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Formulation of Antioxidant Emulgel containing Beluntas China (*Gynura pseudochina* (L.) DC)

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ABSTRACT

Skin exposed by the environmental stresses constantly, such as pollutants, solar radiation, heat, and cold, causing the free radicals that which triggered premature aging. This bad effects of free radicals can be reduced by natural antioxidants such as Beluntas china (*Gynura pseudochina* (L.) DC) extract. The antioxidants use of beluntas china extract for skin will be more optimal if it is applied by appropriate form, emulgel, which has stronger consistency and longer contact time than gel due its lipophilic content. The aim of this research was to formulate an antioxidant emulgel from beluntas china extract, which is effective, stable, and safe with the best gelling agent. The extract was formulated by variety types of gelling agents which were carrageenan, hydroxypropyl methylcellulose (HPMC), and carbomer 934. Then, the physical stability was evaluated, including organoleptic, homogeneity, pH, viscosity, and freeze thaw. The results showed that formulation of carbomer 934 1% 2xIC_{50} extract concentration give the best physical stability evaluationat at room temperature for 60 days storage time.

Keywords: antioxidant, beluntas china extract, emulgel, free radicals, skin

1. Introduction

Skin is one of the body's largest organs and protects the body from various types of stimuli, external damage and loss of moisture. However, the skin is constantly exposed by daily environmental stresses such as pollutants, solar radiation, heat, and cold, which form reactive oxygen species (ROS) from oxygen-based molecules that contain unpaired electrons (free radicals) such as super oxide (O_2^{2-}) or hydrogen peroxide (H_2O_2) [1]. Free radicals cause damage to DNA, collagen, elastin, and hydration balance which is important for elasticity and skin renewal process, so that cause aging and inflammation [2-6].

Antioxidants are compounds that inhibit oxidation reactions with free formation chain reactions, thus prevent the formation of peroxides, and even cell damage will be inhibited [7, 8]. There are 2 types of antioxidants, which are natural and synthetic. However, the use of synthetic antioxidants could be carcinogenic and toxic if it is used for a long time and high doses [9]. Therefore, natural sources of antioxidants are needed, one of it is Beluntas China (*Gynura pseudochina* (L.) DC).

Beluntas China is one of Indonesian native plant that has been used by the ancient as traditional medicine [10-12]. Based on several research, it is known that this plant has effects as an anticancer, analgesic, and decreasing cholesterol levels [13]. Beluntas China contains chemicals that are useful for humans, such as flavonoids, phenolics, alkaloids, saponins, tannins, terpenoids, and sterols. Phenolics and flavonoids are the main antioxidant components of Beluntas China leaves [14, 15].

Emulgel is a gel consist of lipid phases dispersed in water and a two-phase system that contains water and lipid molecules. Emulgel has a better consistency, lower risk of forming coalescence and more stable viscosity, so it can reduce the foam structure of the emulgel itself. Emulgel has the advantage of being a hydrophobic material carrier that cannot be integrated directly into a gel base [16]. Based on this background, research on the formulation of emulgel antioxidants containing Beluntas China extract has been carried out. Emulgels were formulated using various gelling agents to optimize its physicochemical stability during storage.

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2. Methods

2.1 Extraction

Gynura pseudochina (L.) DC was obtained from the Jambi area, Jambi Province. Beluntas china was cleaned, air-dried for 7 days, chopped until they are somewhat powdery and weighed 1 kg. Simplisia of beluntas china macerated with 70% ethanol solvent for 3x24 hours at room temperature. Then the liquid extract was taken and filtered so that the filtrate is free of pulp. The filtrate was evaporated with a rotary evaporator so that a thick extract was obtained [17]. To obtain the extract yield value, the extract is calculated by the following equation:

$$\% \text{ Rendement} = \frac{mass\ extract}{Total\ mass\ of\ simplisia} \times 100\% \quad \text{..... (Eq. 1)}$$

2.2 Phytochemical Screening

Phytochemical screening was carried out on both simplisia and extract of beluntas china leaf to determine the content of secondary metabolites contained, including alkaloids, flavonoids, tannins, polyphenols, saponins, steroids and triterpenoids, quinones, monoterpenoids, and sesquiterpenoids.

