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The Effect Of Giving Pegagan *(Centella Asiatica)* Ethanol Extract On Incised Wound Healing In White Rats *(Rattus Norvegicus)*

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ABSTRACT

This study aims to determine the effect of giving *Centella asiatica* on incised wound healing through the treatment of *Centella asiatica* on white rats *(Rattus norvegicus).* This study uses Experimental method in the form of a post-test only group design to determine the effect of *Centella asiatica* ethanol extract on the healing time of incised wound in white rats *(Rattus norvogicus)*. The sample used in this study was 20 white rats divided into five treatment groups. Data analysis used quantitative analysis with helped of SPSS 29 software. The data test consisted of normality, homogenecity, and one way ANOVA test. The result showed 10% *Povidone iodine*, *vaseline*, 10% ointment of *Centella asiatica* ethanol extract, *15%* ointment of *Centella asiatica* ethanol extract, and 25% ointment of *Centella asiatica* ethanol extract had the same effect on incised wound healing in white rats *(Rattus norvogicus).* Intervention with 10% *Povidone iodine* had average healing time of 12,75 days; intervention with 10% ointment of *Centella asiatica* ethanol extract had average healing time of 10 days; intervention with 15% ointment of *Centella asiatica* ethanol extract had average healing time of 8,75 days; and intervention with 25% ethanol extract *Centella asiatica* had average healing time of 12,75 days. The normaly test shows that the entire group has a significant value of p>0,05, so it says that the data is normally distributed. The homogeneity test shows an overall significance of p>0,05, so the data is nuanced and homogeneous. The ANOVA test showed a significance of p = 0,152, so the value of p >0,05, meant that there was so significant difference between groups. This study proved that the application of *Centella asiatica* ethanol extract ointment can be used as an alternative in the treatment of incised wound, such as post-section caesarean wound care.

1. INTRODUCTION

A wound is a condition of damage to the body's tissue structure due to various factors, such as an opening with a sharp object, scratches, animal bites, and others (Harsa, 2020). The wound must be treated seriously in order to achieve a complex regeneration process (Suryanti & Supriyadi, 2008). Care and treatment of open wounds is very important to avoid infection (Nurdiatini et al., 2017). In general, Povidone iodine 10% is widely used as an antiseptic for wound treatment. However, inappropriate use can negatively affect the development of granulation tissue in the wound (Nurdiatini et al., 2017). Traditional medicine is an alternative choice for at least 49% of the Indonesian population in treating wounds (Oktaviani et al., 2019). The results of the literature search found that there are at least seven plants that meet the criteria as wound healing plants based on traditional use. One of these herbs is Pegagan (Sutardi, 2017).

Several studies have been conducted to prove the role of Pegagan (Centella asiatica) in the wound healing process but remain unclear. Various studies show Centella asiatica has compounds with anti-microbial properties (Arumugam et al., 2011). In addition, it is also believed that complex compounds such as saponins, phytosterols, phenolic compounds, tannins and terpenoids are also capable of inhibiting pathogenic microorganisms (Kannabiran et al., 2009). Other studies have also shown Pegagan to be efficacious for blood circulation, laxative urine (diuretic), high blood pressure, reduce fever (antipyretic), improve memory, treat measles, tonsils, treat skin diseases, antibacterial, anti-

inflammatory (anti-inflammatory), insecticide, anti-inflammatory. allergies, tuberculosis drugs, and improve memory (Putri et al., 2021). Some of them are Harsa's research (2020) which obtained the results that Centella asiatica extract can heal wounds faster than the administration of 0.9% Nacl and povidone iodine in wound management of male white rats (Rattus norvegicus) (Harsa, 2020). Another study was also conducted by Galomat (2021) which succeeded in proving that the incision wound in white rats experienced an accelerated healing process (Galomat et al., 2021).

The focus of this study was to examine more deeply the effect of Centella asiatica ethanol extract in ointment preparations with different concentrations to determine the fastest concentration for wound healing in white rats (Rattus norvegicus). Ointment preparations are preparations that are commonly used in society. In addition, this study also focused on how this gotu kola extract compares with povidine iodine antisepsis which is commonly used in the community.

