Colloid Polym Sci (2004) 283: 194–199
DOI 10.1007/s00396-004-1122-3

ORIGINAL CONTRIBUTION

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Photochemical properties of UV-absorbing chemicals in phase-controlled polymer microspheres

Received: 27 October 2003
Accepted: 25 February 2004

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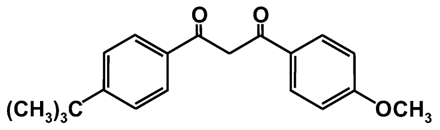
Abstract In this study, a different UV (ultra-violet) ray absorption system is presented in which butyl methoxydibenzoylmethane (BMDM, a model UV-A absorbent, 320–400 nm) is stabilized in phase-controlled poly(methyl methacrylate) (PMMA) microspheres. The photochemistry of BMDM in the microspheres was investigated considering its phase characteristics therein. Analysis by differential scanning calorimetry and X-ray diffraction showed that the BMDM in the microspheres was present in a non-crystalline state. The phase control of BMDM in the polymer microspheres has an excellent ability to protect against UV-A, whilst maintaining its photostability and thermal stability. The results obtained in this study illustrate well that the phase control of the UV absorbents in polymer microspheres is another key factor that determines their photochemistry and photostability in the final formulations.

Keywords UV ray absorption · Phase-controlled · Non-crystalline · Photostability · Photochemistry

Introduction

Recently, there has been an intensive concern about protection against ultra-violet (UV) light, since UV exposure induces serious damage to human skin [1, 2]. UV light can be classified as UV-A (320–400 nm) and UV-B (290–320 nm), depending on its wavelength. Many studies have proved that UV-A is the reason for sunlight-induced skin damages, such as, cutaneous photoaging, immunosuppression, and photocarcinogenesis [3, 4]. Therefore, there have been many attempts to protect against UV-A by using appropriate UV-A-absorbing chemicals in sunscreens. However, when exposed to UV light, UV-A-absorbing chemicals are decomposed or rearranged easily, which happens because the (excited) absorbed energy cannot be transferred efficiently into other forms, such as light and/or heat. UV-induced decomposition of the chemicals not only reduces their UV-protecting performance, but also promotes phototoxic or photoallergic contact dermatitis [5, 6].

In this contribution, we introduce a different approach to stabilize a UV-A absorbent, whilst maintaining its UV-absorbing performance in the formulations. We selected butyl methoxydibenzoylmethane (BMDM, refer to Scheme 1) as a model UV-A absorbent. As far as we know, BMDM is one of the most well known chemicals that provide excellent protection against UV-A. In particular, BMDM has an excellent UV absorption in the UV-A wavelength region (320–400 nm). However, it has been reported that BMDM is also decomposed easily by UV radiation in solutions and emulsion formulations [7, 8, 9]. Hence, to improve its stability, a number of methods have been proposed, including chemical modification, coacervation with polymer, and complexation with cyclodextrins [10, 11, 12, 13, 14]. To the best of our knowledge, however, an acceptable result related to its stabilization has not been reported in the literature.



Scheme 1 Chemical structure of butyl methoxydibenzoylmethane (BMDM)

In this study, we emphasize the importance of phase control, especially the crystallinity of BMDM molecules, in achieving excellent photostability. The phase characteristics of BMDM are controlled by considering its compatibility with polymer in the microsphere system. Finally, this paper describes the effects of the BMDM phase in the polymer microspheres on the photostability, thermal stability, and UV-A-absorbing performance for the purpose of designing a new UV-A-absorbing system.

Experimental

Materials

Butyl methoxydibenzoylmethane (BMDM) was purchased from Roche Vitamins Inc. (Zurich, Swiss) and used without further purification. Poly(methyl methacrylate) (PMMA, $M_w = 3.5\times10^5$ g mol^{-1}) and methylene chloride (MC) were all of reagent grade and purchased from Aldrich (USA). Poly(vinyl alcohol) (PVA, $M_w = 8.8\times10^4$–9.2×10^4 g mol^{-1}, 87–89% degree of saponification) was kindly supplied from Kuraray (Japan).

