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BINAHONG [*Anredera cordifolia* (*Tenore*) *Steenis*] LEAF INFUSA FOR SUTURE WOUND INFECTION CONVALESCENCE

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Abstract

Background: Postpartum infections are the top 4 main causes of the high maternal mortality rate in Indonesia at 2022 of 183 per 100,000 live births. Efforts to prevent complications due to infection of puerperal suture wounds with pharmacological therapy using antibiotics and antiseptics, as well as non-pharmacological ones using plant extracts. Binahong is believed to contain flavonoids, terpenoids, saponins, tannins, essential oils, and alkaloids, which are especially useful in healing wound infections. The aim of the study was to determine the effectiveness of infusion of binahong leaves (Anredera cordifolia (Tenore) Steenis) on the healing of suture wound infections in rats (Rattus norvegicus) experimental animals. **Method:** The research method was a true-experimental posttest only control group design, the study was conducted from June to August 2023 at the Microbiology and Pharmacology Laboratory of Muhammadiyah Sidoarjo University, the research variables were binahong leaf infusion and healing of suture infection, assessment and data collection using the REEDA scale instrument, statistical analysis with the one-way ANOVA, and post-hoc follow-up tests. **Result:** The results showed p <0.05, so there was a significant effect of giving binahong leaf infusion on the healing of suture wound infections. In terms of the difference in the mean value and the results of the post-hoc significant difference test, it appears that the 5% binahong leaf infusion group showed the most effective results in healing suture wound infections and was significantly different from the negative control group with less effective healing of suture infections. **Conclusion :** This is in line with research that states that the group given a 5% concentration of binahong extract was more effective than the group with a higher concentration. Thus, administration of a 5% concentration of binahong leaf infusion can be an alternative for healing suture wound infections due to the important content in it in the form of flavonoids, terpenoids, saponins, tannins, essential oils, and alkaloids. Further research is needed with lower concentrations of binahong leaf infusion to find out the minimum concentration that can have a good effect on the convalescence of suture wound infections.

keyword : *binahong, infection, wound, suture.*

INTRODUCTION

Infection is one of the reasons why the Maternal Mortality Rate (MMR) is still high in Indonesia, because the achievements are still far from the SDGs (*Suitainable Development Goals*) target of 70 per 100,000 live births (KH)(Dinas Kesehatan Provinsi Jawa Timur, 2021). It was recorded that in East Java in 2021 the maternal mortality rate reached 234.7 per 100,000 live births, of which infection

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contributed 7.19%(Dinas Kesehatan Provinsi Jawa Timur, 2021). And in the same year, the MMR in Sidoarjo was 59.69%(*Dinkes Sidoarjo, Profil Kesehatan Kabupaten Sidoarjo Tahun 2021*, 2022).

Suture wound infection is inflammation caused by primary bacterial organisms, especially skin flora including *Streptococcus pyogenes* or *group A streptococcus* (GAS) and *Meticillin resistant Staphylococcus aureus* (MRSA)(Phillips & Walsh, 2020). In addition, stitch wound infections can also be caused by *Streptococcus pneumoniae, Escherichia coli bacteria, Clostridium septicum, Staphylococcus aureus, Clostridium sordellii, Clostridium perfringens*, and *Morganella morganii*(Royal College of Obstetrician & Gynecologist, 2012). When a wound infection develops within 48 hours, the causative organism is usually *group A* or *B hemolytic Streptococcus* or so-called *Streptococcus pyogenes*(Phillips & Walsh, 2020). Puerperal infection by *group A Streptococcus* (GAS) is still a cause of maternal death worldwide, including countries that use modern antibiotic regimens, intensive care measures and infection control practices(Hamilton et al., 2013). The emergence of infection is characterized by fever, tenderness, redness, swelling, and abnormal discharge or exudate(Shinar et al., 2016). Factors that can influence the occurrence of suture wound infections are the result of less clean suture treatment, which causes easy growth of germs and bacteria(Lubis, 2016).

