

## Effect of particle size of TiO<sub>2</sub> and octyl-methoxycinnamate (OMC) content on sun protection factor (SPF)

Jaeyong Choi<sup>1,†</sup>, Suyeon Kim<sup>1,†</sup>, Woonjung Kim<sup>1</sup>, Chul Hun Eum<sup>2,★</sup>, and Seungho Lee<sup>1,★</sup>

<sup>1</sup>Department of Chemistry, Hannam University, Daejeon 34054, Korea

<sup>2</sup>Korea Institute of Geoscience and Mineral Resources, Daejeon 34132, Korea

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**Abstract** Exposure to UV light, i.e., UV-A (320-400 nm) or UV-B (290-320 nm) radiation, can cause skin cancer. Titanium dioxide (TiO<sub>2</sub>) effectively disperses UV light. Therefore, it is used as a physical UV filter in many UV light blockers. Usually, the TiO<sub>2</sub> content in commercialized UV blockers is 25 % at most. To block UV-B, a chemical UV blocker, octyl-methoxy cinnamate (OMC) is used. OMC is commonly used in combination with TiO<sub>2</sub>. In this study, TiO<sub>2</sub> and OMC were mixed in different proportions to produce UV blockers with different compositions. Also the changes in the sun protection factor (SPF) based on the composition and TiO<sub>2</sub> particle sizes were investigated. In order to analyze the TiO<sub>2</sub> particle size, dynamic light scattering (DLS) and asymmetrical flow field-flow fractionation (AsF4FFF) were used. The results showed that the SPF was influenced by the proportion of TiO<sub>2</sub> and OMC, where the proportion of TiO<sub>2</sub> induced a more significant influence. In addition, changes in the TiO<sub>2</sub> particle size based on the proportion of OMC were observed.

**Key words:** Titanium dioxide (TiO<sub>2</sub>), Octyl-methoxy cinnamate (OMC), Sun protection factor (SPF), Asymmetrical flow field-flow fractionation (AF4), Dynamic light scattering (DLS)

### 1. Introduction

Sunlight consists of infrared light, visible light, UV rays, X-rays and  $\gamma$ -rays. UV light accounts for 6 % of the total sunlight, which is much lower as compared to visible light and infrared light. However, the human body is the most sensitive to UV light, and UV light can induce skin cancer and skin-aging. UV light is classified as UV-A (320-400 nm), UV-B (290-320 nm), and UV-C (200-290 nm) based on the wavelength.<sup>1</sup> UV-C destroys mono-cellular organisms

through chromosomal abnormalities, which leads to hazardous effects on the body, such as damage of the cornea. However, most of the UV-C light is absorbed by the ozone layer and does not reach the ground surface or come in contact with the human skin. On the other hand, UV-A and UV-B radiations are not absorbed by the ozone layer and hence have hazardous consequences on the body, such as skin cancer and skin-aging. In particular, UV-A has the longest wavelength and most of the UV-A emitted by the sun reaches the ground surface. Therefore, it accounts

★ Corresponding author

Phone : +82-(0)42-629-8822, +82-(0)42-868-3675 Fax : +82-(0)42-629-8811, +82-(0)42-868-3393

E-mail : [slee@hnu.kr](mailto:slee@hnu.kr), [cheum@kigam.re.kr](mailto:cheum@kigam.re.kr)

<sup>†</sup>Co-first Author, Jaeyong Choi and Suyeon Kim contributed equally to this work.

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for 90-95 % of the UV light coming into contact with the skin. Since the content of UV-A is high during the day and at night, and the amount that reaches the ground is constant, UV-A is also called “everyday UV light.” UV-A can penetrate into dermis and is known as a main factor that leads to skin-aging by causing pigmentation, decreasing skin elasticity, and causing wrinkles.<sup>2,3</sup> UV-B has a relatively shorter wavelength and higher energy levels. Hence, UV-B can reach the dermis in a shorter span of time.<sup>4</sup> UV-B is responsible for skin burns during the summer, and it can inhibit nucleic acid and protein synthesis in skin cells and cause pigmentation. Moreover, UV-B can lower the immune system, increase the possibility of bacterial infections, and induce cancer.<sup>3,5,6</sup> Since different types of UV light have different penetration levels and frequencies, their effects on the skin are also different.