2. METHOD

The method used in this study is True Experiment method and the form of the study design is a post-test only group design. White rats that have been given a incision on their body are divided into 5 groups. The five groups of rat will get different treatments. The first group will be given povidone iodine 10%, the second group will be given vaseline, the third group will be given 10% Pegagan ethanol extract ointment, the fourth group will be given 15% Pegagan ethanol extract ointment, and the fifth group will be given 25% Pegagan ethanol extract ointment. All treated groups will be observed for wound healing progress. The sample in this study was 20 white rats *(Rattus norvogicus)* divided into five groups. The sample in this study were selected using purposive sampling with the criteria of healthy white rats, male, 2-3 months old, weighing 150-200gr, having disabilities, and not wanting to eat.

The data from the observation activities were analyzed using the help of SPSS software, the analysis used is a follow : 1) Normality testing is carried out though the Shapiro-Wilk test to determine whether the research data sample consist of normally distributed data populations, 2) The homogenecity test was conducted using Levene-Statistic with the purpose of obtaining information about sample groups with varied origins and similar populations, and 3) One way ANOVA testing was applied with the purpose of determining whether there was a difference in the mean length of incised wound healing in each group.

3. RESULTS AND DISCUSSION

Table 1. The Result of Normality Test (Shapiro-Wilk)

	Groups	Statistic	df	Sig.
The length of Incised wound Healing (days)	Group I	.945	4	.683
	Group II	.994	4	.976
	Group III	.827	4	.161
	Group IV	.828	4	.163
	Group V	.971	4	.850

Shapiro-Wilk data analysis of the first group resulted in a significance value of 0,683 (p=0,683), a value of 0,976 (p=0,976) for the second group, a value of 0,161 (p=0,161) for the third group, a value of 0,163 (p=0,163) for the fourth group, and a value of 0,850 (p=0,850) for the fifth group. All groups have a significance value of p>0,05, which means that the research samples are normally distributed (parametric).

Table 2. The Result of Homogeneity Test (Levene Statistic)

	Groups	Levene-Statistic	df1	df2	Sig.
The length of Incised wound Healing (days)	Based on mean	2.088	4	15	.133
	Based on median	1.161	4	15	.367
	Based on Median and with adjusted df	1.161	4	7.410	.400

	Based on trimmed mean	1.918	4	15	.160

Based on the Levene Statistic data analysis, the result show that the mean shows a value of p=0,133; the median shows a value of p=0.357; the standard deviation have a value of p=0.160. thus the significance value in all data meets the requirements of p>0,05, which mean all research data are similar variants (homogenous).

Table 3. The Result of One Way ANOVA Test

	Sum of Squares	df	Mean Square	F	Sig
Between groups	51.500	4	12.875	1.966	0.152
Within groups	98.250	15	6.550		
Total	149.750	19			

Based on ANOVA testing, can be seen that the significance value is 0,152 (p=0,152) it means that the significance value is qualified as p>0,05. So it can be concluded that the groups in the research do not have significant differences. Because no significant differences were found in the groups, testing was not applied to analyze differences between groups through Post Hoc.

The wound was observed macroscopically by measuring the length of the wound to see the wound healing process with the purpose of comparing the length of healing between the five groups with different treatment. The result of observation in the study of the provision of different interventions in each group, which are group I wound incision with 10% povidone iodine; group II wound incision with vaseline; group III wound incision with 10% *Centella asiatica* ethanol extract ointment thereapy; group IV wound incision with 15% *Centella asiatica* ethanol extract therapy; group V wound incision with 25% *Centella asiatica* ethanol extract ointment therapy, are listed in Figure 1.

