THE INFLUENCE OF VARIATION OF HYDROXYPROPYL METHYLCELLULOSE AND TWEEN 80 CONCENTRATIONS ON PHYSICAL CHARACTERISTICS AND PHYSICAL STABILITIES GEL OF WATER DRY EXTRACT OF TEMULAWAK

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ABSTRACT

Objective: Water extract of temulawak (Curcuma xanthorrhiza Roxb.) contains curcumin, which known has antibacterial, antiinflammation, and antinginal activity so that it has potential used as wound healing. The purpose of this study was formulating gel of water extract of temulawak made by variation of hydroxypropyl methylcellulose (HPMC) and tween 80 concentrations and investigating the influence of formulations on physical characteristics and physical stabilities gel.

Methods: Gel was made by variation of HPMC and tween 80 concentrations (3.00%: 1.00%; 5.00%: 1.00%; 3.00%: 2.00%; 5.00%; 2.00%). Gel preparations were evaluated the physical characteristics by organoleptic test, homogeneity test, pH, viscosity, spreadability, adhesiveness, and stability. The physical properties were analyzed by software Design Expert 9.

Results: The results showed that HPMC has dominant influence on viscosity, spreadability, and adhesiveness. HPMC and tween 80 have not influence on organoleptic, homogeneity, and pH of the gel. Optimum formula is HPMC 5.00% and tween 80 1.00%. Optimum formula is stable on organoleptic, homogeneity, pH, viscosity, and adhesiveness; however spreadability of gel is not stable during 3 mo storage.

Conclusion: Variation of HPMC and tween 80 concentrations influenced viscosity, spreadability, and adhesiveness, while they were not influence on organoleptic, homogeneity, and pH of gel. HPMC had dominant influence on viscosity, spreadability, and adhesiveness gel.

Keywords: Gel, Temulawak, Hydroxypropyl methylcellulose, Tween 80

INTRODUCTION

Wound is damaged skin tissue which needed protection. Staphylococcus aureus bacteria that often founded in wounded skin tissue. Infected burns have bacteria such as S. aureus, P. aeruginosa, and E. coli [1, 2]. Candida sp. is fungi that colonizes in burns [3]. Dried water extract of temulawak is a natural ingredient and contains curcumin, which has antibacterial and antifungal activity [4, 5] so it has potential as a wound medicine. Gel dosage form can facilitate the use of temulawak dried water extract as a wound medicine. Gel can retain and create a moist environment around the wound, which can accelerate wound healing [6].

In-gel preparations, it is necessary to choose the right gel base to obtain the expected gel properties. Temulawak dried water extract contains curcumin compounds which are unstable at alkaline pH, so that it requires a gel base that can maintain the pH of curcumin to remain stable. Hydroxypropyl methylcellulose (HPMC) is a gel base that can produce a neutral, clear, and stable gel at pH 3-11 so it is suitable as a base gel for maintaining pH of curcumin. Furthermore, HPMC provides a good film layer strength when it dries on the skin [7]. Dried water extract of temulawak is insoluble in water, so it is necessary to add surfactant to help them soluble in water. Surfactant has the ability as a wetting agent and solubilization of compounds in micelles from surfactants so that it can increase the solubility of compounds in water. Tween 80 is a surfactant used in formulas and is safe to use on the skin [8].

In this research, gel preparations were made from temulawak dried water extract using various concentrations of HPMC and tween 80, then the effect of variation of concentrations was observed on the physical properties of the gel. The gel was made using the Factorial Design approach and the results of the physical properties of the gel were optimized with Design Expert 9. Physical stability testing with centrifugation was carried out on all four formulas, while the accelerated physical stability test was carried out for 3 mo on the optimum formula.

MATERIALS AND METHODS

Materials

Powder of Temulawak dried water extract (PT Phytochemindo Reksa), Methocel K15M (Colorcon), tween 80 (PT Bratchem), metil paraben (PT Bratchem), aquadest (CV Genera Labora), and sweet orange essence (Tekun Jaya). All chemicals were purchased from Indonesia.

Methods

Specification of dried water extract of temulawak

Temulawak dried water extract was obtained from PT. Phytochemindo Reksa with specifications as listed in table 1.