2.3 Formulation of Emulgel Antioxidant Beluntas China Extract

Emulgel base optimization was conducted by determining the two best concentrations between three types of gelling agent, which were carrageenan, HPMC, and carbomer. Emulgel base optimization was shown in Table 1.

Table 1. Emulgel Base Optimization

Ingredients	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)
Carrageenan	1	1.25	-	-	-	-
HPMC	-	-	5	6	-	-
Carbomer	-	-	-	-	0.5	1
Liquid Paraffin	7.5	7.5	7.5	7.5	7.5	7.5
Tween 20	1	1	3	3	1	1
Span 20	1.5	1.5	4.5	4.5	1.5	1.5
Propylene glycol	10	10	10	10	10	10
Nipagin	0.03	0.03	0.03	0.03	0.03	0.03
Nipasol	0.01	0.01	0.01	0.01	0.01	0.01
TEA	-	-	-	-	1	1
Aquadest	Ad 100	Ad 100	Ad 100	Ad 100	Ad 100	Ad 100

F1 = Carrageenan 1%; F2 = Carrageenan 1,25%; F3 = HPMC 5%; F4 = HPMC 6%; F5 = Carbomer 0,5%; F6 = Carbomer 1%

Antioxidant emulgel formula containing beluntas china extract is listed in Table 2. The concentration of beluntas china was determined based on the antioxidant activity test using the DPPH method which is 2 x IC_{50}. Emulsions were made by heating each oil phase (Liquid Paraffin and Span 20) and water phase (Propyleneglycol, tween 20, nipagin, and nipasol in aquadest) on a water bath at 60-70°C. Both phases were mixed, then added by extract of Gynura pseudochina, methylparaben, and propylparaben (preservative) that had been dissolved in propylene glycol (humectant). It was stirred until homogenous. Furthermore, gelling agents (carrageenan, HPMC, and carbomer) in which concentration based on optimization results were then added to the emulsion and stirred homogeneously.

Table 2. Formulation of Emulgel Antioxidant Beluntas China Extract

Ingredients	F1a (%)	F1b (%)	F4a (%)	F4b (%)	F6a (%)	F6b (%)
Beluntas China Extract	-	2 x IC_{50}	-	2 x IC_{50}	-	2 x IC_{50}
Carrageenan	1	1	-	-	-	-
HPMC	-	-	6	6	-	-
Carbomer	-	-	-	-	1	1
Liquid Paraffin	7.5	7.5	7.5	7.5	7.5	7.5
Tween 20	1	1	3	3	1	1
Span 20	1.5	1.5	4.5	4.5	3	3
Propylene glycol	10	10	10	10	10	10
Nipagin	0.03	0.03	0.03	0.03	0.03	0.03
Nipasol	0.01	0.01	0.01	0.01	0.01	0.01
TEA	-	-	-	-	1	1
Aquadest	Ad 100	Ad 100	Ad 100	Ad 100	Ad 100	Ad 100

F1a = Carrageenan w/o extract; F1b = Carrageenan 2x IC50 extract; F4a = HPMC w/o extract; F4b = HPMC 2x IC50 extract; F6a = Carbomer w/o extract; F6b = Carbomer 2x IC50 extract

2.4 Physical Stability Evaluation of Emulgel Antioxidant Beluntas China Extract

Physical evaluations involved organoleptic, homogeneity, pH, viscosity, and freeze – thaw

were done at day- 0, 3, 7, 14, 28, 42, and 60. The organoleptic and homogeneity evaluations were carried out by visually observing the changes in shape, color, and odor of the emulgel [18]. The pH measurement was done using a pH meter by dissolving a sample of 1 g into 10 mL of distilled water. Emulgel is stable if there is no significant pH change during storage time [19]. Viscosity was obtained by using a Brookfield Viscometer with the appropriate spindle and speed (rpm) [20]. Freeze thaw was done by storing the sample at 4ºC for 48 hours then transferred to 40ºC for 48 hours (1 cycle). It was done for 5 cycle. Every one cycle was complete, then checked if there was a phase separation occurs [18].

