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Influence of Emollient on The Penetration and The Stability of Sodium Ascorbyl Phosphate Cream

Yanni Dhiani Mardhiani, Deny Puriyani Azhari, Silviana Wulansari

Research Group of Pharmaceutics, Bandung School of Pharmacy,
Bandung, West Java, 40266, Indonesia

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ABSTRACT

Sodium ascorbyl phosphate (SAP) often used in topical formulation due to its more stable properties than ascorbic acid. However, it is difficult to deliver SAP into the dermis in a sufficient dose. To overcome the problem, occasionally we can add a penetration enhancer. In some literature, emollients that often added in cosmetic preparations also have another effect as a penetration enhancer. The purpose of this research was to observe whether emollient addition could influence the penetration of SAP in the cream formulation. SAP was formulated into four formulations with three different emollients: dimethicone (F1), capric triglyceride (F2), isopropyl myristate (F3) and a formulation without emollient addition (F4). The diffusion test was performed using male wistar rat's abdominal membrane as a standard model of the skin barrier. The result of stability test showed that SAP cream was stable at room temperature but unstable on freeze thaw condition described by significant different values for all formulas. Nonetheless, the diffusion test showed that F2 had the highest ability to pass SAP through the membrane, followed by F3 and F1. We concluded that emollient addition could influence the penetration of the SAP cream.

Keywords: vitamin c, ascorbic acid, sodium ascorbyl phospate, emollient, penetration enhancer

1. Introduction

In cream preparations, vitamin C is an active ingredient that very unstable because it is easily oxidized [1], in the presence of light, water, and air that can decompose vitamin C in the form of L-ascorbic acid into L-dehydroascorbat (DHA) and then changed to L-gluconic acid and oxalate as non active ingredient [1, 2]. To overcome this stability problem, it is often used ascorbic acid derivative, namely SAP, magnesium ascorbyl phosphate, ascorbyl palmitate, ascorbyl glucoside, and calcium ascorbyl as more stable form of vitamin C [3]. However it is difficult to deliver SAP into the dermis in the optimum dosage. To overcome the problem, occasionally we can add penetration enhancer [4]. Emollients usually was added in cream preparation as moisturizers when applied to the skin [5]. It can also act as penetration enhancers of the active substance [6]. The effect of increased penetration of active substance by emollients can be obtained from the modification of the type or number of emollients used, or their combination with emulsifiers [7]. The effect of increasing penetration of emollients can occur due to the hydration mechanism of the skin with occlusion and moisturizing effects, other mechanisms that may occur are increased solubility of active compounds in the stratum corneum and changes in the structure of intercellular lipids by changes in brick and mortar conformation in the stratum corneum [8, 9]. There is several categories of emollients [10], In this study, it was done by comparing the penetration ability by using three different emollients based on its chemical class i.e., Tegosoft M® (Isopropil Miristate) as polar emollient [11], Tegosoft CT® (Capric Triglycerides) as nonpolar natural oil [12], and Abil 350® (Dimeticon) as non polar skin conditioning agent.

*Corresponding author,
e-mail : yanni.dhiani@stfb.ac.id

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2. Method

The first stage of this study was optimization of cream base by varying the concentration of the emulgators then evaluated including organoleptic, pH, and viscosity. Base optimization was done by making 5 formulas with different emulgator concentrations, the emulgator used was Fancor uni-embase, in which already contains a combination of several emulgators that are formulated in such a way as to form a stable cream base. The fancor uni embasse concentration used was 17%, 19%, 21%, 23%, and 25% formulated with other excipients such as preservative DMDM hydantoin, and aquademin as solvents. The base was evaluated by simple stability test which it was stored for 7 days at room temperature, then compared statistically to determine the best formula [13].

After getting the best emulgator concentration, the next step is the cream formulation of SAP as we presented in table 1.

After the cream preparations were made, evaluation of the preparations included organoleptic, viscosity measurement, pH measurement, scattering power test and homogenity, emulsion type test, accelerated centrifugation test was done [14]. Stability evaluation was presented for 28 days at room temperature storage and Freeze and Thaw method. This test was carried out for 6 cycles in which 1 cycle consisted of storage at 40ºC for 48 hours then transferred to storage at 4ºC for 48 hours. Then evaluated by observing the organoleptic and measuring the pH value and viscosity as a parameter of stability of a preparation [15].

Penetration rate testing of active SAP contained in cream preparations using franz cell diffusion method. The membrane used was the skin of male Wistar mice. The test cream sample was weighed 1,0 g and flattened on the membrane. The media temperature was 37 ± 1ºC with a total volume of phosphate buffer pH 7,4 as 15 mL receptor fluid for 8 hours. Then the concentration of SAP was determined spectrophotometrically at a wavelength of 258 nm [16, 11].