Preparation of BMDM/PMMA microspheres

BMDM/PMMA microspheres were produced by a solvent evaporation technique [15, 16]. Both BMDM and PMMA were dissolved in MC, and then the BMDM/PMMA/MC solution was poured into 1 wt% PVA solution and emulsified with a MX-5 homogenizer (Nihonseiki Co., Japan). Then, MC in the emulsion droplets was eliminated completely by the evaporation at 40°C for 1 h. The microspheres produced were repeatedly washed by decantation in water and dried at ambient temperature. A typical recipe is summarized in Table 1.

Table 1 A standard recipe for BMDM/PMMA microspheres

Ingredient	Composition (g)		
	BMDM-C10	BMDM-C30	BMDM-C50
PMMA	18	14	15
BMDM[a]	2	6	15
MC	70	70	70
PVA[b]	2	2	2
Water	198	198	198

[a] Butyl methoxydibenzoylmethane
[b] 1 wt% against total water weight

Analytical characterizations

The apparent image of microspheres was observed with an optical microscope (OM, Nikon) and a scanning electron microscope (SEM, JSM-6300, JEOL). A differential scanning calorimeter (DSC, TA Instruments, DSC 910) was used to measure the thermal properties of the microspheres. DSC traces were recorded from 20°C to 100°C with a heating rate of 5°C min^{-1} under a stream of a nitrogen gas. The crystallinity of BMDM was investigated by measurements on an X-ray diffractometer (XRD, Riguka Denki, model RAD-C) in the 2θ range. Cu Kα radiation ($\lambda = 1.542$ Å) was used in XRD measurements. To evaluate the in vitro photostability of BMDM, UV-vis spectrophotometer (Shimadzu Co., UV 1601, Japan) measurements were carried out. First, BMDM and BMDM/PMMA microspheres were mixed evenly in capric/caprylic acid triglyceride oil, respectively. Then, the samples were irradiated with UV-A with an intensity of 9.09×10^{-3} W cm^{-2} for 0.5 h at room temperature (UV-A Tech. Inc.). The net concentration of BMDM was controlled to be 10 ppm in dimethyl sulfoxide solution, and the UV absorption behaviors were then compared.

Thermal stability measurements

To evaluate the stability of BMDM in the microspheres, HPLC (HP1100 series) measurements were carried out at various storage times. First, the BMDM/PMMA microspheres were formulated together with a simple oil-in-water (O/W) emulsion consisting of liquid paraffin (10 wt%), cetearyl alcohol (2 wt%, Croda Inc.), sorbitan monostearate (0.5 wt%, Uniqema America), polysorbate 60 (1.2 wt%, Uniqema America), and deionized water. The concentration of BMDM in the O/W emulsion was adjusted with 2 wt%. The formulations prepared were then sealed in a plastic tube and stored at 40°C. In the HPLC measurements, chromatographic separations were achieved by using a Nova-Pak C18 column (3.9×150 mm, Waters). The flow rate of the carrier solvent composed of methanol/water (90:10, v/v) was 1 mL min^{-1}. The detection wavelength was set at 350 nm. The sample injection volume was 10 μL. The stability of BMDM was defined by the ratio of measured concentration to initial concentration, $[\text{BMDM}]_m/[\text{BMDM}]_0$.

