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A New Ultraviolet Protective Agent of the Intercalation Compound of Aminobenzoic Acid Esters (UV Absorber) and Synthetic Mica (Inorganic Layered Compound)[1]

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The interaction between a sodium-type synthetic mica (Na-TSM), a material of reactive layered compounds which exhibit characteristic light scattering, and some aminobenzoic acid derivatives which act as UV absorbing agents (UV absorber), was investigated. Due to the observed elongation of interlayer spacing (increase in the *d*-value) by X-ray diffraction analysis, it was found that the powdered form of 4-aminobenzoic acid ethyl ester (4-ABE) interacts with Na-TSM, and can be immobilized in the interlayer space of Na-TSM. Consequently, an intercalation compound of 4-ABE and Na-TSM was obtained. The formation of the intercalation compound of 4-ABE and Na-TSM was accelerated by heat processing, particularly at temperatures exceeding the melting point of 4-ABE. When 2-aminobenzoic acid methyl ester (2-ABM) in liquid form at room temperature was used instead of 4-ABE, the intercalation compound of 2-ABM and Na-TSM was formed in a similar manner to that of 4-ABE and Na-TSM. The heat processing again accelerated the formation of the intercalation compound of 2-ABM and Na-TSM. Interestingly, a difference in the formation behavior of intercalation compounds between 4-ABE and 2-ABM was observed. The intercalation compound of Na-TSM and 4-ABE or 2-ABM showed efficient UV absorption in the UV_B and UV_A wavelength regions. Therefore, application of a layered compound of Na-TSM and 4-ABE or 2-ABM as a novel UV screening system is promising.

Key words intercalation compound; ultraviolet absorber; synthetic mica; inorganic layered compound; X-ray diffraction analysis; diffuse reflectance spectrum analysis

The interaction of reactive inorganic layered crystals (host material), such as mica-type layered silicates, with various organic compounds (guest material) which exist among layers due to intercalation has been successfully studied.[2] The combination of inorganic layered crystals with organic compounds offers new materials with useful physicochemical characteristics. We have investigated the intercalation between synthetic and natural micas of inorganic layered compounds and organic drugs. Recently, we reported on the interaction between synthetic inorganic mica and phosphatidylcholine (PC) in a solid dispersion with indomethacin (IM, a model drug) *via* intercalation by use of heating, instead of by the conventional solvent method.[3] Furthermore, the possible formation of a new colored material by the intercalation compound of synthetic mica and water-soluble color methylene blue (MB) has been demonstrated.[4]

Mica is an attractive agent for use as an ultraviolet (UV) screening material since it exhibits characteristic light scattering. Aminobenzoic acid and its related compounds are used in cosmetics as sunscreening agents due to their potent UV absorbing characteristics. Synthetic mica,[5] which is very stable in both acidic and alkaline media, is an attractive model material for reactive layered compounds. If UV absorbing agents (UV absorbers) were to be immobilized within an inorganic layered compound such as synthetic mica, the application of this layered compound as a novel UV screening system might be possible.

In the present study, to elucidate the method of formation of intercalation compounds between aminobenzoic acid esters of UV absorbers and inorganic layered synthetic mica (tetrasilicic fluoro mica), we have evaluated the extent of their interaction by powder X-ray diffraction and UV absorption analysis.

Experimental

Materials Sodium-type synthetic mica (Na-TSM, $Na[Mg_{2.5}Si_4O_{10}F_2]\cdot 2H_2O$) as a host material was supplied by Topy Industry Co., Tokyo, Japan. 4-Aminobenzoic acid ethyl ester (4-ABE) and 2-aminobenzoic acid methyl ester (2-ABM) were obtained from Wako Pure Chemical Industries, Tokyo and from Tokyo Kasei Kogyo, Japan, respectively.

