Effects of particle size, surface coating, and color of titanium dioxide and iron oxides on their ability to protect against UV and blue/visible light

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Introduction

Protection against UVB (290-320 nm) and UVA (320-400 nm) light have been studied for some time, but recently the damaging effects of visible light (400-800 nm) and ways to protect against it have also gained interest. Visible light accounts for almost half of sunlight, and it can penetrate more deeply into the skin than UVB and UVA can, reaching lower layers of the skin. Once in contact to the skin, visible light produces free radicals, proinflammatory cytokines, and matrix metalloproteinase-1, all of which result in photaging. Exposure to visible light has been shown to induce abnormal pigmentation, resulting in age spots or melasma. The portion of the visible light spectrum having the highest energy is referred to as blue light (400-450 nm), and blue light has been reported to induce cytotoxicity and hinder normal growth of both endothelial cells and keratinocytes. Blue light also has been shown to cause oxidative stress in human keratinocytes. A clinical study performed on human skin showed that blue light irradiation caused abnormal pigmentation. Blue light has also been implicated in skin conditions such as solar urticaria, chronic actinic dermatitis, and porphyria. Given these deleterious effects, protection against sunlight should consider not only UVB and UVA light but also blue/visible light. In a study of 40 volunteers, Martini et al. found that sunscreens containing a combination of both UV filter grade and pigment grade titanium dioxide (TiO₂) prevented skin hyperpigmentation better than UV filter grade TiO₂ alone. According to a study by Teramura et al., powdered or liquid foundation makeup containing TiO₂ and iron oxides provided protection against blue light for porphyria patients. A study by Kaye et al. discovered that pigment grade TiO₂ of particle size 2 µm combined with red iron oxide demonstrated better protection against UV-visible light than pigment grade TiO₂ alone. TiO₂ and iron oxides have various physical properties including particle size, surface coating and color. Their properties are also importance factors influencing the effectiveness of sunscreens in UV and blue/visible light protection. Although the protection of UV and blue/visible light have been studied as described, most of them did not give detailed information about these properties. By better understanding the effects of these properties on the UV and blue/visible light protection ability of TiO₂ and iron oxides, the use of these two substances can be optimized by using spectrophotometry. In addition, several combinations of TiO₂ and iron oxides were evaluated for protection against UVB, UVA, and blue/visible light through sun protection factor (SPF), UVA protection factor (UVA-PF), and porphyrin protection factor (PPF) respectively.

Methods

Preparation of the cream base: To prepare the oil phase, glyceryl stearate, PEG-100 stearate, cetylstearyl alcohol, stearic acid, sorbitan monostearate, caprylic capric triglyceride, and C12-15 alkylbenzoate were melted and mixed. For the aqueous phase, carbomer was dispersed in water and neutralized with triethanolamine to form a gel. Glycerine and tetrasodium EDTA were dissolved in water and added to the carbomer beaker. Both the oil phase and aqueous phase were separately heated to 70-75°C. After that, the aqueous phase was poured slowly into the oil phase and the resulting cream
base was continuously stirred until cooling to 40 °C. Phenoxethanol was incorporated and stirred until the cream base was homogenous.

**Preparation of formulations containing titanium dioxide, iron oxides:** The characteristics of TiO₂ and iron oxides used in this study are shown in Table 1. The above preparation of the cream base was modified with the addition of TiO₂ or iron oxides. Formulations were prepared by dispersing either TiO₂ or iron oxides in the liquid oil (i.e. caprylic capric triglyceride and C12-15 alkyl benzoate) of the cream base before adding to the other ingredients of oil phase. The concentration of TiO₂ or iron oxides in formulation were fixed at 10% and 1% by weight, respectively.