Determination of in vitro UV-A protection factor (UV-A PF)

The ability of BMDM/PMMA microsphere to protect against UV-A rays was estimated in the O/W emulsions. The protection against UV-A rays was estimated by measuring the UV-A protection factor (UV-A PF). First, a 2 mg cm^{-2} sample was placed onto a transpore tape (3 M Co.). After 15 min, UV-A PF was measured five times with a sun protection factor (SPF) 290 analyzer system (Optometrics USA Inc.). The UV-A PF was calculated by using Eq. (1), as described by Ferrero et al. [17]:

$$\text{UV - A PF} = \frac{\sum_{320}^{400} E_\lambda I_\lambda \Delta\lambda}{\sum_{320}^{400} E_\lambda I_\lambda T_\lambda \Delta\lambda} \qquad (1)$$

where T_λ is the sunscreen transmittance at wavelength λ; E_λ is the spectral irradiance of terrestrial sunlight at wavelength λ, expected for a clear sky at noon in midsummer for a latitude of 40°N; and I_λ is the biological action spectrum for UV-A.

Results and discussion

Formation of BMDM/PMMA microspheres

In this study, BMDM/PMMA microspheres were produced by a conventional solvent evaporation method. Figure 1 shows OM and SEM photographs for the BMDM/PMMA (BMDM-C50) microspheres after complete elimination of MC. From the OM Image, it is evident that the BMDM was mixed homogeneously with PMMA. There was no phase separation between BMDM and PMMA, meaning that the two phases are very compatible. After recovery of the microspheres, their surfaces were observed with SEM (Fig. 1b). The surfaces of the BMDM/PMMA microspheres were smooth and spherical in shape. The average size of the microspheres was about 20 μm. The maximum loading amount of BMDM in the microspheres was 50 wt%. Up to that concentration, there was no evidence of collapse of the microsphere walls as a result of evaporating and drying.

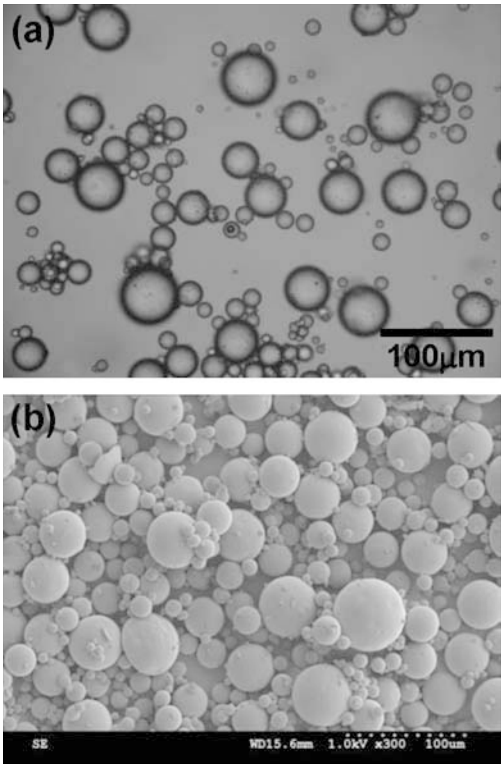


Fig. 1a,b OM and SEM photographs of BMDM/PMMA microspheres (BMDM-C50)

Phase characteristics of BMDM/PMMA microspheres

The phase characteristics of BMDM in the microspheres were analyzed by using DSC and XRD measurements. Figure 2 shows the DSC thermograms of the BMDM/PMMA microspheres. The pure BMDM had a typical endothermic peak at 83.5°C, corresponding to its melting point (T_m). However, when BMDM was incorporated into the PMMA microspheres, the thermal behavior was quite different from the pure BMDM. The BMDM in the PMMA microspheres displayed just a broad weak endothermic peak over the temperature range 20–50°C. From this result, it is assumed that the phase of BMDM in the PMMA microspheres changed from crystalline to non-crystalline. To confirm this unique phase behavior of BMDM in the PMMA microspheres, in this study, the degree of crystallinity of BMDM was observed by XRD measurements, and the results are shown in Fig. 3. In the dried state, the pure

