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Formulation of Micellar Based Water from *Piper crocatum* Leaves Extract Using Various Concentrations of Poloxamer 188

(*Formulasi Micellar Berbasis Air Ekstrak Daun Sirih Merah (Piper crocatum) dengan Variasi Konsentrasi Poloxamer 188*)

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ABSTRACT

Background: Micellar based water (micellar water) is a preparation used to clean the face or makeup with water-based ingredients. Micellar water has moisturizing additives accompanied by antioxidants. *Piper crocatum* leaves is one of the plants that contain flavonoid compounds so it has the potential as an antioxidant. Micelles are the main component in micellar water preparations derived from amphiphilic block copolymer-type surfactants such as poloxamer. **Objectives:** The purpose of this study was to formulate, evaluate, and observe the antioxidant activity of the most optimum formulation of micellar based water preparations of *Piper crocatum* leaves extract with variations in poloxamer 188 concentrations. **Material and Methods:** The stages of this research were material preparation, extract characteristics evaluation, production of micellar preparations at poloxamer 188 concentrations of 1% (F1); 1.5% (F2); and 2% (F3); preparation characteristics evaluation, stability, particle size, antioxidant activity assay for the optimum formula, and irritation test. **Results:** The results of the evaluation showed that the pH of the preparation ranged from 4.54 - 4.76; viscosity values ranged from 16.40 - 24.26 cP; particle size ranged from 170.6 – 349.9 nm; and the entire formula did not irritate the skin. **Conclusions:** Based on the results of this study, it was found that the most optimal concentration of poloxamer 188 was 2% (F3) with IC_{50} value of 119.63 ppm which categorized as a moderate antioxidant activity.

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INTRODUCTION

Micellar water is a preparation used to clean the face or makeup with water-based ingredients. Micellar water contains moisturizing ingredients combined with antioxidants. Micellar water can be used on all skin types, even people with atopic dermatitis or allergic contact dermatitis, and rosacea (Oliveira *et al.*, 2011; Vij, 2022). Research conducted by Guertler *et al.* (2020), that the use of micellar water can collaborate with creams and serums in reducing the symptoms of patients with rosacea and can improve the quality of life of patients. This proves that micellar water has the advantage of being a cleanser for all skin types. Micelles are the main component in micellar water that can be formed from amphiphilic block copolymer-type surfactants. Ricardo *et al.* (2012) argued that amphiphilic copolymer-type surfactants that are often used as micellar agents are pluronic groups or referred to as poloxamer groups (Dzakwan, 2020).

Poloxamer 188 is a type of poloxamer used in cosmetics as a surfactant that forms micelles. The micelle structure in poloxamer 188 is an ABA type block copolymer. Part A of the ethylene oxide polymer block is hydrophilic and part B of the propylene oxide polymer is hydrophobic, through this structure making the micelles in poloxamer 188 work to capture dirt and oil on the face. Poloxamer 188 has several advantages such as low toxicity, high solubility, easy to dissolve in water, stable according to thermodynamics in solution, and has a hydration effect. Based on Dzakwan's (2020) research on the formulation of micellar water preparations from telang flower extract using poloxamer as a surfactant, poloxamer has good biocompatibility properties with telang flower extract. Telang flowers and *Piper crocatum* leaves have the same active substance like flavonoids, so poloxamer is expected to also be compatible with *Piper crocatum* leaves extract (Bodratti & Alexandridis, 2018; Samith *et al.*, 2013; Tadros, 2015 in Dzakwan, 2020; Rosen, 2015).

Based on Dzakwan's research (2020), the formulation of micellar-based water preparations of telang flower extract at various concentrations of poloxamer 188 gave the best results at a poloxamer concentrations of 1% (F5). F5 had a clear physical appearance of the preparation, no precipitation occured and had a particle size of 46.67 nm with a zeta potential of -28.4 mV. In addition to being used for cleaning, micellar water is formulated with antioxidant content as a preparatory value-added. Antioxidants are substances that can prevent oxidation by stabilizing free radicals. One plant that has antioxidant activity is the *Piper crocatum* leaves. *Piper crocatum* leaves contain phytochemical compounds such as alkaloids, saponins, tannins, and flavonoids that can be formulated into natural antioxidants (Reefani, 2016).

According to the results of research by Febriani *et al*. (2022), *Piper crocatum* leaves extract tested for antioxidant activity gave an IC_{50} value of 38.30 ppm which is classified as very strong. Then *Piper*

crocatum leaves extract was made at a concentration of 1.5%; 2%; and 3% for serum preparations. A concentration of 3% is the best concentration to be formulated and is included in the strong antioxidant category with an IC_{50} value of 58.13 ppm.

