

# Sun Protection Effect of 2-Hydroxy-4-(Octyloxy) Benzophenonein Sunscreen Creams Formulations by a Combination of Inorganic UV Filters

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## Sun Protection Effect of 2-Hydroxy-4-(Octyloxy) Benzophenone in Sunscreen Creams Formulations by a Combination of Inorganic UV Filters

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### Abstract

Overexposure of ultraviolet (UV) radiation, especially UVB (280-320 nm) and UVC (200-280 nm) have a harmful effect on the skin. Sunscreen such as derivatives of benzophenone can protect the skin from these detrimental effects. In this research, we evaluated the potency of 2-hydroxy-4-(octyloxy) benzophenone as a sunscreen and improved the ability by combining it with the physical blocker TiO<sub>2</sub> or ZnO in the form of a cream formulation. We use a D-optimal mixture design to obtain the cream formulation with high Sun Protection Factors (SPF) and acceptable characteristics. Several cream formulations containing 2-hydroxy-4-(octyloxy) benzophenone and TiO<sub>2</sub> or 2-hydroxy-4-(octyloxy) benzophenone and ZnO were prepared with concentrations of 5-10%. The creams were tested for the physicochemical parameters such as pH, color, odor, homogeneity, viscosity, and stability. The SPF was observed by spectrophotometry and the value was calculated using the Mansur equation. SPF value of 2-hydroxy-4-(octyloxy)benzophenone, TiO<sub>2</sub>, and ZnO were 25.21±0.47; 24.74±0.35; 3.20±0.05, respectively. SPF value of creams combining 2-hydroxy-4-(octyloxy) benzophenone and TiO<sub>2</sub> were in the range of 4.140-6.326. Furthermore, the SPF value of creams combining 2-hydroxy-4-(octyloxy) benzophenone and ZnO were in the range of 3.609-8.052. The creams meet the requirement of physicochemical properties with acceptable characteristics. They were stable when the creams kept at room temperature for one month. In this current study, the formulation of sunscreen creams with high SPF and acceptable characteristics obtained by a combination of 10% 2-hydroxy-4-(octyloxy) benzophenone and 5% titanium dioxide or ZnO.

**Key words :** 2-Hydroxy-4-(octyloxy) benzophenone . Sunscreencream.Sun protection factor. TiO<sub>2</sub>.ZnO

### 1. Introduction

Exposure of solar ultraviolet (UV) radiation in excessive conditions can cause skin problems including sunburn, edema, erythema, immune suppression, wrinkles, dermatitis, urticarial, aging, hypopigmentation, hyperpigmentation and skin cancer [1-2]. The ozone layer can absorb 100% UVC (200-290 nm), 90% UVB (290-320 nm), and a little amount of UVA (320-400 nm). However, depletion of the ozone layer causes increased UV transmission to the earth's surface. Sunscreen is used to reduce skin damage from UV radiation. Sunscreen is offered in many formulas like gel, lotion, stick, cream, lip balm, and spray. Gel preparations are commonly used for sunscreens because the gel provides some advantages including a cooling effect on the skin, elastic, and transparent appearance.

Based on the basis of its mechanism of action, there are 2 types of sunscreens including chemical absorbers (organic) which absorb the UV radiation and physical blockers (inorganic) which reflect and scatter UV radiation [3-4]. Previously, sunscreen only focuses to cover UVB radiation. Currently, the FDA recommends the use of broad-spectrum sunscreens which cover not only the entire spectrum of UVB but also the UVA. Zinc oxide, a physical blocker sunscreen, was able to protect skin from UVA radiation [5]. However, physical blocker is less proficient against UVB protection [6]. A combination of sunscreen that can protect the skin not only in the UVB region but also in the UVA regions, will provide added value.

The benzophenones derivativ 2-hydroxy-4-(octyloxy) benzophenone (HOB) is commercially available. The compound has been used extensively in organic synthesis. Based on the structure, we considered the molecule to be applicable as a UV filter. Furthermore, the compound was prepared to develop sunscreen cream

formulations with satisfactory characteristics. The purpose of this study was to evaluate in-vitro sunscreen activity of a cream formulation containing HOB and improved the ability by combining it with the physical blocker TiO<sub>2</sub> or ZnO.

