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Formulation and Evaluation of N-Hexane Fraction of Libo Fruit based Emulgel for Sunscreen

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Abstract

Libo fruit (*Ficus variegata* Blume) has activity as a sunscreen. Topical form of certain pharmaceuticals can be used to protect the skin from sun exposure. This study aims to determine the best gel-emulsion formula from the libo's N-Hexane fraction, its stability, and its sunscreen activity. The formula was consist gelling agents variations type and concentration, i.e. carbopol 940 and hydroxypropyl methylcellulose (HPMC). The best formula were chosen based on physicochemical characteristics. the freeze-thaw test deployed to check the stability, and the sunscreen activity was tested using UV-Vis spectrophotometry. The results showed that the best formula was formula 1 with carbopol 940 (1%), there were no changes in physicochemical characteristics during the stability test, and experienced a decrease in sunscreen activity after the stability test.

Keywords: emulgel, libo (*Ficus variegata* Blume), sunscreen

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1 Introduction

Libo is widely found in the forests of Kalimantan. It is known by regional names such as kedadai, ara, ayak, kara, kendang, nyawai, tantilan and tentabau. Libo is from the genus Ficus with the Latin name *Ficus variegata* Blume [1].

Several studies shown that Libo has pharmacological activity and has the potential as a medicinal plant. The fruit of the libo plant exhibited antioxidant, antibacterial, and larvicide against *Aedes aegypty* mosquito larvae and cytotoxic or anticancer [2]. Other studies indicated that the ethanol extract of *Ficus variegata* tree bark has high antioxidant activity against DPPH compared to several other medicinal plants [3]. The methanol fraction of libo leaves has very strong antioxidant activity with an IC50 value of less than 50 µg/mL[1]. In addition, research conducted by Rijai [2], displayed that libo fruit extract and fractions have good antioxidant activity. The n-hexane fraction of libo fruit has sunscreen activity with an SPF value of 20.69 and is included in the ultra-protection type category. Based on research conducted by Hardina et al., secondary metabolites found in the active libo fraction are alkaloids, flavonoids and steroids or terpenoids [4].

the prominent activity of libo makes this plant can be prepared into pharmaceuticals. on the other hand, topical drug delivery systems are used to protect the skin from exposure to ultraviolet (UV) rays. Commonly used topical drug delivery systems are lotions, creams, ointments, and gels. Gel are generally able to release drugs faster than ointments and creams. emulsion-gel (emulgel) is a development of the pharmaceutical form of gel. Currently, emulgel are starting to develop using natural resources as their active ingredients. Emulgel has some advantages such as not oily, easy to spread, easy to wash, and has a more attractive appearance [5].

In this study, the formulation and stability test of emulgel will be carried out using the N-Hexane fraction of libo fruit (*Ficus variegata* Blume) as its active ingredient which functions as a sunscreen. For this purpose, the best formula is determined by comparing the physicochemical characteristics of the various types and concentrations of gelling agents, which are then tested for sunscreen activity in vitro using a UV-Vis spectrophotometer by comparing the sunscreen activity before and after the stability test.

2 Methods

2.1 Preparation of N-Hexane Fraction of Libo Fruit

Libo fruit (*Ficus variegata* Blume) is dried into simplicia and then extracted by maceration method using methanol solvent. The methanol extract is then fractionated using n-hexane solvent.

2.2 Fabrication of Emulgel

The emulsion phase and gel phase are made to produce emulgel. The emulsion is made by mixing span 80 and olive oil and as the oil phase of the emulsion and tween 80 is mixed in distilled water as the water phase of the emulsion. Then methyl paraben and propyl paraben are dissolved in propylene glycol and then mixed into the water phase of the emulsion. The oil phase and water phase are heated at a temperature of 70-80°C then mixed and the n-hexane fraction of libo fruit is added to the emulsion and stirred using a magnetic stirrer until homogeneous [6]

The gel phase was made using various types and concentrations of gelling agents. The gel phase was made by dissolving carbopol or HPMC into distilled water and stirring using a magnetic stirrer until a gel phase was formed. After that, the emulsion and gel were mixed in a ratio of 1:1 while stirring slowly [6]. The formula for the n-hexane fraction emulgel of

libo fruit (*Ficus variegata* Blume) can be seen in Table 1.