Preparation of Intercalation Compounds The heating method of Watanabe *et al.*[3] was applied. Briefly, an aliquot (100 mg) of a powdered mixture containing each drug and Na-TSM (sieved through an 80-mesh screen), and weighed (weight ratio of drug to Na-TSM, 5:95—40:60), was heated in a glass tube in a nitrogen gas atmosphere using a dry block oven (Scinics Co., Tokyo, Japan) at a constant temperature for a predetermined time. The heated materials were cooled to room temperature by placing the tubes in ice water. These products of heat processing were then collected and crushed using a mortar. The drug-synthetic mica (an intercalation compound of UV absorber and Na-TSM (inorganic layered compound)) was obtained by sieving the crushed products of heat processing through an 80-mesh screen. The resulting mixture was then characterized by powder X-ray diffraction analysis as described in a previous report.[3]

X-Ray Diffraction and UV Absorption Analysis The intercalation products were characterized by X-ray diffraction analysis (Powder X-ray Diffractometer, MAC Science (Yokohama, Japan): Cr-$K\alpha$ radiation ($\lambda = 2.29$ Å) using a monochromator). For UV absorption analysis of the products, the diffuse reflectance spectra were evaluated. The reflectivity spectrum of each product in the UV_B and UV_A regions was measured using a UV-VIS recording sepectrophotometer (model UV-2400 (PC), Shimadzu Co., Kyoto, Japan) equipped with an integrating sphere assembly (model ISR-240A, Shimadzu Co., Kyoto, Japan: white reflectance standard, barium sulfate). Then, the diffuse reflectance spectrum was determined using the Kubelka-Munk function,[6] *i.e.* Eq. 1:

$$f(R_d) = (1 - R_d)^2 / 2R_d \qquad (1)$$

where R_d is the relative diffuse reflectivity. The diffuse reflectance spectrum ($f(R_d)$-wavelength curve) corresponds to the absorption

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spectrum for solid materials.

Results and Discussion

Intercalation of 4-ABE or 2-ABM into Na-TSM Aminobenzoic acid derivatives[7] and mica are used as sunscreening materials in pharmaceutical and cosmetic fields. Previously, we studied the possibility of the formation of an intercalation compound of 4-ABE (UV_B absorber)[8] and natural white mica (Muscovite) or Na-TSM.[1] Consequently, it was found that 4-ABE intercalated into Na-TSM by means of heat processing without requiring for solvents. However, 4-ABE could not intercalate into Muscovite. These findings led us to investigate whether the intercalation of Na-TSM and another aminobenzoic acid derivative could be formed using the method described in the Experimental section. However, a weak formation of the intercalation compound of 4-ABE and Na-TSM in powder form was observed at room temperature. Therefore, in this investigation, to facilitate the formation of intercalation compounds, the drug in solid form (powder) at room temperature was liquefied by heating at temperatures exceeding the mp of each compound by 10 °C.

Figure 1 illustrates the X-ray diffraction patterns of the mixture of 4-ABE and Na-TSM (weight ratio, 4-ABE : Na-TSM = 20 : 80) before (curve 2) and after (curve 3) heat processing at 100 °C (mp 88—90 °C of 4-ABE + 10 °C). The X-ray diffraction pattern of Na-TSM as a control (curve 1) is also shown in Fig. 1. The interlayer spacing (*d*-value) of Na-TSM obtained from the peak of the X-ray diffraction pattern (2θ value) was 1.2 nm. The X-ray diffraction pattern of the mixture of 4-ABE and Na-TSM at room temperature shows a similar peak profile (*d*-value, 1.2 nm) for Na-TSM without drug. However, a new peak, indicating a *d*-value of 1.9 nm, was observed in the X-ray diffraction pattern of the mixture of 4-ABE and Na-TSM. This indicates that the intercalation compound of 4-ABE and Na-TSM was formed between 4-ABE and Na-TSM. When the mixture of 4-ABE and Na-TSM was heated at 100 °C, then cooled, the peak indicating a *d*-value of 1.2 nm disappeared and a new peak indicating a *d*-value of 1.9 nm was significantly increased in the X-ray diffraction pattern of the heated product of the mixture of 4-ABE and Na-TSM. These results suggest that the interlayer spacing of Na-TSM had increased, and the formation of the intercalation compound of 4-ABE and Na-TSM was accelerated by heat processing. To evaluate the immobilization of 4-ABE in Na-TSM, mixtures of 4-ABE and Na-TSM before and after the heat processing were set on filter papers and then rinsed by ethanol (20-fold volume of the mixture of 4-ABE and Na-TSM). The estimated recovery (%) of 4-ABE in the filtrate (ethanol) from the mixture of 4-ABE and Na-TSM and its heated product was approximately 90% and 75%, respectively. This difference in the recovery of 4-ABE suggests that 4-ABE is immobilized into Na-TSM; thus, the intercalation compound of 4-ABE and Na-TSM was prepared by the heating method.

