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Topical delivery of retinol emulsions co-stabilised by PEO-PCL-PEO triblock copolymers: effect of PCL block length

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Abstract

This article describes enhanced skin permeation and UV/thermal stability of retinol emulsions by the co-stabilisation of Tween20 and biodegradable poly(ethylene oxide)-*block*-poly(ϵ-caprolactone)-*block*-poly(ethylene oxide) (PEO-PCL-PEO) triblock copolymers having different lengths of hydrophobic PCL block. A triblock copolymer with a longer PCL block has a lower hydrophile-lipophile balance (HLB) value. Commercial Retinol 50C® (BASF Co., Ludwigshafen, Germany) was used as the source of retinol. Ultrasonication of the Retinol 50C® emulsion with the triblock copolymers led to an increase in retinol solubilisation and a decrease in average particle size of the resulting retinol emulsion. These characteristics improved skin permeation of retinol through the stratum corneum of artificial skin and subsequent proliferation of viable epidermis cell. Employment of the triblock copolymer with a longer PCL block increased both UV and thermal stabilization of the retinol. These results suggest that HLB and PCL block length are important factors to enhance the topical delivery of retinol into the skin.

Keywords: biodegradable polymers, encapsulation, transdermal drug delivery, retinol

Introduction

As a model drug in topical delivery, retinol and its derivatives have been extensively studied for pharmaceutical and cosmetic applications since they are proven as essential ingredients for the proliferation of epidermis cell (Senoo et al., 1996; Jenning et al., 2000; Biesalski et al., 2001; Hwang et al. 2005). However, a suitable encapsulation process is generally needed because they are vulnerable to heat and UV light (Tran et al., 2001; Sapino et al., 2007; Favaro et al., 2011). Over the past few decades, numerous strategies have been developed to improve the stability of retinol using surfactants, block copolymers, lipids, and so on. Among them, amphiphilic and biodegradable block copolymers (e.g. di- and tri-block copolymers based on poly(ϵ-caprolactone) (PCL) (Choi et al., 2005; Hyun et al., 2006; Kim et al., 2006; Cho et al., 2008, 2009a, 2009b), poly(lactic acid) (PLA) (Chognot et al., 2003; You et al., 2004; Choi et al., 2008), and poly(ethylene glycol) (PEG or PEO) (Jeong et al., 1999; Kwon and Okano, 1999; Ge et al., 2002; Kim et al., 2006) have been of great interest for the topical delivery of retinol.

Amphiphilic block copolymers in an aqueous solution show similar behavior to short-chain surfactants in terms of micellization and aggregation above critical micelle concentration (CMC) or critical aggregation concentration (Cho et al., 2010). Nano-scale aggregates consisting of amphiphilic block copolymers exhibit a hydrophobic core domain and a hydrophilic hairy shell layer, facilitating solubilisation and protection of hydrophobic drugs and active agents. Therefore, the nano-scale aggregates are often used as potential vehicles for drugs and active agents (Kim and Taton, 2006; Adams et al., 2008; Hu et al., 2008; Shum et al., 2008). Nano-scale dimension of vehicles generally ensures intimate contact to the stratum corneum of human skin, eventually enhancing the amount of drugs penetrating into

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the viable epidermis (Ghouchi Eskandar et al., 2009). Since the stratum corneum of human skin is composed of hydrophilic ''bricks'' (bundles of keratins) and hydrophobic ''mortar'' (mixed lamellar structure of ceramides, cholesterols, fatty acids and so on), amphiphilic feature is essential for effective transdermal permeation through the stratum corneum.

Several groups have reported the potential of block copolymers as vehicles for topical delivery (Cho et al., 2009a, 2009b). However, to the best of our knowledge, few studies discussed the relationship between hydrophile–lipophile characteristic of block copolymers and skin permeation behavior. Herein, we demonstrate stabilisation and topical delivery of retinol by co-stabilisation using both Tween20 and triblock copolymers of poly(ethylene oxide)-*block*-poly(ϵ-caprolactone)-*block*-poly(ethylene oxide) (PEO-PCL-PEO) with different PCL block lengths. We chose commercial Retinol 50C® as a retinol source and performed Franz diffusion cell analysis in order to investigate skin permeation and proliferation of viable epidermis cell layer of an artificial skin. The aim of this work is to study on the effects of PCL block length on the UV/thermal stability and skin permeation of the retinol emulsions.

