Journal of Photochemistry and Photobiology B: Biology 148 (2015) 277–283

Contents lists available at ScienceDirect

Journal of Photochemistry and Photobiology B: Biology

journal homepage: www.elsevier.com/locate/jphotobiol

Improvement in UV protection retention capability and reduction in skin penetration of benzophenone-3 with mesoporous silica as drug carrier by encapsulation

C.C. Li [a,c], Y.T. Lin [b], Y.T. Chen [a], S.F. Sie [a], Y.W. Chen-Yang [a,*]

[a] Department of Chemistry, Center for Nanotechnology, Center for Biomedical Technology, Chung Yuan Christian University, 200 Chung-Pei Road, Chung-Li 32023, Taiwan, ROC
[b] Master Program of Nanotechnology, Chung Yuan Christian University, 200 Chung-Pei Road, Chung-Li 32023, Taiwan, ROC
[c] Department of Cosmetic Science, Vanung University, 1 Van-Nung Road, Chung-Li, Taoyuan County 32061, Taiwan, ROC

ARTICLE INFO

Article history:
Received 29 December 2014
Accepted 30 April 2015
Available online 8 May 2015

Keywords:
Benzophenone-3
Mesoporous silica
Organic UV-filter
Drug carrier
In vitro release and skin penetration

ABSTRACT

In this study, various amounts of benzophenone-3 (BP-3), a solid-type of organic UV-filter, were encapsulated in mesoporous silica (MS) to form the BP-3 encapsulated by MS UV-filters (BESs), BES-1 and BES-2, via *in-situ* sol–gel process. The characterization of BESs was completed using Fourier transform infrared (FTIR) spectroscopy, thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC). The results showed that of the BES filters, BES-2 containing emulsion (BES-2-E) exhibited about 2 times and 1.64 times higher SPF and erythemal UV-A PF values, respectively, and after 3 months about 7–8 times higher protection retention capability than the free BP-3 containing emulsion (BP-3-E). Moreover, the result of the *in vitro* skin penetration test using Franz glass diffusion cell indicated that the skin permeation of BP-3 from BESs was about 3 times lower than from BP-3-E. This property is particularly important for sunscreens because the amount of sunscreen penetration inside the stratum corneum directly correlates to its UV protection ability, and consequently its ability to reduce phototoxic and photo-allergic reactions that are damaging to the skin. The results of this study demonstrated the potential of *as*-prepared BES-2 as a UV-filter for cosmetic products.

1. Introduction

Ultraviolet (UV) radiation is responsible for a wide variety of acute and chronic skin problems. Acute responses of the human skin to UV radiation include sunburn and erythema. Chronic UV radiation effects include photo-aging and photo-carcinogenesis, which are considered to be caused by the induction of immunosuppression. The use of sunscreens has been known as a good prevention against UV-induced skin damages [1–3]. The effectiveness of sunscreens depends on factors such as: the physicochemical properties of the active components, the lipophilicity of the carrier and the particular type of formulation used, etc. The active components in the sunscreen are the UV-filters, which can either be organic based UV radiation-absorbing molecules or inorganic based compounds which specialize in scattering, and reflecting UV radiation [4–6]. In order to optimize the effectiveness of UV-filters several studies have combined the merits of the organic filters and inorganic filters to improve their UV-prevention abilities [7–12]. Similarly, our previous work have demonstrated the encapsulation of a liquid-type organic UVB-filter, Octylmethoxycinnamate (MCX), into the inorganic UV-filter mesoporous silica using *in situ* sol–gel process, and found about 57% enhancement on its *in vitro* sun protection factor (SPF) value [13]. To further include UVA filter ability, in yet another work we looked to a solid-type organic UVA-B filter, 2-hydroxy-4-methoxy-benzophenone (BP-3), which is widely used as cosmetic additive, pigment initiator, medicine, etc. due to their excellent absorption of the UV wavelengths between 290 nm and 400 nm [14]. In this particular work, BP-3 was adsorbed onto mesoporous silica (MSBP-2) and found to increase the solubilization and reduce the crystallization in the sunscreen emulsion to improve its UV-protection ability [15]. Specifically our study showed that not only the *in vitro* SPF but also the *in vitro* UV-A values of the MSBP-2-based sunscreen was increased by about 17% more than that of the free BP-3-based sunscreen. Although the adsorption method was a more economical method over encapsulation due to its simplicity which cuts down on cost and time; the improvement in SPF value was not as significant as what have been observed from the MS-encapsulated MCX UV-filter [13]. Therefore, in this work we set out to test the sunscreen ability of MS encapsulated BP-3 UV-filter (BESs) made through *in situ* so gel process.