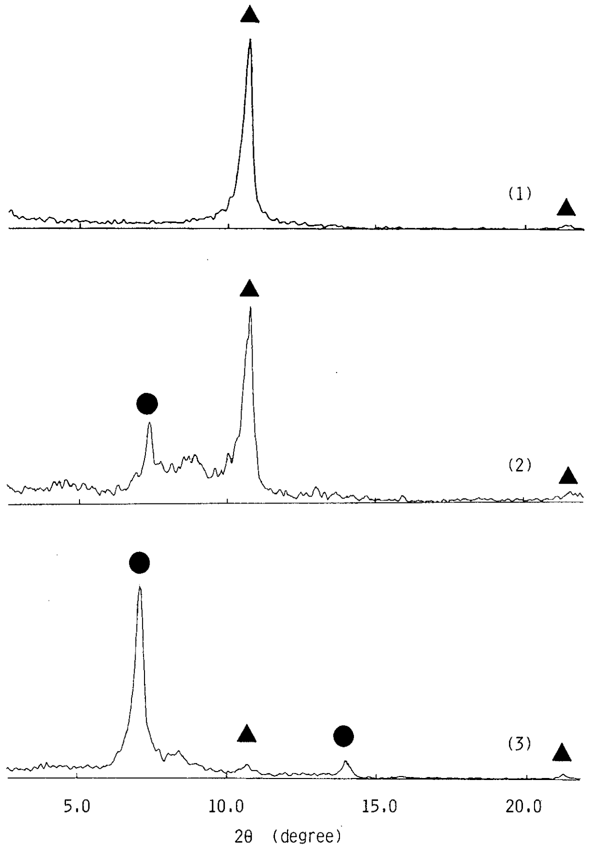

Fig. 1. X-Ray Diffraction Patterns of Na-TSM, a Mixture of 4-ABE and Na-TSM, the Intercalation Compound of 4-ABE and Na-TSM (Heat-Processed Product) Obtained by the Heating Method

Curves: (1), Na-TSM; (2), mixture of 4-ABE and Na-TSM at room temperature; (3), intercalation compound of 4-ABE and Na-TSM (weight ratio, 4-ABE (mp 88—90 °C): Na-TSM = 20 : 80, after heating at 100 °C for 6 min). Key: ●, peak for intercalation compound of 4-ABE and Na-TSM (*d*-value = 1.9 nm); ▲, peak for Na-TSM (*d*-value = 1.2 nm).

