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Note

Polymer Nanoparticles Containing Sunscreen Ingredients for UVA and UVB Coverage

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Solar radiation in ultraviolet (UV) ranging 400–290 nm exerts harmful effects on humans. Although the atmospheric ozone layer filters out most UVB (320–290 nm), photochemical damage is primarily caused by UVB. Proteins and nucleic acids exposed to UV can cause structural changes via photochemical reactions. As a result, the structural changes disturb critical genetic processes such as transcription, DNA replication, and translation, leading to severe diseases. In addition, UVA (400–320 nm) exposure also affects skin irritation. Therefore, it is essential to use sunscreen covering both UVA and UVB absorption to protect the skin from solar radiation as shown in *Fig.* S1.[1]

Another condition for good sunscreen is that it must be chemically stable materials so that long-term UV blocking can be achieved. Above all, the UV absorber should not have any harmful effect on the human body when applied to the skin. Some of the representative sunscreen ingredients used in cosmetics are still presented with safety issues regarding their toxicity. For example, avobenzone, oxybenzone, octocrylene (OCR), homosalate, octisalate, and octinoxate were absorbed systemically and exceeded the critical plasma concentration suggested by the Food and Drug Administration (FDA). Understandably, these results do not mean that sunscreens containing the above substances should not be used. However, the problems that can arise from the adsorption of these ingredients into the body should not be ignored. Safety issues that can occur in the endocrine system have not been demonstrated, especially when the ingredient is above a critical amount. Among the sunscreen ingredients, avobenzone can be decomposed by UV rays. A strong enol to keto photoisomerization is generated by UV irradiation, and the protonation dramatically interferes with the stability of the enol tautomer.[2] Avobenzone cannot be used alone in sunscreens because this process is irreversible.[3] However, photolabile UV absorbers can be stabilized by other photostable UV absorbers, such as OCR and homosalate.[4–7] Therefore, using OCR as a quencher, it could create a combination with excellent UVA and UVB blocking capability. This combination has already been confirmed for stability.

There are also environmental issues. For instance, the toxicity of sunscreen ingredients adsorbed or uptaken to various plant species is severe to cucumber, phytoplankton and algal.[8] By inhibiting photosynthesis and respiration, the structure and function of plant cells are damaged due to the excessive production of reactive oxygen species and the formation of lipid peroxides. In addition, OCR accumulates in the form of fatty acid complexes in corals, causing dysfunction.[9]

A polymer micelle structure, consisting of a core of the organic UV absorber surrounded by a polymer shell, was adopted to reduce the damage caused by the sunscreen.[10] Pluronic® F127 (PF127) triblock copolymer consisting of poly(ethylene oxide) and poly(propylene oxide) (PEO_{100}-*b*-PPO_{65}-*b*-PEO_{100}) has been widely utilized as a cosmetic ingredient.[11] Its amphiphilic property can be used as emulsifier, gelling agent, and thickener. In an aqueous solution, PF127 self-assembled micelles, which have a shell dominated by the PEO blocks and a hydrophobic core consisting of the PPO block. These core of aggregates can load hydrophobic sunscreen ingredients such as bis-ethylhexyloxyphenol methoxyphenyl triazine (BEMT), butyl methoxydibenzoylmethane (BMDM), ethylhexyl salicylate (EHS), ethylhexyl methoxycinnamate (OMC), Lumogen® Violet (LV)

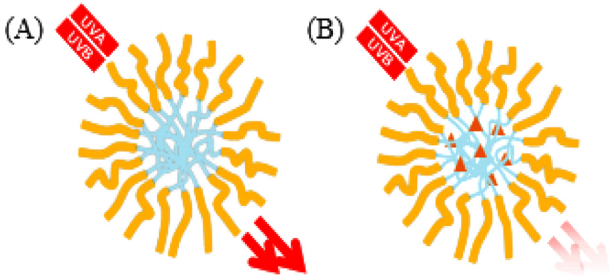

***Figure* 1.** Effect of organic molecules within polymeric NPs upon UV irradiation. While pristine nanoparticles transmit UV light (A), nanoparticles with UV absorbers screen UV (B).

and OCR (*Fig.* 1).[12-14] Chemical structures of sunscreen ingredients were shown in the *Fig.* S2.

However, spontaneous micellization of PF127 can signify that temperature change can alter the micellar structure in water. Below the critical micelle temperature (CMT), the spherical micelle can be dissociated into unimers.[15] To prevent the dissociation of PF127 micelles, we prepared thermodynamically enhanced PF127 nanoparticles (NPs).

