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Test of Breadfruit Leaf Extract Cream Preparation (Artocarpus Altilis) and Antioxidant Activity Test with DPPH Method

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ABSTRACT

The skin, which accounts for approximately 15% of body weight, is the body's outermost organ and serves as a barrier between the body and the environment. Skin color varies, ranging from fair to dark, with different shades on various parts of the body. Protecting the skin from inflammation, cancer, and premature aging caused by free radicals is crucial, and skin care cosmetic preparations are essential for achieving this goal (Wahyuni, 2005). This research aimed to investigate the antioxidant activity of breadfruit leaf extract and assess its suitability for use in cream preparations. This experimental laboratory study evaluated the potential of breadfruit leaf extract cream as an antioxidant agent. The experimental method involves manipulating the research object and using controls to investigate the cause-and-effect relationship between treatments and their effects (Sugiyono, 2014). Phytochemical screening of breadfruit leaf simplisia powder showed the presence of flavonoids, alkaloids, saponins, tannins, triterpenoids/steroids and glycosides. The content water of the simplisia was 7.30%, while the water-soluble juice and ethanol-soluble juice contents were 26.70% and 15.14%, respectively. The total ash content was 9.99%, and the ash content was 5.06%. Breadfruit leaf essence exhibited strong antioxidant activity, with an IC50 score of 28.10 ± 0.15 compared to quercetin, which also demonstrated strong antioxidant activity with an IC50 score of 9.76 ± 0.07 µg/mL. Breadfruit leaf extract has potent antioxidant activity, and its cream preparations meet the necessary requirements

INTRODUCTION

The skin, as the outermost organ of the body, serves as a barrier that separates body from the environment external. An adult's skin has an area of 1.5 m2 and weighs approximately 15% of their body weight, with a wide range of colors from fair skin to blonde and black, pink hues on the soles of a baby's feet and hands, and dark brown pigmentation on adult genitalia (Graham et al., 2005). Skin color is predominantly determined by the presence of melanin, which is synthesized through the highly reactive enzyme tyrosinase. Melanin gives the skin a brown or blackish-brown color by undergoing spontaneous polymerization from dopachrome (Charissa, Djajadisastra, & Elya, 2017). Aging is a physiological process that can be accelerated by free radicals, and skin hyperpigmentation is a manifestation of increased tyrosinase enzyme activity caused by free radicals (Siregar et al., 2019). Antioxidant compounds have been found to inhibit free radicals, thus reducing tyrosinase enzyme activity (Dwikarya, M, 2007).

Despite the rapid and sophisticated progress of modern science, natural medicine remains relevant and popular among enthusiasts due to a lack of knowledge and information about plants used for certain treatments (Dalimartha, 2000). The use of antioxidant compounds, both topically and systemically, is increasingly popular for preventing diseases and protecting the skin from free radical damage. Topical anti-aging products are commonly used in cosmetic preparations (Trifina, 2012). Skin care cosmetics are necessary to protect sensitive skin from inflammation, cancer, and premature aging caused by free radical oxidative effects (Wahyuni, 2005). Antioxidants are substances that can counteract the harmful effects of free radicals, which are formed due to oxidative metabolism resulting from chemical reactions and metabolic processes in the body. Antioxidants can mitigate skin harm caused by free radicals, which are major factors in the aging process and tissue damage.

For a long time, Indonesian people have utilized plants as medicine and cosmetic ingredients in skincare due to the belief that natural compounds are safer than synthetic ones, which is consistent with the "back to nature" trend. The significant diversity of hayati in Indonesia supports the development of natural-based skincare products (Nelly et al., 1999).

Creams that are applied externally on the skin can be formulated as m/a or a/m emulsions, depending on various factors such as the desired effect of the preparation, the nature of the therapeutic substance, and the condition of the skin surface (Howard, 1989). A cream is a semisolid preparation composed of two immiscible substances, usually oil and water, which liquid is dispersed in small droplets throughout the other liquid, and is designed for external use (Anief, 2003).

The breadfruit tree (Artocarpus altilis) is a highly versatile plant with a rich composition of calcium, carbohydrates, phosphorus, vitamins and minerals. Its several parts have been utilized as food, cosmetic ingredients, clothing material, and traditional remedies for treating ailments such as asthma, high blood pressure, and diarrhea (Pradhan et al., 2012). The leaves, fruits, bark, and sap of the breadfruit tree have all been used as medicine, with breadfruit leaves containing polyphenols, alkaloids, tannins, and flavonoids (Rinaldi, Kamadjaja, & Sumarta, 2018).

This research aims to formulate and evaluate the characteristics of cream preparations containing breadfruit leaf essence, as well as test their antioxidant activity using the 1,1-diphenyl-2-picrylhydrazil (DPPH) method. By conducting this study, we hope to provide valuable information on the potential of breadfruit leaf essence cream preparations as antioxidants, which can ultimately benefit the public in maintaining healthy skin.

