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Formulation and Activity of Sunscreen Cream from Ethanol Extract of *Calendula Officinalis* L Flowers

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ABSTRACT: Sunscreen made of natural ingredients is an alternative to protect the skin from excess UV radiation and a substitute for chemical products that have side effects. It was reported that *Calendula officinalis* L. has flavonoid and saponin metabolite compounds, which function as photoprotective agents. This research aims to formulate sunscreen cream and examine the effect of variations in *Calendula officinalis* L flower extract (5%;7%;10% w/v) on physicochemical properties, stability, and values of the Sun Protecting Factor (SPF) in vitro using UV-Vis spectrophotometry and in vivo using Wistar line rat test animals to see the time of formation of Minimum Erythema Dose (MED). It has been proven that variations in the concentration of *Calendula officinalis* L. extract affected the physicochemical properties, such as pH value, viscosity, spreadability, and adhesion strength. However, the overall results of the physicochemical properties still met the requirements. Variations in extract concentration affected the SPF value. In vitro SPF test showed the minimum protection category for F1, extra protection for F2, maximum protection for F3, and no protection for F0. Meanwhile, the in vivo SPF test showed the minimal protection category for F1, medium protection for F2, extra protection for F3, and no protection for F0.

Keywords: **sunscreen; cream; *Calendula officinalis* L.; SPF.**

Introduction

Indonesia has an almost entirely tropical climate with quite a high intensity of exposure to sunlight. However, excessive exposure or UV radiation can cause acute changes in the skin, such as pigmentation, photosensitivity, erythema, and long-term effects that cause premature aging and skin cancer [1]. Skin protectants like sunscreen can protect the skin from exposure to UV rays. Sunscreens commonly contain active ingredients that can absorb, reflect, or scatter UV rays to prevent skin damage due to UV rays [2]. However, chemical sunscreens on the market have side effects, such as contact dermatitis, irritation, phototoxic reactions, photoallergy, and photosensitivity [3].

The need to protect the skin from UV exposure and find a substitute for chemical sunscreens that have side effects motivates the use of sunscreens derived from natural ingredients. Nowadays, natural compounds are considered potential agents for sunscreen formulations due to their photoprotective activity. Moreover, natural compounds have been widely discovered, abundant, and relatively affordable [4].

It has been reported that Calendula officinalis L. can reduce melanin content in the skin and function as an anti-inflammatory that can reduce erythema on the skin [5]. Many cosmetic formulations are starting to use Calendula Officinalis L. due to the phenolic compounds in its chemical composition. Considering the content of secondary metabolites that have the potential to act as photoprotective agents, this research aims to formulate sunscreen cream and examine the effect of variations in Calendula officinalis L flower extract on physicochemical properties, stability, and SPF values in vitro and in vivo. There have not been many studies examining Calendula Officinalis L. flowers as a sunscreen cream that have been tested in vivo. In vitro SPF value testing is carried out using a spectrophotometer, and in vivo testing uses test animals. The SPF value is calculated by comparing the time the Minimum Erythema Dose (MED) forms on skin protected by sunscreen to the time MED forms on unprotected skin [6].

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Methods

Materials

The material used in this research is the Calendula officinalis L. flower, which comes from Karanganyar district Central Java, ethanol 70% (*Merck, Jerman*), phenoxyethanol (*Fagron Hellas, Greece*), cetyl alcohol (technical) (, stearic acid (Cipta Kimia, Indonesia), paraffin liquid (Cipta Kimia, Indonesia), sorbitol (Cipta Kimia, Indonesia), propylene glycol (Cipta Kimia, Indonesia), glyserin (*Wilmar Nabati, Indonesia*), triethanolamine (*Petreonas Chemicals, Malaysia*), aquadest (Cipta Kimia, Indonesia), buffer solution (Cipta Kimia, Indonesia), wistar strain of white rats, methoxalen 1% (Surya Dermato Medica Laboratories).