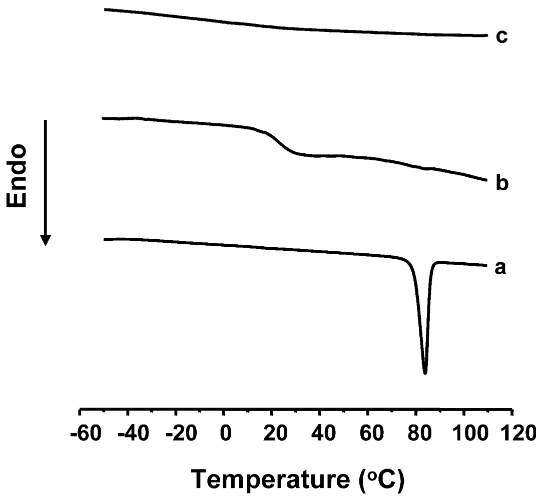


Fig. 2a–c DSC thermograms of BMDM/PMMA microspheres: **a** BMDM, **b** BMDM/PMMA microspheres (BMDM-C50), and **c** PMMA microspheres

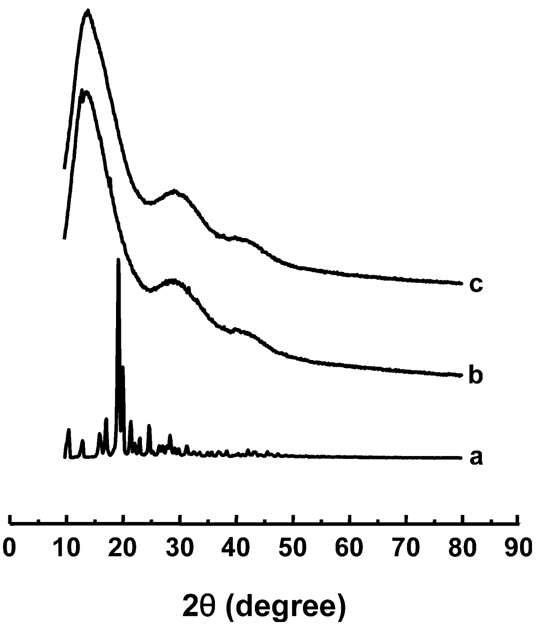


Fig. 3a–c X-ray diffractograms of BMDM/PMMA microspheres: **a** BMDM, **b** BMDM/PMMA microspheres (BMDM-C50), and **c** PMMA microspheres

BMDM showed a bundle of typical crystal peaks. However, when the BMDM was incorporated into the PMMA microspheres, its crystal peaks could not be detected. The XRD pattern of the BMDM/PMMA microspheres was exactly consistent with that of PMMA. From the DSC and XRD data, it is verified that the BMDM was mixed homogeneously in the PMMA microspheres, forming a non-crystalline state owing to its good compatibility with PMMA.

Photostability and thermal stability

In this study, in vitro photostability of the BMDM was evaluated by measuring the progress of photodegradation by UV-vis spectrophotometry. Figure 4 shows UV-vis spectra of BMDM after UV irradiation for 0.5 h at room temperature: BMDM itself therefore had a very low photostability. With only 0.5 h UV radiation, the maximum intensity of UV absorbance was lowered significantly to about 44% of the initial state. In contrast, the BMDM located in the PMMA microspheres showed a high photostability. Even after 0.5 h UV irradiation, only 9% of BMDM was photodegraded, thereby indicating that most of the BMDM molecules in the microspheres remained safely active against strong UV rays.

Furthermore, the thermal stability of BMDM was measured as a function of the storage time at 40°C in the O/W emulsions, and the results are shown in Fig. 5. One can easily see that the BMDM located in the PMMA microspheres has an enhanced thermal stability. Irrespective of the loading concentration, the BMDM located in the PMMA microspheres was very stable at high temperature for a long time.

