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Physical Properties and Irritation Index Essential Oil of Clove (*Syzigium aromaticum*) in Absorption Base Ointment with Variation Concentration

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Abstract. The essential oil of clove (*Syzygium aromaticum*) contains eugenol which has antiinflammatory activity. Development of the dosage form for this essential oil was needed to increase its acceptability. The aim of this study was to know the influence of concentration variations of the essential oil of *Syzigium aromaticum* in an absorption ointment base to the physical properties and irritation index of the ointment. The ointment was formulated by melting method. The concentrations of essential oil were 2,5% (FI), 5% (FII) and 10% (FIII), respectively. The ointment was evaluated for its physical properties (spreadability, adhesivity and pH) and irritation index. Data were analyzed by anovaone way with 95% confidence level. The results of this study showed that the concentration variation)of essential oil of *Syzygium aromaticum* influenced the physical properties except pH. The increasing concentration of essential oil of *Syzygium aromaticum* caused increasing spreadability and decreasingadhesivity. On the other hand the concentration variationof essential oil did not influence the irritation index of the ointment. The irritation index of the ointment was negigible.

Keywords: essential oil, *Syzygium aromaticum*, physical properties, irritation index, absorption base

INTRODUCTION

Clove bud essential oil (*Syzygium aromaticum*) is derived from cloves. The clove tree, which belongs to the family Myrtaceae, is widely grown in Indonesia, India and Madagascar [1]. Clove oil has biological activities because of its high level of eugenol that is efficacious as an antiseptic and analgesic in dental and oral treatments [2], antioxidant, analgesic and neuroprotective activity [3]. Other studies also show that eugenol has anti-inflammatory activity with the mechanism of action of lowering the levels of cytokines (TNF-α) [4] and suppresses the expression of COX-2 [5].

Based on the potential of clove bud essential oil as an anti-inflammatory needs further research to develop a dosage form. Since the disadvantage the oral dosage form include unspecific target and high doses, the topical dosage form will be choiced [6]. An example of a topical dosage form is absorption ointment base. Absorption ointment base was chosen because it has good physical stability when compared to other ointment base [7].

Related to the use of the ointment on the skin, it is necessary to evaluate the physical properties of the ointment and potential skin irritation. It is based on the consideration that the physical properties which include spreadability, adhesivity and pH will affect the therapeutic effectiveness of the ointment. Ointments are expected to have a wide spreadability so that it can cover all the affected areas of the skin, adhesive in long period that results in the active substance diffusing from ointment base, give a therapeutic effect and have the same pH in the range of the skin pH so it can not cause skin irritation. There fore irritation test is also required because the essential oil of clove bud contains eugenol and some of derivative compounds potentially irritate the skin [8]. The aim of this study was to determine the effect of variations in the concentration of clove bud essential oil to the physical properties and potential irritation in the absorption ointment base.

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EXPERIMENTAL METHODS

Materials

Materials used in this study include the essential oil of clove bud. The essential oil of clove bud was obtained from the Center of Essential Oils Studies Islamic University of Indonesia (CEOS-UII). The ingredients for the absorption ointment base are pharmaceutical quality (adeps lanae, stearyl alcohol, cera alba, white vaseline). Animals test was used to irritation skin test is rabbit. The whole procedure was approved by the Research Ethics Committee of Ahmad Dahlan University (UAD KEP) No. 011504040.

Procedure

Ointment Formulation

The absorption ointment base was made using fusion method by dissolving stearyl alcohol, cera alba, and white vaseline together in a porcelain cup until dissolved and homogeneous in a water bath (*mixture 1*). On the other porcelain cup, adeps lanae was heated until melted and fed into mixture 1, stirred continuously until homogen. The mixture was poured into a mortar, stirred constantly, and after chilled clove bud essential oil was put then stirred until homogen. The ointment composition is presented in Table I.