Procedures

Maceration of *Calendula officinalis* L. Flowers

The flowers were separated from the bottom of the flower and then dried in an oven (Memmert, Germany) at 45 °C. After that, dry sorting was carried out to separate foreign materials attached to the simplicia. The clean and dry sample was ground in a blender and sieved until it became a fine powder [7]. The flower powder was weighed, and then 70% ethanol was added (the ratio of ingredients to solvent was 1:5 w/v) [8]. The extraction process was carried out for 3 days and the stirring process was done every 24 hours. The maserate was filtered, then soaked again with the same solvent in a ratio of 1:5 and filtered again. A rotary evaporator was used to concentrate the resulting filtrate to obtain a thick extract [7].

Sunscreen Cream Formulation

The composition of the cream formulation is shown in Table 1, with several variations in extract concentration, namely F1 (5% w/v), F2 (7% w/v) and F3 (10% w/v).

Sunscreen Cream-Making Process

Mixing cetyl alcohol, stearic acid, liquid paraffin, & phenoxyethanol (oil phase) and propylene glycol, sorbitol glycerin, TEA, & distilled water (water phase) was carried out at a temperature of 70-75°C. After the cream base was formed, *Calendula officinalis* L. extract was added and then mixed at a temperature of ± 40°C, while stirring until it became a homogeneous cream.

Physical Characteristics of *Calendula officinalis* L. Extract:

Organoleptic

Organoleptic is determined using the five senses in describing form, aroma, and color.

Water Content

Water content is determined using a moisture analyzer. A total of 1 gram of extract sample was put into the moisture analyzer and waited until the tool showed the results of the water content in percent (%). Based on the Decree of the Minister of Health of the Republic of Indonesia, the water content requirement meets the standard of <10% [9].

Table 1. Sunscreen cream formulations

Bahan	F0 (%w/v)	F1 (% w/v)	F2 (% w/v)	F3 (% w/v)
Calendula flower extract	0	5	7	10
Phenoxyethanol	0.2	0.2	0.2	0.2
Cetyl alcohol	4	4	4	4
Stearic acid	8	8	8	8
Paraffin liquid	10	10	10	10
Propylen glykol	1	1	1	1
Sorbitol	7	7	7	7
Glyserin	7	7	7	7
Triethanolamine	2	2	2	2
Aquadest	Ad 100	Ad 100	Ad 100	Ad 100

Information :
F0 : Cream formula without extracts
F1 : Cream formula with 5% extract
F2 : Cream formula with 7% extract
F3 : Cream formula with 10% extract

Rendement

Rendement calculation:

$$\%\ Rendement \quad \frac{extract\ weight\ \ final}{extract\ weight\ \ initial} x\ 100\%$$

Flavonoid Phytochemical Screening

A total of 1 mL of sample was put into a test tube, and then 2 drops of 10% sodium hydroxide (NaOH) were added and shaken vigorously [10].

Saponin Phytochemical Screening

A sample of 0.5 grams was put into a test tube and added with 10 ml of heated distilled water, then cooled and shaken vigorously for 10 seconds until foam appeared in no less than 10 minutes as high as 1-10 cm. Next, 1 drop of 2N hydrochloric acid (HCl) was added; If the foam did not disappear, it indicated the presence of saponin [10].

Sunscreen Cream-Making Process

Mixing cetyl alcohol, stearic acid, liquid paraffin, & phenoxyethanol (oil phase) and propylene glycol, sorbitol, glycerin, TEA, and distilled water (water phase) was carried out at a temperature of 70-75°C. After the cream base was formed, *Calendula officinalis* L. extract was added and then mixed at a temperature of ± 40°C, while stirring until it became a homogeneous cream.

Physicochemical Evaluation of Sunscreen Cream: Organoleptic Test

Organoleptic tests include smell, color, and texture [11].

