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CARICA PAPAYA L. WITH SUTURE WOUND HEALING IN MICE EXPERIMENTAL ANIMALS

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Abstract

Background: Stitches are a condition in which skin tissue damage results from incisions or surgery and trauma. Carica Papaya Linn contains flavonoids which are efficacious as anti-inflammatory or antiseptic in inhibiting bacterial growth. Carica Papaya Linn is effective in repairing cells damaged by free radicals. The purpose of this study was to see the effectiveness of papaya leaf extract (Carica Papaya Linn) against stitches. **Method:** This research was quantitative research with a True Experimental design with the one group post-test method using the REEDA scale assessment. The population in this study were mice (Mus Musculus) which were divided into 5 groups, control group, nebacetin group, 5% test group, 10% test group and 15% test group. Research was conducted in the Lab. Medical Laboratory Technology at Muhammadiyah University of Sidoarjo and for making extracts from the Faculty of Mathematics and Natural Sciences, Surabaya State University. Data was collected and then the results were analysed using the One Way ANOVA statistical test. **Result:** The results of the statistical test showed a value of P = 0.000 in the 7th day group, which means there was a difference in each group of mice and the mean results showed the lowest result was 0.2 in the 15% extract which stated the best wound healing. **Conclusion :** The conclusion of the study was that there was an effect of giving papaya leaf extract (Carica Papaya L.) on wound healing in experimental mice.

keyword : *Carica Papaya L, Suture Wound*

INTRODUCTION

A wound is a con that results in disruption of a tissue in the body, which can cause the body's function to decrease and can interfere with daily activities. According to the process of occurrence, wounds are divided into surgical wounds or can be called incised wounds. These are wounds caused by damage to skin tissue. resulting in wounds (Diana Damayanti, 2016). The stages of wound healing consist of three phases, namely the inflammatory phase, the fusion phase, and the maturation phase, when wound granulation occurs directly. This process includes the formation of new connective tissue consisting of leukocyte cells, fibroblasts, and new blood vessels (Septiningsih, 2018).

Wound treatment consists of 2 factors, namely pharmacological and non-pharmacological. Pharmacologically, you can use antibiotic drugs such as nebacetin, amoxicillin and many more. Antibiotics are a class of antimicrobial compounds that have the effect of suppressing or inhibiting a biochemical process in an organism, especially in the process of infection by bacteria. Meanwhile,

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non-pharmacology means using herbal medicines such as papaya leaf extract, betel leaf, binahong leaf. Contains flavonoid, saponin and tannin compounds which are useful for anti-inflammatory and antiseptic properties(P. A, 2019).

Nowadays, the use of herbal therapy is increasingly popular because apart from being effective, it also tends to have a very low risk of side effects. One of the plants that is receiving great attention is the papaya plant, because various parts such as leaves, fruit, stalks, stems and roots have a number of benefits in a medicinal context(Syahruddin, 2019).

Papaya leaves (Carica Papaya L.) are a type of herbal that can be an alternative choice in wound care. The compounds contained in papaya leaves (Carica Papaya L.), namely flavonoids, are useful as anti-inflammatory and antiseptic in suppressing the growth of bacteria which can cause infection in wounds. Flavonoids are the same as antioxidants, which have many uses for the body, such as being able to replace cells that die due to free radicals. Flavonoid content is found in many parts of fruit, leaves, roots and skin(Seila Aprilliani Y. Robert B).

The treatment method using papaya leaf extract (Carica Papaya L.) is a non-pharmacological treatment in the herbal world. Papaya leaves (Carica Papaya L.) are a herbal plant that can be an alternative choice in wound care. Flavonoids play a role in the wound healing process against Staphylococcus aureus bacteria which often produce pus (pus) in wounds(Chritina, 2014). Recent research indicates that papaya leaf extract has potential in wound care. The active components in papaya extract include flavonoids(A. Syah, 2022). Based on the introduction, this research aims to analyze papaya leaf extract (Carica Papaya L.) on healing suture wounds.

METHOD

Research methods

The method used is quantitative research with a True Experimental design with the one group posttest method. This research is an experimental preclinical trial with a completely randomized design (CRD) and is also comparative. The data observed is the average time in days needed by each group of mice to close the wound. The experimental animal group was divided into several therapy groups, namely the Negative Control group (K-) which was not given treatment, the Positive Control group (K+) given the antibiotic nebacetin powder, test group 1 (P1) given 5% papaya leaf extract, test group 2 (P2) was given 10% papaya leaf extract, test group 3 (P3) was given 15% papaya leaf extract.