METHODS

Types of Research

This study adopts an experimental laboratory approach to investigate the potential of breadfruit leaf essence cream as an antioxidant agent. Sugiyono (2014) defines experimental research as a method used to examine the effects of specific treatments on other variables in controlled conditions. Thus, it can be inferred that the experimental method involves

manipulating the research object and utilizing control groups to explore causality and the relationship between treatments and outcomes in the experimental group.

Place and Time

This research was carried out at the Phytochemistry Laboratory and Cosmeseutics Laboratory of the University of North Sumatra, Medan. In December 2022 to January 2023.

Tools and Materials

The study will employ several tools, including glassware, stirring rods, cotton, evaporators, mortars and pestles, water baths, porcelain dishes, cream containers, pH meters, petri dishes, transparent glass, filter paper, horn spoons, analytical scales, and a UV-Vis spectrophotometer. Meanwhile, the materials used in the study consist of breadfruit leaves, 96% ethanol, filter paper, distilled water, liquid paraffin, beeswax, sorbitan monostearate, and triethanolamine.

Data Analysis

The observed data were analyzed statistically with *One way ANOVA* (variance analysis). This statistical analysis uses SPSS (*static product and service solution*) and $p < 0.05$ is chosen as the minimum level of significance. One *way ANOVA* was chosen because this study used more than two groups to test generalizations so that, data sample was considered delegate of the population. The conditions that must be met by the *ANOVA one way test* are as follows:

1. Numerical data on categorical groups
2. Data distribution should be normal
3. Data variance must be the same

If it does notmeet the requirements, then efforts are made to transform the data so that the normal distribution and variance become the same.

RESULTS AND DISCUSSION

1. Plant Identification Results

Based on the identification conducted at the Herbarium Medanase (MEDA), Herbarium Laboratory of the Faculty of Mathematics and Natural Sciences (FMNS), University of North Sumatra, the plant under study was identified as Artocarpus altilis, commonly known as breadfruit leaves.

2. Results of Breadfruit Leaf Phytochemical Screening Test

Phytochemical screening tests are carried out to establish and identify the components of bioactive compounds contained in breadfruit leaves. Some of the active compound components identified include: steroids/triterpenes, alkaloids, saponins, tannins, glycosides and flavonoids. Screening results of breadfruit leaves extracted using ethanol solvent, can be showed in Table

Table 1. Results of Phytochemical Screening Test of Breadfruit Leaf Extract

Bioactive Compounds	Fruit Extract Breadfruit Leaves
Alcolloids	+
Flavonoids	+
Saponins	+
Tannins	+
Streroid/Triterpenoid	+
Glycosides	+

Description:
(+) = Contains Compounds
(-) = Contains No Compounds

The ethanol extract of breadfruit leaves was qualitatively analyzed for its active components, which revealed the presence of all secondary metabolites. The compounds that act as antioxidants in the extract are alkaloids, flavonoids, glycosides, saponins, and tannins. Alkaloids have pharmacological effects as analgesics and anesthetics, as well as antibacterial abilities by disrupting the peptidoglycan components in bacterial cells. Saponins have potential as antimicrobial compounds by reducing the permeability of bacterial cell walls. Phenolic compounds known as tannins can cause harm to the polypeptides present in the cell wall and obstruct the growth of bacteria by coagulating the protoplasm within the bacterial cell. The antibacterial effect of tannins stems from their ability to inhibit the enzymes reverse transcriptase and DNA topoisomerase by affecting their mechanisms of action.

Robinson (1995) noted that alkaloids possess antibacterial abilities as well as pharmacological effects such as analgesics and anesthetics. The compound is believed to inhibit the formation of intact cell wall layers in bacterial cells by disrupting the constituent components of peptidoglycan, causing cell death. Meanwhile, saponins found in breadfruit leaf extract have the potential as antimicrobial compounds by reducing the permeability of bacterial cell walls, allowing them to enter the bacterial cytosol and inhibit their growth, according to Safitri (2010).

Tannins are another type of metabolite compound found in breadfruit leaf extract. Maharani et al. (2014) discovered that tannins, Phenolic compounds known as tannins are capable of damaging the polypeptides present in the cell wall. The mechanism of tannin inhibition occurs through the lysis of bacterial walls, facilitated by the presence of saponin and flavonoid compounds. This process allows tannin compounds to easily penetrate the bacterial cells and coagulate the bacterial cell protoplasm.. Additionally, Robinson (1995) found that tannins act as antibacterials by inhibiting reverse transcriptase enzymes and DNA topoisomerase, preventing bacterial cells from forming.

