Majalah Farmaseutik Vol. 15 No. 1: 35-41
ISSN-p : 1410-590x
ISSN-e : 2614-0063

Antifungal Cream Preparation of Galangal rhizome Extract (*Alpinia galanga* L.)

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ABSTRACT

Cream is a semi-solid emulsion dosage form of both water-in-oil (W/O) or oil in water (O/W) type containing one or more dissolved or dispersed ingredients in the corresponding base material (containing no less than 60% water). Cream is usually used as emollient or containing active pharmaceutical ingredients on the skin (Ansel, 2008). The advantage of cream are the application practicallity, water washeability, and the easiness to spread evenly. In this research, we formulated cream containing rhizome Galangal rhizome. According to Darmono (2008), Galangal rhizome has various properties such as antifungal and antibacterial activities. Galangal rhizome contains *1-asetoksikhavikol asetat* (ACA). ACA is an antifungal. ACA has good solubility in 70% ethanol. We maserated Galangal rhizome (*Alpinia galangal* L.) to extract ACA from the simplicia. As for the cream base, we use hidrophilic base containing emulgators stearic acid and triethanolamine, with glycerin as humectant. During the optimization, we chose three formulas, formula 1 (10% stearic acid , 2% triethanolamin, 5% glycerin, and 0.01% vitamin E), formula 2 (15% stearic acid , 3% triethanolamin, 10% glycerin, and 0.05% vitamin E), and formula 3 (20% stearic acid, 4% triethanolamin, 7.5% glycerin, and 0.09% vitamin E). We used the bases to contain 10% of the extract. The results show that formula 1, formula 2, and formula 3 had typical smell of Galangal rhizome, brown color, and thick consistency. All formulas are homogenous. Formula 1 the best stability. We conclude that Galangal rhizome (*Alpinia galanga* L.) can be formulated in cream form with our formula 1 had the best stability among others.

Keyword: cream formulation, antifungi, Galangal rhizome *(Alpinia galanga* L.)

INTRODUCTION

The climate in Indonesia supports the incidence of various tropical diseases, particularly skin infections caused by microbes, especially fungi. Skin infections caused by fungi is a difficult problem to overcome, because fungi survive more easily in the environment that is less favorable than other microscopic substances (Fatrotin, 2010). One of these diseases is dermatophytosis, caused by the infection of *Trichophyton, Microsporum* and *Epidermophyton*. This fungi infect the surface of human or animal bodies such as the skin, nails, hair, horns and feathers (Darmono, 2008).

The use of herbs as an alternative medicine tends to increase along with the expensive of several types of synthetic compounds. This is due to the growing awareness of the community to return to nature (Fitriati, 2007). One of medicinal plants used as a cure for skin diseases caused by fungi is Galangal Rhizome (*Alpinia galanga* L.). Galanga is a member of the Zingiberaceae family. Galangal rhizome is easy to obtain in Indonesia and works as a liniment for fungal skin disease (*panu* in bahasa) before modern medicine develops as it is now. Galangal rhizome has various properties including anti-fungal and antibacterial activities. Yuharmen *et al*., 2002 showed microbial growth inhibition activity by essential oils and methanol fraction of Galangal rhizomes in several species of bacteria and fungi. Suaib *et al*.,

2016 stated that the overall inhibitory effect of Galangal rhizome extract on the highest growth of *O. theobrema* fungi is at a concentration of 0.75% where the overall treatment showed a significant difference that had been tested at each concentration. The inhibitory effect of Galangal extract on the growth of fungus *O. theobremae* during observation at 0.25% was 20.47%, at 0.50% was 27.10%, and at 0.75% was 38.77%.

Cream is a semi-solid emulsion dosage form of both water-in-oil (W/O) or oil in water (O/W) type containing one or more dissolved or dispersed ingredients in the corresponding base material (containing no less than 60% water). Cream is usually used as emollient or containing active pharmaceutical ingredients on the skin (Ansel, 2008). The advantage of cream are the application practicallity, water washeability, and the easiness to spread evenly. The concentration of Galangal rhizome extract in the cream was 10%. This concentration was chosen based on the concentration range of Galangal rhizome extract which effectively inhibited the growth of *M. Canis* and *T. Mentagrophytes*. Hezmela (2006) conducted a study to determine the optimal range of extract concentrations to inhibit the growth of the two test fungi. Based on the research conducted, it is known that the concentration range of extract to inhibit the growth of *M. Canis* is 0.3% - 5%, while for *T. Mentagrophytes* is 0.5% - 10%.