Table I. Formula of Absorption ointment base containsclove bud essential oil

Materials	Formula I (%)	Formula II (%)	Formula III (%)
Clove bud essensial oil	2,5	5	10
Adeps Lanae	2,93	2,85	2,7
Cera alba	7,8	7,6	7,2
Stearyl Alcohol	2,93	2,85	2,7
White Vaselin	83,85	81,7	77,4

Physical Properties Evaluation

Adhesivity Test

The ointment was weighed 0.25 grams and then was placed between two glass objects. The glass objects were pressed with a load of 1 kg for 5 minutes. Once the load was lifted from the glass objects and they were placed on the load testing tool that was given load 80 grams. Record of the time was required so that two glass objects were separated [9].

Spredability Test

The ointment was weighed 0.5 g and then was placed on the round glass diameter 15 cm, other glass laid there on and was allowed to stand for 1 minute. Diameter of the ointment spread was measured. Afterwards, the glass was added with 100 grams of additional burden for 1 minute and then the diameterwas measured until getting the constant one[10].

pH Test

The ointment was weighed 0.5 g and then was diluted with 5 ml of distilled water. After that the pH of the solution was checked using universal pH indicator [11].

Irritation Skin Test

The ointment irritation skin test was performed using rabbits as test animals..This study used six male rabbits. This test refers to the Guidelines [12] for Non-Clinical Toxicity Test (in vivo). The rabbits were shaved on the back carefully, then they were applied to hair removal cream to remove fine hairs. After that they were cleaned up the remnants of hair removal cream with warm water. After 48 hours, the backs of rabbits were divided into 6 square parts, each with an area of 2x3 cm^2 area and distance per area + 2 cm, and then was given treatment. Observations were made during the first 4 hours after the rabbits were given the ointment. Next the rabbits observation was continued in 24, 48 and 36 hours. To see reversibility, they were observed until day 14. Response of the ointment was assessed according to the guidelines.

RESULT AND DISCUSSION

Adhesivity Test

Adhesivity test as one of the parameters that need to be evaluated for semi-solid dosage form such as ointments are needed to see how long the ointment ability can stay and be attached to the skin. Ointments that can stay and stick around longer on the skin can produce longer therapeutic effect [13]. Adhesivity test results in this study (Fig.1) show that the bonding of the ointment base strength has a good adhesion of more than 4 seconds [14]. Data shows all formulas fullfill the requirement. The increase in concentrations causes the reduction of adhesivity. The greater level of clove bud essential oil in absorbent ointment bases causes the reduction of consistency so the adhesivity will be decreased.

Spredability Test

Spredability test shows ability of the ointment to spread on the skin surface. The test results in this study (Fig.2) showed that increasing the concentration tends to cause an increasing spredability. The greater level of clove bud essential oil concentration on absorption ointment base cause the ointment consistency becomes more fluid, so that spredability will increase. However, the spredability of all the formula has not complied with a good spredability is between 5-7 cm^2 [14].

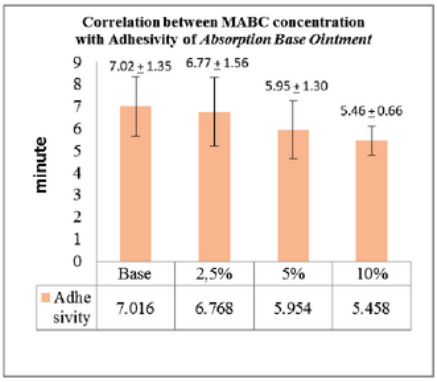

FIGURE 1. Correlation between Clove bud essential oil (MABC) concentration with adhesivity of absorption ointment base