Intervention in puerperal suture wound infection is given pharmacological therapy and non-pharmacological therapy. Pharmacological therapy is by administering antibiotics and antiseptics(BPOM, 2016), meanwhile, the use of non-pharmacological therapy is one of them using plant extracts(BPOM, 2016). Binahong is a vine originating from Central and Eastern South America which then spread to Asia (China, India, Japan, Israel) , parts of Africa, Mexico, the Caribbean, Australia, the United States, New Zealand and other places(BPOM, 2016). Binahong is believed to be useful in the wound healing process because it contains several ingredients including flavonoids, saponins, terpenoids, essential oils and alkaloids which have anti-inflammatory antioxidant properties and antibacterial(BPOM, 2016).

Based on research by Miladiyah and Prabowo in 2012, it was stated that the ethanol extract of binahong leaves in concentrations of 20% and 40% was effective in healing 2 cm incision wounds in guinea pigs(Miladiyah & Prabowo, 2012). The same thing was done by Singh, et al. in 2014 showed that topical administration of binahong leaf paste showed better results in healing 1 cm^2 incisional wounds in mice (*Musmuscularis*)(Gurcharan Singh et al., 2014). The results of research conducted by Violante, et al. 2020 stated that the flavonoids in the hydroethanol extract of dried *Fridericia chica* leaves showed good antibacterial activity against Gram-negative and Gram-positive bacteria including *Streptococcus pyogenes, Pseudomonas aeruginosa, Staphylococcus epidermidis, Staphylococcus aureus,* and *Salmonella typhimurium*(Violante et al., 2021). The same thing was done by Hasyim (2020) which states that the active content of binahong tuber infusion with concentrations of 5%, 10% and 20% also has antibacterial properties against the growth of *Escherichia coli*(Hasyim, 2020). Results of experiments by Gusnimar, et al. (2021) stated that boiled water from binahong leaves is effective in healing perineal wounds in postpartum women(Gusnimar et al., 2021). Based on this background, it is necessary to carry out further research regarding the effectiveness of the active ingredients in binahong leaves using the infusion method for suture wound infection convalescence.

METHOD

The research method used was *true-experimental* "*posttest only control group design*" to test whether an experimental variable was effective or not, in this study the independent variable was binahong leaf infusion [*Anredera cordifolia* (*Tenore*) *Steenis*] and the dependent variable was healing of stitched wound infections. The research was conducted at the TLM (Medical Laboratory Technology) Microbiology and Pharmacology Laboratory, Faculty of Health Sciences, Muhammadiyah University of Sidoarjo. The intervention was carried out for 7 days, and data was collected using the REEDA scale instrument to measure healing of suture wound infections which includes five components related to the healing process, namely redness, swelling, ecchymosis, output, and tissue linkage. In this research, an ethical feasibility test was carried out first through the Ethics

Committee of Nahdlatul Ulama University Surabaya with certificate number 0313/EC/KEPK/UNUSA/2023.

Adaptation of experimental animals(Handajani, 2021)

The stages in this research started from the preparation and maintenance stage of the test animals, namely healthy white rats (*Rattus norvegicus*), the number of samples previously determined using the Federer formula was 24 with a total reserve of 4 female rats aged ± 3-4 months with a weight of around 150 g. -250 grams which are adapted first for 1 month, where there is a quarantine process of ±3 weeks to get the rats used to the new environment and make it easier for the mice to adapt to the stimulus given in the research through habituation to contact between the researcher and the rats, as well as an acclimation process carried out for ± 1 week to adapt rats to new procedures and equipment. Apart from that, also prepare the environment and rearing cages (room temperature 18◦C-26◦C, there is ventilation, and changes between light and dark every 12 hours), as well as providing food (ie rice and soup) and drinking water.

Preparation of binahong extract powder(BPOM, 2016)

The binahong leaves used in this study came from the binahong plant in Magepanda District, SIKKA Regency, Maumere, Flores, East Nusa Tenggara. Binahong leaves were taken and processed until dry and then prepared as much as 200 grams (175 grams used in the study) into thick plastic which was tightly closed and safe which was then sent to Java (research site, Sidoarjo) via ship for 3 days of travel. The steps for preparing the binahong leaf extract powder before being shipped are: a) picking the binahong leaves directly from the plant, b) washing all the binahong leaves which will be used as extract using clean running water, c) drying the binahong leaves which have been washed clean under direct sunlight to dry for ± 1 week, d) dry binahong leaves are blended and filtered to obtain fine powder, e) fine powder and then stored in a safe and clean storage container.

