Preparation and Evaluation of Sunscreens Nanoemulsions Containing Avobenzone and Octyl Methoxycinnamate

Anayanti Arianto[1], Hakim Bangun[1], Josephine Yauvira[1]
[1]*Department of Pharmaceutical Technology, Faculty of Pharmacy, Nanomedicine Centre, Universitas Sumatera Utara, Medan Indonesia*
anayantia@yahoo,com

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Abstract: The use of sunscreen for the purpose of effectively absorbing sunlight in order to prevent the occurrence of premature aging and skin cancer. Nanoemulsion is very effective to be applied as cosmetic preparation due to their characteristic properties of small droplet size with high surface area enables effective delivery of the active ingredients. It is transparent appearance and thermodynamically stable. The formulation of the nanoemulsions was prepared in various ratios of Tween 80 as a surfactant and ethanol as co-surfactant using avobenzone and octyl methoxycinnamate as sunscreen agent.The nanoemulsion was evaluated for particle size, centrifugation, stability during experiment for 12 weeks of storage at room temperature, pH, viscosity, and SPF value. Nanoemulsion in the ratio of tween 80 and ethanol (34:26) had the smallest average particle size of 163.31 nm with yellowish color, clear and transparent appearance, pH value (7.46 ± 0.00), viscosity value (75cP ± 25), did not show any separation or creaming in the centrifugation, stable during experiment for 12 weeks of storage at room temperature. The sunscreen nanoemulsion preparations containing avobenzone and octyl methoxycinamate with the ratio of Tween 80 and ethanol 34:26 contributed to give SPF value of 16.80 ± 0.08. This formulation could be considered efficient for sunscreen cosmetic use

1 INTRODUCTION

The skin is on the outer surface of the body so often exposed to sunlight. Every year, about a million people are diagnosed with skin cancer and about 10,000 die from malignant melanoma. In 2018, an estimated 9,320 deaths from melanoma will occur. The harmful effects of solar radiation caused by solar radiation consist of UVA rays from 320 to 400 nm, UVB from 290 to 320 nm and UVC of 200-290 nm. UVC radiation is filtered by the atmosphere before it reaches the earth. UVB radiation is not perfectly filtered by the ozone layer and is responsible for sunburn damage. UVA radiation reaches the deeper layers of the epidermis and dermis and causes premature aging of the skin. UV radiation is one of the leading causes of skin cancer (Dutra, et al. 2004; Mitsui, 1997; Parkin, et al. 2011).The formulation of sunscreen that is efficient, stable and can be marketed is a challenge. The stability of product appearance obtained during storage is a problem of efficacy and consumer safety (Lionetti and Rigano, 2017). Sunscreen products on the market mostly available in the form of lotions, gels, emulsions and creams. Nanoemulsion is very attractive to be applied in cosmetics (sunscreen products) because nanoemulsi has droplet size smaller than emulsion ie in nano size (20-500 nm) so it is more stable, can prevent creaming, sedimentation or coalescence, besides also increase solubility of an insoluble active ingredient in water.

Nanoemulsion is very useful to be applied in cosmetic because of it is more stable, with low viscosity, and transparent visual aspect, and a high surface area allows effective delivery of the active ingredient for the skin, thereby increasing the efficacy (SPF value) of the sunscreen product.(Rhein, 2007, Devarajan and Ravichandran, 2011). The Nanoemulsion is formed spontaneously, generally without high-energy input. This research uses chemical sunscreen, which is avobenzone as absorbent of UVA and octyl methoxycinnamate as UVB absorbent. The maximum concentration of avobenzone used is generally 3% and the concentration of octyl methoxycinnamate is 7.5% (Rieger, 2000).The aim of this study was to obtain nanoemulsion of avobenzone and octyl methoxycinnamate (OMC), and to evaluate their

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physical stability and in vitro sunscreen activity through Sun Protection Factor (SPF) determination by spectrophotometric methods. *in vitro* testing methods by spectrophotometric methods have been developed because they are more rapid, less expensive and above all because they prevent the involvement of human volunteers with the related ethical problems. The nanoemulsion in this study was made by low energy spontaneous emulsification method using 3% avobenzone and 7.5% octyl methoxycinnamate as sunscreen agent and Tween 80 as surfactants and ethanol as co-surfactant. Tween 80 is widely used as surfactant in the preparation of nanoemulsion. In addition to having a large HLB of 15, Tween 80 is stable against electrolytes, weak acids, and bases (Rowe et al., 2009). However, the use of Tween 80 singly is not enough to reduce surface tension to form nanoemulsion.Therefore, in the preparation of nanoemulsion, surfactants are often combined with cosurfactants.

2 MATERIALS AND METHODS

2.1 Materials

Avobenzone, octyl methoxcinnamate (India), Tween 80, ethanol 96%, paraffin liquid, propylene glycol were purchased from PT.Brataco (Medan, Indonesia). Methyl paraben, propyl paraben, butyl hydroxyl toluene and buffer pH solution purchased from CV Rudang (Medan Indonesia).

