Influenced of Kojic Acid and B-Cyclodextrin on SPF Value Sunscreen Product Contained Oxybenzone and Octyl Dimetyl Paba (3:7) (In vanishing cream base formulation)

by Widji Soeratri

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Abstrack

The aim of this study was to investigate the SPF value of sunscreen product contained oxybenzone and octyl dimetyl PABA (3:7) with the addition of kojic acid 1% w/wr as whitening agent and their complex with β-cyclodextrin in 1:1 molar equivalent. The SPF value was determined by Petro correlation for *in vitro* method. The result Showed that the addition of kojic acid increased the SPF value of sunscreen product from 10,607 ± 0,432 became 11,741 ± 0,479. A different result showed with the addition of complex form of kojic acid with β-cyclodextrin. The SPF value decreased to 9,113 ± 0,295. The complex formation of the sunscreen agent with β-cyclodextrin was suspected to be responsible for this phenomenon. Moreover, it was suggested to make *in vivo* correlation with the result of this study.

Key words : oxybenzon, octyl dimetyl PABA, kojic acid, β-cyclodextrin, SPF, vanishing cream

Introduction

Sunscreen agents are commonly present in whitening products to compensate for the photosensitivity effect caused by the whitening agent. This combination is more efficient but may have a profound effect on the efficacy of the UV filter.

UV filters are generally aromatic compounds conjugated with an electron receiving group or conjugated with a double bond and an electron-releasing group that is substituted in the ortho or para position of the aromatic ring. Chemicals of this configuration absorb the harmful short-wave (high-energy) UV rays (200 - 400 nm) and convert the remaining energy into innocuous longer wave (lower energy) radiation (>400 nm) (Shaath, 2005). The energy absorbed from the UV radiation corresponds to the energy required to cause a photochemical excitation in sunscreen molecule. Thus, cosmetic vehicles, such as pH, λ_{max}, and extinction coefficient (ε), which affect the electron delocalization, have a direct influence to the SPF (Shaath, 1986).

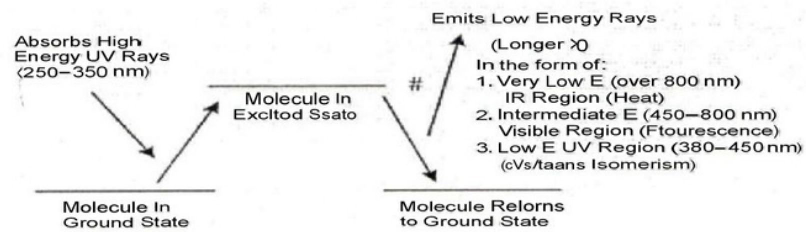


Fig 1. Schematic representation of the process in which a sunscreen chemical absorbs ultraviolet radiation (Shaath, 2005)

Octyldimetyl PABA and oxybenzone are one of kind UV filter that worked with the mechanism above (Shaath, 2005). They absorb UV rays and combined to provide wide range protection from UVA and UVB spectrum. Since they are influenced by the vehicle, their combination with whitening agent may impact their efficacy to protect the skin from harmful UV radiation (Widianingsih and lumintang, 2002).

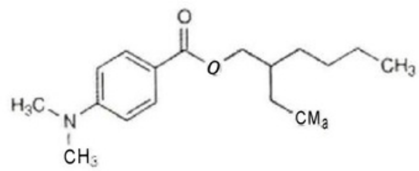


Fig 2. Octyldimetyl PABA (Sweetman, 2007)

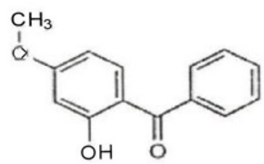
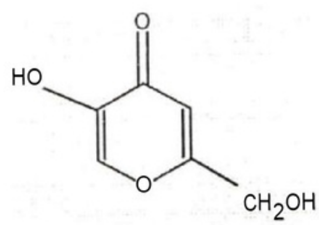


Fig 3. Oxybenzone (Sweetman, 2007)



MW: 142.1
MP: 153-154ºC
pKa: 7.90-8.
Log P (octanol-water): -0,64

Fig 4. Properties of Kojic Acid 5-hidroksi-2-hidroksimetil-4-pyron

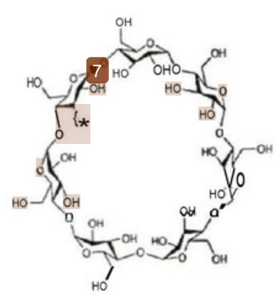


Fig 5. β-cyclodextrin (Sweetman, 2007)

Whitening agent that used in this experiment was kojic acid. Kojic acid is produced mainly by microbial fermentation using aspergillus and penicillium spp. In *in vivo* test, cream containing kojic acid compounds have been reported as effective in preventing pigmentation changes in human skin due to exposure to UVA and UVB. This inhibition has been shown to be due to chelation of Cu, a prosthetic group in tyrosinase (Barel *et all,* 2001).