Interactions of organic materials with a solid surface can be successfully studied using inorganic layered compounds that take up organic materials between their layers by intercalation or ion exchange. Concerning mica-type layer silicates, it was reported that alkylammonium ions are intercalated after exchanging the inorganic interlayer cations, for example, the exchange of potassium ions of $KTiNbO_5$ by an alkylammonium ion[2]; the alkylammonium ions aggregate between the silicate layers to form bimolecular films.[2] Furthermore, the intercalation of *n*-alkylamines into layered transition metal phosphates has been reported.[9] In this investigation, we chose sodium-type tetrasilicic fluoro mica (Na-TSM) with a characteristic of ion-exchange ability. The UV absorber 4-ABE has an amino group in its chemical structure. Therefore, 4-ABE may interact with Na-TSM by ion-exchange with an interlayer ion (exchange of sodium ion of Na-TSM by 4-ABE). In general, the alkyl chains in alkylamine and alkylammonium ions between inorganic layers are directed perpendicularly to the layers and have a bilayer formation.[2,10] Consequently, the intercalation can be detected by increased basal spacing. An increase in the *d*-spacing value (from 1.2 to 1.9 nm) observed in the intercalation compound of 4-ABE and Na-TSM suggests that the conformation in the interlayer space was formed between Na-TSM and 4-ABE, as well as between alkylamines and so on.

In a subsequent study, the formation of the intercalation compound of Na-TSM and 2-ABM (UV_A absorber)[8] in a liquid form (oily) of the chemical at room temperature was examined. Figure 2 shows the X-ray diffraction pattern of a mixture of 2-ABM and Na-TSM (weight ratio, 2-ABM : Na-TSM = 20 : 80). Although heat processing was not carried out in the mixture of 2-ABM and Na-TSM, a new peak indicating the *d*-values of 1.5 and 1.8 nm was observed following the mixture of 2-ABM and Na-TSM at room temperature (shown by curve 2 in Fig. 2). From this result, it was presumed that two conformations of 2-ABM between the layers of Na-TSM exist. The peak indicating a *d*-value of 1.8 nm suggests a bilayer formation of 2-ABM by complete intercalation. On the other hand, the peak indicating a lower *d*-value (1.5 nm) may be related to the incomplete intercalation or monolayer formation of 2-ABM. The heat processing has the effect of promoting intercalation or bilayer formation, as evidenced by the marked increase in the peak, indicating a *d*-value of 1.8 nm (shown by curve 3 in Fig. 2) when the mixture of 2-ABM and Na-TSM was heated at 125 °C. With respect to the effect of heating temperature, the peaks indicating *d*-values of 1.5 and 1.8 nm disappeared (shown by curve 3 in Fig. 2) when the mixture of 2-ABM and Na-TSM was heated at a temperature exceeding 135 °C (bp of 2-ABM). Consequently, the X-ray diffraction pattern for the mixture was similar to that observed for Na-TSM without 2-ABM (curve 1 in Fig. 2). The reason for this is that the interlayer spacing of Na-TSM returned to the original length (1.2 nm) because 2-ABM volatilized from the shell layer of Na-TSM. Therefore, when the intercalation compound of 2-ABM and Na-TSM is efficiently formed, it is necessary to heat the mixture of 2-ABM and Na-TSM at a temperature below the bp of 2-ABM.

UV Absorption of an Intercalation Compound of a UV Absorber and Na-TSM Figure 3 illustrates the UV reflectivity spectra of Na-TSM and two of the intercala-