2.2 Preparation of Nanoemulsion

In the preparation of nanoemulsion, Tween 80 as surfactant combined with ethanol as cosurfactant. The ratio of surfactant (Tween 80) and co surfactant (ethanol) mixtures in nanoemulsion formulation as shown in Table 1. The nanoemulsions were prepared according the spontaneous emulsification method (Cinar, 2017), where the oil phase (avobenzone dissolved in ethanol, octyl methoxycinnamate, butyl hidroxyl toluene, paraffin liquid) were mixed with water phase (Tween 80, methyl paraben and propyl paraben dissolved in hot distilled water, propylene glycol) and stirred,then add with deonized water to provide 3% w/w paraffin liquid in final nanoemulsion and then stirred gently at 3000 rpm (magnetic stirrer HI 190 M) for 4 hours until a clear nanoemulsion was produced. Then the nanoemulsion preparation was sonicated for 1 hour (Ultrasonic Cleaner 1510 E-MT)) until a transparent nanoemulsion was produced.

Table 1: Composisiton of nanoemulsions

Ingredients	F1	F2	F3
Avobenzone	3	3	3
OMC	7.5	7.5	7.5
Tween 80	34	36	38
Ethanol 96%	26	24	22
Paraffin liquid	3	3	3
Propylene glycol	5	5	5
Methyl Paraben	0.3	0.3	0.3
Propyl Paraben	0.6	0.6	0.6
BHT	0.1	0.1	0.1
Distilled water	20.5 mL	20.5 mL	20.5 mL

2.3 Physical Stability Assessment

Prepared formulations were subjected to centrifugation at 3750 rpm for 5 hours and were observed for phase separation. (Lachman, et al., 1994). The stability studies were performed by keeping the selected formulation of nanoemulsion at room temperature (25±2^{o}C) for a period of 3 months. The viscosity, and pH were determined at 0, 1, 2, and 3 months (Alam, S M et al. 2015).

2.4 Determination of SPF Value

The SPF value is calculated using the Mansur equation. The sample absorption spectrum was obtained by using a UV-Vis spectrophotometer at 290-400 nm wavelength with 96% alcohol as blank, the absorption value recorded per 5 nm interval wavelength 290-320 nm and 10 nm interval wavelength 320-400 nm. The value of absorption obtained was multiplied by erythemal effects spectrum (EE) x I for each interval. The value of EE x I per interval could be seen in Table 2. The amount of EE x I obtained multiplied with the final correction factor, then the SPF value of the tested sample would be obtained. The value of EE x I and correction factor is a constant where the value of EE x I from the wavelength 290-320 nm and every 5 nm difference and the correction factor 10 has been determined by (Sayre, 1979),

$$SPF = CF \sum_{290}^{320} EE(\lambda) \times I(\lambda) \times Abs(\lambda)$$

CF = Correction factor
EE = Erythemal Effect Spectrum
I = Solar Intensity Spectrum
Abs = Sample absorption

Table 2. Correlation between the erythemogenic effect (EE) and the radiation intensity at each wavelength (I) (Mansyur et al. 1986).

Wavelength (nm)	EE x I
290	0.0150
295	0.0817
300	0.2874
305	0.3278
310	0.1864
315	0.0839
320	0.0180
Total	1

The value of EE x I and correction factor is a constant where the value of EE x I from the wavelength 290-320 nm and every 5 nm difference and the correction factor 10 has been determined by (Sayre, 1979).

2.5 Determination of Nanoemulsion Droplet Size

The mean droplet size of the nanoemulsion was determined by Vasco$^{\gamma}$ CORDOUAN Technologies *Particle Size Analyzer* Measurements were performed at room temperature.

2.6 pH Determination

The pH of the formulation was measured using a digital pH meter (Hanna Instrument). One g of nanoemulsion was dissolved in 100 ml distilled water. The measurement of pH of each formulation

2.7 Viscosity Measurement

The Viscosity of nanoemulsion was measured by using Brookfield DV-E viscometer. The sample was filled in a beaker and the viscosity was measured by using Spindle number S62.

3 RESULT AND DISCUSSION

The result of all formulations showed a light yellow, clear, and transparent nanoemulsion as shown in Figure 1. One characteristic of nanoemulsions is a bluish brightness and translucent aspect, whereas macro emulsions display milky appearance (Mason *et al.*, 2006) The preparations of nanoemulsion by spontaneous emulsification method. This method can produce nanoemulsions at room temperatures and no special devices are required. When an oil phase with a water soluble substance is mixed with water, oil droplets spontaneously forms. The mechanism depends on the movement of water dispersible substance from the oil phase to the water phase. This leads to interfacial turbulence and thus formation of spontaneous oil droplets. The nanoemulsions stable during experiment for 12 weeks of storage at room temperature (Figure 2).