UV blockers are usually used to protect the skin from UV light.<sup>7</sup> UV blockers absorb, reflect and disperse sunlight, and consequentially, block UV light. UV blockers are usually available in the form of as creams, lotions, and sprays.<sup>8</sup> Commercialized UV blockers are marked with their corresponding sun protection factor (SPF), which reflects the ability of the product to block UV-B. A higher SPF means a higher degree of protection from UV-B. For example, when the amount of sunlight is 1, a product with SPF 15 would decrease the sunlight to 1/15. Further, the protection grade of UV-A (PA) is usually shown along with SPF, where PA can be either +, ++ or +++. A Higher number of + signs indicates a higher degree of protection from UV-A.<sup>9,10</sup> Based on the ingredients, UV blockers are classified as organic blockers, inorganic blockers, and organic/inorganic blockers. The most widely used inorganic UV blockers are titanium dioxide (TiO<sub>2</sub>) and zinc oxide (ZnO). TiO<sub>2</sub> is sub-classified into anatase and rutile forms, where the latter is the most commonly used UV blocker.<sup>11</sup> Organic UV blockers include octyl-methoxy cinnamate (OMC), octocrylene, benzophenone, octyl salicylate, and oxybenzone.<sup>12,13</sup> Organic/inorganic blockers are produced by combining organic and inorganic UV blockers.

Previous studies have investigated the effects of optical properties such as UV absorption rate and UV reflection rate on SPF and PA, based on different forms of TiO<sub>2</sub>. Studies confirming the TiO<sub>2</sub> concentration, particle size, and distribution in commercially available UV blockers, as well as changes in the SPF based on different TiO<sub>2</sub> particle sizes, have been conducted.<sup>14-16</sup> A previous study has investigated the synergic effects of organic and inorganic UV blockers mixed together.<sup>17</sup>

Field-flow fractionation (FFF) is widely used to analyze the characteristics of colloids and to separate colloids (ex. nanoparticles, protein, DNA, etc.) based on their sizes. FFF has a wide range of analysis, from a few nanometers to hundreds of micrometers.<sup>18-21</sup> Based on the type of external field, FFF is classified as asymmetrical flow field-flow fractionation (AsFIFFF), sedimentation field-flow fractionation (SdFFF), and thermal field-flow fractionation (ThFFF).<sup>18</sup>

In this study, commonly used methods for size analysis, i.e., microscopy and dynamic light scattering (DLS), as well as the relatively unknown AsFIFFF, were used. The changes in TiO<sub>2</sub> particle sizes based on the proportion of organic/inorganic UV blockers were observed, and the correlation between the physical/chemical characteristics of organic/inorganic UV blockers and the SPF was studied. The appropriate proportion of organic and inorganic UV blockers required for a high SPF was also investigated.

## 2. Theory

### 2.1. Theory of AsFIFFF

AsFIFFF can be used to directly calculate the hydraulic diameter ( $d_H$ ) using retention time ( $t_r$ ), as shown in Eq. (1).<sup>21,22</sup>

$$d_H = \frac{2kTV^0}{\pi\eta w^2 V_c t^0 t_r} \quad (1)$$

Here,  $k$  is the Boltzmann constant,  $T$  is the absolute temperature (K),  $V^0$  is the void volume of the channel,  $\eta$  is the carrier liquid viscosity,  $w$  is the width of the channel,  $V_c$  is the intensity of the external field, and  $t^0$  is the void time of the channel. In Eq. (1), all

variables with the exception of  $t_r$  are constants based on the experimental conditions. Therefore, determination of  $t_r$  of a sample using AsFIFFF can yield the sample size and size distribution.