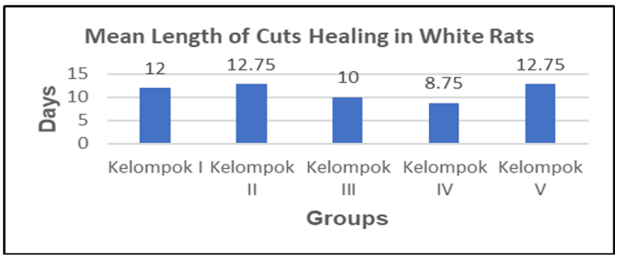

Figure 1. Mean Length of Incised wound Healing in White Rats

The purpose of the study was to prove the effect of *Centella asiatica* ethanol extract on the healing time of white rats (Rattus norvegicus) that had been given a incision wound on their body. Therefore, different interventions were carried out on 5 groups of rats, namely group I was given 10% povidone iodine intervention; group II was given vaseline intervention; group III was given 10% Pegagan (*Centella asiatica*) ethanol extract ointment intervention; group IV was given 15% Pegagan (*Centella asiatica*) ethanol extract ointment intervention; and group V was given 25% Pegagan (*Centella asiatica*) ethanol extract ointment intervention.

This study began with the procedure of making incision wounds on white rats. The fur on the back of white rats was shaved and then cleaned using an alcohol swab. The cleaned back was then anesthetized using ketamine at a dose of 50 mg/kgBB which was injected intramuscularly. After that, the back was incised along 3 cm with a depth of 2 mm using a sterile scalpel. The incision incised wound on each white rat body are given ointment evenly according to the group. Ointment application is done once a day until the wound heals and closes. The wound that has been given ointment is then closed using gauze. Furthermore, observation, recording, and documentation were carried out on the development of the wound healing process.

The difference in the length of healing in each group can be seen in Figure 1. White rats in group I that have been intervened with povidone iodine 10% show the wound closed with the fastest time on

day 11 and while the longest time on day 13 with the average length of the wound healing process occurs within 12 days. Povidone iodine is one of the most commonly used primary dressings in wound care. Povidone iodine has antiseptic properties, which inhibit or eradicate bacteria. Povidone iodine also has toxic properties to fiboblasts, which are known to affect the process of collagen formation for the formation of new tissue in the wound so that it can inhibit the wound healing process (Nurdiatini et al., 2017). Long-term and high-concentration use of povidone iodine may inhibit wound granulation formation.

White rats in group II that had been intervened with vaseline closed the fastest on day 8 and the longest on day 17, with an average length of wound healing process within 12.75 days. Vaseline has emollient properties that soften the skin, skin hydration will increase due to inhibition of water evaporation in the skin layer. The effect of hydration from vaseline can increase drug absorption (Ansel, 1989). Agustina, 2010 in Widianingtyas, (2013) added that a humid environment can accelerate fibrinosis by neutrophils and endothelial cells, encourage the formation of new blood vessels (angiogenesis) quickly, reduce the risk of infection, help the formation of natural body proteins quickly, help the formation of active cells quickly where the invasion of white blood cells and the immune system functions earlier (Widianingtyas, 2013). Moist wound skin conditions can also encourage the rapid healing process by making it easier for epidermal cells to move freely through the wounded skin so that new granulation tissue will form (Smeltzer & BG., 2001). Therefore, because vaseline is emollient which has a role as a skin moisturizer, in this study vaseline was able to close the wound most quickly on day 8.

White rats in group III that had been intervened with 10% *Centella asiatica* ethanol extract experienced wound closure with the fastest time on day 8 and the longest time on day 11 with an average wound healing process occurring within 10 days. White rats in group IV that had been intervened with 15% *Centella asiatica* ethanol extract experienced wound closure with the fastest time on day 6 and the longest wound healing on day 14 with an average length of wound healing process within 8.75 days. White mice in group V that were treated with 25% *Centella asiatica* ethanol extract experienced the fastest wound closure on day 11 and the longest wound healing on day 15 with an average wound healing time of 12.75 days.