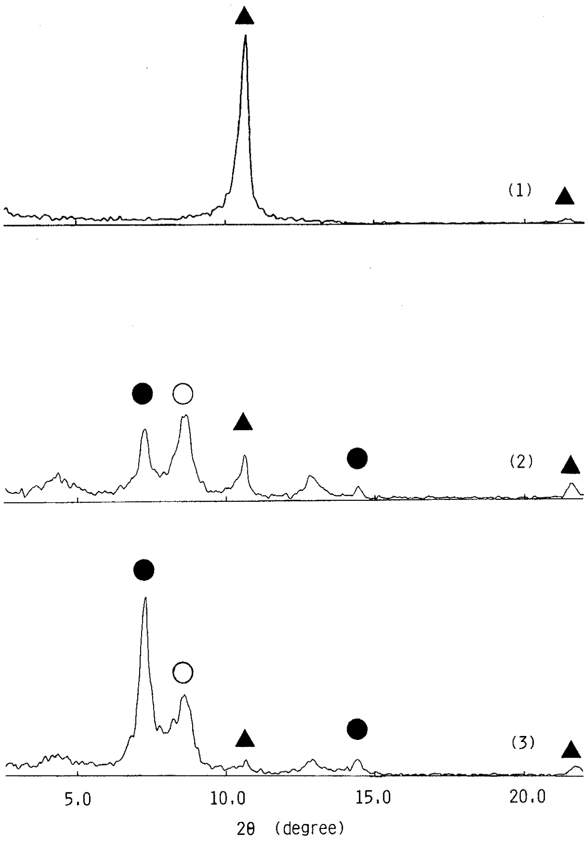

Fig. 2. X-Ray Diffraction Patterns of Na-TSM, a Mixture of 2-ABM and Na-TSM, the Intercalation Compound of 2-ABM and Na-TSM Obtained by the Heating Method

Curves: (1), Na-TSM; (2), mixture of 2-ABM and Na-TSM at room temperature; (3), intercalation compound of 2-ABM and Na-TSM (weight ratio, 2-ABM (bp 135 °C): Na-TSM = 20 : 80, after heating at 125 °C for 6 min). Key: ●, peak for intercalation compound of 2-ABM and Na-TSM (*d*-value = 1.8 nm); ○, peak for intercalation compound of 2-ABM and Na-TSM (*d*-value = 1.5 nm); ▲, peak for Na-TSM (*d*-value = 1.2 nm).

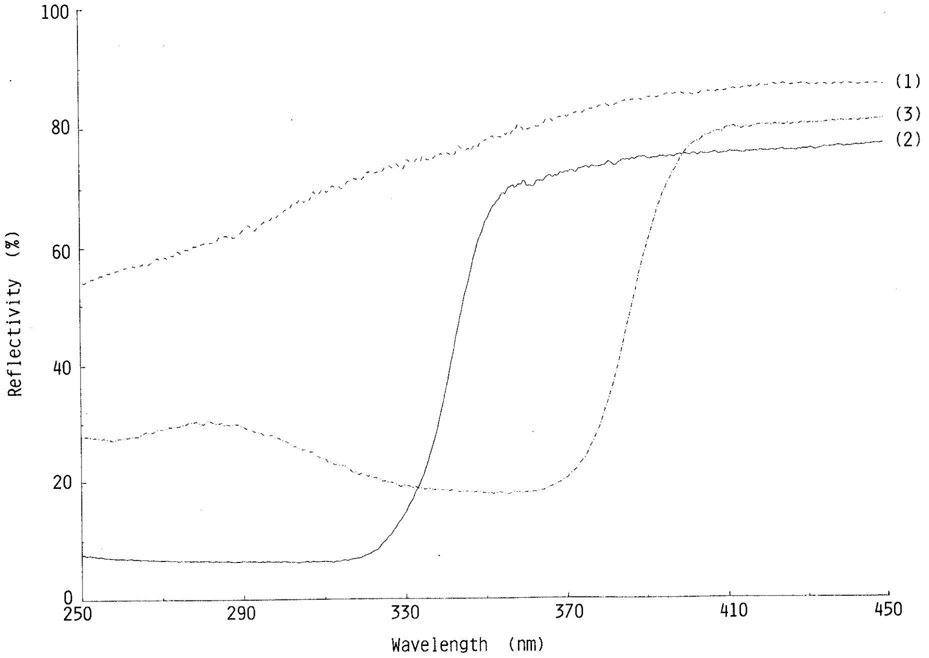

Fig. 3. UV Reflectivity Spectrum of Na-TSM and the Intercalation Compound of Na-TSM and 4-ABE (Heat-Processed Product at 100 °C) or 2-ABM (Mixture with Na-TSM at Room Temperature)

Curves: (1), Na-TSM; (2), intercalation compound of 4-ABE and Na-TSM; (3), intercalation compound of 2-ABM and Na-TSM.