### 3. Experimental

#### 3.1. Materials

TiO<sub>2</sub> used in this study to manufacture UV blockers was of rutile form, and was purchased from Ishihara Sangyo Kaisha, Ltd. (Tokyo, Japan). OMC was purchased from BASF SE (Mannheim, Germany). The ingredients required to manufacture UV blockers (purified water, oil, emulsifier, etc.) were purchased from Ecofactory (Seongnam, Korea). To disperse the manufactured UV blocker, Tween 80 (Sigma-Aldrich, St. Louis, USA) was used. The FL-70 (Fisher Chemical, New Jersey, USA) and sodium azide (NaN<sub>3</sub>, Sigma-Aldrich, St. Louis, USA) were used to prepare the FFF carrier liquid.

#### 3.2. Instruments

The homogenizer used for manufacturing the UV blocker was MS-280D (MTOPS, Yangju, Korea). The SPF and monochromatic protection factor (MPF) were measured with an SPF analyzer-290As (Solar Light, Glenside, USA). The range of measured wavelength was 290-400 nm, at the interval of 5 nm. A total of 12 measurements were carried out, and the measurement site was changed each time. The average value was calculated and reported. The SPF and MPF of the manufactured UV blocker were measured after the UV blocker was spread on Schonberg PMMA plates. The spread amount was determined based on the "UV blocker measurement method and standard" of notice 2012-88 from the Ministry of Food and Drug Safety.<sup>23</sup>

To confirm the sizes and shapes of the TiO<sub>2</sub> particles, transmission electron microscopy (TEM, Tecnai F30 ST, FEI Company, USA) and scanning electron microscopy (SEM, Magellan 400, FEI Company, USA) were used. The sizes and distributions were analyzed using a DLS system (DynaPro NanoStar, Wyatt Tech. Corp., Santa Barbara, USA) and an

AsFIFFF short channel (Wyatt Tech., Europe GmbH, Dernbach, Germany) equipped with a cellulose membrane (Millipore, Bedford, USA) with 10 kDa molecular weight cut-off, and a 250- $\mu$ m-thick Mylar spacer. The carrier liquid used in the AsFIFFF separation was deionized distilled water containing 0.1 % FL-70 and 0.02 % NaN<sub>3</sub>. In order to remove impurities from the carrier liquid, a 0.45- $\mu$ m membrane filter (Membrane Solutions, Plano, USA) was used for filtration before analysis. An HPLC pump (LC-20AD, Shimadzu Corp., Kyoyo, Japan) was used for injecting the carrier liquid, and an Optiflow 1000 Liquid Flowmeter (Agilent Technologies, Palo Alto, CA, USA) was used to measure the flow rate. A UV detector (Model 500, Chrom Tech, Minnesota, USA) was used to detect the samples assorted based on their sizes. 20  $\mu$ L of the sample was injected using a syringe pump (Legato 100, KD Scientific Inc., Mendon, USA) at a flow rate of 0.2 mL/min. Each measurement was repeated 3 times to confirm reproducibility.

### 4. Results and Discussion

#### 4.1. UV blocker effects of TiO<sub>2</sub> and OMC

Prior to preparing UV blockers, the UV blocking properties of TiO<sub>2</sub> and OMC were individually evaluated. In order to approximate the formulation of UV blockers without the effects of other added compounds, TiO<sub>2</sub> and OMC were mixed with Vaseline prior to SPF and MPF measurements. The measurements of pure Vaseline were then subtracted to calculate the SPF and MPF of pure TiO<sub>2</sub> and OMC. In order to determine the changes in the SPF and MPF with concentrations, the concentration of TiO<sub>2</sub> was set to 6, 12, 18 and 25 wt% and the concentration of OMC was set to 0.5, 2.5, 4.5 and 7.5 wt%, respectively. The concentrations were all within the permitted range for functional cosmetics.