## 2. Materials and Methods

**Materials :** Zinc oxide was from KOBO. 2-hydroxy-4-(octyloxy)benzophenone was obtained from Sigma-Aldrich. Methylparaben, propylparaben, mineral oil, propylene glycol, triethanolamine, glycerin, ZnO, and aquadest were obtained from Brataco Chemical (Indonesia). Cetyl alcohol, glyceryl monostearate were

purchased from Cognis. Olive oil and ascorbic acid were from Prima Chemical.

**Optimization of cream formulation :** The experimental design was a two factor two-level general factorial (Design Expert 7.0.0) and seven formulations were prepared (Table 1). The amount of HOB (X1) and TiO<sub>2</sub> or ZnO (X2) were selected as independent variables. The number of independent variables was optimized for dependent variables: viscosity and SPF. The low (5%), and high (10%) are the values of HOB, TiO<sub>2</sub> or ZnO. Mathematical equations were generated for each parameter. The mathematical models were studied for significance.

**Table 1 :** Composition of cream formulations with different amount of 2-hydroxy-4-(octyloxy) benzophenone, TiO<sub>2</sub>, and ZnO

Ingredients	Run1	Run2	Run3	Run4	Run5	Run6	Run7	Negative Control
<b>Ingredients A</b>								
Cetyl alcohol (g)	1	1	1	1	1	1	1	1
Mineral oil (g)	10	10	10	10	10	10	10	10
Olive oil (g)	10	10	10	10	10	10	10	10
Propylparaben (g)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Glyceryl monostearate(g)	16	16	16	16	16	16	16	16
<b>Ingredients B</b>	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Methylparaben (g)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Glycerin(g)	7	7	7	7	7	7	7	7
Ascorbic acid	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
HOB	5	10	10	6.25	8.75	7.5	5	0
TiO <sub>2</sub> /ZnO	10	5	5	8.75	6.25	7.5	10	0
Aquadest ad (ml) qs ad to	100	100	100	100	100	100	100	100

**Cream formulation :** The basic sunscreen formulation was prepared according to the formula recommended by EIRI with some modifications [7]. The Ingredients B (methylparaben, glycerin) were first heated (70°C) as well as ingredients A (glyceryl monostearate, cetyl alcohol, mineral oil, and propylparaben). The ingredients A were poured into a warm porcelain mortar and a required quantity of olive oil was added to the mixture. The water phase (B) was added slowly to the oil phase (A). The ascorbic acid was added and grinded well. After that, ZnO or TiO<sub>2</sub> was dissolved in hot distilled water and added to the mixture. Finally, HOB was added to form a homogeneous cream.

**Organoleptic evaluation :** All creams were observed for physical form including texture, color, and odor. These physical characteristics were observed by visual tested.

**Physicochemical evaluation :** Physicochemical evaluation of cream was tested for homogeneity, pH, viscosity, and spreadable. Homogeneity was observed by applying the cream on a glass object. The cream must give indicate of a non-grained appearance and no visible spot. The pH was measured using a pH meter. Viscosity was measured in Brookfield viscometer (DV-1 Prime) using a LV-4 spindles and a rotation rate of 60 RPM. Finally, the spreadable test of the cream was measured by applying the cream (500 mg) between two pieces of circle glass plates (diameter 15 cm) for one-minute compression. After that, the standard weight (50 g) was applied to the upper plate. After one minute's compression, the spreading diameter of the cream was measured. All measurements were made in triplicate.

**Determination of SPF value of HOB, TiO<sub>2</sub>, ZnO, and cream formulation :** Samples were prepared according

to the method recommended by Dutra [8]. One gram of sample was weighed and diluted to 100 ml with ethanol. The solution was ten milliliters. Afterwards 5.0 ml of filtered solution was transferred to a 50 mL volumetric flask, adjusted with ethanol. The absorbance of the final solution was measured by spectrophotometry in the range of 290 to 320 nm for every 5 nm wavelength interval. Finally, the SPF value was calculated using the Mansur equation [9].