Homogeneity Test

The cream was smeared on a glass object and then observed under a microscope. The cream is said to be homogeneous if it has an even aroma and color, does not show fine grains, and looks homogeneous when viewed using a microscope (Nikon E100, Indonesia) [12].

pH Test

A total of 1 gram of cream extract was diluted with 10 ml of distilled water, then measured using a pH meter (LUTRON PH-208, Taiwan); The pH of a good preparation corresponds to the pH of the skin, namely 4.5 – 6.5 [11].

Spreadability Test

A total of 1 gram of the cream preparation was placed carefully on the glass. It was then covered with another glass with a weight on top, and the diameter was measured after 1 minute [13].

Adhesion Test

A total of 0.5 grams of cream was smeared on a glass plate and given a load of 250 grams for 5 minutes. The load was lifted, and the two attached glass plates were taken, with the time recorded until the two plates were separated from each other. The standard for cream adhesion is >4 seconds [11].

Viscosity Test

The viscosity of the preparation was determined using a viscometer (RION VT-04, Japan). The preparation was put in a container, then the spindle was inserted into the immersion limit and the rotor was run until it showed a constant number [14].

Test Cream Type

The emulsion was put into a cup or beaker and then diluted by adding water. If the emulsion can be diluted, the emulsion is said to be oil in water [15].

Cycling Test

The cycling test was carried out by storing the preparation at 2 different temperatures in 6 cycles. The cream preparation was put into a conical, stored in a refrigerator at 4°C ± 2°C for 24 hours, and then transferred to an oven at 45°C ± 2°C for 24 hours. The storage time at these two temperatures in 2 days is considered 1 cycle. Observations were carried out in 6 cycles [16].

Sun Protection Factor Values Are Determined In Vitro

SPF value is determined in vitro using a spectrophotometer (Genesys UV-VIS, China). As much as 0.0125 grams of each preparation sample was taken and then diluted with 70% ethanol to 50 ml. The 70% ethanol solution was used as a blank. The absorbance results of the sample at a wavelength of 290 - 320 and an interval of 5 nm were recorded, and then the SPF value was calculated. The SPF value was calculated using the Mansur method:

$$SPF = CF\ x \sum_{290}^{320} EE\ (\lambda)\ x\ I\ (\lambda)\ x\ Abs\ (\lambda)$$

Description:

CF : Correction Factor (10)
EE : Spectrum of effects of erythema
I : Solar intensity spectrum
Abs : Sample absorbance

Sun Protection Factor Values Are Determined In Vivo

The test animals used were male white Wistar rats aged 2-3 months with a body weight of 200 g. Approval was received from the Research and Health Ethics Commission from Dr. Moewardi General Hospital Surakarta No. 1.691/XII/HREC/2022. Five test animals were given negative control (not smeared with sunscreen), positive control (smeared with sunscreen available on the market), and treatment (smeared with sunscreen made of *Calendula officinalis* L. extract with concentrations of 5%, 7%, 10%). Before the test, the five groups of test animals were acclimatized for 7 days, during which each group was separated by the cage, and their body weight was measured. The backs of the test animals were shaved and marked with an area of 5x5 cm^2 and then sensitized with methoxalen at a dose of 10 mg/kg of BW. In the next stage, the unprotected Minimum Erythema Dose (MED) was determined by shining UV B light on the animal's back with the negative control test and protected MED by shining UV B light on the back of the animal with the positive control and treatment. The SPF value is calculated from a comparison of the MED value on skin protected by sunscreen and the MED value on skin not protected by sunscreen [17].

Result and Discussion

Organoleptic Test of The Extract

The resulting extract was observed using aroma, color, and texture parameters. Based on observations, the extract has a brown color, thick texture, and a distinctive smell of Calendula officinalis L.

Water Content Test of The Extract

Water content calculations were carried out to determine the amount of water content in the extract. Based on the test results, the water content value was 8.54%, and thus, it can be concluded that this value meets the specified requirements, which is less than 10%. Extracts with high water content can become a growth medium for microorganisms, thereby damaging the quality and compound content of the extract. Since the water content value is below 10%, it can prevent hydrolysis reactions, insect disturbances, and microbial growth in the extract [9].