3. Result

3.1 Cream base optimization

Based on the evaluation and statistical analysis of the cream base during 7 days simple stability test including organoleptic, viscosity, and pH, F1 with a 17% emulgator concentration was chosen as the cream base which was then used for the SAP cream formulation.

3.2 SAP cream evaluation

3.2.1. Organoleptic and homogeneity evaluation

Organoleptic and homogeneity evaluation of SAP cream was presented good appearance and homogeneity during 28 days storage at room temperature

3.2.2. Centrifugation Test

The observations of centrifuged tests showed that the cream of SAP from F1 to F4 is physically stable where phase separation does not occur.

3.2.3. Emulsion Type Test

Observations on all formulas with methylene blue method showed that the type of SAP cream in this study is oil in water.

3.2.4. Room temperature stability test

Organoleptically, based on pH, viscosity and dispersion test observation, there was no significant differences among all formula during 28 days.

The measurement pH results of all formulas can be seen in figure 1. The results of data analysis with the one way anova method showed that there were significant differences between viscosity to storage time in all formulas from day 1 to day 28. The measurement results of F1, F2, F3, and F4 viscosity can be seen in figure 2. The value of SAP cream spreadability can be seen in Figure 3.

3.2.5. Freeze and thaw stability test

Organoleptic examination performed every 1 cycle for 6 cycles of accelerated stability testing, including examination of color, odor, and cream dosage form. It showed discoloration in the 2nd cycle to the 6th cycle. pH evaluation of SAP cream at freeze thaw stability test can be seen in Figure 4. Viscosity evaluation of SAP cream at freeze thaw

stability test can be seen in Figure 5. Diffusion test of SAP cream can be seen in Figure 6.

Table 1. Formulation of SAP cream

Materials	Concentration (%)			
	F1	F2	F3	F4
SAP	1.5	1.5	1.5	1.5
DMDM Hydantoin	0.6	0.6	0.6	0.6
Na-Metabisulfite	0.1	0.1	0.1	0.1
Fancor uni embasse	17	17	17	17
Abil 350®	1.0	-	-	-
Tegosoft CT®	-	1.0	-	-
Tegosoft M®	-	-	1.0	-
Citric acid	0.5	0.5	0.5	0.5
Aquademineral	up to 100	up to 100	up to 100	up to 100

Note : Fancor uni embase: Cream base; Tegosoft M®: Isopropil Miristat; Tegosoft CT®: Capric Triglycerides; Abil 350®: Dimetikon

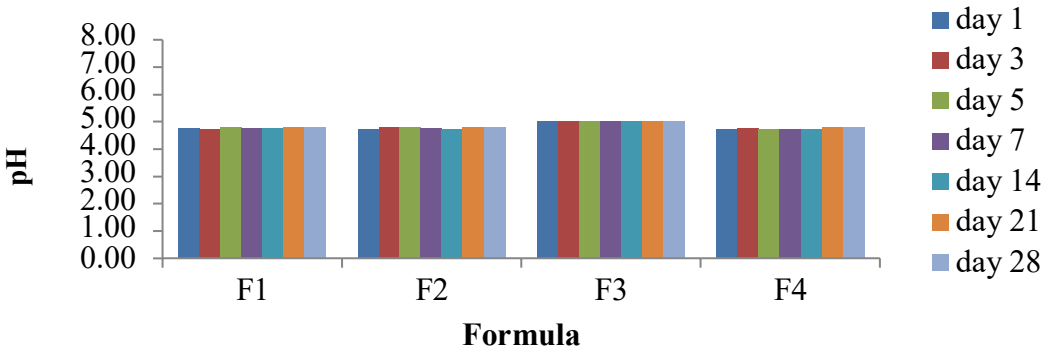

Figure 1. Graph of SAP cream pH in the room temperature stability test
Note: [F1: Abil 350®; F2: Tegosoft CT®; F3: Tegosoft M®; F4: no emollient]

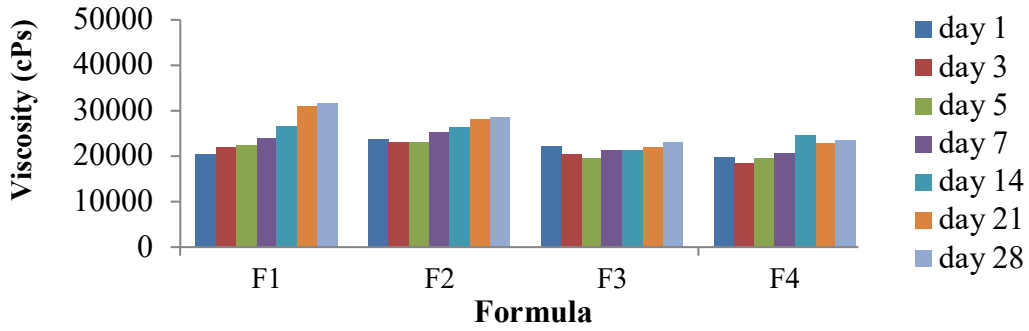

Figure 2. Graph of SAP cream viscosity at room temperature storage
Note: [F1: Abil 350®; F2: Tegosoft CT®; F3: Tegosoft M®; F4: no emollient]