**Table 1 The characteristic of titanium dioxide and iron oxides**

<table>
<thead>
<tr>
<th>Sample code</th>
<th>Compositions</th>
<th>Surface coating</th>
<th>Manufacturer</th>
<th>Particle size*</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-35</td>
<td>Rutile, Titanium dioxide and hydrated silica and dimethicone</td>
<td>Uncoated</td>
<td>Tayca</td>
<td>35 nm</td>
</tr>
<tr>
<td>TD-35</td>
<td>Rutile, Titanium dioxide and Aluminium hydroxide and dimethicone</td>
<td>Dimethicone</td>
<td>Tayca</td>
<td>35 nm</td>
</tr>
<tr>
<td>TT-60</td>
<td>Rutile, Titanium dioxide and Aluminium hydroxide and triethoxycaprylsilane</td>
<td>Triethoxycaprylsilane</td>
<td>K.S.Pearl</td>
<td>60 nm</td>
</tr>
<tr>
<td>T-250</td>
<td>Rutile, Titanium dioxide and aluminium hydroxide and hydrogen dimethicone</td>
<td>Uncoated</td>
<td>Daito Kasei Kogyo</td>
<td>250 nm</td>
</tr>
<tr>
<td>TT-250</td>
<td>Rutile, Titanium dioxide and aluminium hydroxide and hydrogen dimethicone</td>
<td>Hydrogen dimethicone</td>
<td>Daito Kasei Kogyo</td>
<td>250 nm</td>
</tr>
<tr>
<td>TT-300</td>
<td>Rutile, Titanium dioxide and aluminium hydroxide and triethoxycaprylsilane</td>
<td>Triethoxycaprylsilane</td>
<td>Miyoshi Suzhou</td>
<td>300 nm</td>
</tr>
</tbody>
</table>

* Reported by the manufacturer: particle size less than 100 nm (nanosize); particle size 100-1000 nm (submicronsize); particle size more than 1000 nm (micronsize).

The effects of particle size, surface coating, and color of TiO₂ and iron oxides on protection against UV and blue/visible light were performed using spectrophotometry as following:

**Effect of particle size and surface coating of TiO₂:** The effect of particle size and surface coating of TiO₂ on the UV and blue/visible light protection were performed using a UV-Vis spectrophotometer (UV-1800®; Shimadzu, Kyoto, Japan). Briefly, each formulation was applied on a quartz plate (size 5.0 cm×2.5 cm) at 1.3 mg/cm². The sample was spread over the whole plate using a fingertip (pre-saturated with the sample). The plate was kept in the dark at room temperature for 15 minutes. The transmittance spectra at wavelengths between 290 to 800 nm were recorded. Samples were measured in triplicate.

**Effect of particle size and color of iron oxides:** The measurement was performed using the UV-1800® spectrophotometer following the procedure as described above.

**Determination of SPF, UVA-PF, and PPF:** TiO₂ and iron oxides yielding high protection were selected to be combined and incorporated into a cream base. The UV-visible absorption of the combined samples were measured using the UV-1800® spectrophotometer as described above. Then, the effectiveness of these combined samples in the protection of UVB and UVA were determined by SPF and UVA-PF values using the following equations:

\[
SPF = \frac{\int_{290 \text{ nm}}^{400 \text{ nm}} E(\lambda)I(\lambda)d(\lambda)}{\int_{290 \text{ nm}}^{400 \text{ nm}} E(\lambda)I(\lambda)10^{-Abs(\lambda)}d(\lambda)} \quad \text{...(Eq.1)}
\]

\[
\text{UVA-PF} = \frac{\int_{320 \text{ nm}}^{400 \text{ nm}} P(\lambda)I(\lambda)d(\lambda)}{\int_{320 \text{ nm}}^{400 \text{ nm}} P(\lambda)I(\lambda)10^{-Abs(\lambda)}d(\lambda)} \quad \text{...(Eq.2)}
\]

Where \(E(\lambda)\) is the erythema action spectrum, \(I(\lambda)\) is the spectral irradiance (W/m²/nm) at wavelength 290-400 nm, \(Abs(\lambda)\) is the mean absorbance of combined samples at wavelength 290-400 nm.