3. Result

3.1 Extraction

200 grams of simplicia were extracted using ethanol 70%. The content of phenolic and flavonoid compounds is higher in extracts with hydro-catholic solvents compared with extracts that use ethanol or pure methanol [21]. The extraction process was done by maceration. The thick extract was obtained for 14.84 grams with a yield of 7.42%. Organoleptic examination of beluntas china ethanol extract showed that the extract was in the form of thick liquid, distinctively smelling, dark green and bitter.

3.2 Phytochemical Screening

Phytochemical screening was carried out to determine the content of secondary metabolites contained in the extract qualitatively. Based on the results of phytochemical screening-detected in simplicia and ethanol extracts of beluntas china plants are alkaloids, flavonoids, polyphenols, saponins, and steroids. Flavonoid and polyphenols detected by phytochemical screening are the active compounds used as antioxidants [22-24].

3.3 Formulation of Emulgel Antioxidant Beluntas China Extract

The formula with the most stable evaluation results of each type of gelling agent for 7 days will be used as a base for variations of the formulation added by the extract later. The parameters observed were Organoleptic and Homogeneity, pH (Figure 1), and Viscosity (Figure 2). Based on observations, all emulgel bases are white, odorless, and homogeneous. The selected base concentration from each type of gelling agent are F1 (carrageenan 1%), F4 (HPMC 6%), and F6 (carbomer 1%).

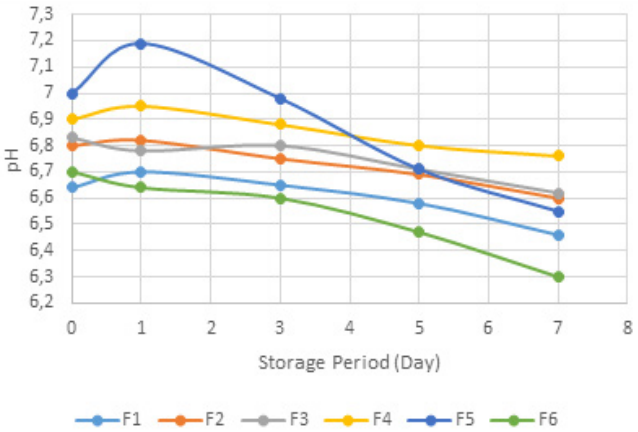

Figure 1. pH During the Optimization Period

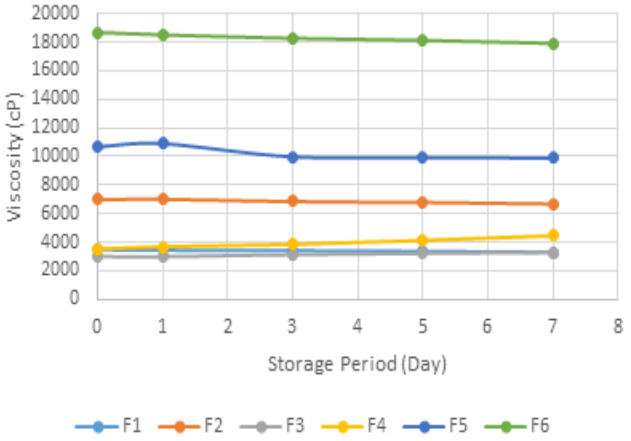

Figure 2. Viscosity During the Optimization Period (F1 = Carrageenan 1%; F2 = Carrageenan 1,25%; F3 = HPMC 5%; F4 = HPMC 6%; F5 = Carbomer 0,5%; F6 = Carbomer 1%)

3.4 Physical Stability Evaluation of Emulgel Antioxidant Beluntas China Extract

The result of organoleptic and homogeneity evaluations is shown in Table 3, while pH in Figure 3, and Viscosity in Figure 4. The results of the freeze-thaw test showed that F1a, F1b, F6a, and F6b showed physical stability for 5 cycles, but F4a and F4b showed phase separation in the 3rd cycle. This indicated that the formula was not resistant to temperature stress.

