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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 photoaging.[1] 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.[2] Blue light also has been shown to cause oxidative stress in human keratinocytes.[3] A clinical study performed on human skin showed that blue light irradiation caused abnormal pigmentation.[4] Blue light has also been implicated in skin conditions such as solar urticaria,[5] chronic actinic dermatitis[6], and porphyria[7]. 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.[8] found that sunscreens containing a combination of both UV filter grade and pigment grade titanium dioxide (TiO_2) prevented skin hyperpigmentation better than UV filter grade TiO_2 alone. According to a study by Teramura et al.[9], powdered or liquid foundation makeup containing TiO_2 and iron oxides provided protection against blue light for porphyria patients. A study by Kaye et al.[10] discovered that pigment grade TiO_2 of particle size 2 µm combined with red iron oxide demonstrated better protection against UV-visible light than pigment grade TiO_2 alone. TiO_2 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 TiO_2 and iron oxides, the use of these two substances can be optimized by using spectrophotometry. In addition, several combinations of TiO_2 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 alkyl-benzoate 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. Phenoxyethanol was incorporated and stirred until the cream base was homogenous.

Preparation of formulations containing titanium dioxide, iron oxides: The characteristics of TiO_2 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 TiO_2 or iron oxides. Formulations were prepared by dispersing either TiO_2 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 TiO_2 or iron oxides in formulation were fixed at 10% and 1% by weight, respectively.

Table 1 The characteristic of titanium dioxide and iron oxides

Sample code	Compositions	Surface coating	Manufacturer	Particle size*
Titanium dioxide samples				
T-35	Rutile, Titanium dioxide	Uncoated	Tayca	35 nm
TD-35	Rutile, Titanium dioxide and aluminium hydroxide and hydrated silica and dimethicone	Dimethicone	Tayca	35 nm
TT-60	Rutile, Titanium dioxide and aluminium hydroxide and triethoxycaprylylsilane	Triethoxycaprylylsilane	K.S.Pearl	60 nm
T-250	Rutile, Titanium dioxide and aluminium hydroxide	Uncoated	Daito Kasei Kogyo	250 nm
TD-250	Rutile, Titanium dioxide and aluminium hydroxide and hydrogen dimethicone	Hydrogen dimethicone	Daito Kasei Kogyo	250 nm
TT-300	Rutile, Titanium dioxide and aluminium hydroxide and triethoxycaprylylsilane	Triethoxycaprylylsilane	Miyoshi Suzhou	300 nm
Iron oxide samples				
IYT-200	Yellow iron oxide and Triethoxycaprylylsilane	Triethoxycaprylylsilane	Athena Corp	200 nm
IRT-200	Red iron oxide and Triethoxycaprylylsilane	Triethoxycaprylylsilane	Athena Corp	200 nm
IBT-200	Black iron oxide and Triethoxycaprylylsilane	Triethoxycaprylylsilane	Athena Corp	200 nm
IYT-1500	Yellow iron oxide and Triethoxycaprylylsilane	Triethoxycaprylylsilane	K.S.Pearl	1500 nm
IRT-1700	Red iron oxide and Triethoxycaprylylsilane	Triethoxycaprylylsilane	K.S.Pearl	1700 nm
IBT-3000	Black iron oxide and Triethoxycaprylylsilane	Triethoxycaprylylsilane	K.S.Pearl	3000 nm

** 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 TiO_2 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 TiO_2: The effect of particle size and surface coating of TiO_2 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/cm^2. 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: TiO_2 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;

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

Where $E(\lambda)$ is the erythema action spectrum, $I(\lambda)$ is the spectral irradiance (W/m^2/nm) at wavelength 290-400 nm, $\mathrm{Abs}(\lambda)$ is the mean absorbance of combined samples at wavelength 290-400 nm.

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

Where $P(\lambda)$ is the persistent pigment darkening action spectrum, $I(\lambda)$ is the spectral irradiance (W/m^2/nm) at wavelength 320-400 nm, $\mathrm{Abs}(\lambda)$ is the mean absorbance of combined samples at wavelength 320-400 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.[9] 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.

$$PPF = \frac{\int_{400\ \mathrm{nm}}^{450\ \mathrm{nm}} PP(\lambda)\cdot I(\lambda)\cdot d(\lambda)}{\int_{400\ \mathrm{nm}}^{450\ \mathrm{nm}} PP(\lambda)\cdot I(\lambda)\cdot 10^{-Abs(\lambda)} d(\lambda)} \quad \text{…(Eq.3)}$$

Where PP(λ) is the mean absorbance value of PPIX solution, I(λ) is the standard spectral irradiance of the solar source based on an air mass of 1.5 G (received from IEC 60904-3), Abs(λ) is the mean absorbance of combined samples at wavelength 400-450 nm.