PPF is a value indicating the effectiveness of samples in blue light protection. *In vitro* PPF was determined according to the method of Teramura et al. Briefly, protoporphyrin IX (PPIX) (95% purity, ALX-430-041, Enzo Life Sciences, New York, USA) was dissolved in dimethyl sulfoxide (Sigma-Aldrich, Missouri, USA) and diluted to a final concentration of 0.0025 mg/ml. The absorbance of PPIX solution and the combined samples were measured using a UV-1800® spectrophotometer. The PPF value was calculated using equation 3.
The commercial sunscreen CC Dermaction® (Watson, Bangkok, Thailand), which claimed to protect against blue/visible light, was used as a control.

Data analysis: The data was analysed using one-way analysis of variance (ANOVA), followed by Tukey's test for multiple comparisons (SPSS Statistic 22.0, International business machine Corporation, New York, USA). *P*-values less than or equal 0.05 were considered significant.

Results and discussion

Effect of particle size and surface coating of TiO$_2$: In the UV wavelength, nanosize TiO$_2$ (i.e. T-35, TT60, and TD-35) showed better protection than submicronsize TiO$_2$ (i.e. T-250, TD-250, and TT-300) (Figure 1). Decreasing the particle size to nanosize resulted in shifting the wavelength from blue/visible to UV regions, which lead to reduce protection in blue/visible light but more transparency, and improved cosmetic appearance. The effect of surface coating on nanosize TiO$_2$ seemed to show less effect on UV protection than that on submicronsize TiO$_2$. In contrast to submicronsize TiO$_2$, T-250 was uncoated TiO$_2$ that showed significantly better UV and blue/visible light protection than TT-300 and TD-250 which were coated TiO$_2$. For blue light wavelength, only T-250 and TT-300 showed the better protection than nanosize TiO$_2$. TD-250 showed the least in protection against blue/visible light. This may be due to its appearance. From the observation, TD-250 possesses transparency appearance after dispersing in oils. T-250 and TT-300 were selected to combine with iron oxides. TT-60 which has the same surface coating with TT-300 and iron oxides was also included in further studies.

Effect of particle size and color of iron oxides: Yellow, red and black iron oxides were selected based on their color used in tinted sunscreens. In each color, submicronsize iron oxides yielded better protection in all wavelengths compared to micronsize iron oxides (i.e. IYT-200>IYT-1500; IRT-200>IRT-1700; and IBT-200>IBT3000) (Figure 2). This implies that the reflection or scattering efficiency goes down (increase transmission) when the particle size goes up to micronsize. This result is consistent with previous study showing that the particle size having best at reflection or scattering blue/visible light are in ranging from 200 to 500 nm. For the effects of color, yellow iron oxides showed higher protection in both UV and blue light wavelengths compared to red and black iron oxides, respectively. On the other hand, in visible wavelength, red iron oxides also showed higher protection compared to yellow and black iron oxides, respectively. However, white pigment TiO$_2$ (i.e. T-250 and TT-300) still showed better UV and blue/visible light protection than those of iron oxides. Next study, tinted sunscreen formulations were aimed to prepare. Therefore, YT-200, RT-200 and BT-200 were selected to incorporate with T-250, TT-300 and TT-60.
Effect of the combination of TiO₂ and iron oxides on UVB, UVA, and blue light protection:
The formulations of combination between selected TiO₂ and blended iron oxide are shown in Table 2. These formulations were determined for their protection efficacy against UVB, UVA, and blue light by using SPF, UVA-PF, and PPF values respectively. Comparing between sample A and E, blended iron oxide did not enhance the efficacy of T-250 in UVB, UVA, and blue light protection. Although the UVB, UVA, and blue light efficacy of TT-300 was poor compared to T-250, its efficacy could be enhanced after combining with blended iron oxide (i.e. sample F). For TT-60 which yielded high UV protection but low blue light protection, its efficacy in protection against all wavelengths could also be enhanced following combining with blended iron oxide (i.e. sample G). This enhancement effects may be due to the increasing opacity of their combinations, which results in increasing of reflection or scattering. Sample E, F and G formulated in this study showed similar protection against blue light compared to the commercial product.