* Corresponding author. Tel.: +886 3 265 3317; fax: +886 3 265 3399.
E-mail address: yuiwhei@cycu.edu.tw (Y.W. Chen-Yang).

http://dx.doi.org/10.1016/j.jphotobiol.2015.04.027
1011-1344/

In addition, the degree of skin penetration is also an important factor to be investigated for the UV filter in the sunscreen formulated. In fact, recent studies have indicated that some UV filters with particular formulation can be absorbed through the skin, further metabolized and eventually bioaccumulated and/or excreted , which can simultaneously trigger the phototoxic and photo-allergic responses [16], causing unfavorable effects such as skin allergy, endometriosis, antiestrogenic, antiandrogenic activity [17–19] and estrogenicity [20,21].

Therefore, in addition to testing the improvement in the screen ability of BESs, their degrees of skin penetrability were also investigated. Due to the encapsulation by the MS, we anticipated that the *in vitro* release and skin penetration of BP-3 would be significantly reduced. Indeed, our finding showed that the BES-2 containing emulsion (BES-2-E) exhibited about 2 times and 1.64 times higher SPF and erythemal UV-A PF values, respectively, and after applied for 24 h the skin permeation of BP-3 from BES-2-E was about 3 times lower than that from the free-BP-3 containing emulsion (BP-3-E).

2. Experiment

2.1. Materials

The precursor, tetraethyl orthosilicate (TEOS), methanol, ethanol, 1-chlorobutane, acetonitrile, sodium tetrafluoroborate isopropyl alcohol, and 1-methylimidazol were purchased from Acros Company. Propylene glycol (PG), 1, 3-butylene glycol (1,3-BG), Carbopol 940, disodium EDTA, cyclopentasiloxane (KF995), glyceryl stearate & PEG-100 stearate (Arlcel165), glyceryl monostearate (GMS), cetearyl alcohol and triethanolamine (TEA) were purchased from Top-Thyme. In addition, cetyl octanoat, Phenonip-XP, triglyceride (M-318) and benzophenone-3 (BP-3) were purchased from Kosfarm Corporation, Eugeni Company and Essence Plus Company, respectively. All the reagents were used as received.

2.2. Preparation of mesoporous silica (MS) and BP-3 encapsulated mesoporous silicas, BES-1 and BES-2

The MS and BESs were prepared by the *in situ* sol–gel process using the ionic liquid (IL) 1-n-butyl-3-methylimidazolium tetrafluoroborate (BMIBF) as the pore-forming agent and solvent and BP-3 as an additive according to our previous method [22]. In a typical run for preparation of BES-1 or BES-2, 5.8 g (28 mmol) of TEOS, 1.45 g (6.4 mmol) of BP-3 or 1.16 g (5.0 mmol) of BP-3, 1.9 g (58 mmol) of methanol, 3.0 g (12 mmol) of BMIBF and 3.4 g (189 mmol) of water were mixed in a bottle. The monolithic BES-1 or BES-2 gel was formed by gelatinizing at room temperature within 3 h after mixing. The gel was cured at ambient temperature for five days in open air. Then the entrapped ionic liquid was Soxhlet-extracted with water until the IL was removed. The *as*-prepared mesoporous material BP-3-MS was then obtained by freeze-drying. For comparison with the encapsulated samples, mixtures of MS and BP-3 with the same composition as BES-1 and BES-2 (BES-1-Mix and BES-2-Mix, respectively) were prepared by mixing and milling MS and BP-3 powders. The corresponding BP-3 adsorbed MS (MSBP-2) was prepared as reported [15] for actual comparison.