*Fig. 1* shows the SPF and MPF measured at various concentrations of TiO<sub>2</sub> and OMC. *Fig. 1(a)* shows that, as the TiO<sub>2</sub> and OMC concentrations increase, the SPF increases accordingly. When the rate of increase in the SPF with the concentration

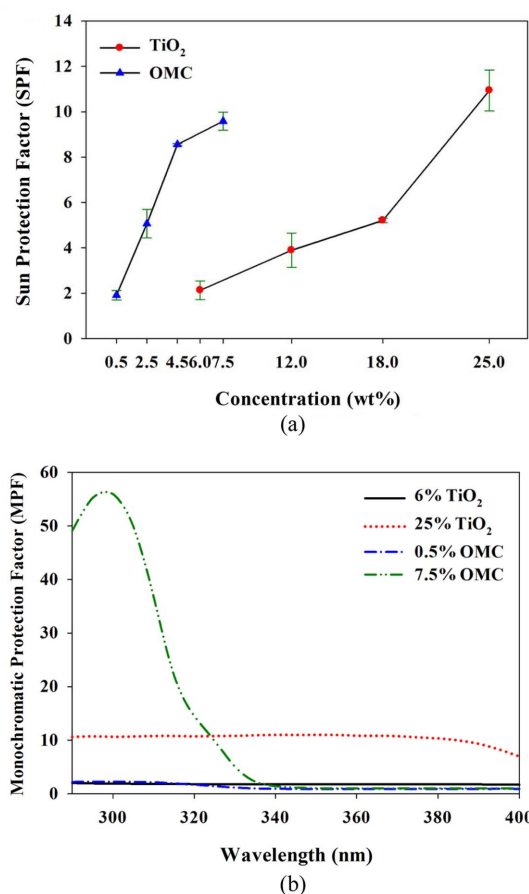


Fig. 1. Results of sun protection factor (SPF) (a) and monochromatic protection factor (MPF) (b) for different concentration of TiO<sub>2</sub> and OMC.

was compared using the slope of the plot, TiO<sub>2</sub> was 0.45 and OMC was 1.11. These results indicate that OMC is twice as sensitive as TiO<sub>2</sub> in terms of changes in the SPF. Although the SPF was not measured for identical concentrations of the two

compounds, the highest concentration was comparable to the upper limit of the permitted range in cosmetics. The SPF of pure TiO<sub>2</sub> and OMC in UV blockers can be estimated to be close to 10. Fig. 1(b) shows the range of UV light that TiO<sub>2</sub> and OMC can block. It was observed that TiO<sub>2</sub> effectively blocks UV light at 290–400 nm, which corresponds to both UV-A and UV-B. On the other hand, OMC effectively blocked UV light at 290–320 nm, which corresponds to UV-B. The results suggest that UV blockers solely composed of OMC can be specialized for protection from the UV-B range, while those solely composed of TiO<sub>2</sub> can block both UV-A and UV-B. Furthermore, it can be inferred that combination of organic and inorganic UV blockers result in more effective blocking of UV light.

#### 4.2. Effects of TiO<sub>2</sub> and OMC proportions on SPF

In order to systematically confirm the effects of organic and inorganic UV blocker proportions on the SPF and MPF, the permitted limits in cosmetics were disregarded. The TiO<sub>2</sub> and OMC concentrations were set to 0%, 4.5%, 9% and 13.5%, and the standard method provided by the Ministry of Food and Drug Safety was used for the manufacturing UV blockers.<sup>23</sup>

Table 1 shows the proportions of the organic and inorganic UV blockers, concentrations, and the measured SPF.