3. Results of Characterization of Breadfruit Leaf Simplisia

1. **Results** of **Characterization** of **Breadfruit Leaf Simplisia**

   Results of the characterization examination of breadfruit leaf simplisia in the form of water content, water soluble juice, ethanol soluble juice, total ash content and acid insoluble ash content can be seen in Table 1

Table 2. Results of Characterization of Breadfruit Leaf Simplisia

No	Examination	Breadfruit Leaf Simplisia Powder (%)
1.	Water content	7.30%
2.	Water Soluble Juice Content	26.70%
3.	Ethanol Soluble Water Content	15.14%
4.	Total ash content	9.99%
5.	Ash content is not acid soluble	5.06%

The purpose of determining water content is to establish the minimum limit or range of water present in the simplisia and extract materials (Ministry of Health RI., 2000). The higher the water content, the better the mushroom growth since water is an ideal medium for it (Mutiatikum, et al., 2010). As seen in the table above, the moisture content of the simplisia and extract satisfies the requirements. The moisture content for the extract should not be more than 30% (Voigt, 1995) while the moisture content for the simplisia should not exceed 10% (MOH, 1995).

The purpose of determining the levels of water-soluble juice is to measure the quantity of polar water-soluble juice (Ministry of Health RI., 1995). Conversely, the goal of determining the levels of soluble juice in ethanol is to identify the

compounds that are dissolved in ethanol, including those that are both polar and nonpolar.

The determination of the total ash content provides a comprehensive view of the internal and external mineral content that emerges during the extract formation process (Ministry of Health RI., 2000).

This plant contains internal mineral content such as K, Ca, Mg, Mn, and Fe (Barua, et al., 2014). The determination of acid-insoluble ash content is performed to evaluate the simplisia and extract against contamination by materials containing silica, heavy metals such as Pb (Ministry of Health RI., 1995).

4. Results of Determination of Total Phenol Levels

The Folin-Ciocalteau method was used to establish the total phenol content compound in the ethanol essence of breadfruit leaves. This method is chosen for its specificity and sensitivity to phenol compounds, and the reagents used in small quantities. The Folin-Ciocalteau reagent is initially greenish-yellow but turns dark blue when it reacts with a sample solution that has been added with Na2CO3. The principle of this steps is based on the formation of blue complex compounds that can be measured at a wavelength of 775. To create a standard solution, gallic acid was used because it is a natural and stable phenolic compound. According to Viranda (2009), Gallic acid is a type of simple phenolic acid that is derived from hydroxybenzoic acid. When gallic acid reacts with the Folin-Ciocalteau reagent, it produces a yellow color that indicates the presence of phenolic compounds. Next, an alkaline solution of Na2CO3 is added, resulting in a more concentrated blue color that is proportional to the concentration of phenol ions that are formed. As a result, a higher concentration of phenolic compounds will lead to a greater amount of phenolic ions, which will reduce heteropoly acid into a molybdenum-tungsten complex, resulting in a more intense color (Sari and Ayuchecaria, 2017).

1. **Maximum Absorption Wavelength Determination Result**

   Maximum absorption wavelength of gallic acid was established by adding Folin-Ciocalteau reagents, 10% Na2CO3, and aquades with a concentration of 125 μg/ml, and then measuring it using a UV-Visible spectrophotometer, which resulted in a maximum absorption wavelength of 775 nm. The graph showing the results of measuring the maximum absorption wavelength of gallic acid is presented in Figure 4.1.

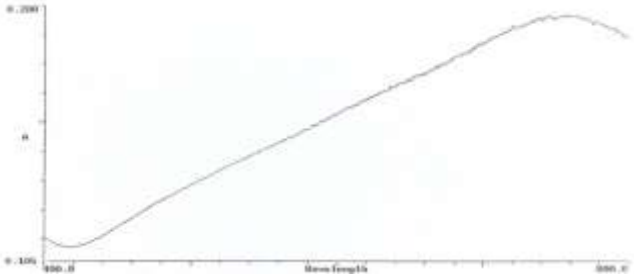

Figure 1. Maximum Wavelength of Acid Error

2. **Results of Determination of Error Acid Absorption Curve**

   Determination of gallic acid absorption curve is done by measuring gallic acid absorbance at concentration variations from 250 – 15.625 μg/ml with a wavelength of 775 nm. The absorption curve of gallic acid can be seen in Figure 2.