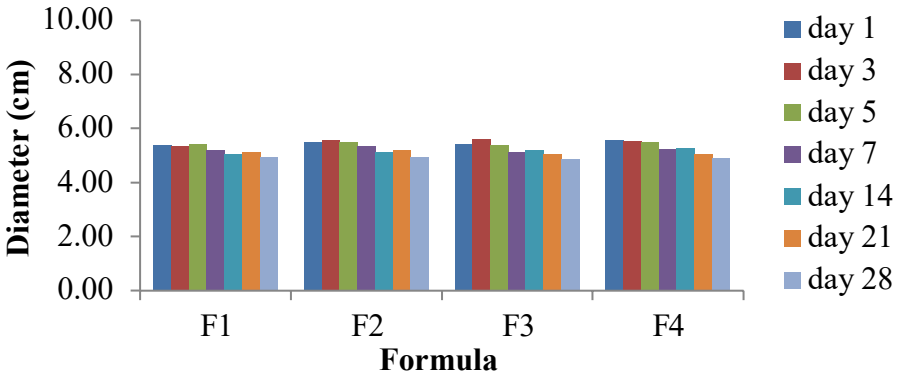

Figure 3. Graph of spreadability value at room temperature storage
Note: [F1: Abil 350®; F2: Tegosoft CT®; F3: Tegosoft M®; F4: no emollient]

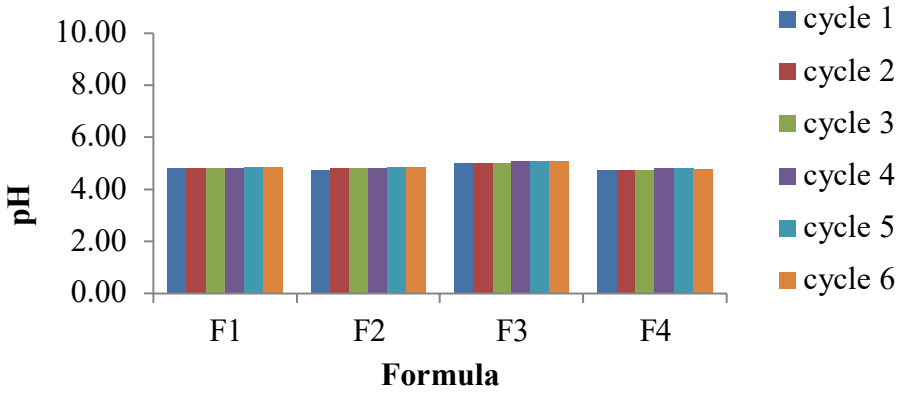

Figure 4. Graph of pH value at freeze thaw stability test
Note: [F1: Abil 350®; F2: Tegosoft CT®; F3: Tegosoft M®; F4: no emollient]

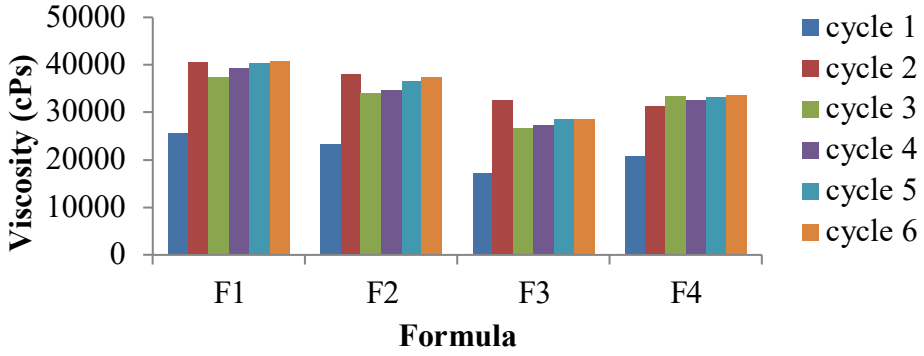

Figure 5. Graph of viscosity value at freeze thaw stability test
Note: [F1: Abil 350®; F2: Tegosoft CT®; F3: Tegosoft M®; F4: no emollient]