Based on the background above, this study formulated a water-based micellar preparation using the addition of *Piper crocatum* leaves extract with variations in poloxamer concentration 188. The formulation of this research problem is what is the most optimal concentration of poloxamer 188 to obtain a good *Piper crocatum* leaves extract water-based micellar preparation, and whether the water-based micellar preparation can meet the evaluation parameters. The purpose of this study was to formulate, evaluate, and test the antioxidant activity of the most optimal formulation of water-based micellar preparations of *Piper crocatum* leaves extract with variations in poloxamer concentration of 188.

MATERIAL AND METHODS

Materials

The equipment used for this study were glassware (Duran®), analytical balances (Fujitsu FS), scales (Kenko®), magnetic stirrer (Scilogex), UV-Vis spectrophotometer (Thermo Scientific®), rotary evaporator (Heidolph®), Brookfield viscometer (Ametek®), pH meter (Hanna Instruments®), Particle Size Analyzer (PSA) (DelsaMax Pro®), refrigerator (Liebherr®), vortex (Scilogex®) and oven (Memmert®). The materials used include *Piper crocatum* leaves, 70% ethanol, poloxamer 188 pro analysis (Merck®), sodium gluconate, propylene glycol, glycerin, phenoxyethanol, lactic acid (Merck®), purified water (One Med®), vitamin C (Merck®), DPPH solution (Himedia®), and ethanol pro analysis (Merck®).

Methods

Material Preparation

Piper crocatum leaves were obtained from Desa Setiamekar, Kecamatan Tambun Selatan, Bekasi, West Java for 7 kg. Harvested leaves were medium aged or 4 months old. Determination was carried out at Organisasi Riset Ilmu Pengetahuan Hayati Pusat Riset Biologi BRIN (Badan Riset dan Inovasi Nasional).

Preparation of Simplisia

The *Piper crocatum* leaves were wet-sorted and cut to the same size then spreaded on the drying container. The drying process was carried out with the help of indirect sunlight. After dry-sorting was carried out, the leaves were mashed using a blender and sifted with sieve number 60. Simplisia of *Piper*

crocatum leaves powder then stored in airtight containers at room temperature (Handoyo & Pranoto, 2020; Okzelia & Mardiyyah, 2023).

A total of 1 kg of simplisia of *Piper crocatum* leaves powder was added with 70% ethanol with a ratio of 1:10, then stirred and allowed to stand for 24 hours. Then remaceration was carried out for 24 hours. The filtrates were evaporated with a rotary evaporator at 40ºC (Sanjaya *et al*., 2020; Departemen Kesehatan RI, 2008).

Test Characteristics of Extracts

Organoleptic Test

This organoleptic examination was carried out by observing the shape, odor, and color of *Piper crocatum* leaves extract powder.

Water Content Test

A total of 1 g of sample was weighed then put into an evaporating dish. Samples then dried at 105ºC within 5 hours and weighed. This procedure was carried out until there the difference between two consecutive weighings of no more than 0.25% (Kementerian Kesehatan RI, 2017).

Extract Yield

The comparison between the weight of extracts obtained and the weight of initial dried simplisia was stated as yield of extract (Agustien & Susanti, 2021).

Phytochemical Screening

Alkaloid

A 0.1 grams of *Piper crocatum* leaves extract was dissolved with 5 mL of chloroform and 3 drops of NH_4OH. The chloroform fraction was acidified and separated with 2 drops of H_2SO_4 2M. The upper layer (acid) was added with Dragendorff, Mayer, and Wagner. Alkaloid compounds are detected if there were an orange precipitate formed with Dragendorff reagent, a white precipitate formed with Mayer reagent, and reddish-brown precipitate formed with Wagner reagent (Puspita *et al*., 2018).

Flavonoid

A 1 gram of *Piper crocatum* leaves extract was added by 1 mL of concentrated HCl and 0.2 grams of mg powder. Flavonoid compounds are detected (positive flavonoids) if yellow, orange, or dark red color is formed (Kasitowati *et al*., 2017).

Tannin

A 0.1 grams of *Piper crocatum* leaves extract was added with 5 mL of pure water and brought to a boil. The filtrate then added with 1% $FeCl_3$. If it is blackish-green, tannin compounds are detected (Puspita *et al.*, 2018).

Saponin

A 0.1 grams *Piper crocatum* leaves extract was added to 5 mL pure water then heated for 5 minutes at a temperature of 100°C then shaken up to 5 minutes. If there is a foam that is formed no less than 1 cm high and stable after 15 minutes of silence, it indicates that there are saponin compounds (Puspita *et al.*, 2018).