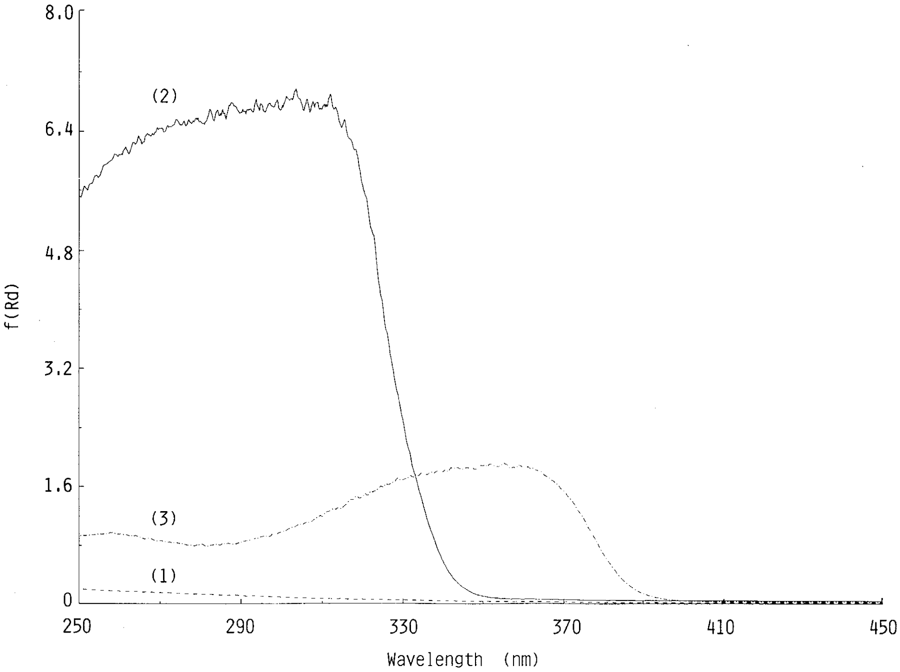

Fig. 4. Diffuse Reflectance Spectrum of the Intercalation Compound of Na-TSM and 4-ABE (Heat-Processed Product at 100 °C) or 2-ABM (Mixture with Na-TSM at Room Temperature)

Curves: (1), Na-TSM; (2), intercalation compound of 4-ABE and Na-TSM; (3), intercalation compound of 2-ABM and Na-TSM.

tion compounds prepared using Na-TSM and 4-ABE or 2-ABM. The diffuse reflectance spectra of the intercalation compounds of 4-ABE and Na-TSM and 2-ABM and Na-TSM are shown in Fig. 4. As shown in Fig. 3, Na-TSM (curve 1) exhibits high reflectivity in the UV_A and UV_B regions due to its light scattering characteristics. On the other hand, Na-TSM alone did not absorb UV light because the $f(R_d)$ value is negligible (Fig. 4). High levels of $f(R_d)$ values for the intercalation compound of 4-ABE (UV_{max} (ethanol): 290 nm) and Na-TSM were obtained in the UV_C wavelength region[11)] (less than 290 nm) and the UV_B region (290—320 nm). In addition, $f(R_d)$ values for the intercalation compound of 2-ABM (UV_{max} (ethanol): 340 nm) and Na-TSM were obtained in the UV region, particularly, in the UV_A wavelength region[11)] (320—400 nm).

Conclusion

An intercalation compound was formed from a mixture of Na-TSM and a UV absorber of 4-ABE or 2-ABM at room temperature, and the heat processing, particularly at a temperature exceeding the mp of the added compound, accelerated the formation of the intercalation compound of UV absorber and Na-TSM. Thus, it seems that the UV absorption in the UV_A and UV_B wavelength regions can be efficiently achieved by the intercalation compound of Na-TSM and a UV absorber. The application of the layered compound of Na-TSM and 4-ABE or 2-ABM as a novel UV screening system is promising.

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References and Notes

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