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FORMULATION AND EFFECTIVENESS TEST OF THE WOUND HEALING GEL RED PIDADA FRUIT (*Sonneratia Caseolaris)* SKIN EXTRACT

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ABSTRACT

Red pidada fruit peel extract gel preparation can increase the efficiency and comfort of topical use because of its activity in the healing of open wounds. The aim of this research was to determine how variations in HPMC levels affect the physical quality and stability of red pidada fruit peel extract gel preparations, using the maceration method to obtain thick extracts and formulations with different HPMC concentrations (1% HPMC, 3% and HPMC 5% formula were tested for physical quality and stability, including the Storage Stability Test for 4 weeks. Effectiveness testing was also carried out in white mice using an incision wound method with a depth of 1.5 mm and macroscopic observation. The effectiveness test concentration was set to 5%. The results of data analysis using the Spss One Way ANOVA test showed that higher HPMC levels resulted in a thicker gel, viscosity, stickiness, spreadability, and higher pH. It can be concluded that the gel formulation that meets the requirements is that formula 2 provides organoleptic test results with a thick green color typical of red pidada, good homogeneity test, spreadability test 5.52 cm, adhesion test 2.61 minutes, viscosity test 2700cCps, pH test 4.92. During storage, the gel exhibited good consistency. The longer the storage time, the closer the pH changes to alkaline values. With the Anova value, there is a significant difference in the three formulas with a value of p=0.005

Keywords: red pidada (*Sonneratia caseolaris*) fruit peel, wound healing, HPMC, gel

INTRODUCTION

Mangrove red pidada plants are not poisonous and can be eaten directly; therefore, they can be used as a traditional medicine by coastal communities for natural treatment (Niken, Putri and Gusti, 2019). The active compounds in the skin of red pidada fruit are steroids, flavonoids, saponins, and quinones. The content of active flavonoid compounds can be useful for eliminating inflammation that can be caused by injury and infection, can stop the infection process by bacteria, and can stimulate the growth of new cells in the skin. Saponins are antiseptic agents (Srinengri, Arryati and Yuniarti, 2019).

An open wound occurs when skin tissue is damaged by a sharp object, gunshot, or impact with a hard object. Abrasions, bites, cuts, lacerations, and gunshots are examples of open wounds. Natural ingredient extracts are used to remove chemicals from the natural ingredients. This is achieved by separating the mass of the substance components into the solvent. The migration begins at the interfacial layer and then diffuses into the solvent. Using 96% ethanol solvent, it is carried out using the maceration method so that the process of extracting the simplicia using stirring several times is kept at room temperature. (Sari and Moulina, 2020).

Gel preparations have high viscosity and adhesion, so they do not flow easily on the surface of the skin, spread evenly when applied, do not leave scars, only form a thin layer, are easy to wash off with water, provide a cool sensation when applied, and can penetrate better than other preparations (Loni, Beta, and Eni, 2023). Gelling agents can form a gel base that is clear and easily soluble in water and can increase the viscosity of the gel preparation. The HPMC base is a hydrogel-forming material that can float in water and is able to bind a number of polymer fibers where more liquid will be retained and the gel former will bind water, producing a clear gel that is slightly cloudy, has a cool effect, is easy to wash with water, does not clog skin pores, does not irritate the skin, and produces a gel with good viscosity during long-term storage (Risma, Ekowati and Ningsih, 2022).

Based on this research, we used red idada fruit peel as a treatment for open wounds in the form of a gel preparation with varying concentrations of HPMC as a gelling agent and observed the effect on the physical quality and stability of the red pidada fruit peel extract gel preparation.

RESEARCH METHODS

Tools and Materials

The tools used in this research are mortar and stemper, analytical balance, measuring cup, porcelain cup, watch glass, preparation test, preparation storage container, stopwatch, spreadability test tool, adhesion test tool, pH meter test tool (Mettler Toledo, Germany), a viscosity test tool, and an ointment pot.

The materials used in this study were red pidada fruit peel extract as the active ingredient, hydroxypropylmethylcellulose (HPMC) PT.barco. barco as a gelling agent, methyl paraben as a preservative, glycerin as an emollient, and propylenglycol as a humectant.