Yield Test

Based on the maceration results, the extract yield was 9.82%. Yield is a comparison of the weight of the produced extract and the amount of extracted simplicia. The yield test is carried out to determine the number of active compounds extracted. The greater the yield produced, the more active compounds there are in the extract [18].

Phytochemical Screening of *Calendula officinalis* L.

Phytochemical screening was carried out using the principle of a color-testing reaction with a reagent. Screening aims to detect metabolite compounds in natural materials [19]. Secondary metabolite compounds in Calendula officinalis L. flowers with the potential to be sunscreen agents are flavonoids and saponins.

Based on the results of phytochemical screening, as shown in Table 2, it has been proven that this extract qualitatively contained flavonoids, which were observed in significant color changes in the extract sample. It supports the previous research which stated that if plant extracts changed color from red to brown, the sample is declared positive for flavonoids. This reaction is caused by the formation of acetophenone compounds when the sample is reacted with NaOH [20].

In the saponin test, positive results were obtained, as indicated by the formation of foam , since saponin compounds have physical properties that dissolve easily in distilled water and will create foam when shaken [10]. Foam can form because saponin can reduce the surface tension of water. Like soap, saponins have large molecules containing hydrophilic and lipophilic groups. In water, saponin molecules align vertically on the surface with the hydrophilic groups facing away from the water. The formation of foam begins with the adsorption of saponin molecules on the water surface, which can result in a decrease in the surface tension of the water, thus forming foam.

Table 2. Results of flavonoid and saponin phytochemical screening tests

Parameter	Reaction	Indicator	Result
Flavonoid	Extract + NaOH 10%	Brown	+
Saponin	Extract + H2O	Foam	+

Table 3. Organoleptic test results of cream

Parameter	Sebelum cycling test				Setelah cycling test			
	F0	F1	F2	F3	F0	F1	F2	F3
Consistency	Thick	Thick	Thick	Thick	Thick	Thick	Thick	Thick
Color	White	Light yellow	Yellow	Dark yellow	White	Light yellow	Yellow	Dark yellow
Smell	No smell	distinctive aroma of *Calendula officinalis* L.	distinctive aroma of *Calendula officinalis* L.	distinctive aroma of *Calendula officinalis* L.	No smell	distinctive aroma of *Calendula officinalis* L.	distinctive aroma of *Calendula officinalis* L.	distinctive aroma of *Calendula officinalis* L.

Organoleptic Test of The Cream

Organoleptic evaluation of cream preparations was carried out using the senses by observing several cream parameters, including color, texture, and aroma. This evaluation is important as a first indication of formulation stability. Moreover, cosmetic formulations must be aesthetically appealing [4]. The results of the organoleptic evaluation of this research formulation are presented in Table 3.

The test results show that F0 (cream base) has a white color since the color of the cream base is white, while FI, F2, and F3 have a yellow color because the base color of the Calendula officinalis L. extract is brown. All formulas indicate a thick consistency. F1, F2, and F3 have the characteristic odor of Calendula officinalis L. extract because, in this research formulation, no additional ingredients were added to improve the odor (Corrigens odoris).

Homogeneity Test of The Cream

Homogeneity evaluation was carried out due to its influence on the effectiveness of therapy. This is caused by the level of the active substance being evenly dispersed and all the ingredients mixed when used are always the same, so that can be a parameter for the dosage used during therapy [21]. All formulations showed homogeneous results visually, as indicated by the absence of granules and color differences in the cream mass when tested using a microscope. Thus, it can be concluded that the materials are well-mixed or homogeneous.

pH Test

The pH evaluation in skin care formulations is an important parameter since too acidic or alkaline pH can cause skin irritation [4]. The pH evaluation of the cream aims to determine whether the topical preparation made has the same pH as normal skin pH. The pH testing is very necessary in topical preparations since the skin is sensitive to the degree of acidity. Too acidic preparations (6.5) can