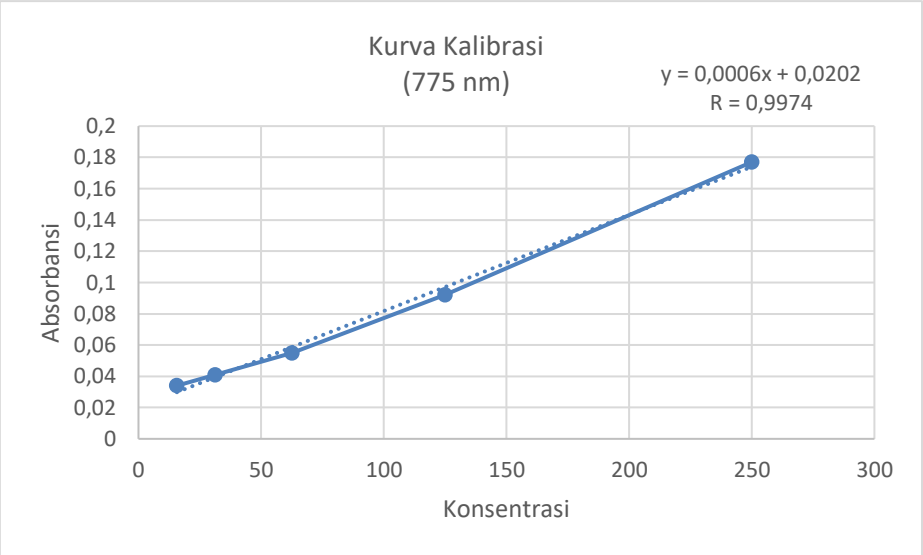

Figure 2. Error Acid Calibration Curve

The gallic acid calibration curve in Figure 2 shows an r value of 0.9974 and a regression equation of y = 0.0006x + 0.0202. An absorption curve illustrates the relationship between the absorption of a solution and the radiation wavelength, with absorption score on the Y axis and concentration on the X axis. The relevancy coefficient r is used to determine the linear relationship in the regression equation y = ax + b. A perfect linear relationship is achieved when b = 0 and r = ±1, depending on the direction of the line (Harmita, 2004).

3. Determination of Total Phenol Levels Result in Breadfruit Leaf Ethanol Extract

The concentration of the total content phenol in breadfruit leaf ethanol essence is determined by substituting the average absorbance values of the sample into a linear regression equation obtained from the calibration curve. The total phenol content is expressed in part of milligrams equivalent to gallic acid per gram of sample (mg/GAE), which represents the amount of gallic acid in milligrams equivalent to 1 gram of sample (Hapsari, et al., 2018). Table 3 presents the results of the total phenol content determination in breadfruit leaf ethanol extract.

Table 3. Total Phenol Content in Breadfruit Leaf Ethanol Extract

Sample	Total Phenol Levels (mg GAE/g sample)	Average Total Phenol Content (mg GAE/g sample)
Breadfruit Leaf Ethanol Extract	293 294,67 293	293.56 ± 1.3

According on Table 3 above, it can be showed that the total phenol content obtained is 293.56 ± 1.3 mg GAE / g sample. These results mean a total phenol of 1 gram of breadfruit leaf ethanol essence is equivalent to 293.56 ± 1.3mg of gallic acid.

4. Results of Determination of Total Flavonoid Levels

The established of total flavonoid levels is based on the reaction between flavonoids and the yellow AlCl3 complex. Addition of sodium acetate results in the formation of a pink complex

compound, whose absorption is measured using a UV-Visible spectrophotometer. The colorimetric method uses AlCl3 10% and acetic acid 5% as reagent adders (Sari and Ayuchecaria, 2017).

Quercetin is commonly used as a standard in determining total flavonoid content due to its high antioxidant activity and prevalence as a type of flavonoid (Sari and Ayuchecaria, 2017).

1. Maximum Absorption Wavelength Determination Result

The maximum absorption wavelength of quercetin was determined by adding a 10% aluminum chloride reagent (AlCl3), 1 M sodium acetate (CH3COONa), and aquadest at a concentration of 25 µg/ml, which led to a maximum absorption at 432 nm. Figure 3 displays the measurement results of the maximum absorption of quercetin

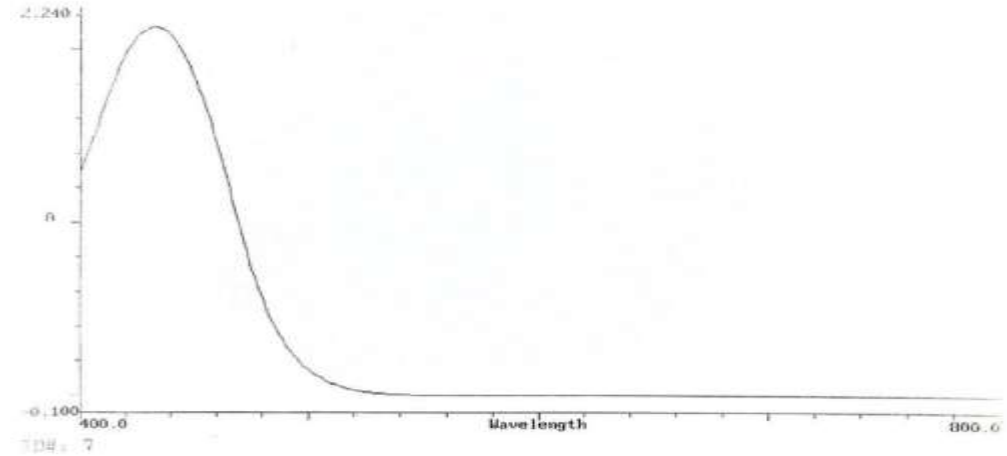

Figure 3. Maximum Wavelengths of Quercetin (432 nm)

2. Results of Determination of Quercetin Uptake Curve

Determination of quercetin absorption curve is done by measuring quercetin absorbance at concentration variations of 100 – 6.25 µg/ml with a wavelength of 432 nm. The absorption curve of gallic acid can be seen in Figure 4

