ANTIBACTERIAL ACTIVITY OF HYDROGEL PLASTERS OF RED BETEL LEAVES EXTRACT (*Piper ornatum*) AND PORANG FLOUR AS GELLING AGENT AGAINST *STAPHYLOCOCCUS AUREUS*

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Abstract

Wounds require treatment to prevent infection by covering, one of which is by using a plaster. Hydrogel plaster has flexible, transparent, and soft properties that are non-irritating, providing a soothing and cooling effect. Red betel leaves have germicidal, antioxidant, fungicidal, and antifungal properties and play a role in the wound healing process. The aim of this study was to determine the flavonoid content of red betel extract, physical quality and antibacterial activity of red betel extract hydrogel plaster and porang flour against *Staphylococcus aureus* bacteria. The methods used were spectrophotometry and diffusion. The type of research used was quantitative research with a descriptive design. Red betel leaves extract has flavonoid content of 14.846 ± 0.17 mg QE/g. Three formulas of hydrogel plaster were made, namely F0, F1 and positive control. The physical quality of the hydrogel plaster includes organoleptic tests on 3 formulas which are in the form of solid preparations, soft and elastic, transparent and dark brown in color, distinctive odor of red betel leaves, pH 4.5-7, thickness 0.630-0.673 mm not more than 1 mm, f olding resistance >200 times, and drying shrinkage of 1.002-1.006% meeting the requirements <9.29%. The antibacterial activity test shows that the hydrogel plaster has antibacterial activity against *Staphylococcus aureus* bacteria at F0 of 0.00 mm with a very weak inhibition zone category and F1 of 19.47 mm strong category, positive control of 21.43 mm very strong and on red betel extract of 20.5 mm strong category.

Keywords : hydrogel, red betel leaves, porang, flavonoids, antibacterial

1. INTRODUCTION

The wound needs treatment so that it does not cause infection. Wound care can be done by the closed method, one of which is by using wound plaster. Wound plasters that have more effective characteristics are needed, such as hydrogel wound plasters (Hou et al., 2020). Hydrogel is a flexible, transparent, and soft polymer wound dressing that does not cause irritation (Saputra et al., 2020).

In addition to having a soft texture, hydrogel must also have antibacterial activity against *Staphylococcus aureus* bacteria. This study was conducted to determine the antibacterial activity of hydrogel plasters containing red betel leaf extract and porang flour against S*taphylococcus aureus* bacteria.

Red betel (*Piper ornatum*) is often cultivated as a medicinal plant because it contains flavonoids, alkaloids, alcohol, polyphenols, tannins, and essential oils (Octavia, 2021). Red

betel leaf extract has antibacterial activity against Staphylococcus aureus bacteria, which inhibits at a concentration of 20% with an inhibition area diameter of 19.5 mm based on research conducted by Sari & Furqan (2021).

Porang (*Amorphophallus muelleri* Blume) is used because of its high glucomannan content. Glucomannan has good film-forming ability, is biocompatible, easily decomposed, and has the ability to form gels. Therefore, porang tubers can be used as a basic raw material for making biopolymers or biodegradable polymers (Falah et al., 2021).

2. METHOD

The research was conducted in the laboratory of the Department of Pharmaceutical and Food Analysis, Health Polytechnic, Ministry of Health, Surakarta. The research time is January-March 2024.

Single variable used is a variation in the concentration of antibacterial activity of hydrogel plaster extract of red betel leaf (*Piper ornatum*) with the addition of porang flour (*Amorphophallus muelleri* Blume) as a gelling agent.

Materials

Red betel leaf, porang, etanol p.a, aquadest (Merck), propilen glikol, gliserol, media Mueller Hinton Agar (Merck), media Nutrient Agar (Merck), bakteri Staphylococcus aureus, klindamisin, glassware, incubators, Laminar Air Flow (LAF), uv-vis spectrophotometer.

Research Path

Determination was made at the Functional Implementation Unit of Traditional Health Services Tawangmangu Dr. Sardjito Hospital, then red betel leaves were extracted while porang tubers were made into flour. Determining flavonoid levels in red betel leaf extract using the UV-Vis spectrophotomeric method. Conducting the manufacture of hydrogel plasters, testing the physical quality evaluation of hydrogel plasters includes organoleptic tests, pH tests, folding resistance tests, thickness tests, and drying shrinkage tests, gram staining identification, antibacterial activity tests.