The cream contained stearic acid as a base of cream and emulsifier in the oil phase, triethanolamine as emulsifier in water phase, glycerine as humectant, α-tocopherol as antioxidant, methylparaben as preservative in oil phase, and propyl paraben as preservative in water phase. The formula design is formula 1 (10% stearic acid , 2% triethanolamin, 5% glycerin, and 0.01% vitamin E), formula 2 (15% stearic acid , 3% triethanolamin, 10% glycerin, and 0.05% vitamin E), and formula 3 (20% stearic acid, 4% triethanolamin, 7.5% glycerin, and 0.09% vitamin E).. Galangal rhizome extract in the cream was 10%. The formulation cream can be seen in Table 1.

O/W cream was formulated by combining stearic acid and triethanolamine (TEA). TEA was chosen as an emulgator because TEA will form an oil emulsion in water which is very stable when combined with free fatty acids. The most suitable fatty acids to be combined with TEA are stearic acid because stearic acid does not experience discoloration like oleic acid (Cosmetic Ingredient Review Expert Panel, 1995). Stearic acid reacts with TEA in situ to produce a salt, triethanolamine stearate which functions as an emulgator for oil-in-water type emulsions (Aulton, 2002). The salt formed is the result of a stoichiometric reaction. Each component reacts with an appropriate comparison. 2-4% of TEA and 5-15% stearic acid generally used depends on the amount of oil to be emulsified (Jenkins *et al*., 1957). Stearic acid in Allen (2009) was used at concentrations of 1-20%. Stearic acid is neutralized using a flavoring agent or triethanolamin to avoid skin irritation because of the compounds. This research used 10-20% stearic acid and 2-4% TEA.

Glycerin as humectants with the consideration that glycerin will resist evaporation of water in the cream preparation and in the skin serves as a moisturizer (Hendradi *et al*, 2013). The use of glycerin is common between 10-20% (Tranggono and Latifah, 2007).. This research use 5-10% glycerine as humectant.

Vitamin E is a fat-soluble antioxidant that protects the skin from oxidative stress, one of which is photoaging. Photoaging is premature aging due to the continuous production of oxygen radicals in the skin from UV light. Many studies documented that vitamin E has major antioxidant and photoprotection activities efficient enough to reduce the frequency and severity of pathological events in the skin (Nachbar & Korting, 1995). The use of 0.5% vitamin E in cream preparations only enough to penetrate 4.3% of the skin, so it is

recommended to use at least 1% of vitamin E in order to penetrate into the skin and produce the expected therapeutic effect. According to a survey conducted by the Personal Care Products Council in 2013, the maximum concentration of vitamin E used in products with dermal / skin contact is 5.4%. Most of the α-tocopherols used in topical cosmetic products had 5% or less (Hasibuan *et al.*, 2014). This research use vitamin E in the range of 0.01-0.09%, expected to be enough to penetrate the skin.

METHODS

Galangal Rhizome (*Alpinia galanga* L.) Extraction

Cutting tool (knife), grinder, maseration container, rotary evaporator, extract container, and oven. Cream production, analytical balance, porcelain cup, glass watch, paper parchment, spoon horn, glass beaker 250 ml, glass beaker 1000 ml, small glass beaker, 100 ml measuring cup, 10 ml measuring cup, drops, waterbath, stirrer, spindle, and mortar.

Materials

100 g of simplicia Galangal rhizome, 70% of ethanol, aluminum foil, and filter paper. While the ingredients used in the preparation of the cream are the ethanol extract of Galangal rhizome, stearic acid, triethanolamine (TEA), glycerine, α-tocopherol, methyl paraben, propyl paraben and aquadest.

Samples of Galangal rhizome (*Alpinia galanga* L.) were freshly taken in Pepedan village, Karangmoncol district, Purbalingga regency. Samples were washed thoroughly in running water. Clean samples were sorted wet and aerated to reduce moisture content. Samples were chopped and dried by aerated in a place that is not exposed to direct sunlight. After drying, it was dry-sorted and milled. Simplicia of Galangal rhizome was weighed 100 g and put into a container. Two liters of 70% ethanol (until the simplicia is submerged) were added to the jar containing the sample. The container was then closed tightly. The maceration process was for 3 days at room temperature, protected from light, and occasionally stirred. Filtrate was collected and evaporated using waterbath to obtain thick extract. Evaporation was stopped at 10% yield (MOH, 2010).