Making media and rejuvenating the bacteria *Streptococcus pyogenes*(Nurhidayanti, 2019)

The first step is to make *Blood Agar Plate* (BAP) media by weighing 20 grams of BAP media into an Erlenmeyer and dissolving it with 500 ml of distilled water, then heating over a Bunsen until the media is clear. After that, the media was

sterilized using an autoclave at 121◦C for 15 minutes. After being sterilized, the media was added with 25 ml of sheep blood or 5% of 500 ml, then shaken. After the next step, the media was poured into the prepared petri dish and sterilized again in UV light with *laminar air flow* for 30 minutes. Next, the media was wrapped in plastic wrap and incubated for 24 hours.

The next step was planting the pure culture of *Streptococcus pyogenes* ATCC 19615 which had been taken from BBLK Surabaya into BPA media which had been made by taking it using sterile wire loops and planting it evenly on the media by scraping. Next, the bacteria are incubated for 24 hours in an incubator to help the bacteria grow.

Preparation of 0.5% McFarlan solution and bacterial suspension(Rosmania & Yanti, 2020)'(Postol et al., 2013)

The next step is to make a 0.5% McFarlan solution which is equivalent to the number of bacteria 1.5 x 10^8 as a standard solution for comparison to the turbidity of the bacterial suspension with the following steps: a) make a 1% $BaCl_2$ solution by weighing 1 gram of $BaCl_2$ into a tube measure and dissolve with 100 ml of distilled water, b) make 1% H_2SO_4 using concentrated H_2SO_4 taken as much as 1.02 ml into a tube that already contains 100 ml of distilled water, then stir until mixed, c) mix 0.05 ml of 1% $BaCl_2$ and 9.95 ml H_2SO_4 1% then shake until completely mixed.

After the 0.5% McFarlan solution is ready, then a suspension is made which is equalized in turbidity with the 0.5% McFarlan solution with the following steps: a) Make a 0.9% NaCl solution by weighing 0.9 grams of NaCl and dissolving it with 100 ml distilled water into a measuring tube, b) the solution is stirred until completely mixed, c) the solution is then transferred to 2-3 test tubes, d) then the 0.9% NaCl solution is sterilized cleanly in the autoclave with a temperature of 121◦C for 15 minutes, d) 0.9% NaCl was then cooled to room temperature before suspension, e) *Streptococcus pyogenes* bacteria were taken on BPA media using sterile wire loops carefully and mixed into 0.9% NaCl solution and shaken until completely mixed and adjusted to the McFarlan turbidity standard of 0.5%, f) the appropriate suspension, then incubated for 24 hours in an incubator to help the growth of bacteria.

Making suture wound and giving bacteria(Postol et al., 2013)**'**(Rejeki et al., 2018)

This stage was carried out as follows: a) anesthetizing the rats using chloroform, b) the rats that had fainted were placed on the underpad, c) shaving using the *single midline incision* technique, d) wiping the surface of the shaved skin using a 70% alcohol swab, e) make a small vertical incision or incision 2 cm long, f) the wound is sutured using an absorbable needle and thread, g) the sutured wound is cleaned using sterile cotton and then the rat is placed back into the cage, h) after sewing the rat is finished, injected about 0, 2 cc of *Streptococcus pyogenes* bacterial suspension over the suture wound and allowed to stand for 24 hours for bacterial growth, i) on the 1st day of anatomical pathology observations found rats infected with *Streptococcus pyogenes* which was characterized by redness around the lesion area (wound), slight swelling and tissue damage around the lesion, as well as causing an abscess in the form of pus.

Sampling(Phillips & Walsh, 2020)**'**(Kemenkes, 2021)**'**(Setyawan, 2015)

Total of 24 infected rats were grouped randomly (*simple random sampling*) by lottery into 4 groups with each group containing 6 rats (experimental group 1 infusion of 5%, experimental group 2 infusions of 20% with an infusion dose of 3.6 ml/200 gr BW rats/day, the positive control group was given the antibiotic *Co-Amoxiclav* dose of 11.25 mg/200 g BW rats/8 hours, as well as the negative control group or no treatment, only normal care). The dose in each treatment was readjusted to the weight of each rat and given 3 times a day or an interval of 8 hours, namely at 07.00 WIB (morning), 15.00 WIB (afternoon), and 23.00 WIB (night) orally using a gastric sonde for 7 days treatment.

