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The Effectivity Of Juwet (*Syzygium Cumini*) Leaf Ethanolic Extract In Rabbit's Wound Healing

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ABSTRACT

The medical plant has fewer side effects than chemical drugs and used by people as an alternative to treat wounds. Juwet as a medicinal plant has the potential to be developed as a wound healer. The purpose of this study was to determine the ability or activity of juwet leaf extract (*Syzygium cumini*) in wound healing. The test was carried out using *New Zealand* rabbits by making wounds on the rabbit's back which were then divided into 5 treatment groups. The treatment group consisted of Group I given *aquadestilata*, Group II given *povidone iodine*, Group III given 25% juwet leaf extract, Group IV given 50% juwet leaf extract, and Group V given 75% juwet leaf extract. The results showed that juwet leaf extract (*Syzygium cumini*) affected wound healing. Average wound diameter consecutively 6,69±1,34, 5,79±2,19, and 4,50±1,70 on day-7. 0,70±0,99, 0,46±0,65, and 0,00±0,00 on the day-10. Based on the results of the research conducted, it can be concluded that juwet leaf extract (Syzygium cumini) has a wound-healing effect on rabbits and the best concentration of juwet leaf extract (Syzygium cumini) for wound-healing activity is 75%.

Keywords: Extract, Rabbit, *Syzygium cumini*, Wound

INTRODUCTION

A wound is a type of tissue damage to the skin caused by exposure to heat sources such as chemical objects, hot water, radiation, fire, electricity, etc., as a result of medical treatment, or changes in physiological conditions. With the presence of work injuries and damage to the anatomy of the body. Wounds that don't heal quickly, of course, make you uncomfortable. If not treated properly, the wound can get worse until an infection occurs (Price and Wilson, 2006). If an infection occurs, it will take longer for the wound to heal, increase in exudate, the wound will become foul smelling, damage the wound boundaries, easy tissue damage, increase in wound size, and increase in pain (Powers *et al.*, 2016)

Wound healing is a process in which the wound experiences an acute inflammatory reaction at the edges which is then followed by the growth of granulation tissue and the surface area epithelializes so that it thickens and matures followed by the maturation of scar tissue at the bottom (Price and Wilson, 2006). When the skin is injured, the process of healing and cell regeneration occurs automatically as a physiological reaction of the body, namely through the hemostasis phase, the proliferation phase, and the remodeling phase.

Generally, people use antiseptics on minor wounds and use antibiotics for infected wounds. Both of these treatments generally have adverse side effects if used inappropriately. Medicinal plants are used by the community as an alternative to healing wounds because their side effects are smaller than chemical drugs. Juwet is a medicinal plant that can be developed as a wound healer. Fruit, fruit skin, and leaves are parts of plants that are often used as medicinal ingredients (Ulung, 2014). Juwet leaf extract contains compounds as secondary

metabolites namely tannins, flavonoids, terpenoids, steroids, and polyphenols (Rahmitasari *et al.,* 2020). Juwet plants are efficacious as antibacterial, antipyretic, anticancer, antioxidant, antiviral, and diabetes drugs because of the flavonoid and tannin compounds contained in juwet plants (Ulung, 2014) and have never been studied for their wound-healing properties.

METHODS

A. Tools and Material

Analytical balance, glass jar for maceration, grinder for grinding Simplicia, rotary evaporator for evaporating the result of extraction. The tools used at the animal testing stage included cages, a 1 cc injection needle, a biopsy punch with a diameter of 8 mm, surgical scissors, tweezers, and calipers. The materials used in this study were juwet leaf Simplicia originating from the City of Madiun and its surroundings, 96% ethanol, *betadine solution*, *aquadestilata*, and *New Zealand* rabbits for the test animals.

B. Extract Preparation

Fresh juwet leaves are washed, chopped, then dried using an oven at 50°C. The dried Simplicia was crushed and weighed as much as 500 g. Then put it in a glass jar and soak it with 96% ethanol solvent (Sutrisna *et al.,* 2018) as much as 2,500 ml (1:5 b/v ratio). Maceration was carried out for 3×24 hours while stirring once a day and re-maceration was carried out. The re-maceration process was carried out by adding 96% ethanol in a ratio of 1:3 for 2 days (Tamimi *et al.,* 2020). The filtrate produced in the maceration and re-maceration processes is combined and concentrated using a rotary evaporator.

C. Wound Induction and Wound Healing Activity Test

The experiment used 3 rabbits as test animals. Each rabbit is given 8 damage. The injuries will be grouped into 5 groups consisting of: Group I (negative), Group II (positive) given *betadine solution*, Group III given juwet leaf extract with a concentration of 25%, Group IV given juwet leaf extract with a concentration of 50% and Group V given juwet leaf extract with a concentration of 75%. The wound diameter was measured on days 0, 7, 10, 11, 13, and 14 using a caliper.