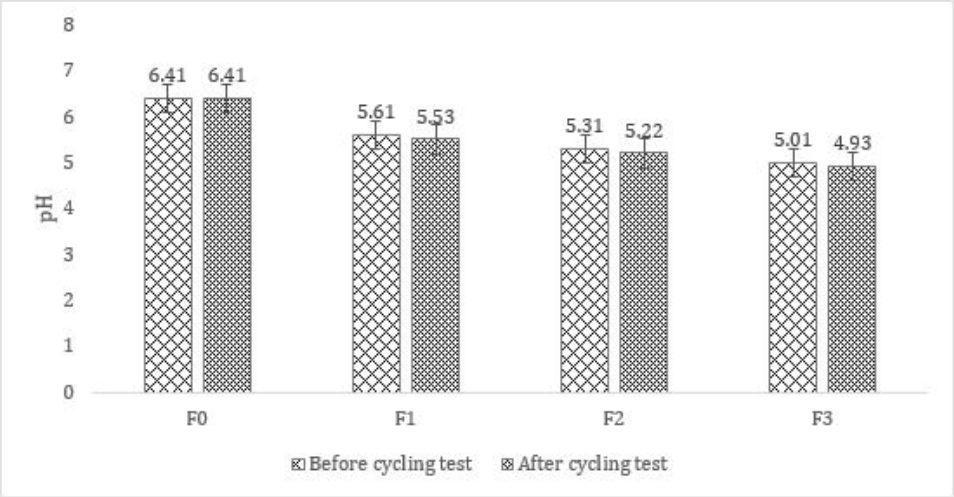

Figure 1. Cream pH test results

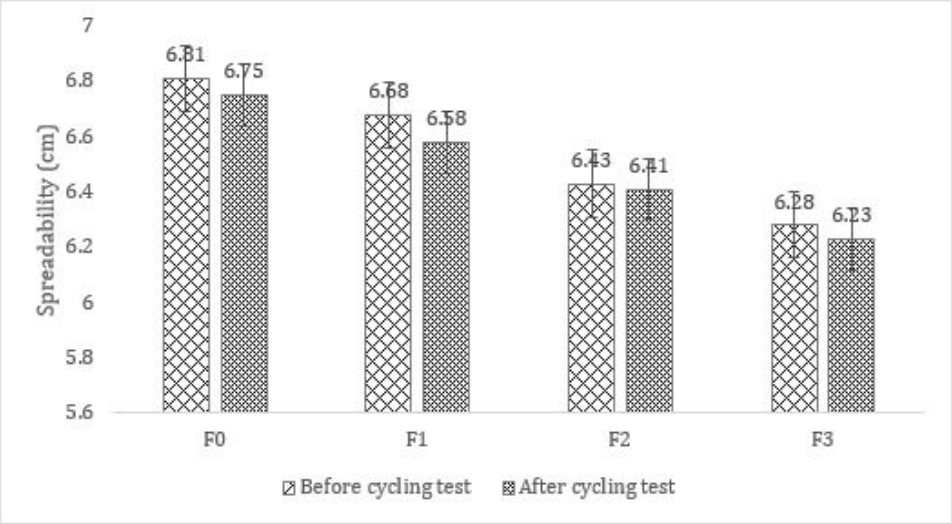

Figure 2. Cream spreadability test results

cause scaly skin [21]. The results of the pH evaluation are presented in Figure 1.

Based on the results of the cream pH evaluation, it can be concluded that the entire formula (before and after the cycling test) meets the range of requirements for topical preparations, namely 4.5 - 6.5 [21]. Based on the graphic results, it can be concluded that the higher the concentration of the extract, the more acidic the pH of the cream preparation will be. This is influenced by the pH value of the Calendula officinalis L. extract obtained, which is 4.7.

