 40% binahong leaf extract cream and the group treatment with papaya leaf extract 40%, obtained $p > 0.05$, $p = 0.543$. This means they were not significantly different because the active ingredient in both is almost the same. Therefore, their effectiveness in helping the healing process of incision wounds in white rats was not much different.

In this study, base cream has the best effectiveness in incision wound healing after papaya leaf extract cream 40% and binahong leaf extract cream 40%. Base cream shows better incision wound healing effectiveness than gentamicin ointment. This is contrary to the research

conducted by Miryam et al. (2014), who explained that the use of gentamicin cream could accelerate incision wound healing in rabbits infected with *Staphylococcus aureus* bacteria better than base cream. This is suspected because there are different topical medication forms, antibiotic resistance, allergic reactions, and disruption of normal flora. The different types of topical medication form used to affect the absorption of the skin, in this case, the form of gentamicin used in this study is an ointment which is a preparation with a semi-solid fat base material that is not suitable for use in hairy areas, folds and acute inflammation, whereas cream preparations are more moisturizing, more easily applied evenly, easier penetration on the skin, and is more suitable for use in lesions with hairy areas, intertriginous areas, and superficial and dry lesions.^{18,19}

CONCLUSION

1. The application of binahong leaf extract cream affects the wound length in the healing process of incision wounds.
2. The application of papaya leaf extract cream affects the wound length in the healing process of incision wounds.
3. There is no significant difference in effectiveness between giving 40% binahong leaf extract cream and 40%

papaya leaf extract cream in incision wound healing.

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