Preparation of gel

Gel formulas can be seen in table 2. Gel was made by dispersion method: Aquadest was heated into 70 °C. HPMC was put into some hot distilled water, stirred until dissolved. Methylparaben was dissolved in a number of hot water and then put into the HPMC solution. Temulawak dried water extract was mixed with tween 80 and put some water into the extract-tween 80 mixture until dissolved, then the extract-tween 80 extracts were added to the HPMC solution. The mixture was stirred until homogeneous. Next, it was filled into a pot gel to be evaluated.
Table 1: Specifications of dried water extract of temulawak

| Item                      | Formula 1 | Formula a | Formula b | Formula ab |
|---------------------------|-----------|-----------|-----------|------------|
| Extract                   | 0.40      | 0.40      | 0.40      | 0.40       |
| Tween 80                  | 1.00      | 1.00      | 2.00      | 2.00       |
| HPMC                      | 3.00      | 5.00      | 3.00      | 5.00       |
| Metil Paraben             | 0.10      | 0.10      | 0.10      | 0.10       |
| Sweet Orange Essence      | 0.03      | 0.03      | 0.03      | 0.03       |
| Aquades ad                | 100,00    | 100,00    | 100,00    | 100,00     |

Table 2: Formula of temulawak dried water extract gel

| Materials (%b/v) | Formula 1 | Formula a | Formula b | Formula ab |
|------------------|-----------|-----------|-----------|------------|
| Physical stability using centrifugation test
A total of 2 g of gel was inserted into the conical, centrifuged at a speed of 3750 rpm for 5 h and observed the phase separation that occurred.

Optimum formula determination
The result data on the physical properties of gel were analyzed using Design Expert 9 software to determine the optimum composition of HPMC and Tween 80.

Optimum formula verification
The result data on the physical properties of the optimum formula that had been made was compared with the data predicted by Design Expert 9 software with a 95% confidence level.

Accelerated physical stability test of optimum formula
The gels were stored with a temperature of 40 °C±2 °C/75% RH±5% RH for 3 mo and the physical properties of the gel were observed.

Data analysis
Data on gel physical properties were analyzed by Design Expert 9 to obtain the optimum formula. The optimum formula verification was conducted by comparing the data on the optimum physical properties of the experiment with the prediction of Design Expert 9 software. Data were analyzed for their normality with Saphiro-Wilk. Data that were not normally distributed were analyzed by one-sample t-test.

RESULTS
The test results of the physical properties of the gel can be seen in table 3. The contour plot of gel physical properties shown in fig. 1. The magnitude of the influence of each factor can be seen in table 4.
Fig. 1: Contour Plot a) Viscosity b) Spreadability c) Adhesiveness

Table 4: Data analysis on physical properties of temulawak dried water extract gel

| Effect          | Viscosity | Spreadability | Adhesiveness |
|-----------------|-----------|---------------|--------------|
| Tween 80        | -47.83    | 24.65         | -0.23        |
| HPMC            | 84.50     | -25.68        | 0.29         |
| Tween 80 and HPMC| -18.83 | -1.02         | -0.030       |

Response equation were below this:

Viscosity

\[ Y = 71.08 - 23.92(A) + 42.25(B) - 9.42(A)(B) \ldots (1) \]

Spreadability

\[ Y = 57.42 + 12.33(A) - 12.84(B) - 0.51(A)(B) \ldots \ldots (2) \]

Adhesiveness

\[ Y = 0.78 - 0.12(A) + 0.14(B) - 0.015(A)(B) \ldots \ldots (3) \]

Reference: (A) = Tween 80 (B) = HPMC

Physical Stability of formula a and formula ab were stable after centrifugation. The criteria for determining the optimum formula can be seen in table 5. The results of the analysis using Design Expert 9 selected the highest desirability which was 0.841. The optimum desirability formula graph can be seen in fig. 2.