Materials and methods

Materials

Retinol 50C® (vitamin A:Tween20 = 1:1 v/v, BASF Co., Ludwigshafen, Germany) was used as a source of retinol. A series of PEO-PCL-PEO triblock copolymers were synthesised by ring opening polymerisation from poly(ethylene glycol) methyl ether (mPEG, $M_n = 2000$ g/mol, Aldrich, St. Louis, MO, USA), ϵ-caprolactone (Aldrich, St. Louis, MO, USA), stannous octoate (Aldrich, St. Louis, MO, USA), hexamethylene diisocyanate (Aldrich, St. Louis, MO, USA), anhydrous toluene (TCI, Tokyo, Japan), diethyl ether (TCI, Tokyo, Japan). The synthesis and characterisation (IR and proton NMR data) of the triblock copolymers were described in our previous reports (Cho et al., 2008; Cho et al., 2009a, 2009b). Table 1 shows the characteristics of the triblock copolymers. HPLC grade methanol and ethanol were purchased from Aldrich and used without any purification. The artificial skin was purchased from Tego Science (Neoderm® ED, epidermis/dermis, Well type 12, Seoul, S. Korea) (Kubo et al., 2006; Lee et al., 2008, 2011). Ultrapure water (resistivity > 18.2 MΩ cm, Millipore Co., Billerica, MA, USA) was degassed and used throughout all experiments.

Preparation of retinol emulsions

In order to maximise the permeation and stabilisation effects in terms of PCL block length, we fixed the concentrations of triblock copolymers at 1 and 3 wt.%, respectively, for skin permeation and UV/thermal stability analyses through the preliminary tests. For an aqueous solution of 1 wt.% triblock copolymer, 0.1 g triblock copolymer was completely dissolved in 9.8 g pure water (in the case of 3 wt.%, 0.3 g triblock copolymer and 9.6 g pure water were used) and then 0.1 g retinol 50C® was added into the solution, followed by ultrasonication using a horn-type ultrasonicator (VCX-750, Vibracell, 20 MHz, 40% load) at 20°C for 1 min. The concentration of retinol was fixed at 16 700 IU/g (0.5 wt.%). All procedures were under N_2 atmosphere in order to minimise the oxidation of retinol.

Characterisations

Particle size

Hydrodynamic size and size distribution of the retinol emulsions were measured using capillary hydrodynamic fractionation (CHDF-1100, Matec Appl. Sci., Northborough, MA, USA) equipped with a 5.0 μm ID capillary. The sample for CHDF was diluted 10 times with the diluted Matec GR100/pure water solution and injected into the load cell of the instrument at room temperature. The average particle sizes with error ranges were obtained from three measurements of each sample.

Morphology

Morphology of the retinol emulsions was observed by transmission electron microscopy (TEM, H-7600, 100 kV, Hitachi, Tokyo, Japan). The sample for TEM was diluted 100 times in pure water, sprayed on a carbon-coated copper grid, and air-dried without staining.

Table 1. Basic properties of PEO-PCL-PEO triblock copolymers.

PEO-PCL-PEO copolymers	[PCL]/[PEO][a]	M_n^a (g/mol)	M_n^b (g/mol)	M_w^b (g/mol)	M_w/M_n^b (-)	CMC[c] (g/L)	HLB[d] (-)
T1	0.11	6.0×10^3	4.4×10^3	4.9×10^3	1.1	0.40	13.5
T2	0.20	6.3×10^3	6.1×10^3	7.5×10^3	1.2	0.35	11.7
T3	0.31	8.4×10^3	8.0×10^3	11.0×10^3	1.3	0.14	8.3

Source: Cho et al. (2009a, 2009b).

Notes: [a]Determined by measuring the relative areas of the peak at 3.65 ppm (EO unit) and the methylene peak at 2.30 ppm (CL unit) in ^{1}H NMR (AVANCE digital 400, Bruker, Madison, WI, USA, in $CDCl_3$).

[b]Determined by GPC (OmniSEC, Malvern Viscotek, Worcestershire, UK) in THF elution with a narrow polystyrene standard of 580–7 500 000 g/mol).

[c]Determined by pyrene UV absorption analysis (UV-1650PC, Shimadzu) at a wavelength of 372 nm.

[d]Calculated by Griffin's equation (Lowenthal, 1968; Pasquali et al., 2008).

Solubilisation of retinol

UV–vis spectroscopy (UV-1650PC, Shimadzu, Kyoto, Japan) was used to record the UV absorption spectra of 0.002 wt.% Retinol 50C® emulsions co-stabilised by T3 block copolymer at room temperature. The concentrations of T3 block copolymer were 0, 0.005, 0.01, 0.02 and 0.03 wt.%.