Research Procedure

Plant Determination

Red pidada fruit peel was determined at the Botany Laboratory of Sanata Dharma University No: 05/LKTO/Far-USD/X/2024.

Preparation of Red Pidada Fruit Peel Extract

Simplisia of red pidada fruit skin as much as 1.2 kg, mashed and sieved with mesh 60 macerated for 5 days while stirring at least 3 times a day. Filtering was performed using filter paper to separate the liquid extract, and then 96% ethanol separation was carried out using a rotary evaporator to thicken the extract to obtain a thick extract of 60 g. The yield obtained from the extraction of red pidada fruit skins was 5%.

The Quality Test of Red Pidada Fruit Peel Extraction

According to the chemical content analysis conducted by the qualitative test method, red pidada fruit peel extract contains active substances, such as flavonoids, which have anti-inflammatory properties that can heal wounds.

The test of the effectivenness of flavonoid compounds from red pidada fruit peel extract on open wounds

The test used male white mice with weight criteria of 150-200 grams totaling of 4 mice. Anesthesia using as many as 5 drops of chloroform on cotton through inhalation is put into a jar that already contains rats. The mice were shaved in the form of a box, and a 2 cm long incision using a sterile scalpel and a 1.5 mm biopsy punch to measure the depth of the wound, and a test preparation of red pidada skin extract with a concentration of 3%, 5%, and 7% HPMC as a *gelling agent*, and the wound was observed macroscopically for 9 days. Then, the area measured the diameter of the wound healing where the smaller the wound area, the greater the percentage of healing power.

$$\%Wound\ Contraction = \frac{Length\ of\ wound\ on\ day\ 0 - Length\ of\ wound\ on\ day\ n}{Wound\ area\ on\ day\ 0} \times 100\%$$

Gel Preparation of Red Pidada Fruit Peel Extract

The composition of the red pidada fruit peel extract gel formula is shown in the **Table I.**

Table I. Gel Formulation of Red Pidada Fruit Peel Extraction

No.	Material	F1	F2	F3
1	Pidada fruit peel extract	5	5	5
2	HPMC	1	3	5
3	Propylenglycol	15	15	15
4	Glycerin	30	30	30
5	Methyl Paraben	0.02	0,02	0,02
6	Distilled water	ad 50ml	ad 50ml	ad 50ml

At the beginning of the preparation process, HPMC was distributed in distilled water, which was heated to temperatures between 80 and 90 °C. The material was then mashed in a mortar until homogeneous dispersion was formed. Methylparaben was dissolved with propylenglycol, then added with red pidada fruit peel extract (mixture 1). Mixture 1 was gradually added to the developed HPMC base, and the remaining water was added gradually by stirring the gel until it became homogeneous. After that, it was placed into an ointment pot to be tested by replicating the formula three times.

Physical Properties Test of Red Pidada Fruit Peel Extract Gel Preparation

Organoleptic properties (color, shape, and odor that can be seen visually), homogeneity, pH, viscosity, spreadability, and stickiness are some of the tests performed.

Data Analysis

Data on physical properties including pH, viscosity, spreadability, and adhesiveness were analyzed using the SPSS One Way ANOVA test, and the results were declared not significantly different if the significance was ≥0.005 and declared significantly different if the significance was ≤0.005. and the organoleptic properties and homogeneity were tested visually.

RESULTS AND DISCUSSION

The Determination of the Plant

Red pidada is a fruit leather plant native to the Sanga-Sanga region of East Kalimantan. In the the botany Laboratory of Sanata Dharma University. Plant growth was determined. The results showed that the material used for the study was red pidada fruit leather known by the scientific name *Sonneratia caseolaris.*

Red Pidada Fruit Peel Extraction

Being added 5 liters of 96% ethanol totaling 1.2 kilograms. Cover and leave for five days, with occasional stirring at least three times a day. To maintain the ingredients in the extract, it was expected that the extract would be protected from light during maceration. After two remacerations, a filter paper was used to separate the liquid extract. Next, 96% ethanol was separated using a rotary evaporator to stop the extraction, which produced 60 grams of extract with a yield of 5%.