Pegagan (*Centella asiatica*) is known to have a main active substance in the form of triterpene saponins. The saponins in *Centella asiatica* plants are antibacterial (Ramandey & Bunei, 2021). The content of triterpene saponins in pegagan consists of asiaticoside, asiatic acid, thanukunside, isothankuside, madecassoside, brahmaside, brahmic acid, madasiatic acid, mesoinosetol, centellose, caroteinoid, potassium, sodium, calcium, iron, vellarine, tannin, mucilage, resin, pectin, sugar, protenin, phosphot, vitamin B, vitamin C, and a little essential oil (Seevaratnam, 2012; Winarto & Surbakti, 2003). The triterpene saponin content can accelerate the wound healing process because it can increase the attraction and synthesis of collagen. Asiatic acid can stimulate collagen synthesis, while madecassoside can increase type III collagen production and has anti-inflammatory effects (Zheng & Qin, n.d.). In addition to acting as a stimulator of collagen growth in the wound healing process, the saponins contained in Pegagan are also able to neutralize pain and inhibit the overproduction of wound tissue. In wound healing efforts, flavonoids are also known to have a role in anti-inflammatory activity (Harsa, 2020).

Quercetin is a type of flavonoid that can inhibit the metabolism of arachidonic acid containing cyclooxygenase and lipoxygenase so that the production of prostaglandins and leukotriene is inhibited. This results in the appearance of pain symptoms, reduced swelling, and reduced dilation of blood vessels in the local bloodstream. As a result, the development and maintenance of inflammatory cells is reduced (Balqis et al., 2014). Therefore, with the content of Pegagan that has an important role in the wound healing process, this study proves that Pegagan (*Centella asiatica*) is able to close the wound most quickly on the 6th day, which occurred in group IV white rats that received intervention treatment with 15% Pegagan (*Centella asiatica*) ethanol extract ointment.

The difference in the mean length of healing in the groups with the intervention of 10% pegagan ethanol extract ointment, 15% pegagan ethanol extract ointment, and 25% pegagan ethanol extract ointment can be influenced by the viscosity and density produced from each extract concentration. If the concentration of the extract in the ointment is too low, the active substance content in the ointment

is also low so that the ability of the ointment to heal wounds by the active substance of the extract will not work optimally. If the concentration of extract in the ointment is too high, the higher the viscosity and density of the ointment so that the ointment is difficult to be absorbed by the skin which will produce thick necrotic tissue. The thicker the necrotic tissue, the blood supply and nutrients as well as cell migration will be hampered so that the healing process becomes longer (Winarto & Surbakti, 2003).

Based on the results of research on the effect of Pegagan ethanol extract on the length of wound healing in white rats, it can be seen that povidone iodine 10%, vaseline, Pegagan ethanol extract (*Centella asiatica*) 10%; 15%; and 25%, have benefits for wound healing. The effect on the length of wound healing in each group has the same benefit, which is shown from the mean length of wound healing and One Way ANOVA testing. With this, povidone iodine 10%, vaseline, ointment of *Centella asiatica* ethanol extract 10%; 15%, and 25% have an equally good effect on wound healing.

The results show that the treatment of Pegagan (*Centella asiatica*) ethanol extract ointment can be used as an alternative in the treatment of incision wounds such as post section caesarea wound care.

4. CONCLUSION

The intervention treatment with povidone iodine 10%, vaseline, *Centella asiatica* ethanol extract 10%; 15%; and 25% had the same benefit on wound healing. This is evidenced in the mean length of wound healing and the results of the One Way ANOVA test.

The results showed a difference in the mean length of wound healing time, where the incision wounds given intervention with 15% Pegagan ethanol extract ointment had the shortest wound healing results with a mean of 8.75 days. The group treated with 10% Pegagan ethanol extract ointment had the second shortest mean wound healing time with a mean wound healing time of 10 days. The group with povidone iodine 10% intervention had a mean wound healing of 12 days. Meanwhile, the interventions with vaseline and 25% Pegagan ethanol extract had the same mean wound healing time of 12.75 days.

The optimal dose of *Centella asiatica* ethanol extract for the wound healing process is 15% concentration because it has the best effectiveness when compared to other groups, which has an average wound healing process within 8.75 days.

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