Terpenoid & Steroid

A 0.1 grams of *Piper crocatum* leaves extract was added with 5 mL of 30% methanol then heated and filtered. The filtrate was added by 3 drops of anhydrous acetic acid and 1 drop of concentrated sulfuric acid (often called the Liebermann Burchard reagent). If it formed blue or green, it indicated that there were steroid compounds, and purple or red color indicated the presence of triterpenoid compounds (Puspita *et al.*, 2018).

Production of Water-Based Micellar Preparation Formulation of *Piper crocatum* Leaves Extract

Water-based micellar was made using a formulation by Dzakwan (2020) with modifications. The active ingredient that is a value enhancer for water-based micellar preparations is *Piper crocatum* leaves extract which has properties as an antioxidant. Each formula was prepared with a dosage volume of 100 mL.

Table 1. Water-Based Micellar Formulation of *Piper crocatum* Leaves Extract

Materials	**Formula**				**Function**
	F0	F1	F2	F3	
***Piper crocatum* Leaves Extract (%)**	2,81	2,81	2,81	2,81	Active Ingredients (Antioxidants)
Poloxamer 188 (%)	-	1	1,5	2	*Micellar Agent*/ Surfactant
Sodium Gluconate (%)	0,2	0,2	0,2	0,2	*Chelating Agent*
Propylene Glycol (%)	1,5	1,5	1,5	1,5	Humectants
Glycerin (%)	0,25	0,25	0,25	0,25	Humectants
Phenoxyethanol (%)	0,5	0,5	0,5	0,5	Preservatives
Lactic Acid (%)	q.s	q.s	q.s	q.s	Neutralizes pH
Purified Water (mL)	Ad 100	Ad 100	Ad 100	Ad 100	Solvent

Test Characteristics of Water-Based Micellar Preparations

Organoleptic Test

This organoleptic test was carried out by observing the shape, odor, and color of micellar preparations.

pH Test

The pH test was carried out by dipping the electrode of pH meter into a micellar preparation (Zarwinda *et al*., 2022).

Viscosity Test

A total of 100 mL of micellar preparation was prepared. The spindle and speed used were adjusted, then the viscometer was run (Zarwinda *et al*., 2022).

Clarity Test

The clarity test was carried out by observing that the resulting preparation was turbid or clear as seen from the color of the preparation visually (Sari *et al*., 2022).

Particle Size, Zeta Potential, and Polydispersity Index Test

This test was carried out to determine the particle size distribution, polydispersity index, and zeta potential using the Particle Size Analyzer (Dzakwan, 2020).

Stability Test

The stability test was carried out using a cycling test for 6 cycles. The preparation was placed in a room that had a temperature of 4^{o}C for 24 hours. The preparation is transferred into the oven with a temperature of 40^{o}C for 24 hours (calculated one cycle) then observed the physical state of the preparation such as organoleptis, clarity, pH, and viscosity (Nafisah *et al*., 2023).

Irritation Test

The irritation test was conducted with a closed patch test by 10 panelists. Panelists criteria were over than 18 years old, have no history of skin allergies, and were in good health. Test samples were taken for 0.2 mL using a syringe and placed on sterile gauze. The sterile gauze was attached to the inner arm and glued together with plaster for 24 hours. Results were observed after 24 hours (Priani *et al*., 2020; Untari & Robiyanto, 2018).

Antioxidant Activity Assay

Preparation of 100 ppm of DPPH Solution

An exact amount (5 mg) of DPPH was weighed then dissolved by ethanol in a 50 mL measuring flask. The solution that has been obtained was stored by covering it using aluminum foil in a dark condition (Okzelia & Nurdaini, 2019).

Determination of DPPH Maximum Wavelength

An exact amount (1 mL) of DPPH solution was added by 3 mL of ethanol then homogenized using a vortex for 1 minute. Incubation was carried out within 30 minutes at a temperature of 27^{o}C in a dark room. Furthermore, the absorbance examination of the DPPH solution was carried out using a UV-Vis spectrophotometer at a wavelength of 400–600 nm until the maximum wavelength was obtained (Okzelia & Nurdaini, 2019).

Preparation of Water-Based Micellar Solution

Preparation of 1000 ppm Master Solution

An exact amount (0.025 mL) of micellar preparation was put into a 25 mL measuring flask, then dissolved using ethanol and homogenized.