2.3. Characterization of the encapsulation product

The Fourier transform infrared spectra were recorded in KBr dispersion using a JASCO FTIR-4200 spectrometer at a resolution of 4 cm^{-1} over 32 scans. The samples were prepared by gently grounding KBr with the encapsulated or free BP-3.

Thermal gravimetric analysis was carried out on a Seiko TG/DTA 220. The samples were heated at a rate of 10 °C min^{-1} and 5 °C min^{-1} under a nitrogen flow for the measurements from 30 °C to 200 °C and 200 °C to 600 °C, respectively. Before starting the measurements, the samples were flushed in N_2 at room temperature for 15 min.

Differential scanning calorimetry analyses were performed on a TA Instruments Q20. 3–6 mg of samples with the same amount of BP-3 were loaded in aluminum pans and heated under nitrogen flow at a scanning speed of 30–100 °C at a heating rate of 10 °C min^{-1}.

UV–VIS spectra of the samples were collected on a Thermo Evolution 60S spectrometer between the 200 nm and 500 nm wavelengths. All the samples including BP-3, BES-1, BES-2, MSBP-2, BES-1-Mix, and BES-2-Mix contained the same amount of BP-3 and were measured in powder form. The weight of the MS powder sample was kept the same as that of BP-3 sample for comparison.

2.4. Preparation of oil-in-water sunscreen

The oil-in-water sunscreens were prepared by the emulsion method. Briefly, the oil phase containing KF995 (10%), Cetyl octanoate (10%), Arlcel165 (2.5%), GMS (1.5%), cetearyl alcohol (1.5%), MS (2%) or BP-3 (2%) or BES-1 (4.4%) or BES-2 (5.9%) was heated to 80 °C by stirring. The aqueous phase containing PG (4%), 1, 3-BG (4%), Carbopol 940 (0.16%), disodium EDTA (0.2%) and deionized water q.b.a 100 g was heated to the same temperature as the oil phase. Then, the hot aqueous phase was dispersed in the hot oil phase while stirring until the mixture was cooled down to 40 °C. Finally TEA (0.1%) and Phenonip-XP (0.5%) were added into the mixture, constantly stirring until it was cooled to room temperature and form the oil-in-water sunscreen. The sunscreen containing BP-3, BES-1 and BES-2 is abbreviated as BP-3-E, BES-1-E and BES-2-E, respectively. The sunscreen emulsion containing MSBP-2 was also prepared as reported [15].

2.5. In vitro UV protection factor measurement

The performance of the sunscreens prepared were evaluated according to the Food and Drug Administration (FDA) recommendation SPF *in vitro* test by comparing SPF "Sun Protection Factor" values of MS preparations with emulsions containing the same proportion of free sunscreens by using SPF-290S computer operated analyzer system (Optometrics Corp, USA) [23–25]. A surgical patch of Transpore™ tape (3 M Company, USA) with an area of 50 cm^2 was used as the substrate for this experiment. Typically, 2 mg cm^{-2} of each tested sample was distributed on the substrate surface with syringe. The stratification of the sample was done manually by using a latex glove (Global) and distributing the product with three longitudinal movements back and forth. After 15 min, the tape was placed on a free standing film holder. The transmittance was measured in six different points and the results are presented as average values. The *in vitro* SPF measured in this paper represents an indicator of the UVA/UVB protective property of the sunscreen product, which was calculated from the monochromatic protection factor, the solar irradiance, and the erythemal constants according to the following:

$$\mathrm{SPF} = \sum_{290}^{400} E_\lambda B_\lambda \Big/ \sum_{290}^{400} (E_\lambda B_\lambda / \mathrm{MPF}_\lambda) \quad (1)$$

where MPF_λ is the mean monochromatic protection factor, E_λ is the spectral irradiance of terrestrial sunlight under controlled