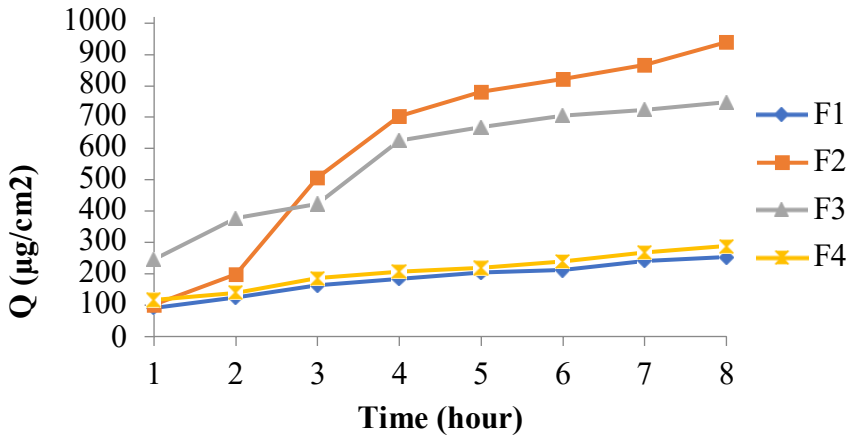

Figure 6. Graph of diffusion test of SAP cream
Note: [F1: Abil 350®; F2: Tegosoft CT®; F3: Tegosoft M®; F4: no emollient]

4. Discussion

From the result of organoleptic and homogeneity evaluation, SAP cream was presented good appearance and homogeneity during 28 days storage at room temperature, thus physically stable.

Based on the results of the data analysis of figure 1, the pH value of each formula on storage time during 28 days at room temperature using the one way Anova method, it was found that F1 and F3 had a significance value> 0.05, so there was no significant difference from pH values F1 and F3 during the day 1 to 28 days, while F2 and F4 there are significant differences (sig <0.05), so it can be concluded that F1 and F3 are stable in the storage period while F2 and F4 are unstable during the storage period. Meanwhile, there were significant differences between viscosity at the same condition in all formulas from day 1 to day 28. The measurement results can be seen in figure 2.

At figure 3, the value of the dispersibillity at room temperature is in the range of 4.7 - 5.7 cm. It was related to the influence of the viscosity value which it was inversely proportional to the viscosity. If there is an increasing in viscosity value, the dispersibillity value will be decreased from day 1 to 28. Spreadability values of all formulas have qualify the spreadability standard (in the range of 5-7 cm). One way anova analysis showed a significant difference in all formulas.

In the freeze thaw stability test, it showed discoloration in the 2nd cycle to the 6th cycle, this color change presennted oxidation of the active substance due to heating when the preparation was stored at 40ºC. Then in the 4th cycle the preparation becomes a scorched or rancid odor, this can happen because in the cream preparations contained ingredients such as emulsifiers and emollients which are oil or fat ingredients so that when stored at high temperatures will result in oxidation of the oil content which can cause rancidity.

At figure 4, the results of pH evaluation at freeze thaw test data analysis using One Way Anova showed a significant difference in all formulas (sig <0.05). It showed that all formulas are not stable in periods of storage with extreme temperatures based on pH values, this can be caused by the influence of media which are decomposed by high temperatures during the manufacturing or storage process that produces acidic or basic substances, so this can affect the pH value.

At figure 5, the graph showed that F1 had the most stable viscosity value. Based on one way anova analysis, presented that F1 has a significance value (sig > 0.05). The emulsion viscosity will decrease if the temperature is high, and will increase when the temperature is low. This is because the heat obtained will increase the distance between atoms so that the force between atoms will decrease, the distance becomes tenuous resulting in the viscosity of the cream decreasing. After the cream has cooled there will be a release of water to the cream, but if the emulsifying film can work again under ice-induced pressure before coalescence occurs then the emulsion system will

stabilize. Temperature can affect the viscosity where high temperatures can reduce viscosity, conversely low temperatures can increase viscosity [17].

The results of diffusion of sodium ascorbyl phosphate cream at figure 6 showed differences in the percentage of active substances that diffuse between F1, F2, F3, and F4. F1 and F4 tend to have a cumulative number of penetrated (Q) active substances that are almost the same, F3 has a high Q value and F2 reaches the highest Q value. This is related to the different types of emollients used in cream formulations, where F1 using dimethicon 1% produces the same Q value as F4 as a negative control that does not use emollients, indicating that in this study dimethicone has no potential to increase the penetration of active substances, whereas F3 using isopropyl myristate as emollient has a sufficiently high diffused cumulative value, indicating that in this study isopropyl myristate can increase the penetration of active substances, and F2 using capric triglycerides has the potential to increase the penetration of the active substance most compared to isopropyl myristate and dimethicone. This is related to the different polarity of the three types of emollients [8].

5. Conclusion

It could be concluded that cream formula which employ capric triglyceride as emollient had the highest ability to pass SAP through the membrane, followed by isopropyl miristate, and dimethicone. Therefore the addition of emollient could influence the penetration of the active substance in formulation.

Acknowledgement

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