Preparation of binahong leaf infusion and antibiotic solution(Phillips & Walsh, 2020)**'**(BPOM, 2016)

Making an infusion solution of binahong *Anredera cordifolia* (*Tenore*) *Steenis* leaves using the following steps: a) weighing the crushed binahong leaves according to the desired extract concentration, namely a concentration of 5% or 50 mg/ml (5 grams/100 ml of distilled water) and a concentration of 20% or 200 mg/ml (20 grams/100 ml distilled water) into a beaker b) heat the extract using a Bunsen for 15 minutes after the temperature of the extract solution reaches 90°C, c) then

filter while the liquid is still hot. The antibiotic *Co-Amoxiclav* 625 mg is made by grinding the drug until it is fine and dissolving it in 100 ml of distilled water until completely dissolved.

Data analysis

Research data on days 1, 5 and 8 which were collected using the REEDA scale observation sheet were analyzed using SPSS with the *One-Way ANOVA* statistical test to see the average value (*Mean*) and its significance value to assess whether there was the influence of each group. The criteria for reading the average value of the REEDA scale for each group are that the smaller the number of values, the more effective it is in healing suture wound infections, and the results of the *One-Way ANOVA* test are if the *P-value* < 0.05 then Ho is rejected and Ha is accepted which means there is The effect of giving binahong leaf infusion on the healing of stitched wound infections in *Rattus norvegicus* experimental animals. The test results were continued with the *Post-Hoc Tukey* test to assess real differences between groups. If the *P-value* < 0.05 then Ho was rejected and Ha was accepted, which means there was a group influence on healing of suture wound infections in *Rattus norvegicus* experimental animals.

RESULT AND DISCUSSION

3.1. Result

Table 1. Samples's group and demographic

Group	Normality *Shapiro-Wilk*	Homogeneity
Extract 5%	0.212	
Extract 20%	0.091	0.712
Positive Control	0.421	
Negative Control	0.167	

Based on Table 1, it appears that the significance value is > 0.05, so that the four study groups have data that is normally distributed and homogeneous.

Table 2. Intervention Effect on Suture Wound Infections Convalescence

	Group	N	Mean±SD	CI 95%	*P-value*
1st Day	Extract 5%	6	13.17 ± 0.753	13.96-12.38	0.806
	Extract 20%	6	13.33 ± 0.816	14.19-12.48	
	Positive Control	6	12.83 ± 1.169	14.06-11.61	
	Negative Control	6	13.00 ± 0.894	13.94-12.71	

5th Day	Extract 5%	6	8.75 ± 0.509	9.29-8.22	0.008
	Extract 20%	6	8.85 ± 0.720	9.61-8.10	
	Positive Control	6	9.37 ± 0.623	10.02-8.71	
	Negative Control	6	10.03 ± 0.619	10.68-9.38	
8th Day	Extract 5%	6	3.11 ± 2.177	5.50-0.83	0.027
	Extract 20%	6	4.69 ± 2.502	7.31-2.06	
	Positive Control	6	5.71 ± 2.260	8.08-3.33	
	Negative Control	6	7.40 ± 2.101	9.60-5.19	

Based on Table 2, it can be seen in the test results that the average value (*Mean*) shows that there are differences between the four groups, it can be seen from the average value that decreases until the eighth day, which means that giving binahong leaf infusion has a good effect on healing suture wound infection. There was also a significance value on the first day, namely 0.806 which was > 0.05, which meant that there was no significant difference in the four groups on the first day because it was the value of the infection that was found 24 hours after the bacteria were given and no intervention had been given. The significance value on the fifth day (0.008) and the eighth day (0.027) which is <0.05, then Ho is rejected and Ha is accepted. So, it can be said that there is a significant difference between groups.