Spreadability Test of The Cream

The cream preparation is expected to spread easily on the skin without pressure. The evaluation of cream spreadability aims to ensure that the cream preparation shows the desired application properties, spreads sufficiently, and is evenly smeared on the skin [4]. The greater the diameter value of the spreadability, the greater the surface area covered. A good cream has a wide spreadability, so that contact between the active substance and the skin is more optimal. The greater the spreadability value of the cream, the softer the consistency of the cream

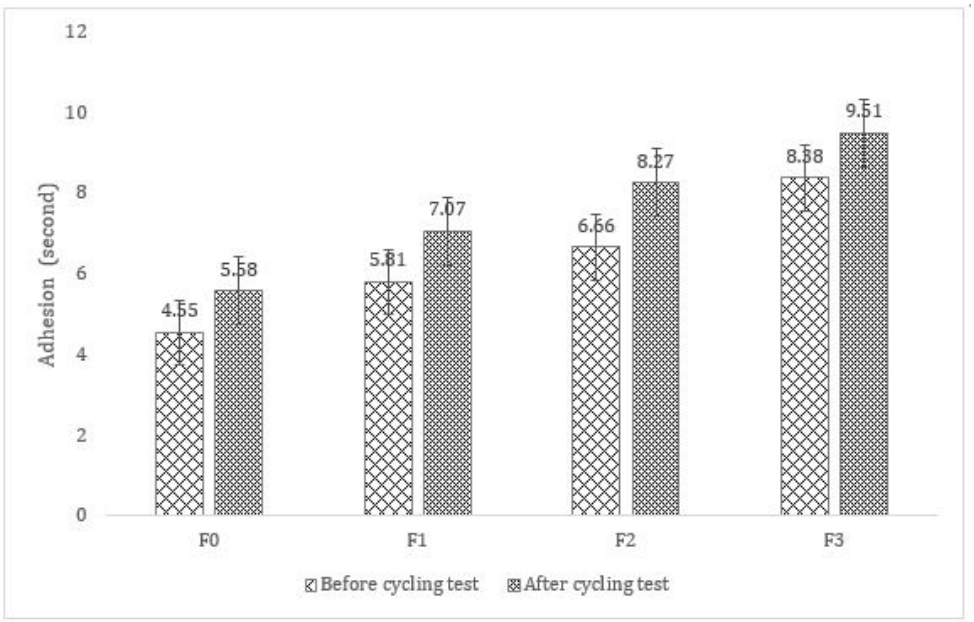

Figure 3. Cream adhesion test results

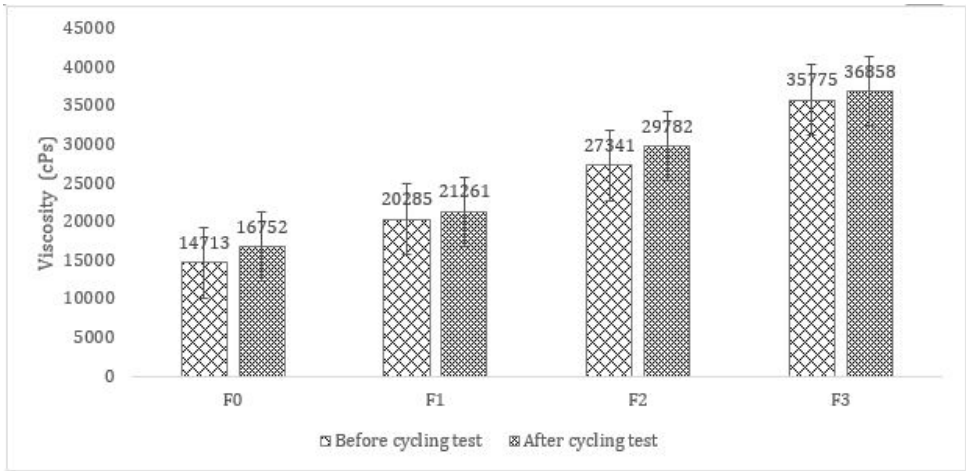

Figure 4. Cream viscosity test results

[21]. The results of the pH evaluation are presented in Figure 2.