Preparation of Series Solutions

The 1000 ppm master solution was put into a 10 mL measuring flask to get a series concentrations of 40 ppm, 80 ppm, 120 ppm, 160 ppm, and 200 ppm.

Preparation of Vitamin C Control Solution

Preparation of 100 ppm Master Solution

An exact amount (2.5 mg) of micellar preparation was put into a 25 mL measuring flask, then dissolved using ethanol and homogenized.

Preparation of Standard Series Solutions

The 1000 ppm master solution was put into a 10 mL measuring flask to get a standard series concentrations of 2 ppm, 4 ppm, 6 ppm, 8 ppm, and 10 ppm.

Antioxidant Activity

All series of water-based micellar and vitamin C solutions put 1 mL each to a test tube, then 1 mL of DPPH solution and 2 mL of ethanol. The solution then allowed to stand at room temperature in a dark condition for 30 minutes. Absorbance was measured in a maximum wavelength of DPPH 100 ppm with a UV-Vis spectrophotometry tool (Sukmaningrum *et al*., 2021). Antioxidants are divided into several categories, if the IC_{50} value of <50 ppm is categorized as having very strong antioxidant activity, the IC_{50} value of 50 - 100 ppm is categorized as having strong antioxidant activity, the IC_{50} value of 100 - 50 ppm is categorized as having moderate antioxidant activity, the IC_{50} value of 151 - 200 ppm is categorized as having weak antioxidant activity, and the IC_{50} value of >200 ppm is categorized as very weak (Molyneux, 2004).

Data Analysis

Physical characteristics such as pH and viscosity analysis tests for comparison between F0 - F3 preparations use one-way parametric analysis ANOVA, and use the T test as a comparison before and after cycling test. The antioxidant test data of IC_{50} results were processed using linear regression with x as the sample concentration and y as the percent antioxidant activity.

RESULTS AND DISCUSSION

Material Preparation

A medium-aged or 4 months old *Piper crocatum* leaves were collected due to high levels of active substances in *Piper crocatum* plants (Agoes, 2019). Plant determination becomes the starting point in research to identify and validate specific plants to be used for formulation. The results of the determination stated that the sample used had the name red betel type *Piper cf. fragile* Benth., is a synonym of *Piper crocatum* Ruiz & Pav and a tribe of the genus Piperaceae (Tjitrosoepomo, 2005).

Preparation of Simplisia

Simplisia is a natural material that has gone through the drying stage used for treatment and has not undergone processing (Kementerian Kesehatan RI, 2017). The purpose of preparation of simplisia is to extend the shelf life of raw materials without reducing the quality of raw materials so as not to reduce their quality. A total of 7 kg of *Piper crocatum* leaves was sorted and washed due to clean them from dirt which still attached to the leaves. *Piper crocatum* leaves were cut to the same size to speed up the drying process. Black cloth is used as a cover to keep simplisia from dust and insects attached to simplisia, as well as being a protector from direct ultraviolet rays to minimize damage to the active substance of simplisia (Kawiji *et al.*, 2010). Dried simplisia was re-sorted to be separated from the disrupting materials (Patria & Soegihardjo, 2013). Simplisia was mashed using a blender to get the results of powder-shaped simplisia. Simplisia powder was sifted with sieve number 60 mesh to equalize particle size and facilitate the withdrawal of chemical compounds contained during the extraction process by enlarging the sample surface area (Azzahra & Budiati, 2022). The simplisia powder obtained was 1000 grams. Simplisia of *Piper crocatum* leaves powder was stored in airtight containers at room temperature.

Extraction of *Piper crocatum* Leaves

Extraction is the process of withdrawing a chemical compound from its mixture with the help of a solvent. The purpose of extraction is to separate potentially efficacious substances for treatment with substances that are not needed so that they are easier to use (easy to absorb, taste, and use) and stored so that the goal of treatment can be achieved (Syamsuni, 2006). Maceration is the cold method chosen

for extraction. Maceration has the principle of like dissolve like, namely the dissolution of compounds when combined with solvents that have the same properties. The reason for choosing the maceration method is that the tools and procedures used are simple. A total amount of 1000 grams of *Piper crocatum* simplisia were macerated using 70% ethanol solvent for 10 liter. The selection of 70% ethanol solvent was based on the polar properties possessed by 70% ethanol so that it could dissolve a secondary metabolite compound that has polar properties (Riwanti *et al.*, 2020), 70% ethanol solvent also has advantages in attracting compounds that only dissolve in nonpolar solvents so that it was considered to be a universal solvent. 70% ethanol is a non-toxic solvent so it is safe to use (Hasanah & Novian, 2020). Maceration process was carried out for 24 hours with occasional stirring so that all components of compounds contained in *Piper crocatum* leaves can be bound to the solvent and evenly distributed. The macerate was filtered with filter paper to separate the filtrate from the residue. The residue from the first maceration was redissolved with 70% ethanol solvent known as the remaceration process. Remaceration carried out for 24 hours was intended to maximize the effectiveness of extraction by re-dissolving secondary metabolite compounds using solvent turnover (Fatwami & Royani, 2023). The results of remaceration were again filtered until they were separated between the residue and the filtrate. The filtrate obtained was solid brown.