Cream contained 1 % of kojic acid showed steady but slow whitening effect. 14C-labeled kojic acid cream was observed to be quickly absorbed from the skin to the liver, intestines, and kidneys in mice. When the absorption was thus quick, the depigmentation agent did not stay at the epidermis where it had its target organ, melanocytes, for a long enough time to inhibit melanogenesis. Therefore, kojic acid was mixed with β-cyclodextrin to slow the absorption into the dermis (Eisner and Maibach, 2005).

Cyclodextrins are cyclic oligosaccharides with a hydrophilic outer surface and a somewhat hydrophobic central cavity. Cyclodextrins are able to form inclusion complexes with many drugs by taking up the drug molecule, or a lipophilic moiety of the molecule, into the cavity (Loftsson and O'Fee, 2003).

Cyclodextrins can both enhance and hamper drug delivery through artificial and biological membranes. The composition of the drug formulation and the physicochemical and physiological composition of the membrane will determine what kind of effect obtained. Cyclodextrins will enhance drug delivery through a diffusion-controlled barrier but will hamper delivery through a lipophilic membrane-controlled barrier. It will either hamper or enhance drug delivery through porous membranes depending on the relative pore size compared with the effective diameter of the drug/cyclodextrin complex (Loftsson and O'Fee, 2003).

Alteration of SPF value is undesirable. Therefore, this study was aimed to investigate the SPF value of sunscreen product contained oxybenzone and octyl dimetyl PABA (3:7) with the addition of kojic acid 1% $^{b}/_{b}$ as whitening agent and their complex with β-cyclodextrin in 1:1 molar equivalent. Investigation was made in vanishing cream base preparation because it was elegant, smooth, and easy to be washed from our skin that made it preferable for a cosmetic preparation. Moreover, the formula's characteristics were tested to observe the differences between the formulas.

Methodology

Materials

The materials used in this experiment were as follows Oxybenzone (Surya Dermato), Octyldimethyl PABA (Surya Dermato), Kojic Acid (Surya Dermato), β-cyclodextrin p.a (Sigma Aldrich), Stearic Acid (Surya Dermato), cetyl alcohol (Surya Dermato), span 80 (Surya Dermato) tween 80 (Surya Dermato), Methyl paraben (Surya Dermato), Propyl paraben (Surya Dermato), Sorbitol 70% (Surya Dermato), Isopropanol *p.a.,* (Brataco Chemicals). All of the active ingredients used here were in a pharmaceutical grade except for the chemical reagent isopropanol and β- cyclodextrin which were in pro analytical grade. The qualitative analysis is carried out by using a *Fourier Transform Infrared Spectrophotometre* Jasco FT-IR 5300, *Melting Point Apparatus, Bausch and Lomb Refractometre* and the result were compared to the reference and substance certificate of analysis, while the SPF assay were carried out by using a *Double Beam* Spectrophotometer UV- Vis Perkin Elmer Lambda EZ 201, *Ultrasonic Branson* 3510, *Hettich zentrifugen* EBA 20, Mettler Toledo AL 204 analytical balance. Digital pH meter Schott CG 842 and spreading capacity measurer are also used for the organoleptic analysis.

Preparation of the Formula

Formulas were made with inversion technique. Oil phase that made up with stearic acid, cetyl acohol, propyl paraben, and span 80 was heated until reached 70°C on water heater, then, the remaining base ingredients which part of water phase in 75°C temperature was added to the oil phase. It was mixed until it dispersed and smooth. Active ingredients were added to the base when its temperature reached 40-50°C. Oxybenzone was dispersed in octyldimetyl PABA before they were added. Kojic acid was added in aqueous solution form, and freeze dry complex form of kojic acid with β-cyclodextrin was added in dry condition and dispersed to the preparation.

Determination of Sunscreen Characteristics

The characteristics of the finished product evaluated were emulsion type, pH, spreading-ability, and organoleptic such as colors, odors, and consistency. The finished product was observed with microscope and stained using methylene blue and Sudan III to evaluate its emulsion type. To get the pH value, 2 gram formula was dissolved in 18 mL free-CO_2 aquadest. In order to determine the spreading capability, approximately 1 gram of the gels was weighed and put on a glass plate with a millimeter scale. This glass plate was then covered with another glass plate. And its change in spreading diameter was observed along with an increase of the given load.