Cream Production

Before used a raw material for cream, no characterization of Galangal rhizome was carried out. Reference to the anti fungi possessed by Galangal rhizome is taken from the research of (Yuharmen *et al*., 2002) and (Suaib *et al.,* 2016). Suaib *et al*., 2016 states that the overall inhibitory effect of Galangal rhizome extract on the highest growth of *O. theobrema* fungi is at a concentration of 0.75% where the overall treatment showed a significant difference. The inhibitory effect of Galangal extract on the growth of fungus *O. theobremae* during observation at a 0.25% was 20.47%, 0.50% was 27.10%, and 0.75% was 38.77%. It is expected that the levels of 10% Galangal rhizome extract can stop fungal activity better than those obtained in Suaib's (2016) study. In addition, the concentration of Galangal rhizome of 10% was chosen based on the concentration range of galangal extract which effectively inhibit the growth of *M. Canis* and *T. Mentagrophytes*. Hezmela (2006) conducted a study to determine the optimal range of extract concentrations to inhibit the growth of the two test fungi. Based on the research conducted, it is known that the concentration range of extract to inhibit the growth of *M. Canis* was 0.3% - 5%, while for *T. Mentagrophytes* was 0.5% - 10%. Formula 1, 2 and 3 (Table I). The choice of formula was based on the function of each ingredient used and the expected cream product. The amount ingredients were used was decided by considering the combination.

All materials were weighed according to the results of the calculations contained

Table I. Cream Formulas

Components	Concentrations (w/w)		
	Formulation 1	Formulation 2	Formulation 3
Galangal rhizome extract	10%	10%	10%
Stearic acid	10%	15%	20%
-tocopherol (Vitamin E)	0.01%	0.05%	0.09%
Methyl paraben	0.15%	0.15%	0.15%
Triethanolamine (TEA)	2%	3%	4%
Glycerine	5%	10%	7.5%
Propyl paraben	0.03%	0.03%	0.03%
Aquadest ad	30g	30g	30g

in (Table I). Separate the materials to be dissolved in the oil phase and water phase. Oil phase was made by combining between stearic acid, α-tocopherol, and methyl paraben successively above the waterbath while stirring until homogeneous. Temperature was maintained at 50°C. For the water phase, triethanolamine, glycerin, and propylparaben were dissolved above the waterbath while continuously stirring. The temperature was maintained at 70°C. The water phase was put into the heated mortar. The oil phase was gradually loaded into the water phase while crushed to form a cream base, then water was added. Galangal rhizome extracts were fed into the cream base in bits. The mixture was stirred until homogeneous (Sulastri *et al.*, 2016).

Cream Physical Stability Testing

Organoleptic Testing

Organoleptic testing was including the check for the color, consistency, and smell of cream preparations.

Homogeneity Testing

Samples of cream were taken as much as 0.1 g then smeared on a transparent glass. Observation was the made in the event of phase separation.

pH Testing

pH measurements were carried out using a universal pH indicator.

RESULTS AND DISCUSSION

Yield of Thick Extract

Evaporation process yielded 26.17 grams or 26.17% extract. When evaporation process in waterbath, ethanol will evaporate first than water. This means that in the yield of 26.17% was still containing water. The amount of rendement in the extract according to Afif (2006) was caused by factors of extraction method, amount of solvent, extraction time, powder size and temperature. Water levels that exceed the requirements allow fungal growth (MOH, 1986). Figure 1 shows thick extract of Galangal rhizome (*Alpinia galangal* L.).

Figure 1. Thick extract of Galangal rhizome (*Alpinia galangal L.*)

Table II. Organoleptic Test

Formula	Test	Physical apparence
1	Smell	Specific
	Color	Brown
	Consistency	Soft and tend to be thick
2	Smell	Specific
	Color	Brown
	Consistency	Thick
3	Smell	Specific
	Color	Brown
	Consistency	Very thick

Organoleptic Testing

In the preparations of the first formula, the cream were soft and tend to thick. In the second formula, it was thick, and in the third formula was very thick. This was because the concentration of the base and emulgator that played a role in the formation of cream consistency in each formula (Table II).

The brown color of cream is obtained from the color of Galangal rhizome extract. This was different with the yellowish white color obtained in the research of (Rahmalia *et al.,* 2010).