Preparation Of Ingredients

Red betel leaves are taken that are still fresh, the color of the leaves looks dark green with a bright red color. A total of 3 kg of betel leaves are dried in the oven at a temperature of 40 °C for 5 hours. Then it is mashed until it becomes a powder. 500 g of macarated powder is soaked in 70% ethanol up to a volume of 5000 mL, for 3x24 hours. The filtrate is evaporated in a water bath at a temperature of 60 °C. The extract that will be obtained is 88.76 g with a yield of 17.57%

Porang bulbs of 2 kg are cut into small pieces then dried in the oven ± 8 hours at a temperature of 55 °C. Dried porang is made into powder by grinding it. 100 g of porang flour is macerated for 4 hours using aquadest at a temperature of 40 °C with a ratio of 1:15 to which 10 g of aluminum sulfate has been added. The filtrate is then centrifuged at 1500 rpm for 15 minutes. Supernatants that have been separated from impurities are added 96% ethanol in a ratio of 1:1 to precipitate glucomannan compounds. The glucomannan precipitate was dried in the oven at 55 °C (Septiawan et al., 2021). Porang flour was obtained as much as 15.97 g with a yield of 15.97%.

Determination Of Flavonoid Levels By Uv-Vis Spectrophotometry Method

In determining flavonoid levels, the UV-Vis spectrophotometry method was used using a work procedure according to Mahfirotun (2020):

a. A standard solution of quercetin 200 ppm was made

   Weighed as much as 2 mg of quercetin dissolved with 10 mL of ethanol p.a.

b. Standard series dillution

   A 200 ppm quercetin master solution was made in a series of concentrations of 10, 20, 30, 40, and 50 ppm inserted into a 5 mL measuring flask to the limit mark with the addition of ethanol p.a. From each concentration, a master solution is made by pipetting as much as 1 mL added with 1 mL of 10% $AlCl_3$ solution and 8 mL of 5% acetic acid. The solution is incubated for 30 minutes and absorbed readings are taken at maximum wavelength.

c. Determination of maximum wavelength

   The maximum wavelength is carried out by running a quercetin solution at a concentration of 30 ppm in the wavelength range of 400-500 nm.

d. Determination of total flavonoids

   A total of 5 mg of red betel leaf extract was put into a measuring flask, 5 mL was added with ethanol p.a to the limit mark, so that an extract solution with a concentration of 1000 ppm was obtained. From the 1000 ppm extract solution, 1 mL was taken, added with 1 mL of 10% AlCl3 and 8 mL of 5% acetic acid and let stand for 30 minutes. Absorbance readings are taken at the maximum wavelength. Determination of the maximum wavelength is carried out in the range of 400-500 nm (Sari & Hastuti, 2020).

Making Hydrogel Plaster

The manufacture of hydrogel wound plaster uses a porang flour base developed with aquadest for a few minutes. The base that has expanded is homogenized using a hand mixer until it is homogeneous. Glycerin and propylene glycol are added and stirred until

homogeneous. The addition of the extract is carried out in laminar air flow (LAF) and then added aquadest until the total weight of the preparation reaches 100 g (Edy et al., 2019). The solution is left for 30 minutes, poured into a petri dish of 30 g, baked at 50 °C, put the hydrogel in a desiccant for 20 hours. The hydrogel was cut and applied to the plaster by an aseptic method performed in LAF. Hydrogel plasters are stored in sealed containers (Wardani & Saryanti, 2021).

a

b

c

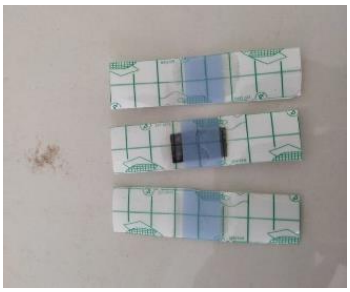

Figure 1. (a) F0, (b) F1 and (c) Positive Control Hydrogel Plaster Preparations

Physical Quality Testing

a. Organoleptic test

Organoleptic examination includes observing the texture, odor, and color of the resulting hydrogel wound plaster (Nitiariksa and Iskandar, 2021).

b. pH test

This test is carried out by adding 10 mL of CO_2 free distilled water to the plaster and leaving it for 1 hour. This test is carried out using a pH meter (Nitiariksa and Iskandar, 2021). The tool is calibrated with a pH 7 buffer followed by pH 4 until the screen shows a constant number. The electrode is immersed in the plaster preparation, the needle on the monitor is waited for to stabilize, then the electrode is rinsed with water to remove cross-contamination and repeated 3 times (Widhowati et al., 2021; Devirizanty et al., 2021).