Table 1. Formula

Material	Percentage (% w/w)			
	Base	Formula 1	Formula 2	Formula 3
Stearic Acid	14	14	14	14
Cetyl Alcohol	2	2	2	2
Methyl Paraben	0,1	0,1	0,1	0,1
Propyl Paraben	0,05	0,05	0,05	0,05
Span 80	0,5	0,5	0,5	0,5
Tween 80	4,5	4,5	4,5	4,5
Sorbitol 70%	3	3	3	3
Oxybenzone	-	3	3	3
Octyldimetil PABA	-	7	7	7
Kojik acid	-	-	1	1
β-Cyclodextrin	-	-	-	8
Aquadest	75,85	65.85	64.85	56,85

Determination of the SPF Value

The SPF value was determined by Petro correlation for *in vitro* method. 2 mg/cm^2 or 2 μL/ cm^2 sunscreen agent for *in vivo* test was equivalent with 10 ppm sunscreen agent dissolved in isopropanol.

First 100.0 mg preparation formula which contained 10 mg sunscreen's active ingredients dissolved in 2.0 ml isopropanol, the solution was then placed in ultra-sonicator and centrifuged for 15 minutes with 50 rpm speed. The 1.0 ml of filtrate was taken and poured into a 5.0 ml metered flask and shake well until it was homogenized (1000 ppm).

The 1.0 ml of mixture was then pipette, put into a 10.0 ml metered flask and diluted to acquire a 100 ppm solution. The 100 ppm solution that we acquired was pipette for 1.0 ml solution and moved into another 10.0 ml metered flask before isopropanol was added to dilute it and then it's shake well until it reach a concentration of 10 ppm . An UV spectrum of this solution was then measured at 290-400 nm by using *Double Beam* UV-Vis *Spectrophotometer* Perkin Elmer Lambda EZ 201 at an interval of 2 nm which has absorbance for 0.05 or more

According to Petro, the absorbance was then converted into the absorbance for 10 ppm solution concentration for each wavelength. Then it was proceed in this following equation:

$$AUC_{\lambda_{p-a}}^{Jp} = \frac{Va + \Lambda p}{2} \Lambda_p - \lambda_{7-a}$$

Whereas:
AUC = Area under Curve
Ap = Absorption on p wavelength
Ap-a = Absorption on p-a wavelength

The total AUC were obtained by totaling each AUC between 2 wavelengths in series from 290 nm till 400 nm which has an absorbance value above 0.050 and the SPF value of a formula were obtained by inserting the total AUC into the equation below:

$$LosSPF = \frac{\textbf{Total area}}{i\Lambda i\, r\, x} 2$$

Whereas:
An = longest wavelength above 290 nm that has an absorbance higher than 0.050
A1 = shortest wavelength 290 nm
The Log SPF value obtained from the equation was then converted into SPF value.

Statistical Analysis

The value of pH and SPF obtained were analyzed with SPSS for windows using One-way ANOVA method and continued with Tukey HSD test to asses the significant differences in different formula given. Result where as $p<0.05$ was considered to be statistically significant. Organoleptic and emulsion type test were descriptive analyzed, and spreading-diameter's data was proceed to get its spreading-ability.

Results and Discussions

Organoleptics test showed no definite differences between the formulas. The formulas had yellowish white colors, with soft cream odors and semisolid consistency. These physical characteristics were determined by the active ingredients of sunscreen agents.

The result for emulsion type test was oil in water emulsion preparation. It was homogenous blue that could be seen in the microscope using methylen blue stained, and dispersed orange with Sudan III.

One of the important factors that influence SPF of a sunscreen is pH, besides extinction coefficient and solvent polarity and therefore, it's important to make sure what's the real cause of SPF changes in the treatment formula. The pH of a product is a measure of the free hydrogen ion content and can be a very important chemical characteristic. The value of pH is dependent on the materials used in the formulation and their interactions. The pH can affect the use properties of the product as well as the stability of the actives and stability of the overall formula. The pH value in table 2, compared with formula 1, was slightly increased in formula 2, but in formula 3 it decreased. The fluctuation was significant according to Tukey HSD test was shown in table 3.

Spreading-ability profile was relatively changed. As showed in figure 6, formula 2 had higher mean spreading diameter than formula 1. The reversed could be seen in formula 3, with relatively downward profile of the spreading-diameter.

Table 2. Average pH data

FORMULA	pH* ± SO
1	4,51 ± 0,08
2	4,72 ± 0,26
3	3,80 ± 0,03

* The result were obtained from an average of 3 times replication

Table 4 showed average value of SPF obtained. Compared to formula 1, formula 2 had higher SPF and formula 3 was lower. According to Tukey HSD test, the differences between the formulas were significant.