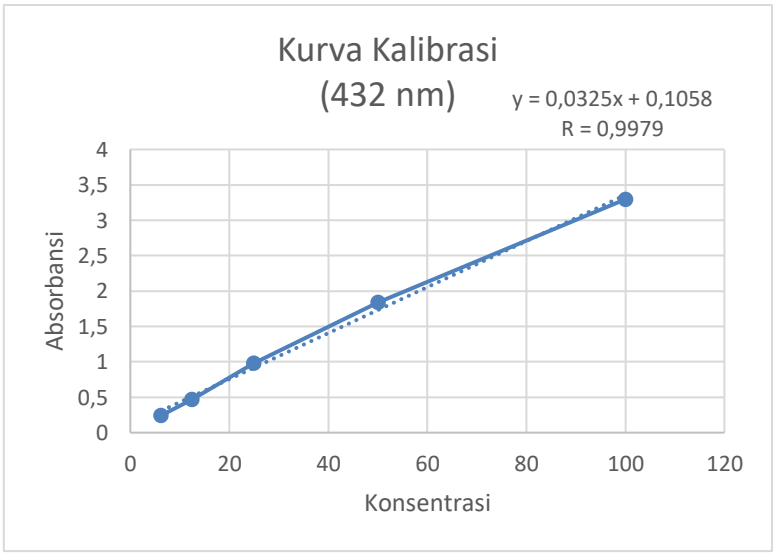

Figure 4. Quercetin Calibration Curve

Based on Figure 4.4 of the gallic acid calibration curve above, The regression equation y = 0.0325x + 0.1058 gave us an r value of 0.9979. An absorption curve is a plot that illustrates the correlation between the absorption of a solution and the wavelength of radiation. The absorption value is plotted on the Y axis, while the concentration is plotted on the X axis. The correlation coefficient r is used as a parameter of the linear relationship in the equation y = ax + b for linear regression. Ideally, a perfect linear relationship is indicated by b = 0 and r = ±1, depending on the direction of the line (Harmita, 2004).

3. **Results of Determination of Total Flavonoid Levels in Breadfruit Leaf Ethanol Extract**

   The total flavonoid content is expressed in QE (quercetin aquivalent) which is the equivalent amount of milligrams of quercetin in 1 g sample (Adhayanti, et al., 2018).

Table 4. Total Flavonoid Levels in Breadfruit Leaf Ethanol Extract

Sample	Total Flavonoid Levels (mg QE/g sample)	Average Total Flavonoid Levels (mg QE/g sample)
Breadfruit Leaf Ethanol Extract	10,96 10,99 10,96	10.97 ± 0.06

Based on Table 4 above, obtained total flavonoid levels of 10.97 ± 0.06 mg QE/g samples. These results mean that a total flavonoid of 1 gram of breadfruit leaf ethanol extract is equivalent to 10.97 ± 0.06 mg of quercetin.

5. Antioxidant Activity Analysis Results of DPPH Method

1. **Maximum Wavelength Determination Results**

   The results of measuring the maximum absorption wavelength of DPPH solution of 12.5 μg/ml in methanol solvent using UV-Vis spectrophotometer can be seen in Figure 5

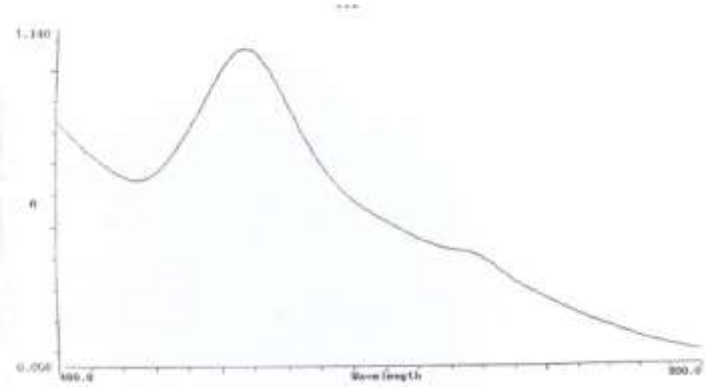

Figure 5. Maximum Wavelength DPPH Solution 12.5 μg/ml in Methanol Using a UV-Visible Spectrophotometer

In Figure 5. it is demonstrated that a 12.5 µg/ml DPPH solution exhibits maximum absorption at a wavelength of 516 nm, which falls within the visible light wavelength range of 400-800 nm. This wavelength is indicative of the point where the maximum absorption occurs and represents the highest sensitivity value (Sayakti, et al., 2022).

6. Results of Antioxidant Activity Analysis of DPPH Method Test Samples

To analyze the antioxidant activity of the ethanol extract of breadfruit leaves, the DPPH method was utilized. This method measures the extract's capacity to eliminate free radicals by gauging the absorbance at 516 nm through a UV-Vis spectrophotometer. The DPPH test is distinguished by a qualitative color shift from purple to yellow, wherein the magnitude of the color alteration is proportionate to the extract's antioxidant activity in lessening free radicals (Rahmawati, et al., 2015).