c. Folding resistance test

The folding resistance test is carried out by applying powder to the sticky adhesive part of the plaster, the plaster is folded repeatedly in the same position until the test patch tears. The number of folds of the plaster preparation in the same position before tearing is considered as the folding resistance value (Buang et al., 2020). The requirement for the number of folding resistances required is >200 (Wardani & Saryanti, 2021).

d. Thickness test

The hydrogel was measured using a screw micrometer with an accuracy of 0.01 mm. In each formula, each was selected randomly and the average thickness of each formulation was calculated. The requirement for the thickness of the plaster must not exceed 1 mm (Nitiariksa & Sukmawati, 2021).

e. Drying shrinkage test

The drying shrinkage test was carried out by weighing the hydrogel plaster and storing it in a silica desiccator at room temperature for 24 hours. After 24 hours, the hydrogel wound plaster was reweighed and its drying shrinkage was determined. The drying shrinkage requirement for a good plaster formulation is less than 9.29% (Yusuf, 2020).

Gram Staining Identification

One ose of bacterial colony was taken, fixed on the glass object using a bunsen flame. A crystal violet solution is added, left for 3-5 minutes and gently rinsed with water. Drip lugol solution left for 3-5 minutes, and gently rinsed with water. The preparation is decolored with a 96% alcohol solution until the crystal violet and lugol color are gone. The glass object is added with immersion oil and covered with other glass objects. The results of the gram staining test can be seen from a microscope with a magnification of 100x (Apriyanthi et al., 2022).

Antibacterial Testing

The tools used must be sterilized first, as well as in the manufacture of Nutrient Agar and Mueller-Hinton agar media sterilized using an autoclave at a temperature of 121 °C for 15 minutes. NA media is used to make the media to tilt on the rejuvenation of *Staphylococcus aureus* bacteria. The bacteria that have been inoculated make a suspension similar to McFarland's standard for turbidity. Furthermore, the antibacterial test uses MHA media that has been poured with bacterial suspension and inoculum until it solidifies. A well hole with a diameter of 6 mm is made on MHA media. The plaster preparation and extract are put into the well hole approximately 50 µL. Then incubated at a temperature of 37 °C. A horizontal obstacle diameter measuring instrument with a caliper is used to measure the resistance zone.

3. RESULTS AND DISCUSSION

The results of antibacterial activity are shown in table 1.

Table 1. Antibacterial Activity Test Results

Formulation	Inhibition zone diameter (mm)	Category (Syari & Aprilia, 2022)
F0	0,00 ± 0,00	None
F1	19,47 ± 0,46	Strong
Positive control	21,43 ± 0,21	Very Strong
Red betel leaf extract	20,5 ± 0,1	Very Strong

Information:

F0 : Control formulation without red betel leaf extract

F1 : Formulation with red betel leaf extract 20%

Positive control : Control formulation with the addition of 20% clindamycin

The results of the quantitative test of the UV-Vis spectrophotometry method obtained the absorbance value of the standard solution of quartz acetate standard solution successively from the standard solution with concentration ranges.

Tabel 2. Absorbance Measurement Results Calibration Curve

Consentration (ppm)	Absorbantion	Equality
10	0,219	Y = 0,0145x 0,0684 R^2 = 0,9995
20	0,354	
30	0,497	
40	0,652	
50	0,795	

From this value, the linear regression equation of the standard curve can be obtained, namely y = 0.0145x - 0.0684 with R^2 = 0.9995.

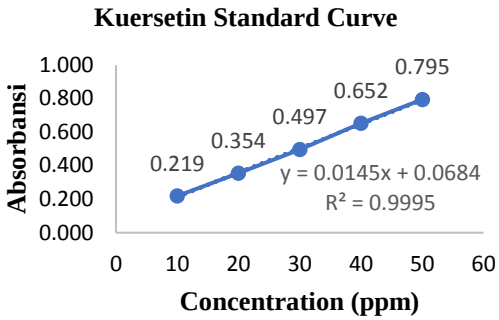

Figure 2. Quercetin Standard Curve

The results of the total flavonoid content of the ethanol extract of red betel leaf (*Piper ornatum*) were obtained on average of 14.846 ± 0.17 mg QE/g. The results of the total flavonoid content obtained from the ethanol extract of red betel leaf obtained a greater result than the previous study from Anggraeni et al. (2023) with an average total flavonoids in red betel leaf ethanol extract of 14.772 mg QE/g.