Table 5: Criteria determination of optimum formula

| Response      | Goal        | Lower       | Upper       |
|---------------|-------------|-------------|-------------|
| Spreadability | In range    | 28.733      | 38.465      |
| Adhesiveness  | Maximize    | 0.47        | 1.16        |
| Viscosity     | In range    | 80.00       | 150.00      |

Fig. 2: Desirability graph of temulawak dried water extract optimum gel formula

Table 6: Comparison data of the prediction value and the actual value of the optimum formula
| Response      | Prediction | Actual  | t-test | Sig (2 tailed) | Conclusion              |
|---------------|------------|---------|--------|----------------|-------------------------|
| Spreadability | 32.77      | 30.51   | -3.194 | 0.086          | Different not significantly |
| Adhesiveness  | 1.05       | 1.23    | 1.244  | 0.339          | Different not significantly |
| Viscosity     | 146.67     | 150.00  | 0.577  | 0.622          | Different not significantly |

The optimum formula chosen consisted of tween 80 at 1.00% and HPMC at 5.00%. The verification results in table 6 showed that the results of the gel physical properties is not significantly different from Design Expert 9 predictions. The physical stability test of the optimum gel formula can be seen in fig. 3.

**DISCUSSION**

The values of viscosity, spreadability, and adhesiveness vary from the four formulas indicating variations in the concentrations of HPMC and tween 80 affect the physical properties of the gel. The four gel formulas had almost the same organoleptic properties, which were yellow, orange-scented (given orange essence), gel-formed, and homogeneous. This shows that the variation of HPMC and tween 80 concentrations do not affect organoleptic properties and gel homogeneity.

The four gel formulas had a pH of 5 and were within the ideal pH range of the skin. This shows that the variation of HPMC and tween 80 concentrations does not affect the pH of the gel. HPMC is a nonionic polymer that cannot interact electrostatically with positive or negative charges in the gel formula [9], while tween 80 is also a nonionic surfactant that does not change the pH of the gel [10].

Gel viscosity is an important characteristic that determines the resistance of the flow of the gel formula so that the gel can spread well on the surface of the skin. The higher the viscosity of the gel, the longer the retention time of gel at the site of action. Tween 80 and the interaction between tween 80 and HPMC produced negative effect values on gel viscosity. This shows that the increase in the concentration of tween 80 in the formula will reduce gel viscosity. Tween 80 is a surfactant that has the ability to bind hydrophilic groups from water resulting in a decrease in interface tension of water phase so that causing a decrease in viscosity [11]. HPMC has the greatest effect value compared to the tween 80 effect and the interaction of both. This means that HPMC has a dominant effect in influencing gel viscosity.

The contour plot of gel viscosity in fig. 1 (a) shows that tween 80 affects the decrease in viscosity shown in the blue gradation area. The addition of HPMC resulted in an increase in viscosity which showed a change in color gradation from blue to bright green. The effect of HPMC is the greatest on gel viscosity. This is because gel viscosity is affected by the concentration of the polymer gelling agent. Increasing the concentration of the gelling agent will further strengthen the gel polymer network so that it can increase viscosity [12]. Hydrophilic polymers such as HPMC have the ability to increase the viscosity of the solution at low concentrations, to expand and absorb the surface. Polymers such as methylcellulose have at least 3 or 4 ether groups and 1 or 2 hydroxyl groups which can be widely hydrated by water. The oxygen ether has two free electron pairs which can bind two water molecules through hydrogen bonds. The result of increasing the size of the unit will increase resistance to flow or solution viscosity [13].

Spreadability of gel is an important characteristic for delivering the right dose to the target site, ease of applying it to the skin, and consumer acceptance. The higher the spreadability, the wider the contact gel above the skin surface. HPMC and the interaction of tween 80 and HPMC produced negative effects on spreadability. The increase in the HPMC concentration in the formula will reduce the spreadability of gel. HPMC has the greatest effect value compared to the tween 80 effect and the interaction of both. This shows that HPMC has a dominant effect in influencing the spread of gel.

The contour plot in fig. 1(b) shows that the greater the concentration of tween 80 will increase the spreadability shown in orange gradations. The addition of HPMC resulted in a decrease in spreadability indicated by changes color gradations from bright blue to dark blue. The effect of HPMC is the greatest on the spreadability of gel. This is because HPMC can increase gel viscosity associated with spreadability. The increasing viscosity, the resistance of fluid to flow is decreased, so that spreadability will decrease [14].
All the authors have contributed equally.

**CONFLICT OF INTERESTS**

Declare none

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