The Chemical Compound Identification Test

The results of the study on the chemical content of red pidada fruit peel extract are

in accordance with the literature, showing that the extract contains active substances such as flavonoids, which are thought to have anti-inflammatory properties that can heal wounds (Lallo *et al*., 2020)

Table II. Identification Test Results of Compound Content of Red Pidada Fruit Peel Extracts

Compound	Identification	Tube reaction	Library
Flavonoids	Sample+ Mg powder 0.2 g and concentrated HCL1-2 drops	Formed orange to red	Formed red-orange

Wound healing activity of Red Pidada Bark extract

Observations were made for 9 days to observe the physical changes that occur in the wound area using 4 male white mice; the negative control observed the development of the wound closure process without using the extract as a drug, 3% extract concentration, 5% extract, and 7% extract.

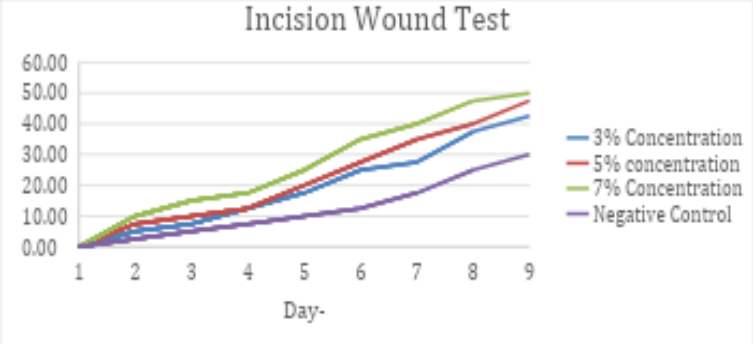

Figure 1. Incision Wound Closure

The results of the above observation indicate that there is a negative control that has the lowest healing power when the wound is performed as a comparison of the healing process because there is no effective substance treatment in wound healing for a long time. Every red pidada fruit peel plant has a metabolite content in the wound healing process, such as flavonoids, which have an important role in stopping bleeding, accelerating wound healing through the mechanism of vasoconstriction in blood vessels, able to ward off free radicals, inhibit hydrolysis and enzyme oxidation, and exert anti-inflammatory effects. At a concentration of 3 %, the inflammatory and wound healing processes take a long time.

concentrations of 5% and 7% have optimal concentrations in the healing process of cut wounds in white mice; however, if we refer to the research objectives and criteria, the 5% concentration is in accordance with the research criteria and objectives, which is quite effective in providing good pharmacological effects. effective in healing of cut wounds. Meanwhile, the negative control had the lowest healing power when the wound was used as a comparison of the healing process because there was no treatment with substances that were efficacious in healing the wound and it took longer. It can be seen that each red pidada fruit skin plant contains metabolites in the wound healing process such as flavonoids which have an important role in stopping bleeding, accelerating wound healing through vasoconstriction mechanisms in blood vessels, being able to ward off free radicals, inhibiting hydrolysis and enzyme oxidation and being anti-inflammatory. Analysis of the data measuring the diameter of the incision using *one-way ANOVA* showed that there were no significant differences in the three concentrations, with a value of p=0.236 (p>0.005).

Stability Test

Stability is the ability of a product to maintain quality according to quality

specifications set over a period of time. The usage and storage. Physical stability is the lack of change in the physical properties of a product during storage. Changes in physical properties are seen during storage, and formulation instability can be seen from changes in physical appearance, color, and taste of the formulation (Lachman & Lieberman, 1994).

Test results of red pidada fruit peel extract gel

Physical gel stability testing of red pidada fruit peel extract preparation aims to determine the physical quality and stability of red pidada fruit peel gel preparation stored for 4 weeks at room temperature. Physical quality testing of gels can include organoleptic, homogeneity test, spreading strength test, adhesion test, pH test, and viscosity test

Physical Properties of Red Pidada Fruit Peel Extract Gel Preparation

Organoleptics

The purpose of this test was to identify the appearance of the gel in terms of color, odor, and consistency. This test is necessary because of the convenience of using the availability of topical agents.

