Characterization of sunscreen cream containing benzophenone-3,3′,4,4′-tetracarboxylate dianhydride

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Abstract. The purpose of this research was to evaluate in-vitro sunscreen activity of a cream formulation containing benzophenone-3,3′,4,4′-tetracarboxylate dianhydride (BTDA). Sunscreen is used to protect skin from the adverse effects of ultraviolet (UV)A (320–400 nm) and UVB (290–320 nm) radiation. The most common chemical sunscreen is derivatives of benzophenone. The potency of benzophenone-3,3′,4,4′-tetracarboxylate dianhydride for sun protection was evaluated using in-vitro spectrophotometric technique. Several cream formulation containing 5% (F1), 6% (F2), and 7% (F3) BTDA were designed. These cream were subjected to physical characteristic such as, organoleptic, viscosity, homogeneity, pH, spreadability, adhesivity, and stability (tuliskan satuan –bila ada). The sun protection factors (SPF) were analyzed by spectrophotometry using samples irradiated with UV in B region. All cream formulations showed good physical characteristics. The formulation of sunscreen cream containing BTDA meets the requirements of physical properties. SPF values of BTDA, F1, F2, and F3 were 6.40±0.21; 0.27±0.03; 0.87±0.01; and 0.56±0.00, respectively. All cream formulations of sunscreen cream containing BTDA meets the requirements of physical properties with satisfactory characteristics, but does not indicate any sun protection activities.

1. Introduction
The sun's UV radiation has both positive and negative impacts on health. The harmful effects from exposures to ultraviolet (UV) radiation vary according to the levels of UV, the duration, the radiation intensity affecting on the person exposed, and the individual skin 'sensitivity of the person to UV. The ultraviolet radiation (UVR) is divided into three types depending on wavelengths region: long wavelengths UVA (320-400 nm), medium wavelengths UVB (280-320 nm), and short wavelengths UVC (200-280 nm) [1]. UVC is extremely harmful to the skin. Fortunately, UVC radiation is completely absorbed by ozone layer as well as large quantities of the UVB radiation. As a result, the UVR that reaches the earth’s surface contains about 5% of UVB and 95% of UVA [2].

UVR can cause a number of skin illnesses such as edema, erythema, hyperpigmentation, immunosuppression, photoaging, and skin cancer. [1]. UVB is the major wavelength that causes sunburn, and directly damages the cellular DNA leading to the formation pyrimidine photoproducts [3], photoaging [4], free radical production [5], and photo carcinogenesis [6]. In addition, UVA penetrates deeper into the epidermis and dermis of the skin (around 1 mm) and indirectly damages the DNA via the production of radical oxygen species (ROS) [7].
The skin of human provides natural protection against the harmful effects of the sun's UV radiation. The constitutive pigmentation was the main element of UV sensitivity [8]. Overexposure to UV radiation can reduce the skin’s ability to protect from these harmful effects of the sun’s UV radiation.

The current strategy for photoprotection from ultraviolet rays is using sunscreen application. Sunscreen is a product combining several active compounds that help prevent the sun’s ultraviolet (UV) radiation from reaching the skin. The sun protection factor (SPF) provides an indication of the effectiveness of the sunscreen. As the SPF increases, the extent of protection increases. Many effective sunscreen preparations are sold commercially. In general, sunscreen preparations are formulated as lotions, creams, oils, or sprays containing an active molecule.

Commercially available active molecule in sunscreen can be classified into two major categories: chemical (organic) and physical. Chemical sunscreen contain an active molecule which can reduce the amount of UVA and/or UVB reaching the skin by absorbing the radiation. Physical sunscreen reduce the amount of light penetrating into skin by building a physical barrier that scatters, reflects, and physically blocks the UV light from reaching the skin [9]. Organic sunscreen has been the mainstay of sunscreen formulation for periods and is still used in greater amounts. Organic sunscreen contain different substances classes which can be classified into derivatives of anthranilates, benzophenones, cinnamates, camphors, dibenzoylmethanes, p-aminobenzoates or salicylates [10-11].

The benzophenones derivative, benzophenone-3,3’-4,4’-tetracarboxylate dianhydride (BTDA), 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 BTDA.