Based on the spreadability results, it can be concluded that the overall diameter meets the requirements for good cream spreadability, which is 5 - 7 cm [21]. The higher the extract concentration in the cream, the lower the spreadability value obtained. Spreadability is related to the viscosity value of the cream inversely proportional to the spread area. large viscosity value requires a large pressure to flow, so the viscosity value affects the spreadability of the preparation. The greater the spreadability value, the smaller the viscosity value [21]. Based on the cream stability test, there is a difference in the spreadability value of the cream before and after the cycling test, where the spreadability decreases after the cycling test. The viscosity of the cream after the cycling test increased.

Adhesion Test

The adhesion test aims to examine the length of time the cream can stick to the skin. The optimum adhesion of the cream means that the cream does not come off easily and adheres better to the skin. The active substances in the cream can be absorbed, producing the desired effect [22]. The results of the adhesion evaluation are presented in Figure 3.

Based on the evaluation of the adhesion of the cream, the entire formula (before and after the cycling test) met the range of spreadability requirements, which is not less than 4 seconds [23]. The higher the concentration of the extract added, the longer the adhesion of the cream preparation will be. This can be interpreted as the ability of the cream that the more it is added with the extract, the longer its ability to stick to the skin and the more optimal the activity of the active substances. Adhesive ability is

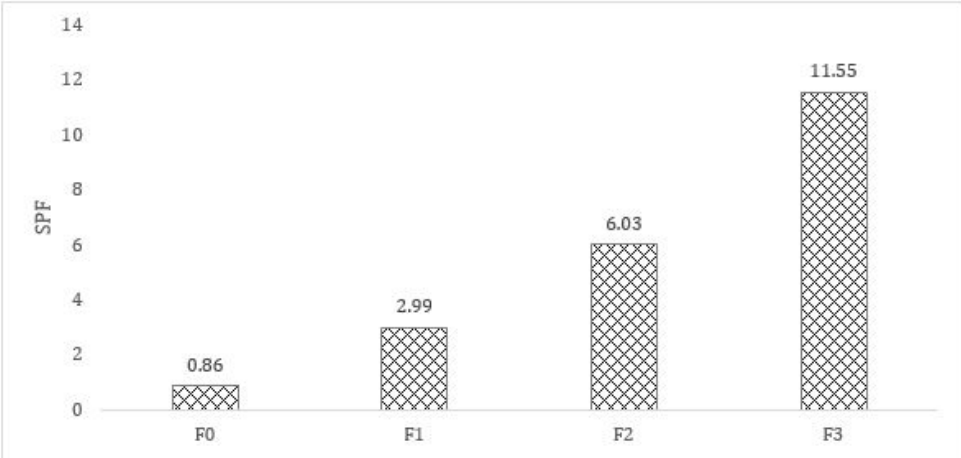

Figure 5. SPF value in vitro

Figure 6. Results of in vivo SPF values

related to viscosity, where the higher the adhesion, the higher the viscosity value [23]. Based on the cream stability test, there is a difference in the adhesion value of the cream before and after the cycling test, where the adhesion decreases after the cycling test. The viscosity of the cream after the cycling test increased.

Viscosity Test of The Cream

The viscosity test of the cream aims to determine the viscosity (thickness) of the cream preparation produced. The viscosity of the preparation is inversely proportional to its diffusion, where low viscosity will increase the diffusion speed in the release of the active substance [24]. The results of the cream viscosity test are shown in Figure 4.

Based on the evaluation of the viscosity of the cream, the entire formula (before and after the cycling test) met the range of viscosity requirements, which is not less than 4000-40000 cps [25]. The higher the concentration of the extract added, the higher the viscosity of the cream preparation will be. This is influenced by the higher the extract added, where the lower the water added to the formulation, the thicker or higher the viscosity of the preparation will be [23]. Based on the cream stability test, there was a difference in the viscosity value of the cream before and after the cycling test, where the viscosity decreased after the cycling test. This is likely due to a decrease in the diameter of the spreadability of the cream, making it difficult for the particles to move and causing the preparation to become thicker, thereby increasing the viscosity of the preparation. Viscosity can increase if the water content in the preparation is lost or evaporated.