## 2. Results and Discussion

Today, many strategies are proposed to obtain sunscreens with high SPF values and can cover a broad spectrum of UV radiation. One strategy is to combine UVA and UVB filters as well as chemical and physical sunscreens. This sunscreen combination method tends to be preferred because it only requires a preparation process that is identical to the conventional one, and only the required formulation ingredients are adjusted. In this study, we used ZnO or TiO<sub>2</sub> as a physical sunscreen and HOB as a chemical sunscreen.

The previous study in our research group show that the HOB has a higher SPF value of 25.2±0.5 compared with benzophenone-3,3',4,4'-tetracarboxylate dianhydride (6.4±0.2) or 2-benzoylbenzoic acid (2.7±0.4) [10]. The SPH value was also higher than that of SPF of natural sunscreen corn cob (4.95±0.86) [11]. The absorbance of

HOB, ZnO, and TiO<sub>2</sub> at UV region (200-400 nm) were recorded and shown in Figure 1. It presented that the absorbance of HOB in the UVB region was higher than that of UVA and part of UVC. The absorbance of TiO<sub>2</sub> in the UVA and UVC region were higher than that of HOB. On the other hand, ZnO has relatively similar absorbance throughout the UV region, and also ZnO has a greater absorbance in the UVA region than that of HOB. The SPF value of HOB, TiO<sub>2</sub>, and ZnO were 25.2±0.5; 24.7±0.3; and 3.2±0.05 which is considered ultra, ultra, and extra protection, respectively, in terms of sunscreen protection.

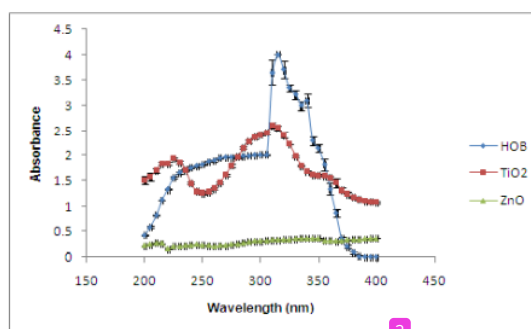


Fig. 1. Absorption curve of the solution of 2-hydroxy-4-(octyloxy)benzophenone, ZnO, and TiO<sub>2</sub> (right). The concentration of 1% in ethanol.

Table 2 : Physicochemical parameter evaluation of HOB-TiO<sub>2</sub> creams

Formulation	Color	Odor	pH	Homogeneity	Viscosity (cps)	Spreadability (cm)
Negative control	White	Characteristic of olive oil	4.01±0.01	Homogenous	9136.66±106.92	4.66±0.07
Run1	White	Characteristic of olive oil	5.95±0.02	Homogenous	9546.66±94.51	4.65±0.10
Run2	White	Characteristic of olive oil	5.90±0.02	Homogenous	7853.33±96.09	4.21±0.11
Run3	White	Characteristic of olive oil	6.56±0.02	Homogenous	8236.66±105.98	4.65±0.06
Run4	White	Characteristic of olive oil	5.58±0.03	Homogenous	8956.66±80.82	4.24±0.10
Run5	White	Characteristic of olive oil	5.09±0.03	Homogenous	8426.66±96.09	4.91±0.06
Run6	White	Characteristic of olive oil	5.86±0.03	Homogenous	8466.66±96.09	4.91±0.05
Run7	White	Characteristic of olive oil	6.19±0.02	Homogenous	9756.66±105.98	4.30±0.01