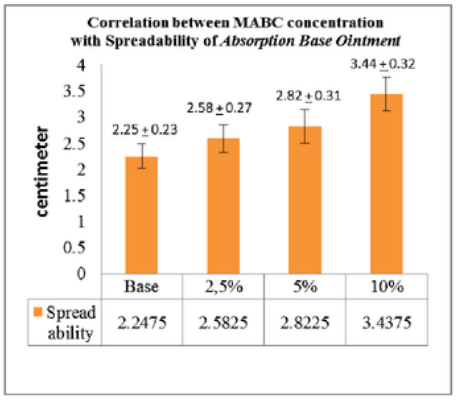

FIGURE 2. Correlation between Clove bud essential oil (MABC) concentration with spreadability of absorption ointment base

pH Test

The pH test was performed to see acidity level of the topical dosage form. The pH of topical dosage form that will be used on the skin should be in the range 4.5 - 7. The dosage form with a pH in the range that does not cause skin irritation because the dosage form are not too acidic and alkaline [15]. The pH test results in this study (Fig.3) showed that the absorption ointment base containing clove bud essential oil has a pH of 5.4 - 5.6 so that it meets the pH requirements of the topical dosage form that will be used on the skin.

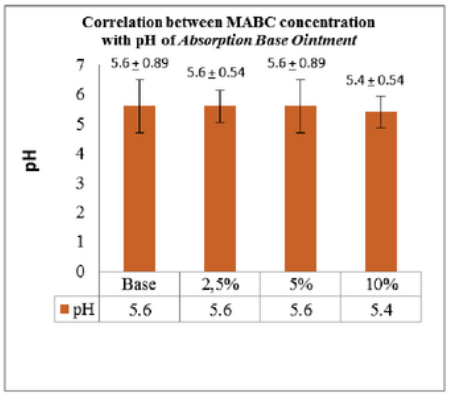

FIGURE3. Correlation between Clove bud essential oil (MABC) concentration with the pH of absorption base ointment

Skin Irritation Test

Irritation index test results showed that with the increase in concentrations of clove bud essential oil also the increase of the irritation index. This is because eugenol also has an activity as an enhancer [16]. Eugenol as one class of terpenes have the potential as enhancers [17]. Enhancer as a compound that helps the penetration of active substances into the skin layer by affecting the structure of skin has chance to give irritation effect. Yet of all the formulas, the increase that occurred was not significant and was still in very slight category(negigible) (Fig. 4).

In this test, croton oil was used as a positive control to test the irritation because it has been proved irritate the skin. Croton oil was also proven as mediators trigger of inflammation in the skin of animals that are affected the dose and duration of administration [18].Through these mechanisms, it is evident in this study (Fig. 4) that the application of croton oil on the back of rabbit skin cause irritation as indicated by the value of the irritation index of 1.75 (Category: Slight).

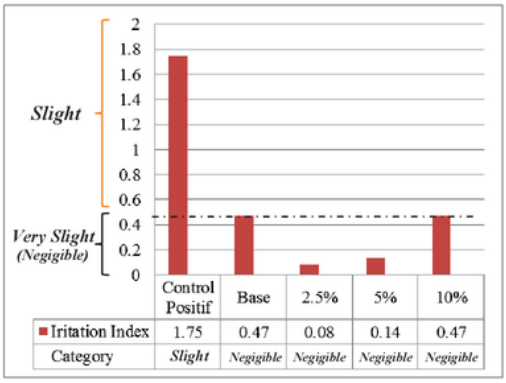

FIGURE 4. Irritation index of each formula absorption ointment base contain clove bud essential oil compared to positive control

Based on the test resulted of adhesivity, spredability, pH and irritation index, it can be determined the most suitable concentration of clove bud essential oil was 10%. Data showed it concentration meet the requirements of adhesivity, pH and has the same irritation index with other formulas were categorized as very slight. Although it concentration has not met the requirements of the spredability, the 10% concentration of clove bud essential oils in absorption ointment base has the most extensive of spredability

.

CONCLUSION

An increasing concentration of clove bud essential oil caused increasing the spreadability and decreasing adhesivity but does not affect the pH of the absorption base oitment. All formulas the ointment give lowirritation index and categorized as *negigible*.

ACKNOWLEDGMENT

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