The SPF for Sun-1 and Sun-2, UV blockers prepared with single compounds, were measured to be  $10.6 \pm 1.6$  and  $18.0 \pm 0.3$ , respectively, which are higher than those shown in Fig. 1. It can be inferred that

Table 1. Compositions of organic-inorganic sunscreen formulations and their SPF values

Number	TiO <sub>2</sub> concentration (wt%)	OMC concentration (wt%)	TiO <sub>2</sub> : OMC Mixing ratio	SPF $\pm$ SD
Sun-1	0	4.5	0 : 1	$10.6 \pm 1.6$
Sun-2	4.5	0	1 : 0	$18.0 \pm 0.3$
Sun-3	4.5	4.5	1 : 1	$18.2 \pm 1.3$
Sun-4	4.5	9.0	1 : 2	$20.3 \pm 1.7$
Sun-5	4.5	13.5	1 : 3	$23.7 \pm 1.8$
Sun-6	9.0	4.5	2 : 1	$23.9 \pm 1.5$
Sun-7	13.5	4.5	3 : 1	$26.5 \pm 1.2$

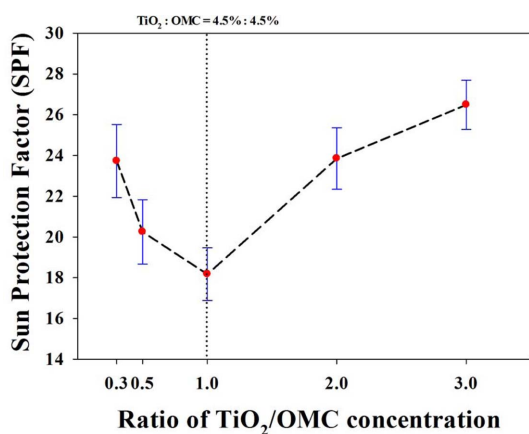


Fig. 2. SPF of sunscreen formulations for compositions of TiO<sub>2</sub> and OMC.

these values are due to the added compounds such as emulsifiers and oils during the manufacturing process. These added compounds led to relatively higher synergic effects with inorganic compounds such as TiO<sub>2</sub> as compared to organic compounds such as OMC. In addition, UV blockers manufactured by mixing TiO<sub>2</sub> and OMC (Sun-3) had an SPF of 18.2 ± 1.3, which was higher than that of Sun-1 and Sun-2, as shown in Table 1.

Fig. 2 shows the changes in the SPF based on the

composition of TiO<sub>2</sub> and OMC. The results were computed by fixing the concentration of one compound and increasing the concentration of the other compound two- or threefold. Table 1 shows the changes in the SPF in the plots of Sun-3, 4, 5, 6 and 7.

The SPF's were similar when the OMC concentration was tripled (Sun-5, SPF=23.7 ± 1.8) and the TiO<sub>2</sub> concentration was doubled (Sun-6, SPF=23.9 ± 1.5). This observation indicates that TiO<sub>2</sub> has a greater effect on the SPF in UV blockers than does OMC. However, this result contradicts those shown in Fig. 1, because of the added compounds and the difference in blocking mechanisms between the two compounds.<sup>24,25</sup> The UV blocking mechanism of OMC is based on the absorption of UV light, while that of TiO<sub>2</sub> is based on a complex process involving the absorption and reflection of UV light, followed by dispersion. Therefore, it is inferred that these differences in mechanisms lead to different outcomes. However, further studies should be conducted to determine the exact reason for the aforesaid difference. Fig. 2 shows that the changes in the SPF are the greatest when the OMC concentration is fixed at 4.5 % and the TiO<sub>2</sub> concentration is increased. As predicted earlier, use of a combined organic/inorganic UV