Cream Type Test

Emulsion type evaluation aims to examine the type of cream emulsion, including water in oil (W/O) or oil in water (O/W). The method used is dilution by dissolving the cream in water or oil. If the cream can dissolve in the water, then it is an oil-in-water emulsion. Based on the evaluation results, the cream formulation is an oil-in-water emulsion type. This is because the volume of the dispersed phase (oil phase) used in the cream is smaller than the dispersing phase (water phase), so the oil globules will be dispersed into the water phase and form an O/W

Table 4. Results of time to appearance of erythema

Treatment	Time of appearance of erythema (hours)							
	24	48	72	96	120	144	168	192
F0	+	+	+	+	+	+	+	+
F1	-	+	+	+	+	+	+	+
F2	-	-	-	+	+	+	+	+
F3	-	-	-	-	-	-	+	+
Positive controll	-	-	-	-	-	-	-	+

Table 5. Results of in vivo SPF values for cream

Controll	MED Protected	MED Not Protected	SPF
Treatment F1	48	24	2
Treatment F2	96	24	4
Treatment F3	168	24	7
Positive	192	24	8

type emulsion [26]. Making a stable emulsion requires an additional emulsifier. The emulsifiers used in this research were stearic acid, TEA, and cetyl alcohol.

In vitro SPF Test

Sunscreen is formulated to prevent sunburn and skin damage caused by UV radiation. Determining the SPF value aims to examine the effectiveness of sunscreen preparation in light protection factors [21]. The results of calculating the SPF value of the cream in this study are shown in Figure 5.

Sunscreen protection categories, according to the US FDA consist of SPF 2-4, the minimum sunscreen protection category; SPF 4-6, the medium protection category; SPF 6-8, the extra protection category; SPF 8-15, the maximum protection category; and SPF >15, the ultra-protection category.

Based on the sunscreen protection category according to the US FDA, the sunscreen formulation in this study can be categorized as minimal protection for F1, extra protection for F2, maximum protection for F3, and no protection for F0 since it does not meet the minimum SPF value, which is 2. Based on the results for the SPF value in Figure 6, it can be concluded that the higher the concentration value of Calendula officinalis L. extract in the sunscreen cream preparation, the higher the SPF value produced.

In vivo SPF Test

Determining the SPF value in vivo was carried out by measuring the protective activity of sunscreen cream on mice exposed to UV B lamps. The SPF value is calculated by comparing the time the Minimum Erythema Dose (MED) forms on skin protected by sunscreen and the time MED forms on unprotected skin. The results of the time when erythema appears are shown in Table 4, and the calculation of the in vivo SPF value is seen in Table 4.

Based on Tables 4 and 5, the MED value on unprotected skin is shown in the negative control when erythema occurs after 24 hours of exposure to UV B light. The negative control is a treatment that uses only the base, so it does not contain sunscreen [6]. MED values on protected skin are shown in positive control and treatment (F1, F2, and F3). Based on Figure 7, it can be concluded that the higher the concentration of Calendula officinalis L. extract in sunscreen cream, the higher the SPF value. According to the US FDA, the sunscreen formulation in this study can be categorized as minimal protection for F1, extra protection for F2, and maximum protection for F3.

Conclusion

Varying the concentration of Calendula Flower Extract affects the testing of the stability of the physical and chemical properties of the cream, where adding the concentration of Calendula Flower Extract increases the viscosity and stickinessbut reduces the pH and spreadability of the cream. In vitro SPF testing shows the minimum protection category for F1, extra protection for F2, maximum protection for F3, and no protection for F0. Meanwhile, the in vivo SPF test results show the minimal protection category at F1, medium protection at F2, extra protection for F3, and no protection for F0.

Conflict of Interest

The authors declared no conflict of interest in the manuscript.

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