Profile of absorbance didn't show any remarkable bathochromic or hipsochromic shift. It has relatively constant λmax at 308 nm. Changes of SPF value in formula 2 were possible because its absorbance was increased. It could be happened because kojic acid has chromophore and auksochrome group.

The SPF value decreased in formula 3. The complex formation of the sunscreen agent with β-cyclodextrin was suspected to be responsible for this phenomenon. The preparation contained water, that could served a good condition to make the reaction happened. Although there was a remarkable fell of SPF value in formula III that observed in this experiment, efficacy of this preparation wasn't definitely decreased. Advanced study about complex formation of the sunscreen agent with β- cyclodextrin was needed to solve this problem. Moreover, it was suggested to make in vivo correlation with the result of this study.

Table 3. Result of HSD test of the sunscreens pH

FORMULA	N	Subset for alpha = .05		
		1	2	2
Formula 3	9	3,8022		
Formula 1	9		4,5056	
Formula 2	9			4,7189
Sig.		1,000	1,000	1,000

a. Uses Harmonic Mean Sample Size = 9,000

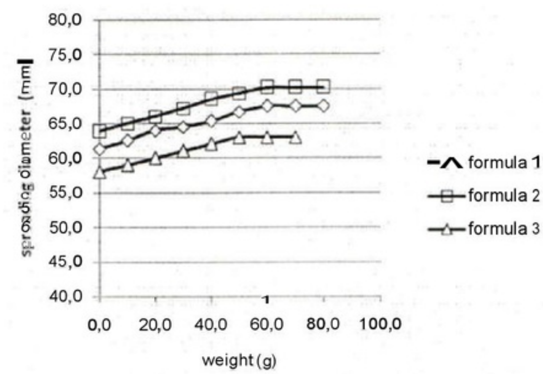


Fig 6. Profile of the Sunscreen's Spreading-ability

Table 4. Spreading-capacity of sunscreen

Formula	Average Slope ± SD (mm/g)	% CV
1	0.100 ± 0.003	3.10
2	0.107 ± 0.006	5.38
3	0.100 ± 0.000	0.00

* The result were obtained from an average of 3 times replication

Table 5. The SPF Value

Formula	SPF (average)
1	10,607 ± 0,432
2	11,741 ± 0,479
3	19,113 ± 0,295

Table 6. Result of HSD test of the sunscreens SPF

FORMULA	N	Subset for alpha = .05		
		1	2	3
Formula 3	9	9,113		
Formula 1	9		10,607	
Formula 2	9			11,741
Sig.		1,000	1,000	1,000

Means for groups in homogeneous subsets are displayed
a. Uses Harmonic Mean Sample Size = 9,000

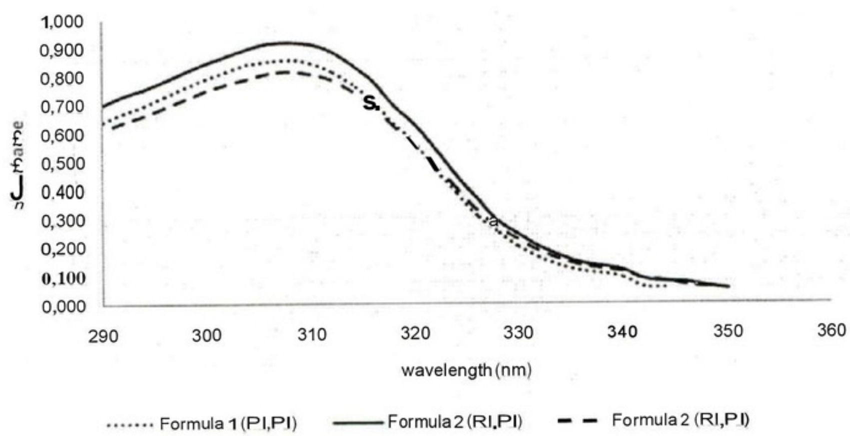


Fig 7. Profile of sunscreens absorbance in formulal, 2, 3 at first replication and measurement.

Conclusion

The result showed that the addition of kojic acid increased the SPF value of sunscreen product from 10,607 ± 0,432 became 11,741 ± 0,479. A different result showed with the addition of complex form of kojic acid with β-cyclodextrin. The SPF value decreased to 9.113 ± 0.295. The complex formation of the sunscreen agent with β-cyclodextrin was suspected to be responsible for this phenomenon. Moreover, it was suggested to make *in vivo* correlation with the result of this study.

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