Table 3. Comparison Effects Between Groups on Suture Wound Infections Convalescence

Group		5th Day	8th Day
Extract 5%	Extract 20%	0.993	0.632
	Positive Control	0.344	0.227
	Negative Control	0.010	0.018
Extract 20%	Extract 5%	0.993	0.632
	Positive Control	0.491	0.862
	Negative Control	0.018	0.196
Positive Control	Extract 5%	0.344	0.227
	Extract 20%	0.491	0.862
	Negative Control	0.289	0.578
Negative Control	Extract 5%	0.010	0.018
	Extract 20%	0.018	0.196
	Positive Control	0.289	0.578

Based on Table 3, it appears that each group has a healing effect on suture wound infections, where the 5% extract, 20% extract and positive control groups show no very significant or very distant differences compared to the negative control group. And the value that most indicated a significant difference was between the 5% extract group and the negative control group with a *P-value* of 0.018 or <0.05.

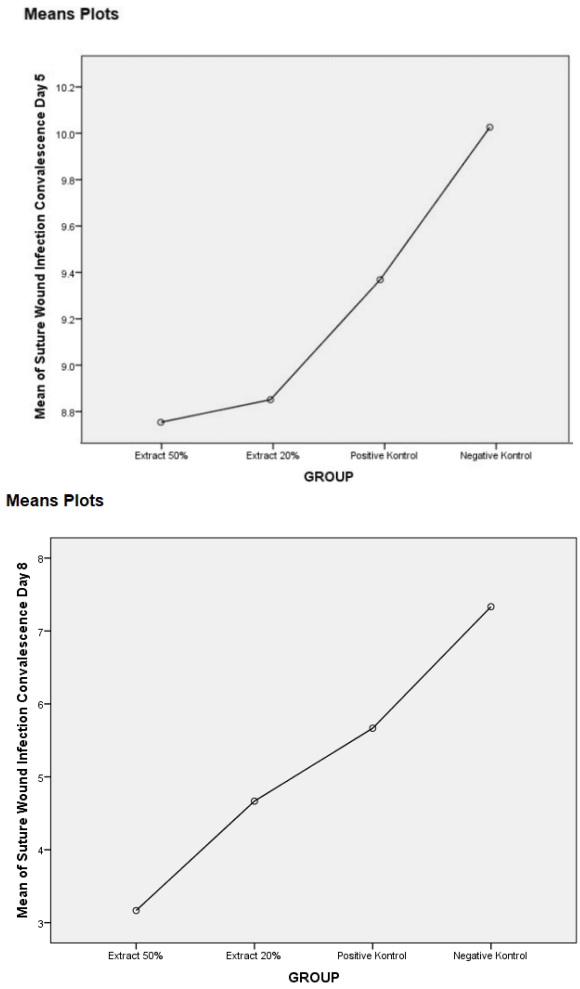

Figure 1. Healing of Fifth and Eighth Days of Suture Infection

Based on Figure 1, there appears to be a decrease in the average healing value, which shows that there is an influence between giving binahong leaf infusion on healing suture wound infections. And the 5% binahong leaf extract infusion group showed the highest reduction or was most effective in healing suture wound

infections, and the negative control group had the least effective healing value. Where in the REEDA scale with assessment components in the form of *Redness*, swelling (*Edema*), bleeding under the tissue (*Ecchymosis*), exudate (*Discharge*), and tissue junctions (*Approximation*), the lower or lower the score obtained from healing, the more effective it is in healing stitched wound infections, and if the value is still high, the healing will be less good.