To stabilize PF127 micelle, we suggest the semi-interpenetrating networks (sIPN) using pentaerythritol tetraacrylate (PETA), as shown in *Fig.* 2.[16] The sIPN formation stabilizes the PF127 micelle (ca. 20 nm in diameter) below its CMT as well as at temperatures above 80 ℃. Also, sIPN formation maintain stable under UV irradiation.[14] It is reported that the core-loaded small molecules are firmly entrapped within the sIPN network. Moreover, this method does not require complicated laborius synthesis.[10,17]

RESULTS AND DISCUSSION

Since the organic UV absorbers inside the NPs are hydrophobic, they can be loaded into the core of the F127 micelles. Each of 6 UV absorbers was individually encap-

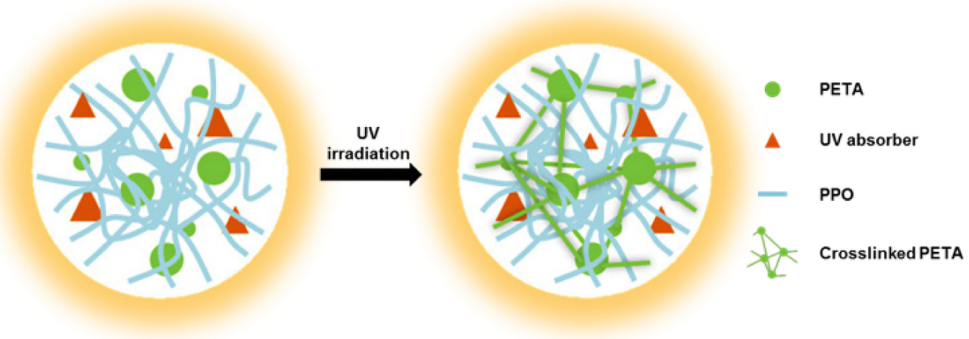

***Figure* 2.** Scheme of sIPN system in the micelle core.

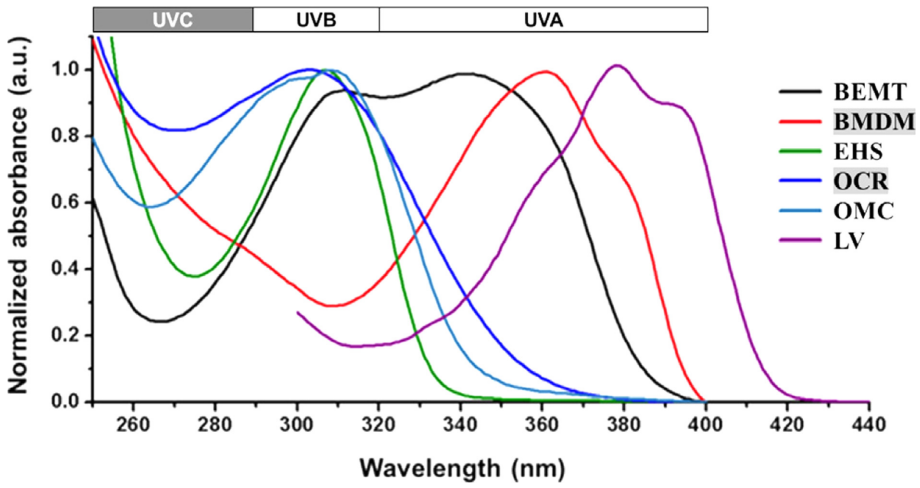

***Figure* 3.** Normalized absorption spectra of NPs containing the listed UV absorbers. Two chromophores to prepare an optimized NP were highlighted. Except LV, other UV absorbers are FDA-approved ingredients, which are commonly used in cosmetics.

sulated in separate F127 micelles. Therefore, the UV absorbers were successfully loaded into the core of micelles in aqueous solution. The absorption spectra of UV absorber-loaded NPs were obtained by a spectrophotometer (*Fig.* 3). NPs containing sunscreen ingredients absorbs specific UV region.

Due to the strong absorptivity of BMDM and OCR (*Fig.* S1) in UVA and UVB range, respectively, the two UV absorbers were selected as sunscreen ingredients resulting in optimized UV absorbing NPs. We carefully screened mixing ratios of the BMDM-OCR NPs so that the NP significantly absorbs both UVA and UVB. The most efficient UV-blocking NPs were selected at the mixing the ratio of BMDM and OCR (1 : 3 and 1 : 4). BMDM and OCR are co-loaded in proportion to the formed NP core. The mixed UV absorber NPs were diluted five times, and the absorption spectra were measured in the 250–400 nm range (*Fig.* 4). Comparing the two spectra, it was confirmed that the optimal ratio of BMDM and OCR was 1 : 3 to cover the entire region more efficiently.

UV-shielding performance and stability of BMDM-OCR NPs need to be considered at the same time. The photostability test of BMDM-OCR NPs under intense light was performed. The effect of UV radiation at 0.5 W/cm^2 on the stability of the BMDM -OCR NPs was investigated as shown in *Fig.* 5. In the both UVA and UVB region, the resulting BMDM-OCR NPs showed no notable photobleaching for 30 min. Here, we should note that usual solar radiation has lower than 0.1 W/cm^2.

In this study, we propose a method for encapsulating organic UV-blocking molecules in polymer micelles. We also optimized the combination of UV absorbers that effectively cover both UVA and UVB for cosmetics applications in near future. Moreover, it is expected that the UV-absorbing small molecules can be prevented from being directly exposed to the skin. Furthermore, the NPs are less harmful to environmental resources because F127 is a FDA-approved substance with thorough examination.