Extract Preparation Method

The extract is made in the Obstetrics Laboratory and then the ethanol filtrate is evaporated in the Lab. Chemistry Laboratory, FMIPA State University of Surabaya. The tools & materials needed in the research to make the extract are a blender, sieve, separating funnel, glassware (pyrex), spatula, maceration container (jar), analytical scales, filter paper and papaya leaves obtained from plantations in Sidoarjo Regency. 1 kg which is still fresh and green and 96% ethanol. The process of making an extraction from papaya leaves is by cleaning the papaya leaves (Carica Papaya L.) by

running them with clean running water and then draining them. The papaya leaves (Carica Papaya L.) are dried in the hot sun until dry for 3 days. Drying papaya (Carica Papaya L.) leaves under the sun must not be done directly exposed to sunlight, papaya (Carica Papaya L.) leaves must be covered with a cloth cover on top. Papaya leaves (Carica Papaya L.) are dried and then pulverized (pulverized). Simplicia (natural ingredients that have not undergone processing) which have been stored in a clean and tightly closed place are extracted by maceration for 1 x 24 hours for 3 days. On the first day, 300 grams of simplicia powder was mixed into a jar and then soaked in 1,500 ml of 96% ethanol, the ratio of alcohol to papaya leaves was 1:5 on the first day. Then soaked again on the second day with the initial amount of simplicia with 900 ml of 96% ethanol and stirred. Then the third soaking was carried out with the same type and amount of solvent as on the second day. Mixing and evaporating the ethanol filtrate using a rotary evaporator is concentrated over a water heater using a temperature of 40-50^0 C. The extract that will be obtained is in the form of a thick extract (liquid) which will be mixed with distilled water and can then be used in research(W. Bodhi, 2021).

Mice Treatment Methods

The experimental animals used are 30 mice (Mus Musculus) obtained from the Sidoarjo rat farm, aged 5-6 months, weighing 10-20 grams and will be kept in the Medical Laboratory Technology Laboratory of the Muhammadiyah University of Sidoarjo in a dry, non-humid room, at a temperature of 30^0 C, with minimal means not being exposed to direct sunlight. Tools used to house mice include 6 mouse cages measuring 30 cm x 20 cm x 15 cm, wooden planks, wire rams, drinking bottles, sterile gauze, rolled gauze, tape, scissors, razors and for feeding. 2 tablespoons of rice 2x (15 grams) a day sprinkled directly and to drink (1000 ml) added once every 2-3 days. Previously, all mice would be adapted for approximately 1 week in the lab. Medical Laboratory Technology before testing. In this study, mice were divided into 5 groups, namely control group, nebacetin group, 5% test group, 10% test group and 15% test group. All groups of mice were anesthetized using 0.2 – 0.5 ml of chloroform, after which the hair was shaved on the mice's back area using scissors and a shaver. The back is smeared with an alcohol swab, then measured and outlined to make it easier to make cuts or incisions 2-3 cm long and subcutaneously deep using a sterile scalpel. After that, the sewing process is carried out using the simple interrupted suture technique (interrupted sutures or one-on-one sutures). The application of papaya leaf extract (Carica Papaya L.) to stitched wounds is given 2 times/day by applying it using a cotton bud, and will be given or carried out aseptically for 7 days. During the treatment process using the extract, observations will be made on the healing of suture wounds(Watung, 2020).

Statistic analysis

Data were analyzed using the SPSS One Way Anova test with the one group posttest method. Sampling was carried out on 30 June – 7 July 2023, where data collection used the REEDA scale assessment instrument, which is an assessment instrument used to assess wound healing which contains five categories, namely Redness, Edema (Swelling), Ecchymosis (Bleeding Spots), Discharge (Expenditure), Approximation (Wound Healing). Each category has a score of 0 to 3,

namely there is no sign of healing. Then the assessment results for each category are presented as a total scale score ranging from 0 to 5, a high score indicates poor wound healing, while a low score indicates good wound healing. This data analysis was carried out quantitatively using normality, homogeneity tests and looking for the average wound healing time. If the p value = value < (0.05) then H1 is accepted which means: There is healing of suture wounds in mice after administering the extract, whereas if the p value is > (0.05) then H1 is rejected which means: There is no healing of suture wounds in mice after administering the extract.