Table 1. Emulgel Formulation

Ingredients	Concentration % (b/v)				
	Formula 1	Formula 2	Formula 3	Formula 4	Formula 5
N-Hexane Fraction of Libo Fruit	1	1	1	1	1
Carbopol 940	1	2	-	-	-
HPMC	-	-	3	4	5
Olive oil	4	4	4	4	4
Tween 80	0.5	0.5	0.5	0.5	0.5
Span 80	1	1	1	1	1
Methyl Paraben	0.03	0.03	0.03	0.03	0.03
Prophyl paraben	0.03	0.03	0.03	0.03	0.03
Propylene glycol	5	5	5	5	5
Distilled water	Ad 100	Ad 100	Ad 100	Ad 100	Ad 100

2.3 Physicochemical Characteristics

2.3.1 Organoleptics

The form, color and odor of the emulgel formula were observed. Observations are carried out immediately after the formula is completed.

2.3.2 pH

pH measurement is carried out using a pH meter. The preparation is placed in a container, then the calibrated pH meter is dipped into the emulgel and the pH is checked on the pH meter.

2.3.3 Viscosity

The viscosity of the emulgel was measured using a Rheosys viscometer. The emulgel was weighed 1 g, then left at room temperature for 10 minutes. The emulgel was put into a measuring container and then measured using spindle no. 2.

2.3.4 Spreadability

Emulgel is placed on a flat glass, another glass is placed on top of it. Then a load of 25 g is added and left for 1 minute. Next, the diameter of the emulgel spread is measured. Then, 50 g of additional load is added and left for 1 minute and then the diameter is measured. Then a load of up to 150 g is added, waited for 1 minute and then the constant diameter is measured.

2.3.5 Homogeneity

Homogeneity testing is carried out by spreading the emulgel sample on a glass object and then covering it with a cover glass, then observing the homogeneity of the emulgel.

2.3.6 Centrifugation

Emulgel was put into a centrifuge tube and then centrifuged at 3800 rpm for 5 hours. Every hour interval, the presence or absence of phase separation was observed.

2.3.7 Freeze-Thaw Stability

Emulgel stability test was conducted using the freezethaw method and storage at room temperature. The freeze-thaw test was conducted by placing the preparation in a refrigerator (±4°C) for 48 hours, then removed and placed in an oven (±40°C) for 48 hours, this process is counted as 1 cycle. In each cycle, organoleptic observations, pH measurements, viscosity measurements, spreadability tests, and homogeneity tests will be carried out. Centrifugation tests are carried out at the beginning and end of the cycle.

2.4 Sunscreen Activity

The preparation of the test solution was carried out by dissolving 1 g of emulgel in 100 mL of methanol. Then the absorbance of the test solution was measured at a wavelength of 290 nm-320 nm with an interval of 5 nm.

3 Results and Discussion

The emulgel formulation was acquired by varying the type and concentration of gelling agent used, i.e. carbopol (1% and 2%) and HPMC (4%, 5%, and 6%). each formula was tested To determine the best formula by physicochemical evaluations. The results of the physicochemical characteristics test of the emulgel formula are presented in table 2.

The results of the organoleptic test of emulgel with active ingredients of the N-Hexane fraction of Libo fruit showed that each formula had a slightly green color, was homogeneous, and had a distinctive odor of the n-hexane fraction of Libo fruit. The viscosity of the emulgel was influenced by the concentration of the gelling agent. The higher the concentration of the gelling agent used, the higher the viscosity [7]. This was supported by the results where the

formula with a large concentration of gelling agent had a high viscosity. According to SNI 16-4399-1996, the semisolid form of pharmaceuticals has a viscosity of 2000-50000 cps or 2-50 Pa.s. Based on the test results, each emulgel formula had a viscosity value within the standard range.

Table 2. The Physicochemical Characteristics of Emulgel

Parameters		Formula 1	Formula 2	Formula 3	Formula 4	Formula 5
Organoleptic	Color	slightly green	slightly green	slightly green	slightly green	slightly green
	Odor	distinctive smell	distinctive smell	distinctive smell	distinctive smell	distinctive smell
	Form	thick	very thick	thick	very thick	very thick
	Homogenity	homogeneous	homogeneous	homogeneous	homogeneous	homogeneous
Viscosity (pa.s)		5.43±0.37	12.17±1.27	8.00±0.86	10.87±0.83	14.82±0.98
pH		4.70±0.07	4.34±0.03	6.64±0.16	6.67±0.17	6.42±0.15
Spreadbility (cm)		5.50±0.10	4.57±0.15	5.54±0.36	4.86±0.13	4.66±0.10
Centrifugation		no separation	no separation	no separation	no separation	no separation