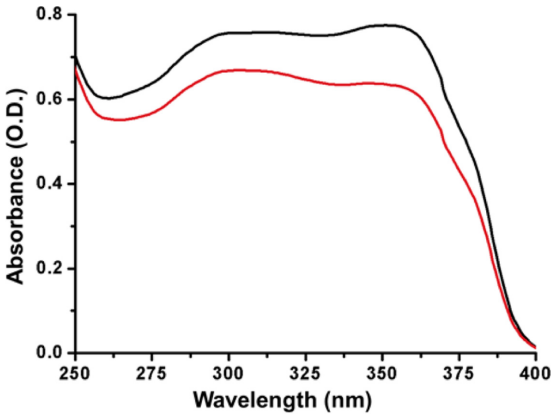

***Figure* 4.** Absorption spectra of NPs containing BMDM and OCR to absorb UVB and UVA. (Black) BMDM:OCR = 1:3, (Red) BMDM:OCR = 1:4.

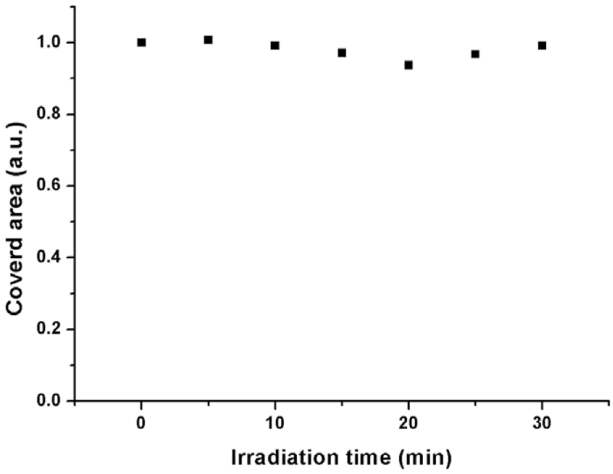

***Figure* 5.** The effect of UV irradiation to UV absorber NP. BMDM-OCR NPs were exposed under 0.5 W/cm^2 UV light source for the given times. The areas are sum of absorbance from 290 to 400 nm.

EXPERIMENTAL

All chemicals were purchased from Sigma Aldrich (Korea) for the preparation of NPs except for UV absorbers. The UV absorbers, BEMT, BMDM, EHS, OCR and OMC were donated by Enprani Co. Ltd (Incheon, Korea). The LV was purchased from BASF (Ludwigshafen, Germany). All of the materials were used without purification. The aqueous solutions were ultra-pure water (resistivity > 18 MΩ) purified by a Milli-Q Millipore system (Millipore, Germany).

Preparation and Characterization of Individual UV Absorber NPs

F127 was dissolved in H_2O to prepare a stock solution of 10 wt% concentration. PETA was prepared in chloroform at 100 mg/mL concentration. UV absorbers were also dissolved in acetone except for BEMT, which was solved in dichloromethane at 1 mg/mL. PETA stock solution of 125 μL and appropriate UV absorbers stock solution was placed in an empty vial. The organic solvent was evaporated to prepare the PETA-UV absorbers film in a fume hood for 24 hours at ambient conditions. The 10 wt% F127 aqueous solutions of 5 mL were transferred to a PETA-UV absorber film vial. Then the solution was agitated for 6 h

using an orbital shaker (Lab Companion SKF 2050 Shaker, Jeio Tech, Koare) at 200 rpm. The vial was filled with Ar and increased the temperature to 50 ℃, at which the micelle was not dissociated in the irradiation chamber. The vial was covered with a cover glass instead of a cap and irradiated with UV lamps (OmniCure series 2000, Lumen Dynamics, Canada) at 1.5 W/cm^2 under stable conditions at 50 ℃ for 6 minutes. The solution was slowly cooled down at room temperature and filtered to remove the remaining reagent with a 0.2 μm syringe filter (Minisart® Sartorius Stedium, Biotechm Germany).

Six UV absorber NPs were diluted with H_2O and examined for optical properties. Each absorption spectrum from 250 to 400 nm was recorded with a UV-Vis spectrophotometer (SpectraMax M2, Molecular Devices, USA). Absorption spectra of UV absorber NPs were obtained by measuring the samples in a 10 mm path length quartz cuvette.

Optimization UV Absorber-blended NPs

Based on the spectra measured with individual UV absorbers, we prepared NPs by selecting appropriate UV absorbers, BMDM and OCR, that can cover both UVB and UVA regions, respectively. The selected mixed UV absorbers at specific mixing ratios formed NPs encapsulated by PF127. The absorption spectra of the optimized UV absorber NPs were recorded.

Stability Test of UV Absorber-blended NPs

UV absorbing NPs were irradiated for 0, 5, 10, 15, 20, 25 and 30 min by UV irradiation at 0.5 W/cm^2. The absorption spectra were recorded by a UV-Vis spectrophotometer.

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Supporting Information. Absorption spectra of commercial sunscreens for comparison and the chemical structures of UV absorbers used in this study are available online.

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