To measure the antioxidant activity of breadfruit leaf ethanol extract, test samples were prepared at concentrations of 100 µg/ml, 50 µg/ml, 25 µg/ml, and 12.5 µg/ml, and each concentration was mixed with 1 mL of DPPH solution. The percentage of DPPH inhibition by breadfruit leaf ethanol extract can be seen in Figure 7

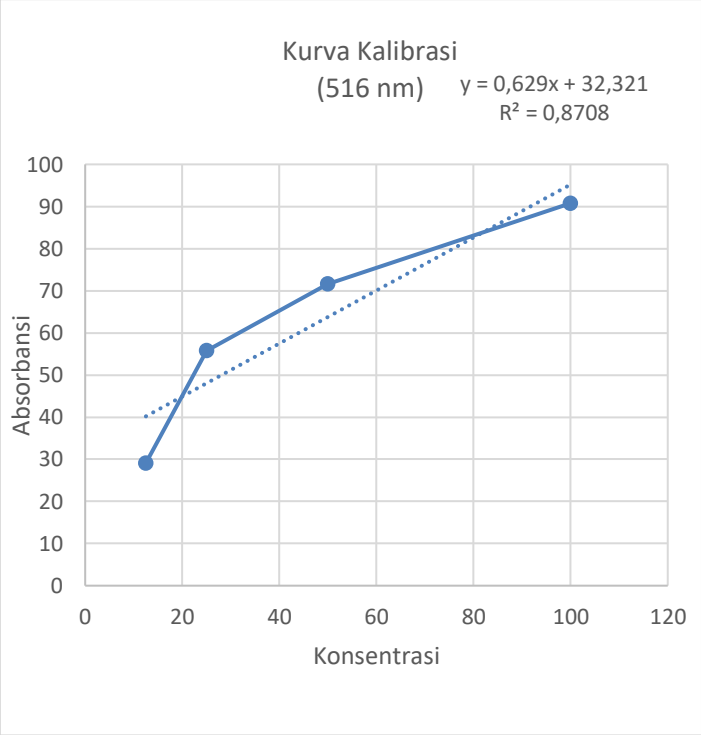

Figure 6. Graph of Antioxidant Activity Test Results of Breadfruit Leaf Samples

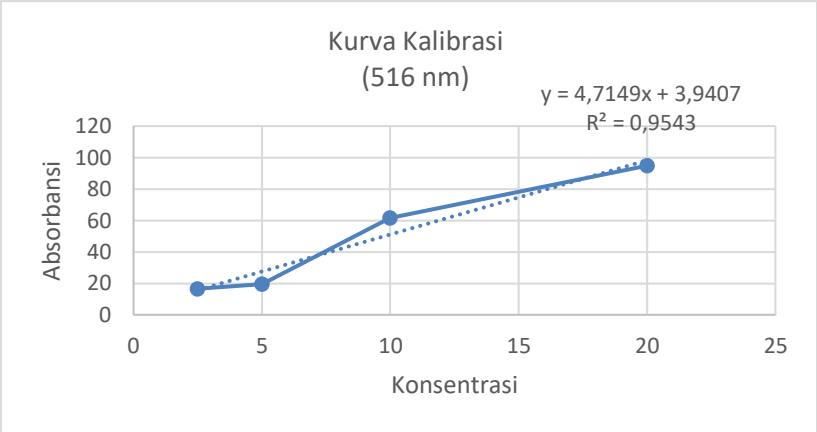

Figure 7. Graph of Quercetin Comparison Antioxidant Activity test Results

Based on the presented graph, it can be observed that the antioxidant activity of breadfruit leaf ethanol extract and quercetin as a comparator exhibited a decrease in absorbance values, indicating an increase in antioxidant activity. The decrease in absorbance values is attributed to the ability of the breadfruit leaf sample solution to scavenge free radicals, which is indicated by the color change from blue to yellow. This color change is evidence of the presence of antioxidant activity in the breadfruit leaf samples (Molyneux, 2004).

The analysis of the chart data suggests that the antioxidant activity of breadfruit leaf ethanol extract is lower than that of quercetin comparator. This is because quercetin is a flavonol compound, which belongs to the largest group of flavonoids and has great potential to ward off free radicals in the body, whereas breadfruit leaf ethanol extract is a mixture of secondary metabolite compounds produced by plants that interact with each other to cause certain activities (Sayakti, et al., 2022).

The percent damping of DPPH with the addition of the sample solution is calculated as the absorbance value. The relationship between the concentration of the sample solution and the percent damping in Figure 4.7 and Figure 4.8 indicates that with an increase in the concentration of the sample solution and a decrease in the absorbance value, the antioxidant activity of DPPH damping also increases.

8. IC50 Analysis Results

The IC50 (Inhibitory Concentration) value is used to calculate the free radical scavenging activity of a compound, which represents the concentration of the test compound needed to scavenge 50% of free radicals. The IC50 value is obtained by plotting the concentration of the sample (µg/ml) on the x-axis and the percentage of inhibition on the y-axis, and then entering the results into a regression equation (Mardawati et al., 2008).