D. Data Analysis

The data obtained were processed with the SPSS application and analyzed using the Shapiro-Wilk normality test and the data homogeneity test with Levene's test. The One Way Anova test is used for normal ($p<0.05$) and homogeneous data. To find out the differences in each group, a post hoc test was carried out. The Kruskal-Wallis test is used if the resulting data is not normal ($p>0.05$) with an error rate of 5% and is continued with the Mann-Whitney test to find out the differences in each group.

RESULTS AND DISCUSSION

The research began with the manufacture of juwet leaf Simplicia. Juwet leaves that have been washed and dried. The juwet leaf extraction method in this study used the maceration method. The maceration extraction method was chosen because it is easy to process, and does not involve high temperatures so that the secondary metabolites contained in juwet leaves are not damaged (Imawati *et al*., 2023; Chairunnisa *et al.,* 2019). After going through the maceration and re-maceration processes, the macerate is evaporated using a rotary evaporator to obtain a thick extract. In this study, 700 g of dry simplicia was obtained with an extract yield value of 14%.

The wound-making stage was carried out on five rabbits that were given wounds on their backs. Before being injured the rabbit's back is first shaved to facilitate the process of injuring the rabbit's skin. The test animals were first given local anesthesia on the part to be

injured. 2% lidocaine injection is used as a local anesthetic injection injected subcutaneously into the part that will be injured so that when the wound is given it can minimize pain in rabbit test animals. Eight wounds were made on the rabbit's back which were then divided into 5 groups (negative control, positive control, extract treatment with concentrations of 25%, 50%, and 75%).

Table 1. Mean ± SD Wound Diameter on Backs of Test Animals

Groups	Day-					
	0	7	10	11	13	14
I	10,61 ± 1,17	4,77 ± 1,14	3,03 ± 0,98	2,07 ± 2,92	0,00 ± 0,00	-
II	9,53 ± 0,75 ts	5,72 ± 2,23 ts	0,00 ± 0,00 *	-	-	-
III	10,45 ± 0,32 ts	6,69 ± 1,34 ts	0,70 ± 0,99 ts	0,00 ± 0,00 ts	-	-
IV	10,02 ± 0,27 ts	5,79 ± 2,19 ts	0,46 ± 0,65 *	0,00 ± 0,00 ts	-	-
V	10,83 ± 0,36 ts	4,50 ± 1,70 ts	0,00 ± 0,00 *	-	-	-

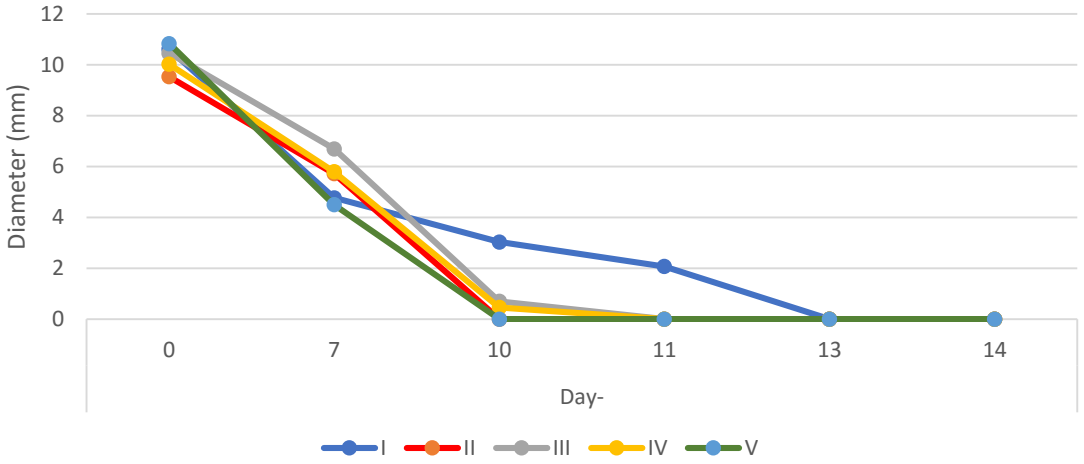
Notes: * significantly different (P<0.05) from the negative control group; ts was not significantly different (P>0.05) from the negative control group; Group I: Given *aquadestilata* treatment (negative control); Group II: Given betadine solution treatment (positive control); Group III: Given 25% juwet leaf extract treatment; Group IV: Given 50% juwet leaf extract treatment; Group V: Given 75% juwet leaf extract treatment.

	Day-0	Day-7	Day-10	Day-11	Day-13	Day-14
I						
II						
III						
IV						
V						

Notes: Group I: Given *aquadestilata* treatment (negative control); Group II: Given betadine solution treatment (positive control); Group III: Given 25% juwet leaf extract treatment; Group IV: Given 50% juwet leaf extract treatment; Group V: Given 75% juwet leaf extract treatment.

Figure 1. Wound Healing Process in Test Animals

Data from observations of wound healing tests in test animals according to (Figure 3) which has been observed shows that the wounds that have been made in all treatment groups experience closure.