All results, both maceration and remaceration, were evaporated with a rotary evaporator to produce a viscous extract that contains certain chemical compounds. The rotary evaporator has a working principle based on the boiling point of the solvent because heating at low temperatures and pressure makes the steam from the solvent retained in the condenser, the condenser part at cold temperatures causes the steam to condense and will change into a liquid by the receiver flask The temperature used in this study was 40^{o}C, because 70% ethanol has a boiling point of 70^{o}C so the temperature used when concentrating the filtrate with a rotary evaporator was below the boiling point of 70% ethanol. Temperatures that are too high cause the compound content in the extract to be lost, so the use of 40^{o}C temperature was chosen to protect the compound content in the sample. The results obtained were a 211.45 grams viscous extract of *Piper crocatum* leaves.

Test Characteristics of Extracts

Organoleptic Test

An organoleptic test was a test that involves the five senses in assessing shape, odor, and color. This test has a subjective nature or has differences in the assessment of each individual (Darmawijaya & Astuti, 2021). The results showed that the *Piper crocatum* leaves extract was in the form of a viscous extract, had a characteristic odor of *Piper crocatum*, and was dark brown color.

Water Content Test

Water content is the amount of water (in percent) that *Piper crocatum* extract has. Water content is one of the important parameters in research, which aims to assess the quality of extracts to be used in accordance or not with standards. The purpose of adjusting the standard is to avoid microbial growth in the extract. The principle of testing water content using the gravimetric method is that the water in the material is evaporated by a heating process, then the material is weighed until a constant weight is obtained (Lestari & Rohmatulaili, 2022).

According to the Farmakope Herbal Edition II, the water content in the viscous extract of *Piper crocatum* leaves is not more than 10%. The water content test results obtained were 6.41% so they met the extract quality standards.

Extract Yield Test

The yield of *Piper crocatum* extract is said to be good if the value is more than 17.0% (Kementerian Kesehatan RI, 2017). A 211.45 grams were obtained with a % yield value of 21.14%. Yield is a result of a comparison between the weight of the extract obtained with the initial simplisia weight. According to Harborne (1987), the high amount of yield obtained, and the active compounds of the sample are also high.

Phytochemical Screening Test

The phytochemical screening test aims to see whether or not the presence of secondary metabolite compounds in *Piper crocatum* leaves extract. The detection of this test is carried out by observing the color change in the extract after being given the test solution (Akasia *et al*., 2021).

Table 2. Phytochemical Screening Results of *Piper crocatum* Leaves Extract

Compound	Reagent	Observations	Information	Positive Results
Alkaloid	Dragendorff	Orange Precipitate	+	Orange, Red Precipitate
	Mayer	Green Precipitate	-	White Precipitate
	Wagner	Brown Precipitate	+	Brown Precipitate
Flavonoid	Mg and HCl Pekat	Orange Solution	+	Yellow, Orange, or Dark Red Solution (Magenta)
Tanin	$FeCl_3$ 1%	Blackish-green Solution	+	Blackish-green Solution
Saponin	Akuades	Stable Foaming	+	Stable Foaming
Steroid	Liebermann-Burchard	Green Solution	+	Green or Blue Solution
Terpenoid	Liebermann-Burchard	Blackish-green Solution	-	Purple or Red Solution

Information:

(+) : Positive result containing test compound

(-) : Negative result contains test compound

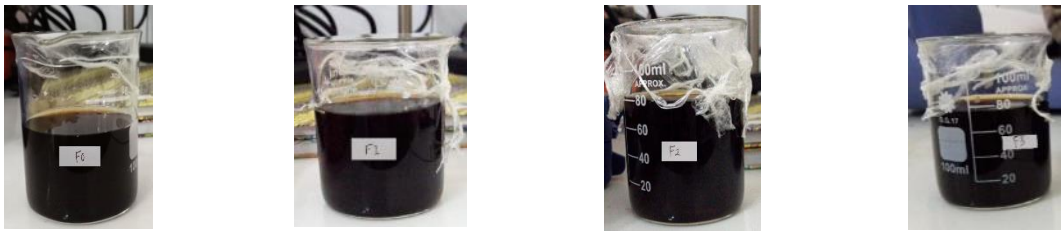
Production of Water-Based Micellar Preparation Formulation of *Piper crocatum* Leaves Extract