2. Methods

2.1. Materials
Benzophenone-3,3’,4,4’-tetracarboxylate dianhydride was obtained from Sigma-Aldrich. Commercial sunscreen Wardah was purchased from local stores. Cetyl alcohol, glyceryl monostearate were purchased from Cognis. Mineral oil, Tween 80, glycerin, Span 80, methylparaben, propylparaben, ceramide, paraffin liquid, fragrance, and distilled water were obtained from Brataco Chemica (Indonesia). Methanol was from Merck.

2.2. Cream formulation
The ingredients used in the formulation of cream are shown in table 1. The cream was prepared by adding ingredients A to the ingredients B with fast speed mixing to avoid separation of water and oil phase (ULTRA TURRAX T25basic IKAR® - WERKE). Ingredients A were first heated together (65-75 °C) and added to the preheated mixture (65-75 °C) of ingredients B. Tween 80 and BTDA were added to a stirred solution of cream. Finally, the volume was made up to 100 mL by adding distilled water. In the experiment, the commercial sunscreen Wardah was employed as a positive control. A BTDA free cream was also prepared as a negative control.

2.3. Organoleptic characteristics
Several tests examining color, texture, odor, and homogeneity were applied to all creams. Homogeneity and texture were tested by applying a certain amount of cream between two pieces of glass. These characteristics were evaluated by visual observation for 30 days, and characteristics assessed on the 1st and 4th weeks.

2.4. pH values
Cream pH was measured with pH indicator stick. One gram of formulation was dispersed in 25 mL deionized water. Measurements were made in triplicate. The pH values were assessed on the 1st and 4th weeks.
2.5. Viscosity measurement
Viscosity was evaluated in Brookfield viscometer using an LV-4 spindle. The rotation rate was adjusted to 60 RPM. All measurements were made in triplicate.

2.6. Preliminary study of stability
The stability test was performed to determine the stability of formulations FI, FII, and FIII. The products were tested during three cycles of temperature testing. One cycle corresponded to 24 hours at room conditions (27 ± 1 °C), 24 hours at 4 ± 1 °C, and 24 hours at 40 ± 1 °C. The stability was evaluated by visual observation examining odor, texture, and appearance of creaming.

2.7. Spreadability
Spreadability of the formulated cream was determined by measuring the spreading diameter of 500 mg sample placed between two pieces of circle glass plates (diameter 15 cm) after one-minute compression. The standard weight applied to the upper plate was 50 g. Each cream was tested three times.

| Ingredients | Formula | I   | II  | III | Control (-) |
|-------------|---------|-----|-----|-----|-------------|
| Ingredients A |          |     |     |     |             |
| Cetyl alcohol (g) | 9.71 | 9.71 | 9.71 | 9.71 |
| Mineral oil (g) | 29    | 29  | 29  | 29  |
| Glyceryl monostearate (g) | 8  | 8   | 8   | 8   |
| Propylparaben (g) | 0.1 | 0.1 | 0.1 | 0.1 |
| Ingredients B |          |     |     |     |             |
| Methylparaben (g) | 0.2 | 0.2 | 0.2 | 0.2 |
| Glycerin (g) | 7.0   | 7.0 | 7.0 | 7.0 |
| Span 80 (g) | 1.15  | 1.15 | 1.15 | 1.15 |
| Tween 80 (g) | 3.29  | 3.29 | 3.29 | 3.29 |
| BTDA | 5  | 6   | 7   |     |
| Distilled water (ml) | qs ad to 100 |

2.8. Adhesivity
Five hundred milligrams of formulation was placed between two glass plates. The load (1 kg) was applied to the upper plate for 5 minutes. After that, the load was removed. The plate was given a load release 80 g. The timing of the release of both plates was noted. Each formulation was tested three times.

2.9. Determination of SPF value
SPF was measured in the samples by an in vitro method using UV–Vis Spectrophotometer (Shimadzu UV-1800). Samples were prepared according to the Dutra’s method [12]. The 1.0 % solution (w/v) of benzophenone derivative, formulated sunscreen creams, control negative, and commercial sunscreen (control positive) were prepared. Briefly, samples were diluted in 100 ml of ethanol and were homogenized by ultrasonication for 5 min. The obtained solution was filtered with a filter paper and the first 10 ml was discarded. Then 5 ml of filtered solution was adjusted to 50 ml volumetric flask using ethanol. Afterward, 5 ml aliquot was transferred to a 25 ml volumetric flask and the volume was adjusted with ethanol. The absorbance of each sample was measured by spectrophotometry in the range of 290–320 nm, every 5 nm intervals, using ethanol as blank. Three replicates of each sample were performed. The SPF of each sample was calculated with the data obtained by spectrophotometric analysis, using the Mansur equation [13].