The results of organoleptic observations on the hydrogel plaster of red betel leaf extract and porang flour were carried out on F0, F1 and positive control, namely solid shape with a soft, pliable, distinctive odor of red betel leaf, transparent in color at F0 and positive control, and dark brown in F1. The difference in color produced was due to the fact that only F1 was given red betel leaf extract, while in F0 and positive control there was no red betel leaf extract so that it still maintained the color given by porang flour containing glucomannan, which was clear.

The pH test is carried out using a pH meter. The test results on the F0, F1 and positive control formulas were obtained on average sequentially, which was 6.01 ± 0.03; 5.02 ± 0.02; 5.38 ± 0.02. These results show that in formulations containing betel leaves, a pH that is more acidic is obtained, but the results obtained are still in the pH range that is in accordance with the pH of the skin, which is in the range of 4.5-7 (Herliyani, 2020). Likewise, in the positive control results that clindamycin was added to it, and F0 without betel leaf extract obtained a pH that was still in the range according to the pH of the skin. The higher the concentration of the extract, the lower the pH obtained. This occurs because the phytochemical content of betel leaf extract is acidic so that it affects the pH of preparations to which red betel leaf extract is added in high concentrations (Hadi et al., 2022).

The folding resistance test aims to determine the flexibility and elasticity of hydrogel plaster preparations. Hydrogel plaster, which has film consistency and has good bonding ability between polymers, will provide flexibility properties that result in the preparation not being easily broken or torn during storage. The number of folding resistance that meets the standard

is >200 (Wardani & Saryanti, 2021). Based on the results of the research obtained the folding resistance in each formula after folding 300 times, it shows that the plaster does not tear, so it can be said that the hydrogel plaster has met the requirements.

The thickness test was carried out to determine the thickness of the wound plaster which aims to determine the thickness of the plaster that will affect the release of active substances from the preparation. The ideal thickness of plaster is thin but not easy to tear (Ismiyati et al., 2019). The results of the plaster thickness test of the F0, F1, and positive control formulas were obtained on average of 0.647 ± 0.01 mm, respectively; 0.673 ± 0.02 mm; 0.63 ± 0.01 mm. The results showed that the positive control had the lowest plaster thickness compared to other formulas. However, the results obtained from each formula are not more than 1 mm, where all results obtained are in accordance with the plaster thickness requirements, which is <1 mm (Nitiariksa & Sukmawati, 2021).

The drying shrinkage test aims to check the water loss of the plaster, where a very dry plaster can cause brittleness and breakage easily (Wardani & Saryanti, 2021). Based on the results obtained in the F0, F1, and positive control formulas, each showed a drying shrinkage value of 1.002% ± 0.0004; 1.006% ± 0.001 and 1.002% ± 0.002. From these results, it was stated that the hydrogel plaster met the good requirements for the drying shrinkage test based on previous research, which was <9.29% (Fuziyanti, 2022).

The results of the gram staining identification test in *Staphylococcus aureus* bacteria are shown in the figure 3.

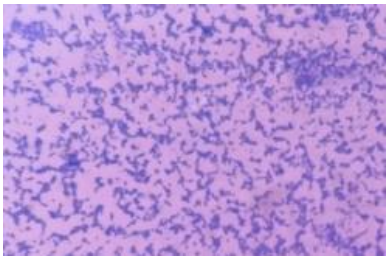

Figure 3. Observation Results of Gram Staining Identification at 100x magnification

Based on the image, the results of gram staining of *Staphylococcus aureus* bacteria belong to the group of gram-positive bacteria with a purple color in the shape of a round cluster like a grape. Gram-positive bacteria will give a purple color when gram staining is carried out because this bacteria has a low lipid content, so the bacterial cell wall will be easily dehydrated due to treatment with alcohol. When the cell wall is dehydrated, the size of the cell pore shrinks and its permeability decreases. Due to the reduced absorption capacity of the cell wall, the violet-lugol crystal complex cannot leave the cell and the cell remains purple (Purwaningsih & Wulandari, 2021).