Figure 2. Red Pidada Fruit Peel Extract Gel

Table III. Organoleptical Test Results

Week	Testing	Formula 1	Formula 2	Formula 3
1	Color	Green	Green	Green
	Smell	Typical	Typical	Typical
	consistency	Somewhat viscous	viscous	Very thick
2	Color	Green	Green	Green
	Smell	Typical	Typical	Typical
	consistency	Viscous	viscous	Very Thick
3	Color	Green	Green	Green
	Smell	Typical	Typical	Typical
	consistency	Dilute	Viscous	Very Thick
4	Color	Green	Green	Green
	Smell	Typical	Typical	Typical
	consistency	Dilute	Somewhat Dilute	Very thick

The results showed that gel preparations F1 and F2. F3 has a distinctive color and smell of red pidada fruit peel extract, while the texture of each formula is different, as F1 has a slightly thick texture, F2 has a thick texture, and F3 has a very thick texture. The higher the concentration of red pidada extract, the sharper the aroma of the preparation; therefore, the formula with a good preparation is F2 with a 3% HPMC concentration with a texture that can maintain consistency stability in the gel during 4 weeks of storage.

Homogeneity

One method that can affect the quality of the gel preparation is homogeneous testing. In this case, the gel is considered homogeneous if the active substance and base can be evenly mixed to produce the desired effect.

Table IV. Homogeneity Test

Week	Formula 1	Formula 2	Formula 3
1	+	+	+
2	+	+	+
3	+	+	+
4	+	+	+

The homogeneity test results of the gel preparation showed a homogeneous composition. Good preparations in F1, F2, and F3 did not have small or rough grains when smeared on glass. Thus, the preparations of the three gel formulas provided good and maximum effects.

Spreadability

The spreadability test aims to determine how well the gel spreads on the surface of the skin that is being treated, because spreadability affects drug absorption and the speed of release of the active substance at the site where it is used.

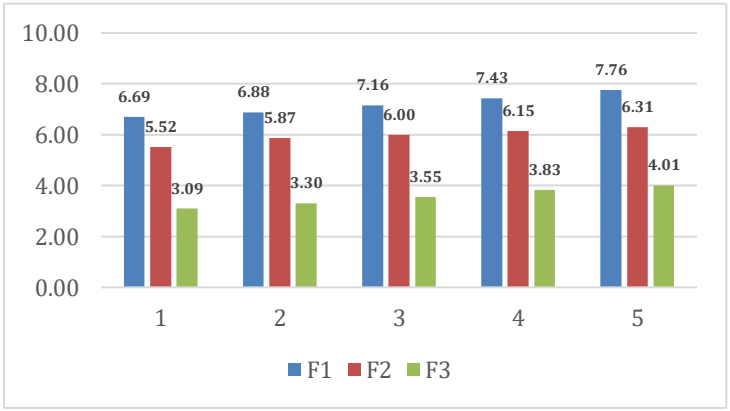

Figure 3. Spreadability Test

The spreading power test obtained varying results for each formula, namely F1, F2, and F3, and there was a different increase in spreading power. These results indicate that F3 does not meet the requirements for good gel spreadability. There was a decrease in the spreadability value due to the difference in the HPMC concentration in each formula. This shows that the higher the gelling agent concentration, the lower the spreadability (Emelda *et al.*, 2020). A one-way ANOVA analysis was then carried out, showing significant differences among the three formulations ($p=0.00$ ($p<0.005$).

Stickiness

Adhesion testing measures the gel's ability to adhere to skin for physical stability testing. Adhesion testing was periodically performed.