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SPF = CF \times \sum_{290}^{320} EE(\lambda) \times I(\lambda) \times Abs(\lambda)
\]
Where, CF (correction factor) =1; EE ($\lambda$) = erythemal effect spectrum, I ($\lambda$) = solar intensity spectrum, and Abs ($\lambda$) = absorbance values at wavelength $\lambda$ of sample. The value of EE x I are constant [14].

3. Results and discussion

BTDA is the organic compound with the formula C$_{17}$H$_{6}$O$_{7}$. It is beige solid. The absorbance values of BTDA at various wavelengths ($\lambda_{\text{max}}$) from 290 to 320 nm are shown in Figure 1. The absorbance of the compound in 290-295 nm was higher than that of 300-320 nm. It showed that the benzophenone derivative has sun protection ability, but only efficient for narrow spectrum of UVB in the region of 290-295 nm. Sunscreen should have wide-ranging spectrum protection against both UVA and UVB radiation.

The SPF value of BTDA was measured and summarized in table 3. The compound was tested in vitro at 1.0 % solution (w/v), and the SPF value obtained was 6.40±0.21, which is considered low in terms of sunscreen protection.

Three different concentrations of benzophenone derivatives were formulated. The organoleptic properties of the formula including color, texture, odor, homogeneity, pH, viscosity, spreadability, and adhesivity, of cream formulations, are displayed in table 2. The results showed that all semisolid creams had smooth texture, beige white color, and characteristic odor of mineral oil. All creams showed satisfactory characteristics. The creams were given a homogeneous composition and no visible granity. The formulation of sunscreen cream containing BTDA meets the requirements of Indonesian National Standard (Standar Nasional Indonesia/SNI) [15].

The viscosity values have no practical correlation with BTDA concentration in the observed range of concentration (5-7%). A cream formulation was prepared using water as one of ingredients. Water may react with an anhydride into its corresponding carboxylic acid. It will affect the viscosity of the cream after being stored for one month at room temperature (table 3). The odor, color, and texture of creams, remained stable throughout the 3 cycles of temperature testing. They showed homogeneity without creaming.

Furthermore, the cream formulations with BTDA were found to possess SPF in the range of 0.27 to 0.87. Cream formulation F2 has better SPF value than other formulations (table 4). According to the statistical analysis, significant differences among the SPF values of negative control, positive control, F1, F2, and F3 (p<0.05) were observed.

Figure 1. Absorbance values of a benzophenone-3,3’,4,4’-tetracarboxylate dianhydride.
Table 2. Evaluation of prepared creams.

| Parameters | Control (-) | FI | FII | FIII |
|------------|-------------|----|-----|------|
| Colour     | White       | Beige white | Beige white | Beige white |
| Texture    | Smooth      | Smooth | Homogeneous | Homogeneous |
| Homogeneity| Homogeneous | Homogeneous | Homogeneous | Homogeneous |
| pH         | 5           | 5   | 5   | 5    |
| Viscosity (cps) | 5530±739.12 | 4163±542 | 4633±515 | 3256±204 |
| Spreadability (cm) | 5.4±0.4 | 5.4±0.2 | 6.1±0.2 | 5.9±0.2 |
| Adhesivity (s) | 26.7±1.5 | 37.0±1.0 | 41.7±1.5 | 42±2.6 |

Table 3. SPF of the benzophenone derivative and creams sunscreen.

| Evaluation Parameters | Control (-) | F1 | F2 | F3 |
|-----------------------|-------------|----|----|----|
| pH                    | 5±0         | 5±0 | 5±0 | 5±0 |
| Viscosity (cps)       | 7456 ± 756.76 | 7115±247 | 7524±245 | 8271±234 |
| Color                 | No change   | No change | No change | No change |
| Creaming              | No          | No     | No   | No  |
| Odor                  | No change   | No change | No change | No change |

4. Conclusion
Our results suggest that the BTDA exhibited low sun protection activity. The formulation of sunscreen cream containing BTDA meets the requirements of physical properties with satisfactory characteristics, but does not indicate any sun protection activities.

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