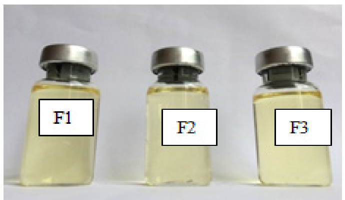


Figure 1: Appearance of the prepared sunscreen nanoemulsion (F1, F2, F3) containing avobenzone and octyl methoxycinnamate.

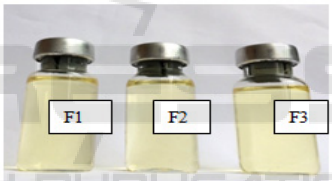
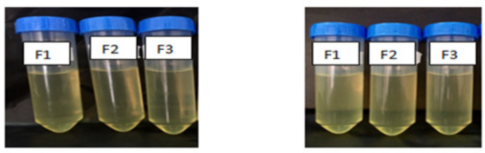


Figure 2: Appearance of the prepared sunscreen nanoemulsion (F1, F2, F3) containing avobenzone and octyl methoxycinnamate after storage for 12 weeks at room temperature

The centrifugation test was performed to determine the stability of nanoemulsion. The centrifugation test describes the stability of the preparation because of the effect of gravitational force equivalent to one year of storage. All of the nanoemulsions (Figure 3) were stable, did not show any a phase separation or creaming.



Before centrifugation   After centrifugation

Figure 3: Appearance of the prepared sunscreen nanoemulsion (F1, F2, and F3) containing avobenzone and octyl methoxycinnamate before and after centrifugation

Table 2: Globule size and globule size distribution distribution of different nanoemulsion samples during storage for 12 weeks at room temperature.

Formula	Ratio of Tween 80 and ethanol	Time (week)	Globule size distribution (nm)	Globule size (nm)
F1	34/260	0	93.35-269.22	163.31
		6	67.63-446.80	196.28
		12	67.63-467.86	202.97
F2	36/240	0	77.65-537.17	230.73
		6	89.15-589.00	255.41
		12	102.36-616.76	279.62
F3	38/220	0	81.30-537.17	232.57
		6	97.75-513.00	246.79
		12	117.52-616.76	291.78

The results of the globule size determination show the nanoemulsion (F1) that used the lowest surfactant concentration with ratio of surfactant Tween 80 and co-surfactant ethanol 34:26 was the smallest globule size and was increased during storage for 12 weeks at room temperature. (Table 2). The results of viscosity and pH measurements of nanoemulsion containing avobenzone and octyl methoxycinnamate during experiment for 12 weeks of storage at different temperature as shown in Table 3. The viscosity of nanoemulsion was increased during 12 weeks of storage and with the decrease in temperature the viscosity will increase and the preparations become more viscous. The pH of nanoemulsion was decreased during 12 weeks of storage and with increasing storage temperature (Table 3.).

Table 3: Viscosity and pH of nanoemulsion (F1) during storage for 12 weeks at different temperature

Time (week)	Temp (°C)	Viscosity (cP) (± SD)	pH (± SD)
0	4.0 ± 2.0	75 ± 25.00	7.46 ± 0.00
4	4.0 ± 2.0	875 ± 12.50	7.23 ± 0.11
8	4.0 ± 2.0	1100 ± 25.00	7.00 ± 0.06
12	4.0 ± 2.0	1750 ± 0.00	6.60 ± 0.10
0	25 ± 2.0	75 ± 12.50	7.50 ± 0.06
4	25 ± 2.0	100 ± 12.50	7.10 ± 0.06
8	25 ± 2.0	175 ± 0.00	6.90 ± 0.10
12	25 ± 2.0	188 ± 0.00	6.60 ± 0.00
0	40 ± 2.0	75 ± 0.00	7.46 ± 0.06
4	40 ± 2.0	88 ± 0.00	6.93 ± 0.10
8	40 ± 2.0	138 ± 25.00	6.60 ± 0.10
12	40 ± 2.0	163 ± 12.50	6.40 ± 0.06

n = 3

From the experimental results, the nanoemulsion F1 that used the lowest surfactant concentration and the small globule droplet size, while still maintaining stability, centrifugal stability that selected for further in vitro SPF value determination. Based on the result that the SPF values resulted from the sunscreen nanoemulsion F1 containing avobenzone and octyl methoxycinnamate was 16.80 ± 0.08. This sunscreen nanoemulsion preparation already has sun protection activity in medium protection level (Lionetti and Rigano, 2017).

4 CONCLUSION

The sunscreen nanoemulsion preparations containing avobenzone and octyl methoxycinnamate are physically stable during experiment for 12 weeks of storage at room temperature and characterized by the absence of discoloration, creaming, or phase and contributed to give SPF value of 16,80. This formulation could be considered efficient for sunscreen cosmetic use.

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