The production of water-based micellar preparations refers to Dzakwan's (2020) research with modifications. The difference in formulation in this study was that the extract used with an increase in concentration, the concentration of poloxamer 188 between formulas was increased, the change of pentylene glycol to propylene glycol, an increase in phenoxyethanol concentration to 0.5%, and the volume of the preparation to 100 mL. The concentration of extracts used refers to the research of Febriani *et al.* (2022) which is a concentration of 3%, but after taking into account the water content, a concentration result of 2.81% was obtained. Poloxamer 188 is a cleaning agent of a polyoxyethylene-polypropylene type block copolymer that can dissolve with pure water. According to Asim *et al.* (2023), Poloxamer 188 becomes a substance with a higher solubility increase when compared to other polymers. *Piper crocatum* leaves viscous extract acted as an added value preparation that has antioxidant potential so that it could minimize the risk of premature aging, and damage to cells, and reduce oxidative stress on the skin. Glycerin and propylene glycol function as humectants that can provide freshness to the skin. Sodium gluconate was useful as a chelating agent in charge of binding polyvalent metal ions to form complexes to increase the stability of the preparation. Sodium gluconate can make the pH of the preparation increase to alkaline so the addition of lactic acid is needed to neutralize the pH of the preparation. Lactic acid is non-toxic, and does not irritate the skin. The antimicrobial preservative used in this micellar preparation is phenoxyethanol, and finally, the material used is pure water which is a solvent in micellar preparations (Dzakwan, 2020; Menteri Kesehatan RI, 2012).

Characteristics Test of Water-Based Micellar Preparations

Organoleptic Test

Organoleptic tests were performed by observing the physical micellar preparations including shape, odor, and color for 6 cycles when the stability test took place. The results before and after the 6-cycle stability test could be seen in Table 3. Water-based micellar preparations after storage testing for 6 cycles produce consistent preparations in color, odor, and shape. The micellar water preparation is shown in Figure 1.



(a) (b) (c) (d)

Figure 1. Micellar Water Preparations of F0 (a), F1 (b), F2 (c), and F3 (d)

Table 3. Organoleptic Test Results of Micellar Preparations

Formula	Before Cycling Test			After Cycling Test		
	Shape	Color	Odor	Shape	Color	Odor
F0	Solution	Blackish Brown	Typical *Piper crocatum*	Solution	Blackish Brown	Typical *Piper crocatum*
F1	Solution	Blackish Brown	Typical *Piper crocatum*	Solution	Blackish Brown	Typical *Piper crocatum*
F2	Solution	Blackish Brown	Typical *Piper crocatum*	Solution	Blackish Brown	Typical *Piper crocatum*
F3	Solution	Blackish Brown	Typical *Piper crocatum*	Solution	Blackish Brown	Typical *Piper crocatum*

pH Test

The pH value is needed because the micellar preparation will be in direct contact with the skin, so standards are needed to avoid skin problems after the preparation is applied. Low pH values (acids) can irritate the skin, and high pH (alkaline) makes the skin scaly (Rompis *et al*., 2019). The pH test aims to determine the pH value of the preparation that has been successfully formulated to adjust to the pH of the topical preparation. The pH value is needed because the micellar preparation will be in direct contact with the skin, so standards are needed to avoid skin problems after the preparation is applied. The value of the skin pH range according to SNI 16-4380-1996 is 4.5 - 7.8. The pH value of micellar preparations were is shown in Table 4. The decrease in pH value can be caused by environmental factors such as temperature changes during storage. The contact between air humidity and preparations also affects the decrease in pH so that acid formation due to CO_2 gas in the air reacts with water in the preparation (Lestari *et al*., 2020). Based on the results of the study, the pH value of all micellar preparations still meets the pH requirements of the skin.

Table 4. pH Test Results

Formula	Before *Cycling Test*	After *Cycling Test*	Standard Value
F0	4.94 ± 0.01	4.71 ± 0.14	4.5-7.8
F1	4.71 ± 0.01	4.59 ± 0.08	
F2	4.62 ± 0.04	4.54 ± 0.07	
F3	4.94 ± 0.01	4.76 ± 0.14	

In the statistical test T-test, the results of the p-value > 0.05 showed no significant difference in pH both before and after the cycling test so that the pH stability was stable.