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.[11] 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.[12] 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.

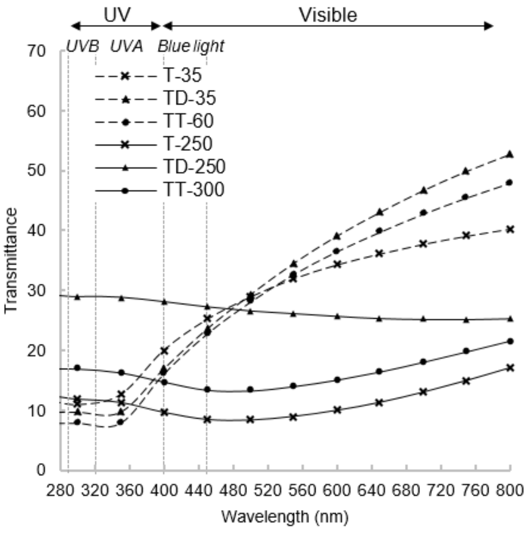

Figure 1 UV-visible transmittance spectra of TiO_2 with various particle size and surface coating.

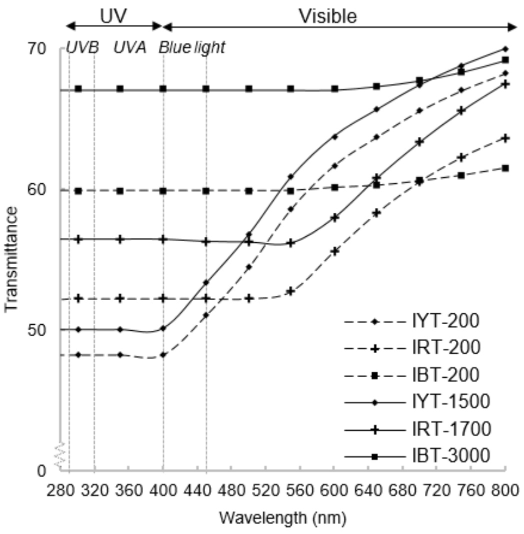

Figure 2 UV-visible transmittance spectra of iron oxides with various particle size and color.

Effect of the combination of TiO_2 and iron oxides on UVB, UVA, and blue light protection: The formulations of combination between selected TiO_2 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 TiO_2 and iron oxides on SPF, UVA-PF, and PPF values.

Sample	Active ingredients	SPF (UVB)	UVA-PF (UVA)	PPF (Blue light)
Cream Base	-	1.22 ± 0.01^h	1.21 ± 0.01^g	1.20 ± 0.02^g
Sample A	10% T-250	8.41 ± 0.74^e	8.61 ± 0.83^d	9.72 ± 1.02^c
Sample B	10% TT-300	5.73 ± 0.53^f	5.93 ± 0.56^e	6.80 ± 0.55^d
Sample C	10% TT-60	12.55 ± 1.18^c	10.45 ± 0.96^b	5.63 ± 0.48^e
Sample D	2.5% blended iron oxide	3.07 ± 0.21^g	3.02 ± 0.19^f	3.06 ± 0.19^f
Sample E	10% T-250+ 2.5% blended iron oxide	8.09 ± 0.73^e	7.95 ± 0.83^d	9.75 ± 0.26^c
Sample F	10% TT-300+ 2.5% blended iron oxide	9.16 ± 0.81^d	9.51 ± 0.84^c	10.33 ± 0.41^b
Sample G	10% TT-60+ 2.5% blended iron oxide	25.94 ± 2.76^b	21.65 ± 2.44^a	11.54 ± 0.76^a
Commercial product	Ethylhexyl methoxycinnamate, Butyl methoxydibenzoylmethane, Ethylhexyl salicylate, Benzophenone-3, Titanium dioxide (CI 77891) and Iron oxides (CI 77492, CI 77491, CI 77499)	187.98 ± 16.72^a	21.00 ± 1.35^a	9.61 ± 0.54^c

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) TiO_2 gives better protection against the UVB and UVA wavelengths than submicronsize (200-300nm) TiO_2. Whether the nanosize TiO_2 is coated or uncoated does not significantly affect protection against UV light. On the other hand, within the blue/visible light wavelength, uncoated submicronsize TiO_2 showed the best protection, followed by coated submicronsize TiO_2 and coated submicronsize iron oxides. It was also found that UVB, UVA, and blue light protection of coated nanosize and coated submicronsize TiO_2 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 TiO_2 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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