Table 3. Organoleptic and Homogeneity of Emulgel Antioxidant Beluntas China Extract

Charac-teristic	Day	F1a (%)	F1b (%)	F4a (%)	F4b (%)	F6a (%)	F6b (%)
Color	1	W	G	W	G	W	G
	3	W	G	W	G	W	G
	7	W	G	W	G	W	G
	14	W	G	W	G	W	G
	28	W	G	W	G	W	G
	42	W	G	W	G	W	G
	60	W	G	W	G	W	G
Odor	1	OL	OL	OL	OL	OL	OL
	3	OL	OL	OL	OL	OL	OL
	7	OL	OL	OL	OL	OL	OL
	14	OL	OL	OL	OL	OL	OL
	28	OL	OL	OL	OL	OL	OL
	42	OL	OL	OL	OL	OL	OL
	60	OL	OL	OL	OL	OL	OL
Homoge-neity	1	H	H	H	H	H	H
	3	H	H	H	H	H	H
	7	H	H	H	H	H	H
	14	H	H	H	H	H	H
	28	H	H	H	H	H	H
	42	H	H	H	H	H	H
	60	H	H	H	H	H	H

Color – W (White); G (Green); Odor – OL (Odorless); SO (Specific Odor); Homogeneity – H (homogeneous); IH (In homogeneous)

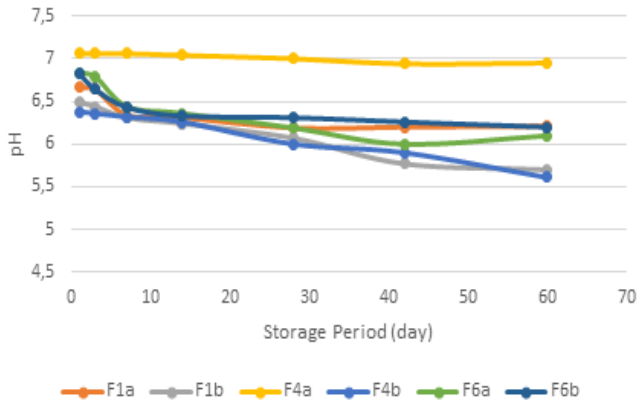

Figure 3. pH of Emulgel after 60 Days (n=3)

4. Discussion

4.1 Formulation of Emulgel Antioxidant Beluntas China Extract

Carrageenan is one of the carbohydrate polymers derived from seaweed, especially Eucheuma cottonii. Carrageenan can form a gel in a thermoreversible manner so that it is widely used as a gelling agent, thickener, and stabilizer in various industries such as food, medicine, cosmetics, and textiles [25]. HPMC produces clear, odorless, and tasteless products. It is commonly used in topical preparations and it resistants to phenol compounds so that beluntas china ethanol extracts will not be damaged [26, 27]. Carbomer 934 has better properties for the release of active substances and easy dispersion [28, 29]. Carbomer is a very acidic compound (pH 2-3), so that triethanolamine (TEA) is needed to balance the pH in the emulgel which was an ionized form. When it is added, the carbomer's pH increases to pH 6-7. Under these conditions, the carbomer becomes thicker, because the carboxyl group of the carbomer will change to (COO^-) so that the carbomer expands and becomes more rigid [30].

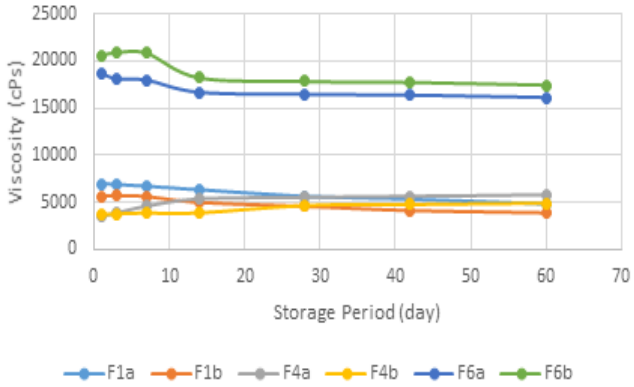

Figure 4. Viscosity of Emulgel after 60 Days (n=3)