RESULT AND DISCUSSION

3.1. Result

Tabel 3.1 Data Normality Test Result

Test Group	Sig.
Ex. 5% Extract Treatment	0,967
Ex. 10% Extract Treatment	0,814
Ex. 15% Extract Treatment	0,325
Ex. Control (+)	0,421
Ex. Control (-)	0,325

Based on table 3.1 it can be seen from the results of the normality test kel. treatment 5% (0.967), ex. treatment 10% (0.814), ex. treatment 15% (0.325), ex. nebacetin treatment (0.421), ex. control treatment (0.325) was declared normality test results for each group of mice on each first day were declared normally distributed because the Sig value. every day p> 0.05.

Table 3.2 Average Results of Stitch Wound Healing

Day	Test Group	Mean ± SD	95% C.I.	Sig.
1	**Ex. 5% Extract Treatment**	8 ± 1,581	6,04 – 9,96	0,626
	Ex. 10% Extract Treatment	8,6 ± 1,140	7,18 – 10,02	
	Ex. 15% Extract Treatment	9 ± 0,707	8,12 – 9,88	
	Ex. Control (+)	8,8 ± 1,304	7,18 – 10,42	
	Ex. Control (-)	9 ± 0,707	8,12 – 9,88	
4	**Ex. 5% Extract Treatment**	2,8 ± 1,140	2,18 – 5,02	0,000
	Ex. 10% Extract Treatment	4,4 ± 0,548	3,72 – 5,08	
	Ex. 15% Extract Treatment	1,8 ± 0,837	0,76 – 2,84	
	Ex. Control (+)	6 ± 1,581	4,04 – 7,96	
	Ex. Control (-)	7,8 ± 2,168	5,11 – 10,49	
7	**Ex. 5% Extract Treatment**	2,4 ± 0,548	1,72 – 3,08	0,000
	Ex. 10% Extract Treatment	2,6 ± 0,894	1,49 – 3,71	
	Ex. 15% Extract Treatment	0,2 ± 0,447	-0,36 – 0,76	
	Ex. Control (+)	6,2 ± 0,447	5,64 – 6,76	
	Ex. Control (-)	6,4 ± 0,707	5,12 – 6,88	

Based on table 3.2 after the data was tested to find out the mean and tested using the One Way Anova test, the mean value on the first day was highest in the treatment group 15% (9) and control (9), then on the fourth day it remained the same in the control group (7 .8) and on the seventh day the lowest value was in the 15% treatment group (0.2). From the mean value, it can also be seen that the average value each day in each treatment group is decreasing, but the treatment group with the best wound healing results is in the 15% treatment group. It can also be seen that the significance value on the first day was 0.626, which means $p > 0.05$, indicating that there were no significant differences in each group on the first day. Then on the fourth and seventh days, a significance value of 0.000 was obtained, which means $p < 0.05$, indicating that there were significant differences that occurred in each group on the fourth and seventh days.

Tabel 3.3 Results of Real Difference Test

Test	Group	Day 1	Day 4	Day 7
Extract 5%	**Extract 10%**	0,917	0,887	0,986
	Extract 15%	0,643	0,273	0,000
	Nebacetin	0,800	0,081	0,000
	Control	0,643	0,001	0,000
Extract 10%	**Extract 5%**	0,917	0,887	0,986
	Extract 15%	0,980	0,051	0,000
	Nebacetin	0,999	0,382	0,000
	Control	0,980	0,007	0,000
Extract 15%	**Extract 5%**	0,643	0,273	0,000
	Extract 10%	0,980	0,051	0,000
	Nebacetin	0,999	0,001	0,000
	Control	1,000	0,000	0,000
Nebacetin	**Extract 5%**	0,800	0,081	0,000
	Extract 10%	0,999	0,382	0,000
	Extract 15%	0,999	0,001	0,000
	Control	0,999	0,273	0,986
Control	**Extract 5%**	0,643	0,001	0,000
	Extract 10%	0,980	0,007	0,000
	Extract 15%	1,000	0,000	0,000
	Nebacetin	0,999	0,273	0,986

Based on table 3.3, it shows very clear differences in the healing of suture wounds in each treatment group on a daily basis. On the first day the significant value was still $p<0.05$ which indicated there was no difference between the groups, but on the seventh day the significant value showed a change, namely $p>0.05$ in the 5% and 15% extract groups with a value of 0.000, the 5% extract group and nebacetin with a value of 0.000, 5% extract group and 0.000 control.