Clarity Test

A clarity test is a test carried out by observing whether or not a preparation is clear, micellar preparations should have a physical solution that is free of particles. The clarity test was observed for 6 cycles. The results show that F0 and F1 look a little cloudy due to the presence of particles that settle. F2 looks very slightly cloudy, and F3 looks like no (clear) precipitate. This is thought to be due to the large size of the particles so that they form aggregates and settle in the micellar solution.

Viscosity Test

A viscosity test is a test that aims to determine the value of how much resistance a liquid has when flowing. According to Dewi & Haminuddin (2017), the standard viscosity value of the solution is 0.24-30.60 cP. The viscosity result indicates the presence of a formula that has an increase and decrease in viscosity. The viscosity test data is shown in Table 5. The rise and fall of viscosity values is influenced by storage, temperature, environmental conditions, and light. Viscosity that is too low causes the contact time between the preparation and the skin does not have a long time so the effectiveness of the preparation is not optimal (Andini *et al*., 2017). The viscosity that is too high causes the solution to become very viscous so it provides a feeling of discomfort when used (Elcistia & Zulkarnain, 2019).

Table 5. Viscosity Test Results

Formula	Viscosity (cP)		
	Before Cycling Test	After Cycling Test	Standard Value
F0	14.80 ± 1.38	16.40 ± 9.25	0.24-30.60
F1	23.20 ± 0.69	20.26 ± 8.42	
F2	22.40 ± 1.38	18.40 ± 5.69	
F3	20.00 ± 0.69	24.26 ± 6.15	

Based on statistical tests using the T-test, a p value of > 0.05 was obtained which indicates that there is no significant difference in viscosity before and after the cycling test, so that it can be concluded that the stability in terms of viscosity is at a stable value.

Test of Particle Size, Zeta Potential, and Polydispersity Index

A particle test is a test that aims to determine the size of particles in a sample. The result of the consecutive particle size test value is shown in Table 6. The particle size values of micellar preparations F2 and F3 were within the standard range of micelle sizes. F3 had the smallest particle size. This is in line with the research of Khoerunisa *et al.* (2020) which states that a more surfactant concentration can reduce particle size. The smaller the particle size will increase solubility so that there is an increase in

bioavailability in the body and makes the preparation easily absorbed by the body. The micelle size range according to Milala (2022) is 10-200 nm.

One of the factors that can assess the stability of colloidal dispersion is zeta potential. Zeta potential can reflect the electric charge on the surface of the particle (Aryani *et al.,* 2021). The higher the potential zeta value, the more stable the preparation. The zeta potential value based on the standard, which is -30 mV and +30 mV, will be electrostatically stable, while the zeta potential value of +20 mV and -20 mV will be sterically stable (Nurdianti *et al*., 2017). The resulting potential zeta value is shown in Table 6. The higher the potential zeta value, the more stable the preparation. The polydispersity index is the size uniformity of the particle diameter. The polydispersity index value of <0.5 indicates a uniform and monodispersed particle size distribution, while if the index value is close to 1, it is categorized as polydispersion (Akbar *et al.*, 2021). A small polydispersity index indicates a relatively narrow or homogeneously distributed nanoparticle size distribution (Kosasih *et al*., 2022).

Table 6. Test Results of Particle, Zeta Potential, and Polydispersity Index

Parameter	Formula				Standard
	F0	F1	F2	F3	
Particle Size (nm)	386.2	349.9	176.3	170.6	10 - 200
Zeta Potential (mV)	7.55	-14.24	-7.7	-16.99	30 mV & +30 mV / -20 mV & +20 mV
Polydispersity Index	0.571	0.571	0.571	0.190	<0,5

Stability Test

The stability test used is an accelerated stability test with the cycling test method. This test is carried out to determine the durability of micellar preparations and determine the stability that occurs during the storage process at extreme temperatures or at cold and hot temperatures. The results of the cycling test for 6 cycles changed the pH value, viscosity, and clarity level. The final pH value of micellar preparations were 4.54 - 4.76 so that it met the pH standards of the preparations. The final viscosity value was in the range of 16.40 - 24.26 cP which still met viscosity standards. The level of clarity of micellar preparations obtained results F0 and F1 had physical changes to be slightly cloudy, F2 was very slightly cloudy, and F3 had a stable physique (clear).

Irritation Test

The irritation test was carried out toward micellar preparations that have been made to determine the presence or absence of potential irritating side effects on the skin. This research irritation test had been declared ethically feasible with permit number EC.081/KEPK/STKBS/V/2023 on May 04, 2023. An ethical review is carried out to ensure that the research carried out is by the principles of research ethics.