Table 3 : Physicochemical parameter evaluation of HOB-ZnO creams

Formulation	Color	Odor	pH	Homogeneity	Viscosity (cps)	Spreadability (cm)
Negative control	White	Characteristic of olive oil	4.01±0.01	Homogenous	9136.66±106.92	4.66±0.07
Run1	White	Characteristic of olive oil	7.04±0.020	Homogenous	8823.33±76.37	4.24±0.07
Run2	White	Characteristic of olive oil	7.02±0.015	Homogenous	8783.33±65.06	4.22±0.09
Run3	White	Characteristic of olive oil	7.00±0.015	Homogenous	8636.66±55.07	4.25±0.04
Run4	White	Characteristic of olive oil	6.92±0.030	Homogenous	8323.33±100.16	4.19±0.05
Run5	White	Characteristic of olive oil	7.10±0.023	Homogenous	7870±62.44	4.10±0.07
Run6	White	Characteristic of olive oil	7.08±0.025	Homogenous	8143.33±25.16	4.13±0.08
Run7	White	Characteristic of olive oil	7.05±0.011	Homogenous	8696.66±115.90	4.20±0.07

The formulated sunscreen creams were evaluated for several physicochemical tests and the results were displayed in Table 2-3. The formulate creams showed good acceptable odor, characteristic odor of olive oil, and were white color. The viscosity of formulated sunscreen creams ranged from 7853 to 9546 cps. The concentration of TiO<sub>2</sub> has a positive effect on the viscosity. It can be concluded that the creams have good viscosity (2.000-50.000 cps, SNI). Viscosity is an important parameter for evaluating cream preparations and the characteristics are related to the spreadable of the creams.

The pH value of formulated sunscreen creams combination of HOB and TiO<sub>2</sub> ranged from 5.09 to 6.56. Whereas the pH value of formulated sunscreen creams combination of HOB and ZnO ranged from 6.92 to 7.08. Cream combination of HOB and TiO<sub>2</sub> has a lower pH value than ZnO. All of formulated sunscreen creams meet the requirements for sunscreen preparation ranging from 4.5-8.0 [12]. The creams would not irritate if applied to the skin.

The SPF values of the sunscreen creams containing both HOB and TiO<sub>2</sub>/ZnO in various concentrations were displayed in Table 4. The results show that the SPF values in the UVB region were directly dependent on HOB or TiO<sub>2</sub>/ZnO concentrations. The creams have a low SPF values compare with the active compounds, this is due to their low amount of active compounds.

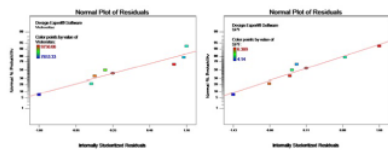
Table 4 : SPF of HOB-TiO<sub>2</sub> and HOB-ZnO cream formulations

Formulation	SPF	
	Combination of HOB and TiO <sub>2</sub>	Combination of HOB and ZnO
Negative control	0.580±0.005	0.498±0.014
Run1	4.872±0.018	4.888±0.067
Run2	6.326±0.013	8.052±0.022
Run3	6.164±0.017	7.606±0.018
Run4	4.140±0.011	3.610±0.009
Run5	6.389±0.018	5.694±0.037
Run6	5.063±0.011	6.419±0.022
Run7	4.489±0.018	4.531±0.034

To optimize the creams for viscosity and SPF value, a general factorial method is applied in this study. The amount of HOB and TiO<sub>2</sub>/ZnO was chosen as independent variables. A statistical model was used to observe the responses.

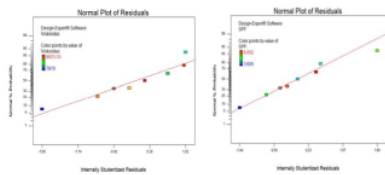
The ANOVA (analysis of variance) of HOB-TiO<sub>2</sub> creams displayed that the viscosity was appropriate to explain the main effect model (P-value 0.0024) as well as SPF (P-value 0.0408). By developing a normal probability plot of internally studentized residuals, a patterned was made for the normality statement (Fig. 2).