3.2. Discussion

Wound healing here uses non-pharmacological methods using papaya leaf extract which contains flavonoid compounds which have anti-inflammatory and antiseptic properties. The wound healing process is caused by a number of factors, one of which is the type of treatment applied, as well as the increasing preference for the use of traditional plant-based medicines. An example of this aspect is supported by Septiningsih (2008), who indicated that ethanol extract from papaya leaves can accelerate the healing process of burn wounds on the skin of New Zealand rabbits(Kamalia, 2017).

Flavonoids are similar to antioxidants, and have various uses for your body, including their ability to reverse cell damage caused by free radicals. Almost all parts of the plant, such as fruit, roots, leaves and outer skin of the stem, contain flavonoids. The benefits of flavonoids include protection of cell structure, increased effectiveness of vitamin C, anti-inflammatory properties, prevention of osteoporosis, and a role as an antibiotic agent(Watung, 2020).

The flavonoid content can help the wound healing process more quickly, one of the leaves that contain flavonoids is papaya leaves. In this study, researchers used papaya leaf extract for the wound healing process, the extract was divided into 3 percentages, namely 5%, 10% and 15%. The content of flavonoid compounds in Carica Papaya L. extract is 15% more, therefore the healing of stitched wounds given or smeared with 15% extract is more effective than others. Especially compared to the group of mice that were not given the extract. From the analysis results it is known that papaya leaves (Carica papaya L.) contain positive flavonoid compounds(Q. A'yun, 2015).

In Indonesia, research conducted by Djunaidi et. al (2015) regarding the effectiveness of papaya leaf extract gel with concentrations of 5%, 10% and 15%, applied 1x/day for 7 days, shows that the content of papaya leaves triggers tissue formation in stitched wounds and the best wound healing is at a concentration of 15 %. Much literature has revealed that papaya leaf extract contains various components that have benefits, including as a wound healing agent thanks to the content of substances such as flavonoids(Ramadhian, 2018). Flavonoids are a type of compound that stimulates collagen production during the wound healing process. Apart from flavonoids, papaya leaves also contain vitamins C, E, beta-carotene and the enzyme papain. Vitamins C, E, and beta-carotene act as antioxidants that balance free radicals that arise due to neutrophil phagocytosis of cell debris and bacteria during wound healing. On the other hand, the papain enzyme functions to accelerate macrophage activity by increasing the production of interleukin which supports the wound healing process, while reducing the potential for more widespread infection(Amanda Nasution, 2017).

Based on other research, papaya leaves have an effect on the wound healing process, this condition is supported by phytochemical screening which states that the papaya leaf part of the papaya plant (Carica papaya L.) contains flavonoid compounds(Adam syah dkk, 2022). Flavonoids are compounds found in papaya leaves (Carica papaya L.) which functions for the wound healing process(Parampasi, 2013).

The flavonoid content contained in papaya leaves has an important role in speeding up the wound healing process. Flavonoids act as antiseptic and anti-inflammatory substances, so they can speed up wound healing. Not only that, flavonoids also have the ability to stop bleeding and

accelerate wound healing. In addition, saponins have an influence on collagen structure and are able to inhibit excessive growth of tissue wounds. Tannins contribute to the wound healing process by increasing blood vessel formation and stimulating fibroblast cell activity. In contrast, steroids suppress the activity of enzymes involved in the synthesis of arachidonic acid, thereby reducing the production of inflammatory mediators(Hertian, 2021).

CONCLUSION AND SUGGESTION

From this research it can be concluded that there are differences in the healing process of stitched wounds on a daily basis in each group. And the best wound healing group was the 15% concentration group which showed the fastest wound healing results compared to other wound groups. So papaya leaf extract with a concentration of 15% can be used as an alternative in the process of healing suture wounds. Suggestions for further research need to be processed to extract a better texture so that it is easy to use.

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