An antibacterial activity test was carried out to determine the ability of hydrogel plasters to inhibit *Staphylococcus aureus* bacteria. The test method used is the well method. The test was carried out using a concentration of 20% red betel leaf extract and clindamycin ointment as a positive control and a hydrogel plaster without extract as a negative control. The choice of clindamycin as a positive control is because clindamycin is an antibiotic of the aminoglycoside class that works by inhibiting the synthesis of proteins of susceptible bacteria at the 50S ribosome level. Clindamycin is active against *aerobic gram-positive* coccus bacteria including *Staphylococcus, Streptococcus pnoumoniae,* but not *Enterococcus* (Dewi, 2019). This is in line with the research of Sumarno et al. (2020), clindamycin ointment as a positive control can inhibit the growth of *Staphylococcus aureus* bacteria with an inhibition of 20.30 mm, which is classified as a very strong inhibitor.

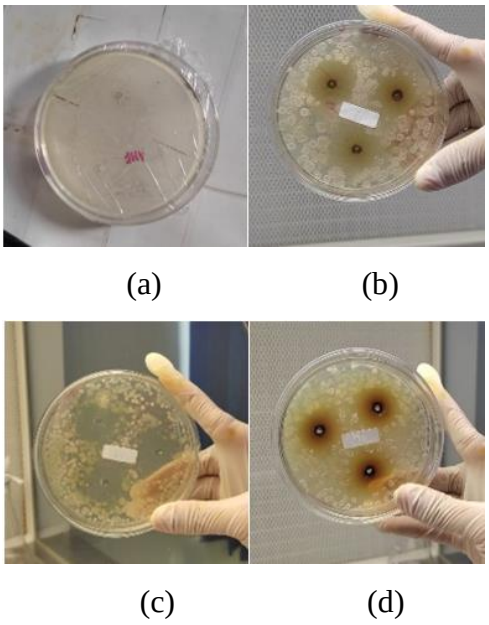

Figure 4. Antibacterial test results

(a) Formulation 0 (F0): Control formulation without red betel leaf extract

(b) Formulation 1 (F1): formulation with red betel leaf extract 20%

(c) Positive control: Control formulation with the addition of 20% clindamycin

(d) Red betel extract

The test results on negative control or F0 without the addition of extracts there was no inhibition zone formed. This is because F0 is a neutral compound that does not contain antibacterial ingredients so that it does not cause an inhibition zone. This is in accordance with the research of Avitri et al. (2022) which uses glucomannan of porang tubers in the manufacture

of edible films, an antibacterial activity test was carried out on *Staphylococcus aureus* bacteria which gave results that there was no inhibition zone. The results of the treatment in F1 with a concentration of 20% red betel leaf extract obtained an inhibition zone with an average of 19.47 ± 0.46 mm obtained in the strong category. The results of the treatment in the positive control with a concentration of 20% were obtained with an inhibition zone with an average of 21.43 ± 0.21 mm classified as very strong. The results of the treatment on red betel leaf extract obtained the presence of an inhibition zone with an average of 20.5 ± 0.1 mm, which is classified as a strong category according to Syari & Aprilia (2022).

Based on the research conducted, the results of the antibacterial test of red betel leaf (*Piper ornatum*) on *Staphylococcus aureus* bacteria are in accordance with previous research. Red betel leaf extract has antibacterial activity against *Staphylococcus aureus* bacteria inhibiting at a concentration of 20% with an inhibition area diameter of 19.5 mm (Sari & Furqan, 2021).

4. CONCLUSION

Based on the quantitative results of the measurement of total flavonoid levels in ethanol extract of red betel leaf (*Piper ornatum*) at a concentration of 14.846 ± 0.17 mg/QE g. The inhibition zone of red betel leaf extract (*Piper ornatum*) against *Staphylococcus aureus bacteria* was obtained with an inhibition zone with an average of 20.5 ± 0.1 mm classified as a strong category. The results of the physical quality test of hydrogel plaster preparations of red betel leaf extract (*Piper ornatum*) with the addition of porang flour (*Amorphophallus muelleri* Blume) at F0, F1 and positive controls have organoleptic, pH, thickness, folding resistance, and drying shrinkage that have met the quality requirements of good plaster preparations. The inhibition zone of the hydrogel wound plaster against *Staphylococcus aureus* bacteria in formula 1 with a concentration of red betel leaf extract of 20% resulted in an inhibition zone of 19.47 ± 0.46 mm classified as a strong category.

Further research needs to use *the Lister Plaster Scissors* tool or a more supportive tool to produce hydrogel plaster with a neater rectangular shape and the same size. There needs to be a study on the sterilization test of hydrogel plaster of red betel leaf extract (*Piper ornatum*) with the addition of porang flour (*Amorphophallus muelleri* Blume). Further research is needed on the levels of alkaloids, tannins, saponins and essential oils contained in red betel leaf extract (*Piper ornatum*).

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