Notes: Group I: Given *aquadestilata* treatment (negative control); Group II: Given betadine solution treatment (positive control); Group III: Given 25% juwet leaf extract treatment; Group IV: Given 50% juwet leaf extract treatment; Group V: Given 75% juwet leaf extract treatment.

Figure 2. Graph of Average Wound Diameter in Test Animals

Based on the data (Table 1 and Figure 1) on the 7th day, there was a decrease in the size of the wound diameter but did not show a significant difference between the other groups with a negative control in the wound diameter of the test animals (P> 0.05). The negative control group experienced wound healing on the 13th day, the positive control group and also the juwet leaf extract group at a concentration of 75% on the 10th day, then on the 11th day the wound healing process occurred in the juwet leaf extract group at a concentration of 25% and 50 %. On the 14th day (the last day of observation) the wounds in all test groups had closed completely. A significant difference in wound diameter between the other groups and the negative control group was only shown on the 10th day (P<0.05). On the 10th day, there was a significant difference between the positive control test group, 50% juwet leaf extract, and 75% juwet extract. This shows that juwet leaf extracts 50% and 75% have the same effect as the positive control. But in the 25% juwet leaf extract test group there was no significant difference from the negative control test group. This is by research conducted by Wijayanti and Safitri (2018) the higher the concentration of the extract used, the higher the antibacterial activity so that the wound closure process occurs more quickly.

Based on (Figure 2) it can be seen from the graph that the average wound diameter in test animals treated with juwet leaf extract has a line pattern that is almost the same as the positive control test group. These results were reinforced by statistical tests which showed that there was no significant difference in the average wound diameter between the positive control test group and the juwet leaf extract test group. This study shows the results of juwet leaf extract (*Syzygium cumini*) affecting wound healing. From the treatment group, the best results were shown by the betadine solution test group after which juwet leaf extract concentration was 75%, 50% then 25% concentration. In the negative control test group it still had a wound healing effect but it lasted longer than the positive control test group and juwet leaf extract. This happened because the negative control test group was only given *aquadestilata* where the *aquadestilata* did not contain active compounds that are antiseptic like the other test groups, so the wound healing process took longer (Budiawan *et al*., 2021). This result is similar to Sari *et al*. (2023) research which explained that wounds treated with *aquadestilata* healed on 11th

day.

In the positive control group, wounds were given *betadine solution* and experienced a faster healing process compared to the negative control group. On the 10th day, the wounds in the positive control group in the test animals had closed completely. *Betadine solution* is a liquid that contains an antiseptic to treat the skin when it is injured (Maudyana *et al*., 2022). Based on this theory the effectiveness of iodine as an antiseptic which has a broad spectrum can support the wound healing process in the positive group of rabbits compared to other test groups due to reduced bacteria that can interfere with the wound healing process. But iodine also has side effects, which can irritate, and burn skin, toxic reactions with iodine content, and skin color that can change due to the content of dyes in iodine (Rahmawati, 2014).

The ability to heal wounds from juwet leaf extract is predicted due to the presence of secondary metabolite compounds in juwet leaves. According to Rahmitasari *et al.,* (2020), juwet leaves contain tannins, flavonoids, terpenoids, steroids, and polyphenols. The antibacterial and anti-inflammatory abilities of juwet leaves can accelerate wound healing in test animals (Rusmalina, 2021). Flavonoid compounds are known as antioxidants (Indriasari, 2022) which have an action against free radicals (Budiawan *et al.,* 2023). Flavonoids have a working mechanism to reduce the growth of g-positive bacteria (Anisa, 2018). In addition, flavonoid compounds are chelating agents that are used to counteract free radicals by transferring free electrons (Banjarnahor and Artanti, 2014). So that the cells in the wounds of the test animals can be protected from damage caused by free radicals. According to Wardani *et al.,* (2018) flavonoids can relieve pain when bleeding occurs.

Tannins can prevent infection in wounds because they have antiseptic properties (Sari *et al*., 2023). Tannins function as antibacterial, antifungal, and astringent which can shrink pores, harden, and stop light bleeding on the skin. As an antibacterial, tannins react with cell membranes, inactivate enzymes, and inactivate genetic material (Handayani *et al.,* 2016). The activity of other tannins is used as a free radical scavenger so that the wound-healing process occurs more quickly (Palumpun *et al.,* 2017).

Terpenoids have actions as antibacterial and antioxidants which can speed up wound recovery (Manoppo, 2021). Terpenoids have an astringent and antimicrobial effect with a representation of recovery activity in wounds so that they can accelerate wound epithelialization and contraction (Setyowati, 2017).

CONCLUSION

Based on the results of the research conducted, it can be concluded that juwet leaf extract (*Syzygium cumini*) has a wound-healing effect on rabbits and the best concentration of juwet leaf extract (*Syzygium cumini*) for wound-healing activity is 75%.

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