Table 2 Effects of the combination of TiO₂ and iron oxides on SPF, UVA-PF, and PPF values.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Active ingredients</th>
<th>SPF (UVB)</th>
<th>UVA-PF (UVA)</th>
<th>PPF (Blue light)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cream Base</td>
<td>-</td>
<td>1.22±0.01n</td>
<td>1.21±0.01n</td>
<td>1.20±0.02n</td>
</tr>
<tr>
<td>Sample A</td>
<td>10% T-250</td>
<td>8.41±0.74n</td>
<td>8.61±0.83n</td>
<td>9.72±1.02n</td>
</tr>
<tr>
<td>Sample B</td>
<td>10% TT-300</td>
<td>5.73±0.53n</td>
<td>5.93±0.56n</td>
<td>6.80±0.55n</td>
</tr>
<tr>
<td>Sample C</td>
<td>10% TT-60</td>
<td>12.55±1.18n</td>
<td>10.45±0.96n</td>
<td>5.63±0.48n</td>
</tr>
<tr>
<td>Sample D</td>
<td>2.5% blended iron oxide</td>
<td>3.07±0.21n</td>
<td>3.02±0.19n</td>
<td>3.06±0.19n</td>
</tr>
<tr>
<td>Sample E</td>
<td>10% T-250+2.5% blended iron oxide</td>
<td>8.09±0.73n</td>
<td>7.95±0.83n</td>
<td>9.75±0.36n</td>
</tr>
<tr>
<td>Sample F</td>
<td>10% TT-300+2.5% blended iron oxide</td>
<td>9.16±0.81m</td>
<td>9.51±0.84n</td>
<td>10.33±0.41n</td>
</tr>
<tr>
<td>Sample G</td>
<td>10% TT-60+2.5% blended iron oxide</td>
<td>25.94±2.76m</td>
<td>21.6±2.44n</td>
<td>11.54±0.76m</td>
</tr>
<tr>
<td>Commercial product</td>
<td>Ethylhexyl methoxyccinnamate, Butyl methoxydibenzoylmethane, Ethylhexyl salicylate, Benzo phenone-3, Titanium dioxide (Cl 77891) and Iron oxides (Cl 77492, Cl 77491, Cl 77499)</td>
<td>187.98±16.72m</td>
<td>21.00±1.35m</td>
<td>9.61±0.54m</td>
</tr>
</tbody>
</table>

Note: Blended iron oxide is the combination of three color of iron oxides to obtain Tint sunscreens. Different alphabets in the column indicate that data are statistically different (p<0.05).

Conclusion
This study has shown that nanosize (35-60 nm) TiO₂ gives better protection against the UVB and UVA wavelengths than submicronsize (200-300nm) TiO₂. Whether the nanosize TiO₂ is coated or uncoated does not significantly affect protection against UV light. On the other hand, within the blue/visible light wavelength, uncoated submicronsize TiO₂ showed the best protection, followed by coated submicronsize TiO₂ and coated submicronsize iron oxides. It was also found that UVB, UVA, and blue light protection of coated nanosize and coated submicronsize TiO₂ can be enhanced by mixing them with blended iron oxide. Adding blended iron oxide in this way also improves cosmetic appearance. Thus it is clear that different physical properties of TiO₂ and iron oxides play a crucial role in their ability to protect against UV and blue/visible light. An understanding of the effects of the different these properties as described here will be helpful in formulating effective sunscreens against UV and blue/visible light. Finally, this study suggests that to maximize protection in the UV and blue/visible light wavelengths, tinted or colored sunscreens should be selected.

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References