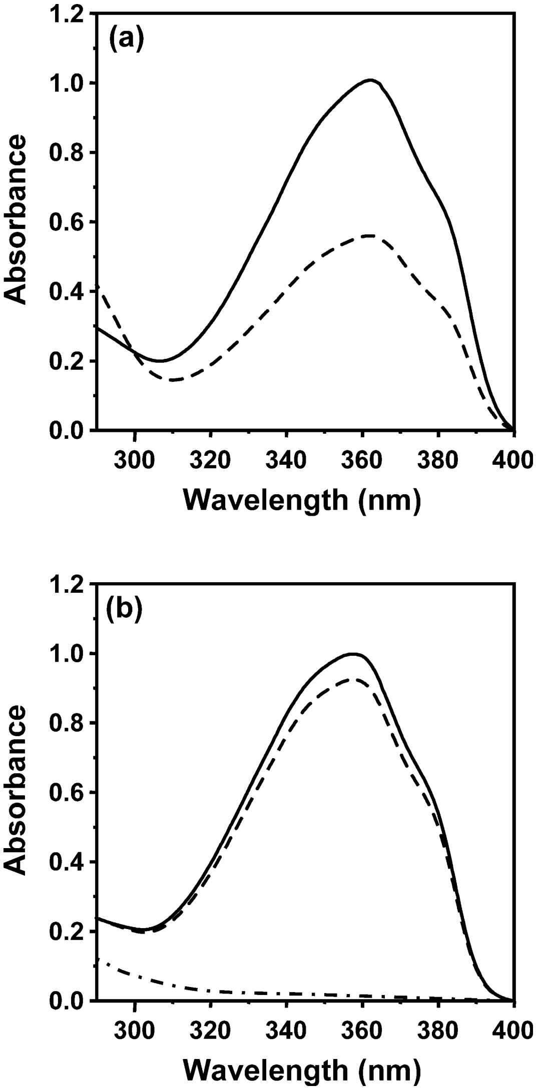


Fig. 4a,b UV-vis spectra of BMDM in solution. **a** BMDM and **b** BMDM/PMMA microspheres (BMDM-C50). The UV-vis spectra were obtained before (—) and after (- -) UV-A radiation, respectively. For comparison, the UV-vis spectrum for 10 ppm of PMMA (- · - · -) before the irradiation is shown in **b**

Generally, by absorption of UV radiation, UV-absorbing molecules are transferred to an excited state from which the energy may dissipate into molecular vibrations and further into heat via collisions with surrounding molecules [18, 19, 20]. Therefore, when an efficient dissipation of the excited-state energy does not occur, the chemical bonds of the UV-absorbing molecules may be broken and new bonds may be formed, thus leading to an irreversible molecular change. BMDM is one of the most unstable UV-absorbing molecules [8, 9]. In our study, however, BMDM located

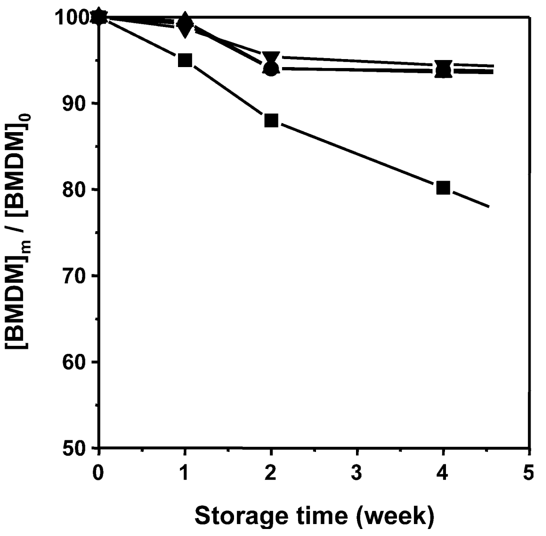


Fig. 5 Thermal stability of BMDM/PMMA microspheres as a function of storage time. Pure BMDM (-■-), BMDM-C10 (-•-), BMDM-C30 (-▲-), and BMDM-C50 (-▼-). To accelerate the degradation speed of BMDM, the stability measurements were carried out at 40°C. The concentration of BMDM was fixed at 2 wt% in the O/W emulsions