Table 5. IC Value Results$_{50}$ Breadfruit Leaf Ethanol Extract and Quercetin Comparator

Sample	Regression equation	$IC_{value\ 50}$ (µg/ml)	Category
Breadfruit Leaf Ethanol Extract	Y = 0.629x + 32.321	28.10 ± 0.15	Very Powerful
Quercetin Comparator	Y = 4.7149x + 3.9407	9.76 ± 0.07	Very Powerful

Molyneux (2004) proposed that the antioxidant capacity of a compound can be categorized as very strong if the IC50 value is less than 50 µg/ml, strong if the IC50 is between 50-100 µg/ml, weak if the IC50 is between 101-150 µg/ml, and very weak if the IC50 is between 151-200 µg/ml. Table 4.7 shows that the breadfruit leaf ethanol extract has an IC50 of 28.10 ± 0.15 µg/ml, indicating that it has very strong

antioxidant activity as its IC50 value is less than 50 μg/ml. In contrast, the quercetin comparator has an IC50 of 9.76 ± 0.07 μg/ml, which also indicates a very strong antioxidant activity. The choice of quercetin comparison is due to its status as a flavonol compound (the largest group of flavonoids) with great potential for reducing free radicals in the body, while the breadfruit leaf ethanol extract is a combination of secondary metabolite compounds produced by plants that interact with each other to generate certain activities (Sayakti, et al., 2022).

9. Preparation Evaluation Results

1. Resultsof physical stability check

   The results of examination of the formulation of breadfruit leaf extract cream preparations visually such as organoleptis and homogeneity can be seen in Table 4.7 and pictures of cream preparations Appendix 2 page 61.

Table 6. Visual Examination Data of Breadfruit Leaf Extract Cream Preparations

	Testing	Cycle 1	Cycle 2	Cycle 3
F0	Organoleptis - Aroma - Color - Shape - Homogeneity	- Distinctive smell - White - Cream - Homogeneous	- Distinctive smell - White - Cream - Homogeneous	- Distinctive smell - White - Cream - Homogeneous
F1 1 %	Organoleptis - Aroma - Color - Shape - Homogeneity	- Distinctive smell - Yellowish green - Cream - Homogeneous	- Distinctive smell - Yellowish green - Cream - Homogeneous	- Distinctive smell - Yellowish green - Cream - Homogeneous
F2 6%	Organoleptis - Aroma - Color - Shape - Homogeneity	- Distinctive smell - Dark Green - Cream - Homogeneous	- Distinctive smell - Dark Green - Cream - Homogeneous	- Distinctive smell - Dark Green - Cream - Homogeneous
F3 9 %	Orgaloleptis - Aroma - Color - Shape - Homogeneity	- Distinctive smell - Dark Green - Cream - Homogeneous	- Distinctive smell - Dark Green - Cream - Homogeneous	- Distinctive smell - Dark Green - Cream - Homogeneous

	Testing	Cycle 4	Cycle 5	Cycle 6
F0	Organoleptis - Aroma - Color - Shape - Homogeneity	- Distinctive smell - White - Homogeneous cream	- Distinctive smell - White - Homogeneous cream	- Distinctive smell - White - Homogeneous cream
F1 1 %	Organoleptis - Aroma - Color - Shape - Homogeneity	- Distinctive smell - Yellowish green - Cream - Homogeneous	- Distinctive smell - Yellowish green - Cream - Homogeneous	- Distinctive smell - Yellowish green - Cream - Homogeneous
F2 6%	Organoleptis - Aroma - Color - Shape - Homogeneity	- Distinctive smell - Dark Green - Homogeneous cream	- Distinctive smell - Dark Green - Homogeneous cream	- Distinctive smell - Dark Green - Homogeneous cream
F3 9 %	Orgaloleptis - Aroma - Color - Shape - Homogeneity	- Distinctive smell - Dark Green - Homogeneous cream	- Distinctive smell - Dark Green - Homogeneous cream	- Distinctive smell - Dark Green - Homogeneous cream

Description: F0: Cream Base, F1: Cream E DS 3% w/w, F2: Cream E DS 6% w/w, F3: Cream E DS 9% w/b

The cream produced without the addition of white extract has a cream color, while with the addition of the extract, the cream turns green to dark green. The intensity of the cream color and characteristic odor increases with increasing concentration of the added extract. As the concentration of the extract increases, the cream base becomes odorless while the aroma of the extract becomes stronger. After 6 test cycles, there were no changes observed in terms of aroma, color, shape, and homogeneity of the preparation.

Organoleptic stability observation is carried out to established any changes in the physical appearance of the preparation during storage by examining its shape, color, and odor (Mappa et al., 2013). Results indicate that all EDS creams were physically stable and did not undergo significant changes in their appearance, color, smell, and consistency after 30 days of storage.

2. Determining the pH of the Preparation Result

The results of determining the pH of EDS cream preparations carried out using pH meters for all dishes can be demonstrate in Table.