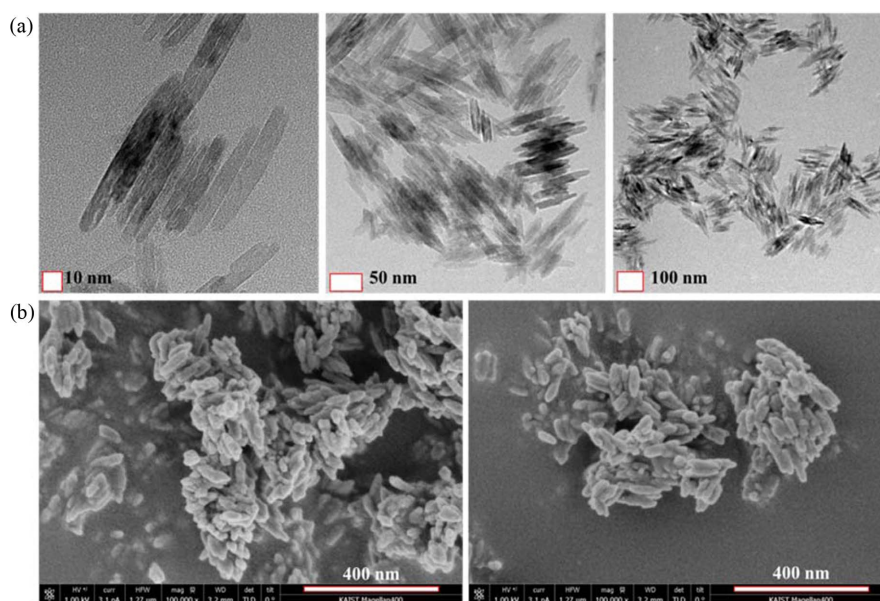


Fig. 3. Electron microscope images of TiO<sub>2</sub> powder. TEM (a) and SEM images (b).

blocker would increase the SPF more effectively and easily than using single UV blocker.

#### 4.3. Changes in TiO<sub>2</sub> particle size

TEM and SEM observations were performed to confirm the particle size and shape of TiO<sub>2</sub> in the inorganic UV blocker used in this study. The results are shown in Fig. 3.

Overall, the TiO<sub>2</sub> particles are rod shaped rather than spherical, with lengths of 50-100 nm and widths of 5-10 nm, as shown in Fig. 3.

During the manufacture of the UV blocker, physical energy may be produced by the high temperature and the use of the homogenizer. In this case, the physical properties of TiO<sub>2</sub> (size, distribution, etc.) could be altered. The sizes and size distributions of TiO<sub>2</sub> in the manufactured UV blocker were measured using DLS and AsFIFFF.

In order to measure the particle size of TiO<sub>2</sub> in the manufactured UV blocker, each sample was diluted to 1 mg/mL in aqueous solution of 1 % Tween 80. The samples were dispersed for 15 min using a sonicator prior to the measurement. The particle size of TiO<sub>2</sub> in the UV blockers Sun-2, 3, 4, 5, 6 and 7 were measured using DLS. The results of size measurements for Sun-2 and 6 by AsFIFFF are shown in Table 2. Unlike the case of DLS, only 2 samples were chosen for the size analysis by AsFIFFF and the remaining 4 samples were not analyzed. The results showed that as the OMC and TiO<sub>2</sub> concentrations increased, the average size of the TiO<sub>2</sub> particles increased, leading to increased SPF.