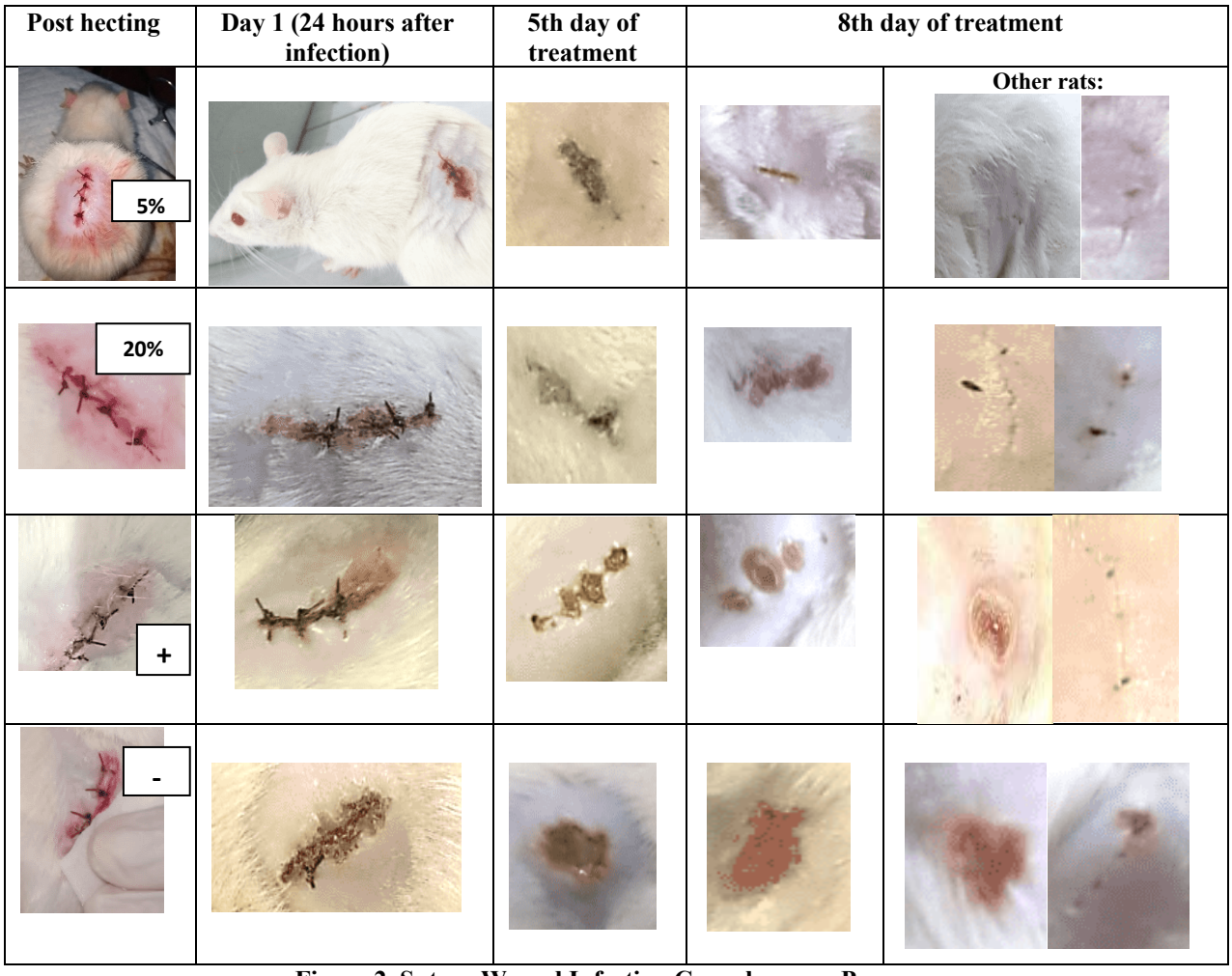

Figure 2. Suture Wound Infection Convalescence Process

Caption :
5% : Binahong leaf infusion 5% concentration
20% : Binahong leaf infusion 20% concentration
\+ : Positive kontrol
\- : Negative kontrol

Based on Figure 2, There appears to be a healing process in each group. Where the 5% group had the best healing effect on stitched wound infections, and

the negative group had the least effective healing effect, indicated by the still high degree of infection in suture wounds.

3.2. Discussion

In this study, white rats (*Rattus norvegicus*) were chosen as experimental animals and infected using *Streptococcus pyogenes* bacteria in stitched wounds and then assessed for healing after treatment. White rats (*Rattus norvegicus*) as experimental animals are similar to humans in their nervous system, tissues, reproductive system, nutritional needs, disease and anxiety because their DNA organization and gene expression are about 98% similar to human genes (Rejeki et al., 2018).

Suture wound infection is inflammation caused by primary bacterial organisms, especially skin flora, including *Streptococcus pyogenes* or *Group A Streptococcus* (GAS) and *Meticillin resistant Staphylococcus aureus* (MRSA)(Phillips & Walsh, 2020). Based on the Republic of Indonesia Minister of Health Regulation No. 28 of 2021 concerning Guidelines for the Use of Antibiotics, skin, gland and soft tissue infections caused by *Group A Streptococcus* (*Streptococcus pyogenes*) bacteria is by administering the antibiotic *Amoxicillin-clavulanate*/oral (*Co-Amoxiclav*/oral) 625 mg/ 8 hours or antibiotic Clindamycin/oral 300 mg/8 hours(Kemenkes, 2021). *Co- Amoxiclav* can be used to treat wound infections because it contains *Amoxicillin* which is 10 times more active than cefuroxime against *Group A Streptococcus* (GAS) (Phillips & Walsh, 2020).