Table 7 pH Measurement Data

Storage Time	pH Measurement Results			
	F0			Avg±STD
Cycle 1	7.3	7.28	7.29	7.29 ± 0.00
Cycle 2	7.21	7.2	7.18	7.19 ± 0.06
Cycle 3	7.16	7.14	7.15	7.15 ± 0.00
Cycle 4	7.02	7.03	7.04	7.03 ± 0.00
Cycle 5	6.95	6.95	6.93	6.94 ± 0.03
Cycle 6	6.86	6.87	6.85	6.86 ± 0.00
Storage Time	pH Measurement Results			
	F1			Avg±STD
Cycle 1	7.19	7.21	7.2	7.2 ± 0.00
Cycle 2	7.14	7.15	7.14	7.14 ± 0.03
Cycle 3	7.05	7.05	7.07	7.05 ± 0.06
Cycle 4	6.97	6.93	6.95	6.95 ± 0.00
Cycle 5	6.89	6.88	6.89	6.88 ± 0.06
Cycle 6	6.78	6.76	6.76	6.76 ± 0.06
Storage Time	pH Measurement Results			
	F2			Avg±STD
Cycle 1	7.08	7.08	7.07	7.07 ± 0.06
Cycle 2	7.07	7.05	7.05	7.05± 0.06
Cycle 3	7	6.98	6.98	6.98± 0.06
Cycle 4	6.85	6.87	6.87	6.86 ± 0.03
Cycle 5	6.75	6.74	6.74	6.74 ± 0.06
Cycle 6	6.65	6.63	6.62	6.63 ± 0.03
Storage Time	pH Measurement Results			
	F3			Avg±STD
Cycle 1	7.04	7.05	7.05	7.04 ± 0.06
Cycle 2	6.95	6.94	6.94	6.94 ± 0.03
Cycle 3	6.88	6.88	6.88	6.88 ± 0.00

Cycle 4	6.71	6.72	6.72	6.71 ± 0.06
Cycle 5	6.55	6.57	6.58	6.56 ± 0.06
Cycle 6	6.46	6.46	6.47	6.46 ± 0.03

Description: F0: Cream Base, F1: Cream E DS 3% w/w, F2: Cream E DS 6% w/w, F3: Cream E DS 9% w/b

The test results indicate that the pH score of EDS cream preparations ranged between 6.0-7.5. The pH of the cream base decreased from cycles 1-6. The decrease in pH can be attributed to the reaction of CO2 from the air with the water phase in the gel, resulting in the formation of acid (Septiani, et al., 2012). Hydrolysis can also cause changes in pH values, which is a process by which compounds interact with water molecules to produce fractional products with different chemical compositions. This process is common in compounds containing ester groups, lactones, and glycosides (Ansel, 2005).

However, the changes in pH in this study were not significant, indicating that the pH of the preparation remained relatively stable during storage and still within the normal pH range of the skin, which is 4.5-6.5. Materials that are more alkaline or acidic can cause the skin to become dry and cracked, as the skin finds it challenging to neutralize them (Tranggono and Latifah, 2007).

Determination of Dosage Viscosity Results

Results of determining viscosity of EDS cream were carried out using a brookfield viscometer on all preparations. The improved results can be seen in Table and the calculation example in Appendix 2 page 63.

The table below shows the viscosity results of stable cream preparations in storage. This can be seen from the viscosity value of the preparation which does not change from day 0 to day 90. The viscosity value of a good gel preparation is 2000-4000 cps (Arikumalasari, et al., 2013) so that the EEDSR gel preparation meets the requirements.

Table 8. Viscosity Measurement Data

Storage Time (Before *Cycling Test*)	Viscosity Measurement Results	
	Viscosity Value (Cp)	Attachment
F0	2030,8	
F1 (3%)	1390,4	
F2 (6%)	1566,6	
F3 (9 %)	1733,2	
Storage Time (After *Cycling Test*)	Viscosity Measurement Results	
	Viscosity Value (Cp)	Attachment

F0	1983.9	
F1 (3%)	1009,8	
F2 (6%)	1042.7	
F3 (9 %)	1052.7	

Description: F0: Cream Base, F1: Cream E DS 3% w/w, F2: Cream E DS 6% w/w, F3: Cream E DS 9% w/b

CONCLUSION

The viscosity of thebag that is too high on the cream will cause the cream structure to be stiffer and the active substance will be more difficult to diffuse through the cream matrix, so the release of the active substance from the cream base will be small (Sanna, et al., 2010; Fulviana, et al., 2013; Goci, et al., 2014). Cream viscosity that is too low will cause the stickiness of the cream to the skin to be smaller so that the contact time of the cream with the skin is shorter (Singh, et al., 2011; Kusumawati, et al., 2012; Dewi, et al., 2013).

The viscosity of a preparation is inversely proportional to its diffusion. The higher the viscosity value of a preparation, the diffusion coefficient will be smaller and the diffusion will be slower while the lower the viscosity value of a preparation, the diffusion will be faster (Hasyim, et al., 2012).

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