In emulgel, increased viscosity can affect the spread of dispersion, increase in adhesion, and inhibit the release of active substances [25]. Based on the viscosity graphic images during optimization, the viscosity will increase along with the high concentration of the gelling agent in the emulgel. Each gelling agent has a different viscosity. This is caused by the structure of each gel base, the more hydroxyl groups (-OH) on the gel base, the higher the viscosity. This hydroxyl group will form hydrogen bonds with water molecules that play a role in the hydration process during the swelling process [26].

The pH stability is also one of the factors in determining the best formula because the pH of the preparation is expected to remain stable during storage so that it stays within the skin's pH range of 4.5 - 6.5 [27].

Formula 1 (carrageenan 1%), Formula 4 (HPMC 6%), and Formula 6 (carbomer 1%) were chosen because they provide better stability, pH, viscosity and organoleptic compared to formula 2 (carrageenan 1.25%), formula 3 (HPMC 5%), and formula 5 (carbomer 0.5%). This can be seen from the standard deviation values of pH and viscosity for 7 days of stable observation.

4.2 Physical Stability Evaluation of Emulgel Antioxidant Beluntas China Extract

Organoleptic and homogeneity test was done by visually observation involved odor, color, and consistency of emulgel. Extracts only affect organoleptic in terms of color. It turned green after the extract was added, while observations of odor, consistency, and homogeneity did not show significant changes.

To see stability during the observation period, the pH value of the preparation needs to be considered. Based on Figure 3, it can be seen that the longer the storage time, the relative pH decreases. However, the pH reduction of the preparation is still in the skin pH range of 4.6 - 6.5 so that changes in pH are still acceptable. The pH value used in this topical preparation must be by the skin's pH range of 4.5 - 6.5. In this range, the skin can accept topical preparations that do not irritate. If the preparation is below pH 4.5 will cause skin irritation while the preparation is above pH 6.5 will cause scaly skin [27].

A decrease in pH value during storage can occur due to the effect of CO_2 which reacts with the aqueous phase on the preparation so that it becomes acidic [20]. The concentration of H^+ ions is used as a measure of the acidity of a solution, if the solvent contains CO_2, the CO_2 will bind to the H^+ ion and then reduce the concentration of H^+ ions in the solution so that the pH becomes higher than the original. The pH will become more alkaline if the amount of H^+ ions in the preparation is low [28]. The decrease in pH can be influenced by temperature, the content of other substances in the preparations that react, which can disturb the stability of the pH [26].

Viscosity is used as an evaluation parameter for semisolid preparation because it affects the dispersion, adhesion, and release of active substances. The speed of drug release will increase with decreasing viscosity. This is because the higher the viscosity will form a strong barrier so that the rate of drug release slows [25, 29]. Viscosity of topical formulation should be physically give good rheology for ease in handling and distributio, as well as process of filling during production. Despite this requirement, there is no specific values of viscosity for topical preparation has been stated.

The optimum viscosity will maintain the active substance to be dispersed and maintain uniformity of concentration on that basis [30]. The longer the storage time, the longer the preparation is affected by the environment, so that it can affect the viscosity. The decrease in viscosity can also occur due to the impermeable preparation of the container so that the preparation can absorb water from the environment so that the volume of water in the preparation increases and decreases the viscosity [20]. The resulting viscosity value based on Figure 4 of each formula is lower when compared to each negative control, namely due to the extract given into the preparation thereby reducing the consistency of the preparation [16].

5. Conclusion

Based on research on the formulation of antioxidant emulgel beluntas china extract (*Gynura pseudochina* (L.) DC), it can be concluded that the best emulgel base formulation of each type of gelling agent based on the evaluation of physical observations shown by 1% carrageenan, 6% HPMC, and carbomer 934 1% base. And, the best formula of antioxidant emulgel beluntas china (*Gynura pseudochina* (L.) DC) extract based on physical evaluation during storage is carbomer 934 1%.

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