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Physical characteristic and irritation index of *Syzigium aromaticum* essential oil in O/W and W/O creams

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Abstract. Essential oil of *Syzigium aromaticum* has been formulated in O/W and W/O creams as anti-inflammatory dosage form. The purpose of this study was to evaluate the physical characteristic and irritation index of *S. aromaticum* essential oil in O/W and W/O creams. The creams were made by fusion method. The creams then were evaluated the physical characteristic including pH, viscosity, spreadability and adhesivity. The irritation index was obtained by irritation skin test in male rabbit. The results showed that the W/O and O/W creams have the value of pH: 6.3 and 6.27; spreadability: 3.18 and 4.17 cm²; adhesivity: 5.59 and 0.07 minutes; viscosity: 4.43 and 2.88 Pa.S, respectively. The irritation test showed that the control enhancer caused mild irritation in both of W/O and O/W creams. These findings indicated that type of cream might influence the physical characteristic and irritation index of *S. aromaticum* essential oil cream.

Keywords: *S. aromaticum*, essential oil, physical characteristic, irritation index, cream

1. Introduction

The essential oil of *S. aromaticum* has efficacy as anti-inflammatory. The previous study have formulated the essential oils in various types of ointment base. The results of this study indicated that the difference in the composition of the formula affected the physical properties of the dosage forms. Data of adhesivity indicated that the increase of essential oil concentration led to an increase in the adhesivity of the ointment with base of W/O cream, lotion, hydrocarbons and the decrease of the adhesivity of the ointment with absorption base. Data of spreadability showed that the increase of the essential oils concentration caused an increase the spreadability of ointment with absorption W/O and O/W creams, and hydrocarbons bases, while on the lotion base there was a decrease of the spreadability. The spreadability of emulgel base was not affected by the increase of concentration of essential oil of *S. aromaticum*. Data of pH showed that the increase of essential oil concentration of *S. aromaticum* did not affect the pH in absorption base, W/O cream, lotion, and hydrocarbon. An increase in pH occur on the O/W cream with the an increase of the concentration of essential oils [1-7]. Other studies have also shown similar results. The formulation of ethanol extract of mangosteen peel in gel showed that variation of gelling agent would affect the adhesivity and spreadability of gel. The results of study showed that carbopol was the most optimal gelling agent in the formulation. The increase of concentration of ethanol extract in gel raised the adhesivity of gel and capability of gel as wound healing. The other study showed that the composition variation of oleic acid and propylene glycol as enhancer affected the activity of the essential oil of *S. aromaticum* as anti-inflammatory. The



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increase of concentration of propylene glycol caused the decrease of the number of cells with COX-2 expression, the number of inflammatory cells and the epidermal thickness of skin [8-10].

In this study the essential oil of *S. aromaticum* was formulated in W/O and O/W creams with the addition of enhancer. The enhancer composition of O/W cream was 50% oleic acid and 50% propylene glycol. While the enhancer composition on the W/O cream was 30% oleic acid and 70% propylene glycol. The results of previous study showed that the difference of composition in the formula would affect the physical properties of the preparation. Thus, the determination of the physical properties and the irritation index of essential oil of *S. aromaticum* formulated in W/O and O/W creams were needed.

1

2. Materials and Methods

2.1. Materials

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This study used essential oil of *S. aromaticum* from the Center for Essential Oils Studies Islamic University of Indonesia (CEOS-UII), Yogyakarta, Indonesia. The ingredients for the O/W and W/O creams were pharmaceutical grade i.e white vaseline, methyl paraben, propyl paraben, propylene glycol, stearic alcohol, natrium lauryl sulphate, aquadest, oleic acid, cetaceum, cera alba, parafin liquidum and natrium tetra borate. Rabbit was used as an animals in irritation skin test. The whole procedure in this study was approved by the Research Ethics Committee of Universitas Ahmad Dahlan with approval number No. 011504040.

2.2. Methods

2.2.1. Formulation of O/W and W/O creams

The O/W and W/O type creams were made using fusion method. Each of the oil phase and the water phase was heated at 70°C. The ingredients of oil phase of O/W cream were white vaseline, propyl paraben, stearic alcohol, natrium lauryl sulphate, oleic acid, whereas in cream type W/O were cetaceum, cera alba, parafin liquidum, oleic acid. The ingredients of water phase of O/W cream were propylene glycol, methyl paraben, aquadest whereas w/o type cream were natrium tetra borate, propylene glycol, and aquadest. After that, the oil and the water phases of each cream were mixed until homogeneous. The essential oil of *S. aromaticum* was added after the base of cream getting cold [11, 12].

2.2.2. Evaluation of physical characteristic

2.2.2.1. Adhesivity test

Briefly, 0.25 g of cream was weighed and put between two glass objects. Then, 1 kg of load has placed upper the glass objects to give a pressure for 5 minutes. After that, the glass objects were placed on the tool that was given load 80 g. The time needed to separate the two glass objects after the load was released was recorded [13].

2.2.2.2. Spreadability test

Briefly, 0.5 g of the cream was weighed and put on the middle of circular glass. The other glass was put on the upper of it for 1 minute. The diameter of cream was measured. The 100 g of load was put on the glass for 1 minute and then the diameter of cream was measured until getting the constant one [14].

2.2.2.3. pH test

Five hundred mg of cream was diluted with 5 ml of distilled water. The pH of cream was then measured using pH meter [15].