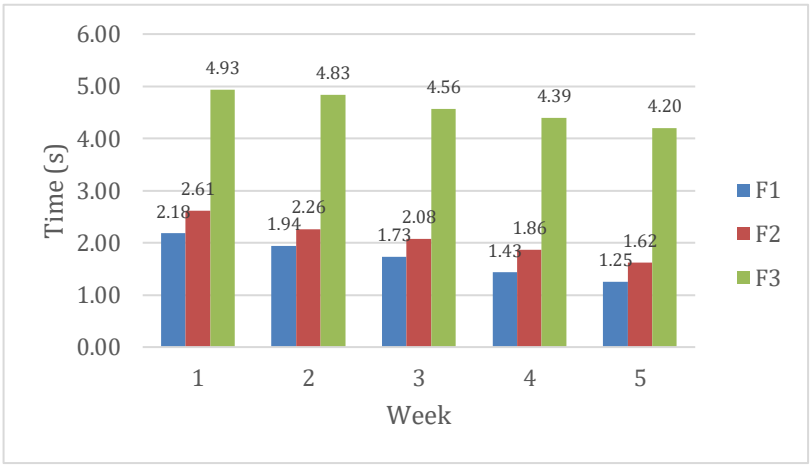

Figure 4. Adhesion Test

Testing for good adhesion on all formulas with the gelling agent used was HPMC at concentrations of 1%, 3%, and 5%, showing that higher concentrations showed longer adhesion time and release of the active substance from the skin. This is because the contact between the gel and skin is longer, which allows the desired therapy to be achieved. The results show that the highest sticking force for F3 was 4.93 seconds, while the lowest sticking force for F1 was 2.18 seconds. With a value of p=0.00 (p <0.05), there was a significant difference among the three formulations (according < one way anova analysis.

Viscosity

The viscosity of a gel, which should be neither too thin nor too thick, determines the ease with which a molecule can move because of the friction between layers of material. The viscosity of the gel affects the effectiveness of the therapy and comfort of gel preparation.

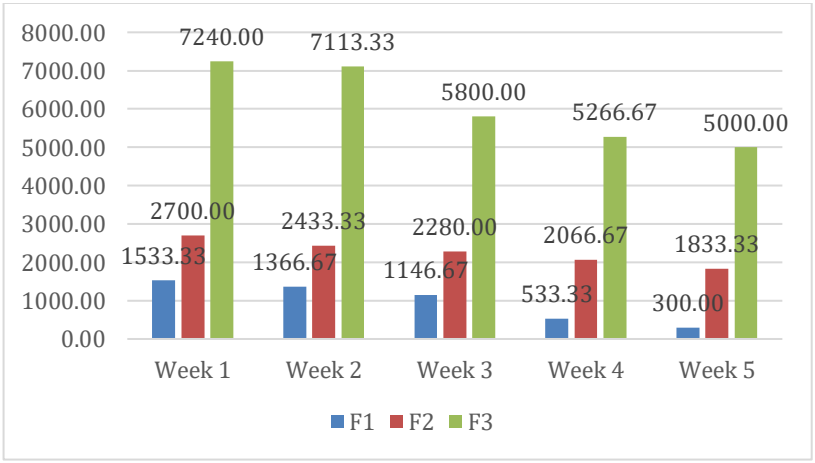

Figure 5. Viscosity

For each formula, the viscosity test results exhibited different values. Each formula contained a different HPMC concentration. Formula F1 has the lowest viscosity, 1533 Cps, and Formula F3 has the highest viscosity, 7240 Cps. With a value of p=0.00 (p <0.05), the one-way ANOVA viscosity data analysis showed that there were significant differences between the three formulas.

CONCLUSION

The identification test of compounds in pidada fruit skin plants yielded positive results for flavonoid content so that it can provide healing results for open wounds so that faster healing time can be carried out using male white mice marked by closing a 2 cm incision wound by applying extract concentrations of 3%, 5%, and 7%. Observations were made for 9 days from the results of observations of 5% concentration providing good wound closure. Research on the effect of HPMC concentration on red pidada fruit skin extract gel on storage stability for 4 weeks can be seen from organoleptic, homogeneity, pH, viscosity, adhesive power, and spreadability, which remain consistent with the gel preparation. The increase in the variation of HPMC levels affected the physical quality of the gel preparation, including a thicker extract gel, a more cloudy gel color, an increase in viscosity and gel adhesion, and a decrease in spreading power. However, this did not affect the homogeneity or pH of the gel. Gel with HPMC variation changes formula II with HPMC concentration of 3% and increases the stability of the gel during being saved in the storage

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