Furthermore, the ANOVA of HOB-ZnO creams showed that the viscosity was appropriate to explain the main effect model (P-value 0.0294) as well as SPF (P-



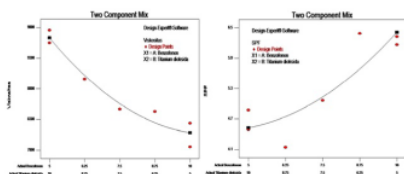
**Fig. 2.** Plot of internally studentized residuals vs. predicted response of viscosity (left) and SPF (right) of HOB-TiO<sub>2</sub> creams.

value 0.0368). A normal probability plot of internally studentized residuals was displayed in Fig 3. The statement of normality is fulfilled when the residual plot is approached along a straight line. The plot is acceptable, so we conclude that the resulting general factorial equation can be used in predicting SPF or viscosity of HOB-TiO<sub>2</sub> creams or HOB-ZnO creams.



**Fig. 3.** Plot of internally studentized residuals vs. predicted response of viscosity (left) and SPF (right) of HOB-ZnO creams.

The fitted equation relating the responses viscosity to the transformed factors of HOB-TiO<sub>2</sub> creams was shown in equation 1 and Fig 4. The equation shows a positive interaction with HOB of 8082.88 and TiO<sub>2</sub> of 9628.80. It means that HOB and TiO<sub>2</sub> will increase viscosity, and TiO<sub>2</sub> has the greatest effect on increasing viscosity compare with HOB. In addition, there is a negative interaction with the combination of HOB and TiO<sub>2</sub> with an interaction coefficient of -1196.14. Furthermore, the fitted equation relating the responses SPF to the transformed factors is shown in equation 2 and Fig 4.



**Fig. 4.** The graph relates to the response of viscosity (left) and SPF (right) to the transformed factors of HOB-TiO<sub>2</sub> creams.

$$Y = 8082,88A + 9628,80B - 1196,14AB \quad (1)$$

Y = viscosity

A = Concentration of HOB

B = Concentration of TiO<sub>2</sub>

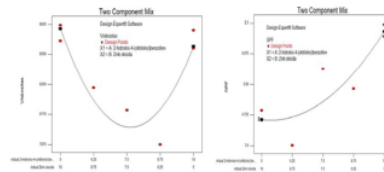
$$Y = 6,41A + 4,52B - 1,34AB \quad (2)$$

Y = SPF

A = Concentration of HOB

B = Concentration of TiO<sub>2</sub>

The same way was used to observe the responses of viscosity and SPF to the transformed factors of HOB-ZnO creams. The results were shown in equation 3-4, and Fig 5.



**Fig. 5.** The graph relates to the response of viscosity (left) and SPF (right) to the transformed factors of HOB-ZnO creams.

$$Y = 1,24A + 0,59B - 0,15AB \quad (3)$$

Y = viscosity

A = Concentration of HOB

B = Concentration of ZnO

$$Y = 1,24A + 0,59B - 0,15AB \quad (4)$$

Y = SPF

A = Concentration of HOB

B = Concentration of ZnO

The desirability value was used to find out the best viscosity and SPF of 7 runs. The optimized of HOB-TiO<sub>2</sub> cream formulation obtained by using design experts was a combination of 10% of HOB and 5% of TiO<sub>2</sub>, with viscosity of 8083 cps, SPF 6.4, and desirability of 1. Furthermore, the optimized of HOB-ZnO cream formulation was a combination of 10% of HOB and 5% of ZnO, with viscosity and SPF of 8651 cps and 7.8, respectively. The desirability obtained by the software was 0.940.

#### 4. Conclusion

The 2-hydroxy-4-(octyloxy) benzophenone, TiO<sub>2</sub>, and ZnO were exhibited sun protection activity. The benzophenone combined with TiO<sub>2</sub> or ZnO can be formulated as a cream with satisfying physical characteristics. In this current study, the formulation of sunscreen creams with high SPF and acceptable characteristics obtained by a combination of 10% 2-hydroxy-4-(octyloxy)benzophenone and 5% TiO<sub>2</sub> or ZnO.

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### Conflict of Interest

The Authors declare that they have no conflicts of interest.

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