Binahong [*Anredera cordifolia* (*Tenore*) *Steenis*] leaves have various benefits including as anti-inflammatory, antioxidant, antibacterial and analgesic (Lestari et al., 2016). Binahong leaves contain bioactive compounds such as flavonoids, tannins and saponins. Flavonoids contained in binahong leaves have an anti-inflammatory effect, while saponins have an antiseptic effect which can prevent or stop the growth of microorganisms in wounds, thereby preventing or treating infections, multiplying fibroblast cells, and stimulating the formation of new tissue (Sasidharan et al., 2010). Regarding toxic effects, *Anredera cordifolia* is not toxic to wistar rats (*Rattus norvegicus*) and does not have a teratogenic effect (Sukandar et al., 2014). In the teratogenicity test, 100, 400 and 1,000 mg/kg doses of binahong leaf extract were administered orally to pregnant rats on the sixth to fifteenth day

of gestation. Exactly on the 20th day of pregnancy, a laparotomy was carried out to remove the fetus. The findings showed that there were no organ and skeletal malformations, nor growth disorders at a body weight of (Sukandar et al., 2014).

In a study conducted by Yuniarti and Lukiswanto (2017) (Misaco Yuniarti & Sektiari Lukiswanto, 2017) it was found that the wound healing process in the 5% binahong leaf extract group was better than the 10%, 15% binahong leaf extract groups, and the group given antibiotics, which showed that binahong leaves with 5% concentration is the optimum dose that can speed up the wound healing process. This is related to the medicinal content in it, including flavonoids, saponins, tannins and ascorbic acid (Misaco Yuniarti & Sektiari Lukiswanto, 2017).

Flavonoids act as antioxidants which can reduce free radicals. Antioxidants then bind to free radicals that damage cell membranes, which then reduces damage to the cell membrane and allows the proliferation phase of wound healing to occur properly(Barku et al., 2015). Apart from that, flavonoids also have an antibacterial mechanism by forming complex compounds from dissolved and extracellular proteins which are able to damage bacterial cell walls, followed by the release of intracellular compounds(Kurniawan & Aryana, 2017). Saponins play an important role in the wound healing process, namely they can increase monocyte proliferation, which then increases the number of macrophages which will release growth factors which are very important in the wound healing process, as well as accelerating the keratinocyte migration process which plays an important role in the recoilization process(Kurniawan & Aryana, 2017). The tannins contained in binahong leaves have a function as an astringent which can cause the pores on the skin to shrink and stop the output of exudate and bleeding in wounds(Kurniawan & Aryana, 2017). Tannins and saponins play a role in the migration and proliferation of fibroblasts in the wound, making the wound contract faster(Kurniawan & Aryana, 2017). Ascorbic acid or vitamin C, also has an important role in the wound healing process. Ascorbic acid is required in activating prolyl hydroxylase, which supports the hydroxylation step in collagen deposition. Collagen is an important component in the formation of scar tissue and wound healing(Kurniawan & Aryana, 2017). Thus, flavonoids, saponins, tannins, and ascorbic acid play an important role in the wound healing process, both through antioxidant, antibacterial mechanisms, and

stimulating the growth and migration of cells involved in wound healing(Kurniawan & Aryana, 2017).

CONCLUSION AND SUGGESTION

Binahong leaf infusion had a good healing effect on sutures infected with *Streptococcus pyogenes* ATCC 19615. On the fifth and eighth day there was a significant difference in the four groups, where each group had an effect on the healing of suture infection. The group with the most significant difference was the 5% binahong leaf infusion group which showed the best effect on healing suture infection compared to the other groups, with the negative control group showing the least effective healing effect on suture wound infection. So that the 5% concentration of binahong leaf infusion can be used as an alternative in the treatment of suture wound infection. For further research, it is necessary to test the lower concentration of binahong leaf infusion to find out the minimum concentration that can have a good effect on the healing of suture wound infections.

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