The irritation test was conducted by 10 panelists in a healthy body condition and all panelists have agreed to undergo this irritation test procession. All tested formulas gave negative results or no signs of irritating the skin after this test. This proves that micellar preparations are safe to use or apply as cleansers and refreshers on the skin.

Antioxidant Activity Assay

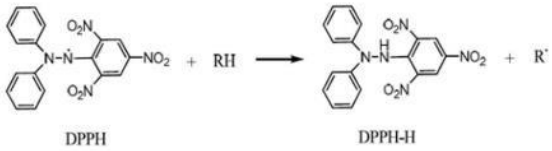


Figure 2. DPPH Reaction with Antioxidants (Tonahi *et al*., 2014)

Antioxidant Test is a free radical test to evaluate the antioxidant activity of a compound or extract sourced from nature. The antioxidant activity of micellar preparations was tested by reacting micellar preparations with DPPH. This work was done in a dark room because DPPH is sensitive to light. The incubation process in the antioxidant test aims to maximize the DPPH reaction with the sample. The positive control used in this study was vitamin C or ascorbic acid. Vitamin C was chosen because it is a pure compound that is proven to have very strong antioxidant activity with a small IC_{50} value. Vitamin C can be oxidized by free radicals because of the double bond it has and there are 2 -OH groups bound (Abdullah & Maryam, 2020). The maximum wavelength measurement result of this study was 515.874 nm with an absorbance of 0.745. The IC_{50} value of vitamin C as a positive control was 9.51 ppm with a very strong antioxidant activity category. The results of IC_{50} values of F3 was 119.63 ppm with moderate antioxidant activity category. Based on the research conducted by Febriani *et al.* (2022), the *Piper crocatum* leaves extract gave an IC_{50} value of 38.30 ppm which categorized as very strong antioxidant activity, but there was a decrease in antioxidant activity to moderate and weak after being formulated into serum preparations. The decrease in antioxidant activity occurs due to temperature changes that affect the physical structure and chemical structure so that it also affects the antioxidant activity contained in the preparation (Rompis *et al.*, 2019). Storage also affects free radicals in inhibiting extracts, causing % of inhibition to decrease. A decrease in antioxidant activity can also be caused by the antioxidant effect of extracts that functioned as antioxidant preparations without additional antioxidants or antioxidant preparations, resulting in a decrease in antioxidant activity. It is expected that the preparation will have additional antioxidants and an increased % concentration of *Piper crocatum* leaves extract so that it can strengthen the antioxidant function in micellar preparations.

Table 7. IC_{50} Antioxidant Results

Sample	IC_{50} value (ppm)
Vitamin C	9.51 ± 0.03
Micellar Based-Water from *Piper crocatum* Leaves Extract (F3)	119.63 ± 0.46

Data Analysis

Data analysis of water-based micellar preparations of *Piper crocatum* leaves extract was carried out using the Statistical Product and Service Solutions (SPSS) program using one-way parametric analysis ANOVA. The parameters tested were pH and viscosity test. The requirement of one-way Analysis of Variance (ANOVA) testing is that the data must be homogeneous and normal. The normality test was performed using the Shapiro-Wilk method because the amount of data tested was <50. Based on the normality test results, a p-value result (>0.05) was obtained so that the test data has been distributed normally. The homogeneity test was carried out by the Levene statistic. Based on the results of homogeneity of variance, a p-value result (>0.05) is obtained so that the test data was homogeneous. Referring to the results of the normality and homogeneity test, the conditions for continuing the one-way ANOVA test have been met. The results of the one-way ANOVA test obtained a p-value (<0.05). This proves that variations in the concentration of surfactant used, namely poloxamer 188, had a significant influence on pH value and viscosity. Then a T test was carried out to compare pH and viscosity before and after the cycling test, the results showed that both tests had a p-value of <0.05 or no significant difference, so that the stability in terms of pH and viscosity was stable.

CONCLUSION

Based on the results of the research conducted, it can be concluded that the most optimal concentration of poloxamer 188 was 2% (F3), then an antioxidant activity test was carried out on F3 which obtained an IC_{50} value of 119.63 ppm with a moderate antioxidant activity category. The results of the evaluation of water-based micellar preparations of *Piper crocatum* leaves extract produced blackish-brown physical preparations, smelled typical of *Piper crocatum*, and had a pH value of 4.54 - 4.76. The viscosity obtained was 16.40 - 24.26 cP and the irritation test results also showed that the entire formula did not irritate so all results of this evaluation met the evaluation parameters.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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