2.2.2.4. Viscosity test

The viscosity of cream was measured by using viscosimeter Rheosys Merlin VR

2.2.3. Irritation skin test

This test referred to the BPOM guidelines for non-clinical toxicity test (*in vivo*). The test used six male rabbits 3 months old. Firstly, the back hair of rabbits were shaved carefully, then the removal cream of hair was applied. After 48 hours, the backs of rabbits were divided into 4 square. It was used to apply

the O/W type cream, W/O type cream and cotton oil 4% (as negative control). One square was used as as normal control. The observations were conducted for 24, 48 and 72 hours. To study the reversibility, the observation was continued after 7 and 14 days. The responses of the cream application were assessed according to the guidelines [16].

3. Results and Discussion

3.1. The physical characteristic of cream

The physical characteristic of O/W and W/O type creams were presented in Table 1.

Table 1. Physical characteristic of O/W and W/O creams

Parameter	O/W type cream $\bar{x} \pm \text{sd}$ (n=3)	W/O type cream $\bar{x} \pm \text{sd}$ (n=3)
Viscosity (Pa.s)	4.43 \pm 0.15	2.88 \pm 0.66
Spreadability (cm ²)	3.18 \pm 0.10	4.17 \pm 0.12
Adhesivity (minutes)	5.59 \pm 0.35	0.07 \pm 0.009
pH	6.63 \pm 0.08	6.27 \pm 0.08

The viscosity of O/W cream was greater than W/O cream. This was due to differences in the composition of the ingredients in each cream. The one of component of the O/W type cream was stearyl alcohol which can provide good viscosity and adhesion [17]. The study on the formulation of several active ingredients in O/W, W/O and amphiphilic type creams also showed that O/W cream had the highest viscosity compared to other types of cream [18].

In addition, the presence of liquid paraffin in W/O type cream also caused the consistency of cream to be softer causing the viscosity becomes smaller [15]. The differences in viscosity may due to differences in composition of enhancer. The enhancer compositions were 50% oleic acid: 50% propylene glycol in O/W type cream and 30% oleic acid:70% propylene glycol in W/O cream. The amount of propylene glycol in W/O type cream was greater than in O/W type cream. The function of propylene glycol was as humectant which caused the w/o type cream had lower consistency.

The viscosity of the cream will affect the spreadability and adhesivity of the cream. The higher viscosity caused the lower of consistency and resulted in the decrease of spreadability. On the other hand, it caused increase of adhesivity. This was also in accordance with the results of previous studies on essential oil of *S. aromaticum* formulations in the base of absorption and base of lotion [1,6]. Based on the previous study, the viscosity of O/W type cream higher than other type cream was caused by the stearyl alcohol in the formulation [17]. The spreadability of cream described the ease of cream in covering the wound. Therefore cream preparations are expected to have a wide spread. Good spreading cream was about 5-7 cm² [19]. The adhesivity described the ability of the cream to adhere to the wounded skin. Therefore, cream was expected to have long adhesive power. The cream should have at least 4 seconds of adhesion [20].

Testing of pH was intended to know the level of acidity of cream which not cause skin irritation [21]. The result of pH test showed that the pH of the O/W and W/O type creams were in the range of skin pH (4.5 to 6.5). Topical preparations were expected to have a pH that was in the range of normal skin. The pH of cream was upper the pH of normal skin will trigger scaly skin, and the pH of cream was under the pH of normal skin will trigger skin irritation [22]. The pH of O/W cream was greater than that of W/O type cream. The amount of oleic acid as enhancer in O/W cream was greater than in W/O cream. The composition of enhancers were 50% oleic acid:50% propylene glycol in O/W type cream and 30% oleic acid:70% propylene glycol in w/o type cream.

3.2. The irritation test

The result of irritation test was presented in Table 2.

Table 2. The index irritation of creams

Group of test	W/O cream	O/W cream
Normal control	0	0
Base of cream	0	0
Base of cream + Enhancer ¹	0	0
Base of cream + Enhancer + Essential oil of <i>S. aromaticum</i> ¹	0	0.03
Base of cream + Essential oil of <i>S. aromaticum</i>	0	0
Enhancer	0.13	0.13

³ Data in Table 2 showed that enhancer caused mild irritation both in W/O and O/W creams. Combination of oleic acid and propylene glycol was used as enhancer in this study. Enhancer have mechanismed by damaging the lipid tissue so it can cause a certain side effects on the skin [23]. The formulation contained each of enhancer and essential oil of *S. aromaticum* did not cause irritation both in W/O and O/W type creams. It mean the formulation could reduce side effect of enhancer. On the other hand, the formulation contained mixture of enhancer and essential oil of *S. aromaticum* in o/w cream caused mild irritation. It may due the amount of enhancer and eugenol in essential oil of *S. aromaticum* was released higher than in w/o cream. The composition of water phase in O/W type cream was higher than in w/o type cream. In this condition, the non polar component such as oleic acid and essential oil of *S. aromaticum* were easier to release from O/W cream than from type w/o cream. There are two components that can cause mild irritation i.e enhancer and eugenol in essential oil of *S. aromaticum*. Based on the literature, essential oil might cause mild irritation[24]. Eugenol is an active compound in *S. aromaticum* essential oil which have enhancer activity [25]. Essential oil could be used as enhancer because it contains of terpenes that can be used as enhancers [26-28]. Terpen has high ability to improve the penetration and low systemic toxicity at low concentrations (1-5%). It can increase the polar drug's diffusion coefficient in the membrane by altering the fat structure of the stratum corneum [29].

4. Conclusions

Type of cream may influence the physical characteristic and irritation index of *S. aromaticum* essential oil cream.

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