Nanoparticles usually have high surface energy

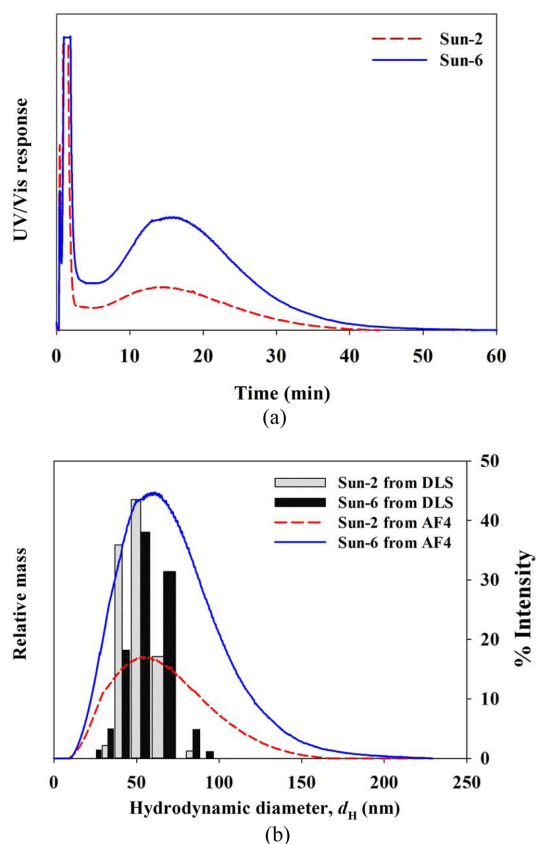


Fig. 4. AF4 fractograms of sunscreen formulations (a) and size distributions from DLS (bar) and AF4 (line) of sunscreen formulations (b). The AF4 channel and the cross flow rates were 1.0 mL/min, and the carrier liquid was water containing 0.1 % FL-70 and 0.02 % NaN<sub>3</sub>.

and easily cohere. Therefore, as the TiO<sub>2</sub> concentration increases, the collision rate between particles also increases and thus may lead to cohesion. The cohesion between the TiO<sub>2</sub> particles increases with an increase

Table 2. Mean diameter of TiO<sub>2</sub> in sunscreen formulations measured by DLS and AF4

Number	TiO <sub>2</sub> : OMC	SPF ± SD	Mean diameter from DLS ± SD (nm)	Mean diameter from AF4 ± SD (nm)
Sun-1	0 : 1	10.6 ± 1.6	-	-
Sun-2	1 : 0	18.0 ± 0.3	46 ± 4.9	66 ± 1.6
Sun-3	1 : 1	18.2 ± 1.3	53 ± 2.9	n.d*
Sun-4	1 : 2	20.3 ± 1.7	57 ± 3.5	n.d*
Sun-5	1 : 3	23.7 ± 1.8	63 ± 5.4	n.d*
Sun-6	2 : 1	23.9 ± 1.5	56 ± 5.0	71 ± 1.4
Sun-7	3 : 1	26.5 ± 1.2	65 ± 1.3	n.d*

n.d\*: not determined

in the OMC concentration. It can be inferred that this is due to the increased degree of emulsification caused by the increased OMC concentration.<sup>26,27</sup> Further studies will be needed to identify the accurate correlation between the degree of emulsification and the cohesion between the TiO<sub>2</sub> particles. Light scattering also increases with the increase in particle size, which leads to light blocking and consequently affects the SPF.

Fig. 4(a) shows the AsFIFFF fractogram of Sun-2 and Sun-6. Fig. 4(b) shows the size distributions determined by DLS and AsFIFFF. The AsFIFFF size distribution was determined by applying Eq. (1). The distribution determined through AsFIFFF differed from that determined by DLS, which is due to the different measurement mechanisms in the two techniques. DLS usually does not separate particles based on their sizes and measures the average particle size. On the other hand, AsFIFFF separate particles according to their sizes and determines their average size and distribution. Therefore, AsFIFFF allows visualization of TiO<sub>2</sub> particles that are too small or too large to be measured by DLS.<sup>28,29</sup>

## 5. Conclusions

In this study, the effects of the organic UV blocker OMC and the inorganic UV blocker TiO<sub>2</sub> on the SPF were compared and analyzed using various methods.

A higher SPF was observed in the case of using pure OMC as compared to that with TiO<sub>2</sub>. In the case of UV blockers manufactured by mixing the two compounds, the TiO<sub>2</sub> concentration had a greater effect (approximately 1.5 times greater) on the SPF than did the OMC concentration.

TiO<sub>2</sub> showed similar UV blocking properties in the wavelength ranges of UV-A and UV-B, while OMC showed greater UV blocking properties in the UV-B range than in the UV-A range.

TiO<sub>2</sub> particle analysis using DLS and AsFIFFF showed that as the concentration of TiO<sub>2</sub> and OMC increased in the UV blockers, the TiO<sub>2</sub> particle size increased. This increase in particle size led to a higher SPF in the UV blockers.

Thus, the correlation between the physical/chemical properties of TiO<sub>2</sub> and OMC and the SPF was investigated. Based on the results, it was confirmed that AsFIFFF and DLS had the potential to evaluate the SPF efficiency in UV blockers.

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