in the PMMA microspheres displayed good stability against UV rays, meaning that the excited-state energy of the BMDM molecules was dissipated efficiently without causing any molecular degradation. It is assumed that the formation of non-crystalline BMDM in the PMMA microspheres was closely related with the high photostability. In the non-crystalline state, the excited-state energy in a BMDM molecule may be transferred easily to other neighboring molecules. In our system, therefore, it is postulated that the excited BMDM molecules returned to their original state by eventually dissipating their excited-state energy as heat, which is evident from the fact that there was no serious molecular degradation at high temperature for a long time.

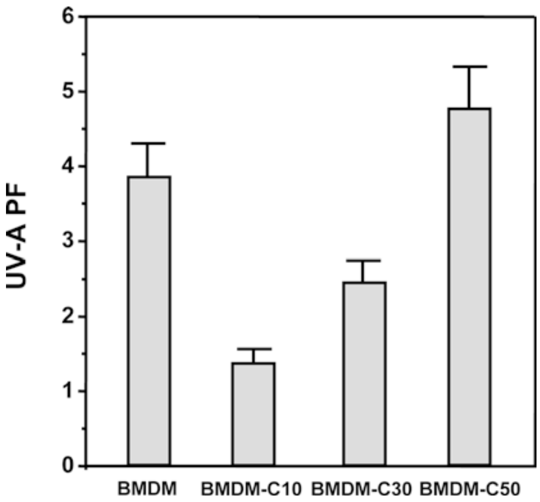


Fig. 6 UV-A protection factors of BMDM/PMMA microspheres in a simple O/W emulsion formulation. The concentration of BMDM was fixed at 2 wt% in the O/W emulsions

UV-A protection behaviors

Figure 6 shows the ability of BMDM/PMMA microspheres to protect against UV-A in the O/W emulsions. The UV-A PF value increased with an increasing amount of BMDM in the PMMA microspheres. At a low concentration of BMDM in the PMMA microspheres, below 30 wt%, the BMDM molecules did not absorb the UV rays effectively, which is fundamentally attributable to the thick polymer phase. However, as the concentration of BMDM increased, the degree of UV-A protection increased dramatically. In particular, when the concentration of BMDM in the microspheres was 50% (BMDM-C50), the UV-A PF value was much higher than that of BMDM at the same concentration in the O/W emulsions. With regard to this interesting result, the solubility of BMDM should be considered in the emulsion formulations. It has been reported that most of the UV-absorbing molecules including BMDM have low solubility in conventional oils [10, 21]. Therefore, when BMDM is solubilized directly in the oil part and emulsified mechanically, its partial precipitation may take place to form small crystals (actually, in our study, the BMDM crystals could be detected in OM observations). However, in the case that the BMDM is confined with a non-crystalline phase in the polymer microsphere, it can absorb effectively UV-A rays, independent of its solubility in oils. Consequently, in our study, it is established that the efficacy of BMDM to absorb UV-A rays could be maximized by controlling its phase characteristics in the polymer microspheres.

Conclusions

In this study, BMDM/PMMA microspheres were prepared by using a solvent evaporation technique. The phase characteristics of BMDM within PMMA microspheres were investigated with DSC and XRD measurements. Uniquely, it was found that the BMDM molecules were present in a non-crystalline state in the PMMA microspheres. The BMDM located in the PMMA microspheres had improved photostability and thermal stability, and excellent ability to protect against UV rays, which seems to be attributed to the formation of the non-crystalline phase in the microspheres. The importance of the BMDM/PMMA microsphere system is found in the fact that it can be applied very usefully to develop highly stable sunscreens against UV rays and heat.

Acknowledgments This work is supported in part from the National Research Laboratory (NRL) program (Project No. 2000-N-NL-01-C-270) by the Ministry of Science and Technology, South Korea.

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