INTRODUCTION

Aspirin is a nonsteroidal anti-inflammatory drug that is efficient as an antplatelet because it can inhibit the activity of the enzyme cyclooxygenase in platelets. Orally administered aspirin has side effects such as the risk of gastrointestinal bleeding and has predisystemic metabolism in the gastrointestinal tract and liver. Transdermal delivery offers an alternative for administering aspirin that by passes the gut and this may be more convenient and safe for long-term use. This study used a form of microemulsion to prevent hydrolysis of aspirin because it contains a high concentration of the surfactant. A microemulsion is a dosage form that can penetrate into the skin for transdermal delivery.

The surfactants used in this study were Tween 80. Surfactants help in forming oil-in-water microemulsions with a cosurfactant, which improves the solubilization. Short to medium chain length alcohols (C3-C8) are commonly added as cosurfactants, which further reduce the interfacial tension and fluidity of the interface. This study used propylene glycol as the cosurfactant. The aim of this study was to investigate the effect of Tween 80 and propylene glycol as a surfactant and cosurfactant on the physical properties of aspirin microemulsions.

MATERIALS AND METHODS

Materials

Aspirin was purchased from of Yixing City, Xingyu. Virgin coconut oil was purchased from LIPi Glibinong, Bogor. Tween 80 was purchased from PT. KAO Chemical. Propylene glycol was purchased from PT. Dow Chemical Pacific. Methylparaben and Propylparaben were purchased from PT. Garian.

Pseudoternary phase diagram construction

For preparing the microemulsion first, preliminary experiments were first carried out using pseudoternary phase diagrams. In the preliminary experiments, the microemulsion formula was optimized with virgin coconut oil as the oil phase, a combination of Tween 80 and propylene glycol (2:1) as the surfactant and cosurfactant, and distilled water as the aqueous phase.

Preparation of aspirin microemulsions

Various microemulsions were chosen from the pseudoternary phase diagrams. The concentration of virgin coconut oil was 5%, and combination (54%, 57%, 60%, and 63%) of Tween 80, and propylene glycol (2:1) concentrations were used. Aspirin was dispersed in the virgin coconut oil as the oil phase and then added to a mixture of distilled water and Tween 80. Then, propylene glycol was added to form a clear and homogeneous mixture (Table 1).

Organoleptic

Organoleptic includes observation of the shape, clarity, and smell. Observations were carried out for 6 weeks, on weeks 0, 3, and 6.

Keywords: Aspirin, Transdermal, Microemulsions, Tween 80.

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Determination of pH

pH measurement was performed using a pH meter, and observations were carried out for 6 weeks, on weeks 0, 3, and 6, at room temperature [4].

Density measurement

Density was measured using a pycnometer. Observations were carried out for 6 weeks, on weeks 0, 3, and 6.

Viscosity measurement

Measurements were carried out using a Brookfield viscometer LVDV-E with spindle number 3 at a speed of 30 rpm for 6 weeks, on weeks 0, 3, and 6.

Particle size measurements

The particle size was measured using a nanoparticle size analyzer. The solution was placed in a cuvette that was inserted into the sample holder.

Surface tension measurement

This measurement was carried out for 6 weeks, every week to 0, 3, and 6 at room temperature. The surface tension was measured using a tensiometer with Du Noüy method [5].

Phase separation

The aspirin microemulsions were centrifuged at 3750 rpm for 5 hrs at room temperature, and then, the phase changes were observed. The aspirin microemulsions were also subjected to a freeze-thaw test at 4°C and 45°C to observe the phase separation that occurs.

Data analysis

The data were statistically tested included with two-way analysis of variance (ANOVA) with a 95% confidence level, to determine significant differences between the formula test results.

RESULTS AND DISCUSSION

Preparation of aspirin microemulsions

The results showed that the formula produces a clear microemulsion is virgin coconut oil (5%) as the oil phase, a combination of Tween 80 and propylene glycol as the surfactant and cosurfactant (2:1) (54%, 57%, 60%, and 63%), and distilled water up to 100%. The microemulsion could be held steady during the observation time of 1 week.

Organoleptic

Based on organoleptic observations for 6 weeks, only the F1 formula was physically opaque since the 1st week. In contrast, the formulas F2, F3, and F4 showed no change, indicating that these three formulas have good stability during storage (Table 2).

Density measurement

The 6 weeks observations revealed that a higher surfactant concentration leads to a higher density (Fig. 1). Further, with a higher surfactant concentration, the solubilization process will increase owing to the increase in the micellar concentration [3]. This makes the microemulsions clear, with smaller particles, so that the density increases.

Determination of pH

Results of pH measurement for 6 weeks showed a decrease in pH during storage (Fig. 2). A higher surfactant concentration led to higher pH of the microemulsions. This probably because the formation of micelles with higher surfactant concentration also increased, and thus, more of the aspirin can be protected in the micelles and hydrolysis can be decreased. In contrast, for F1 and F2 with a smaller concentration of surfactant, much of the aspirin was hydrolyzed to salicylic acid and acetic acid, thus decreasing the pH of the microemulsions.

Surface tension measurement

The measurement results showed that with increasing surfactant and cosurfactant concentrations, the surface tension is lower (Fig. 3). Theoretically, increases in the surfactant concentration will cause a decrease in the surface tension [6]. From the graph, we can see that the formula F3 tends to be more stable than the other formulas.
The results show that the F3 formula particles had an average diameter of 49.46±6.91 nm. This is proved that the F3 aspirin microemulsion met the particle size requirements. However, more research is needed on the pH of the aspirin microemulsions, to obtain the ideal pH preparations. It is also necessary to test the physical and chemical stability of the aspirin microemulsion.

**CONCLUSION**

The results of this research indicated that the optimal concentration of Tween 80 as a surfactant and propylene glycol as a cosurfactant (2:1) is 60%. This microemulsion formula exhibited a pH value of 3.74±0.30, average of 1198.76±56.02 cps, BJ of 1.0669±0.005 g/mL, surface tension of 38.77±0.43 dyne/cm, and particle size of 49.46±6.91 nm.

**REFERENCES**