Table 3. Freeze-thaw test results of emulgel

Parameter		Cycles						
		cycle 0	cycle 1	cycle 2	cycle 3	cycle 4	cycle 5	cycle 6
Organoleptic	Color	slightly green	slightly green	slightly green	slightly green	slightly green	slightly green	slightly green
	Odor	distinctive smell	distinctive smell	distinctive smell	distinctive smell	distinctive smell	distinctive smell	distinctive smell
	Form	thick	thick	thick	thick	thick	thick	thick
	Homogenity	homogeneous	homogeneous	homogeneous	homogeneous	homogeneous	homogeneous	homogeneous
Viscosity (pa.s)		5.71±0.13	5.65±0.13	5.58±0.10	5.56±0.03	5.51±0.13	5.57±0.11	5.56±0.03
pH		4.78±0.02	4.76±0.04	4.77±0.04	4.80±0.06	4.79±0.06	4.77±0.05	4.76±0.03
Spreadbility (cm)		5.54±0.14	5.59±0.17	5.64±0.28	5.70±0.25	5.71±0.17	5.68±0.13	5.77±0.14
Centrifugation		no separation	-	-	-	-	-	no separation

The pH value requirement for topical drug delivery systems must be by the skin pH value range of 4.5-6.5 [8]. If the pH is very acidic, it can cause skin irritation, while the pH of the preparation is very alkaline, it can cause the skin to become dry and scaly [9]. The results showed that formula 1 and formula 2 were within the standard pH range of the skin.

Emulgel spread ability aims to determine the ability of emulgel to spread when applied to the skin. The greater the spread ability, the easier it is to apply emulgel without the need for excessive pressure. In addition, the spread ability of the active ingredient will be more even so that the effect caused by the active ingredient becomes more optimal. The spread ability requirement for emulgel is 5-7 cm. The wider the spread ability, the wider the surface of the skin that can be applied with emulgel so that the diffusion rate of the active ingredient will also be greater. Spread ability can be affected by viscosity, where viscosity is the resistance of the pharmaceutical form to flow so that if the pharmaceutical form has a high viscosity, the resistance to flow will be greater, causing the spread ability of the preparation to be smaller. [10]. The results of the spread ability test showed that formula 1 and formula 3 had spread ability values that met the requirements.

Centrifugation test is a mechanically accelerated stability test that aims to see the stability of emulgel. The parameters seen from this test are the presence or absence of phase separation. The presence of phase separation indicates instability in the emulgel. The effect of centrifugal force carried out for 5 hours at a speed of 3800 rpm is equivalent to the gravitational force received by the preparation during a storage period of 1 year [11]. Based on the results of observations, each formula did not show any phase separation. This can indicate that each formula is physically stable for 1 year. Based on the results of all tests that have been carried out, namely organoleptic tests, homogeneity tests, pH, viscosity, spreadability, and centrifugation tests, formula 1 is the best formula for emulgel.

Freeze-thaw testing was conducted for 6 cycles. The results of the freeze thaw test observations can be seen in Table 3.

The results showed that Formula 1 emulgel did not experience any changes in its physicochemical characteristics or centrifugation testing during the freeze-thaw test, which indicated that Formula 1 was physically and chemically stable.

The results of the sunscreen activity test of the emulgel containing the active ingredient N-Hexane fraction of libo fruit are shown in Table 4.

Table 4. Emulgel SPF Value

Treatment	SPF Value	Type of protection
Base	1.68	ineffective
Before freeze-thaw	16.94	ultra protection
After freeze-thaw	11.80	maximum protection

SPF (Sun Protecting Factor) is a value that states the ability of a sunscreen to protect the skin from exposure to UV radiation. The higher the SPF value, the higher the level of protection of a sunscreen against UV exposure [10]. The results showed that the SPF value for emulgel before freeze-thaw was 16.94, and after freeze-thaw it was 11.80. The protection category for emulgel before freeze-thaw was ultra protection because the SPF value was > 15, while for the sunscreen activity of emulgel after the freeze-thaw test, it was included in the maximum protection with an SPF value range between 8-15. This decrease in activity can occur because, during the freeze-thaw test, temperatures of ±4℃ and ±40℃ were used, which can affect the activity of the n-hexane fraction of libo fruit. The use of temperature in freeze-thaw is thought to damage the chemical compounds in libo fruit that function as sunscreen, causing a decrease in activity.

4 Conclusions

The best emulgel formula with a concentration of carbopol 940 of 1% has good organoleptic, homogeneity, pH, spreadability, and viscosity. The best emulgel formula is stable during the freeze-thaw test. The sunscreen activity of the emulgel preparation with the active ingredient of the n-hexane fraction of libo fruit after the freeze-thaw test decreased.

5 Declarations

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5.2 Author contribution

Concept – Yuni Dwi Anjarwati; Design – Yuni Dwi Anjarwati, Lisna Meylina, Rolan Rusli; Collection and Processing – Yuni Dwi Anjarwati; Analysis– Yuni Dwi Anjarwati, Lisna Meylina, Rolan Rusli; Writing – Lisna Meylina; Critical Reviews – Rolan Rusli

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5.4 Conflict of Interest

The authors declare no conflict of interest.

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