The typical smell of cream was resulted from Galangal rhizome smell. In O/W type of cream, the presence of stearic acid can cause the cream to be softer that its viscosity is lower. Cream base types that have high viscosity will cause the diffusion coefficient of a drug in the base to be low, so the release of the drug from the base will be small (Lachman *et al*., 1989). Stearic acid in Allen (2005) is used at concentrations of 1-20%. Stearic acid was neutralized using a flavoring agent or triethanolamin to not to irritate the skin so that it can be used in cream preparations. Triethanolamine is a mixture comprising mainly 2-2-2-nitrilotreietanol (C_2H_4OH) 3N, together with 2,2-iminoloisetanol and a small amount of 2-aminoethanol (Anonym, 1995). Triethanolamine is usually combined with fatty acidic substances to form water-soluble soaps (Triethanolamine stearate) (Voigt, 1984) used as a regulator of pH, surfactant, foam and cleanser (Anonym, 1995).

Cream viscosity is influenced by the presence of fatty acids contained in the cream, namely stearic acid. The more the amount of fatty acids used, the resulting cream will also be harder. Triethanolamine may also be a water-phase emulsifier which is thinner than the oil phase (stearic acid) so the consistency of the resulting cream was then decreased. The use of stearic acid as an emulsifier in a topical preparation will form a thick base and its viscosity is determined by the amount of triethanolamine used (Allen, 2009). Allen (2009) also mentioned that the formulation of cream preparations with the use of staric acid emulsifier and TEA can affect the viscosity and pH of the preparation.

Homogeneity Testing

Homogeneity test was done by observing the color of the preparation visually and see if there were parts that were not mixed well in the cream. The cream can be claimed to be homogeneous if there is color homogeneity and no particles are found in the cream (Ida & Noer, 2012). Homogeneity affects the effectiveness of therapy because it is associated with the same drug levels in each application. Cream is a preparation in which the application is applied to the treatment site, so that each part of the active ingredient must have

Formula 1 Formula 2 Formula 3

Figure 3. Stability of cream

equal opportunity to occupy the therapeutic site. This condition can be achieved when the cream is homogeneous. All formulas were homogenous.

The homogeneity of a cream preparation is influenced by several factors such as temperature accuracy for melting, and stirring. If the temperature used for the fusion of an ingredient does not match the melting point of the material, then the material will not dissolve and mix with other ingredients. The final result will be fine particles in the glass as a test indicator of its homogeneity. In addition, the cream homogeneity is also influenced by the Galangal rhizome extract which is not evenly mixed and homogeneous during mixing. Figure 2 shows the homogeneinity test of cream.

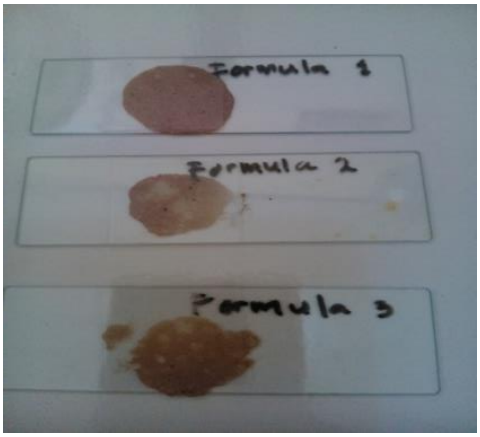

Figure 2. Homogeinity test

pH Measurement

The pH measurement needs to be done to determine the safety of cream preparations when used so that they do not irritate the skin (Juwita *et al.*, 2013). If the preparation is too acidic it will irritate the skin, while too basic cream will cause the skin to become dry during use (Ainaro *et al.*, 2015). Ph testing showed that the pH test results for all formulas of cream preparations were 6. This result was as expected, where both cream preparations have acidity that matches the normal pH range of the skin, which is 4.5 to 6.5 (Naibaho, 2013).

Stability Testing

Stability testing was performed to ensures the identity, strength, quality, and purity of the product to be persist during the expected storage time period.

Formula 1 is more stable than formula 2 and formula 3 because because the less use of emulgator stearic acid. Formula 2 contained 15% stearic acid and formula 3 contained 20% stearic acid. Figure 3 shows the stability of cream.

According to (Rowe *et al.*, 2009), combination of stearic acid and triethanolamine will form a salt of triethanolamine stearate which is anionic and produces fine grains thus stabilize the type of oil emulsion in water or vanishing cream.

CONCLUSION

According to out study, it can be concluded that, galangal rhizome (*Alpinia galanga* L.) can be can be formulated into cream preparation, and the formula of cream using stearic acid of 10% and triethanolamine of 2% as emulgator (Formula 1) has more stable than Formula 2 (stearic acid of 15% and triethanolamine of 3%) and formula 3 (stearic acid of 20% and triethanolamine of 4%) for 10% of Galangal rhizome extract (*Alpinia galanga* L.).

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