UV and thermal stability

High performance liquid chromatography (HPLC system, Waters Co., Milford, MA, USA), equipped with a Waters 600 controller, a Zorbax eclipse XDB-C18 of 5 μm pore size, and a 325 nm UV detector, was used to measure the UV and thermal stability of retinol emulsions. The method for retinol assay was adapted from the literature (Allwood et al., 1992; Padamwar and Pokharkar, 2006). A methanol/pure water solution (9:1, v/v) was used as an eluent and the flow rate was at 1.0 mL/min and the sample injection volume was 20 μL. For the UV stability analysis, the retinol emulsions were treated with UV irradiations of 30 cm distance in a closed chamber (320–400 nm UV-A/TL-D 15 W and 290–320 nm UV-B/ACTINIC BL 15 W, Philips, Amsterdam, The Netherlands) under a N_2 purge at 20°C. For the thermal stability analysis, the retinol emulsions were kept in an incubator of 40°C under N_2 atmosphere for 28 days (Carlotti et al., 2006; Eskandar et al., 2009). After the UV or thermal treatment, 1 g of retinol emulsion taken at predetermined time intervals was added into the 10 mL methanol/water solution, mixed with a vortex mixer (250VM, Hwashin, Seoul, S. Korea) for 1 min at 20°C, and then immersed in a bath sonicator for 5 min, followed by centrifugation at 3000 rpm for 15 min. The supernatant was finally taken and filtered with a cellulose acetate filter (DISMIC-13cp, pore size = 0.45 μm, Advantec MFS Inc., Dublin, CA, USA) for the HPLC measurement at 325 nm to detect the changes of absorbance and molar concentration.

Skin permeation

Franz diffusion cell (FDC) test was performed to study the concentration of retinol permeated through the barrier of skin using the artificial skin, according to the method reported in the literature (Oh et al., 2006; Frelichowska et al., 2009; Forster et al., 2011). First, the artificial skin of 0.785 cm^2 contact area was inserted between a donor chamber and a receptor chamber of the FDC reactor. The receptor chamber of the reactor was filled with a phosphate buffered saline (PBS, pH 7.4, Sigma-Aldrich, St. Louis, MO, USA) and stirred with a magnetic bar. 200 μL of the retinol emulsion was put into the donor chamber and kept for 24 h at 32°C. Skin surface of the sample was washed to remove residual retinol with 50 vol.% ethanol/pure water, cut into small pieces, and then put into methanol. The sample was kept in an ultrasonic bath for 2 min and then in a refrigerator for 12 h at 4°C. After that, the sample was centrifuged at 1000 rpm for 10 min, re-dispersed in an ultrasonic bath for 2 min, and then centrifuged again. Finally, the supernatant was analysed by using the same HPLC instrument in order to measure the amount of retinol in the methanol solution. The same injection volume was 20 μL and the eluent (methanol/pure water = 9:1, v/v) flow rate was 1.0 mL/min. The experiment was repeated three times for each formulation.

Proliferation of epidermis layer

To study the effects of PCL block length of triblock copolymers on the permeation of retinol into a skin and proliferation of epidermis layer, the retinol emulsions were applied to the artificial skin. The skin was cultured for 1 week under aseptic conditions. Two hundred microlitres of the retinol emulsions was applied onto the stratum corneum of the skin every 24 h for 1 week at 32°C. After that, the skin was washed with the PBS solution and fixed with a 10 wt.% formaldehyde aqueous solution. The skin was then cut with a microtome (RM2145, Leica, Nussloch, Germany) and stained with hematoxylin/eosin (Lillie et al., 1976). The cross-section of the skin was observed by optical microscopy (CK41, Olympus, Tokyo, Japan) with counting the number of epidermis cell layer. The control group was an artificial skin grown under the same cultivation conditions without treatment of retinol emulsion. In this analysis, the excess or residual amount of retinol was not assayed.

Results and discussion

Characteristics of triblock copolymers

As shown in Table 1, a series of amphiphilic triblock copolymers (namely, T1, T2 and T3) with different [PCL]:[PEO] ratios were synthesised in order to investigate the effect of PCL block length, where mPEG of 2000 g/mol was used as a macro-initiator. An increase in the PCL block length led to an increase in the molecular weight and a decrease in the CMC and hydrophile-lipophile balance (HLB) values of the triblock copolymer (Cho et al., 2008, 2009a, 2009b).

Hydrodynamic size and morphology of retinol emulsions

Retinol 50C® consists of the same amounts of retinol and Tween20. Therefore, the concentration of Tween20 seems enough to stabilise the retinol emulsion because the CMC of Tween20 is 0.06–0.09 wt.% at 25°C (Tsoler, 1999). Figure 1(a) shows the average hydrodynamic sizes of the retinol emulsions measured by CHDF. The average size of pristine Retinol 50C® emulsion was 34.3 ± 4.6 nm in diameter at the retinol concentration of 0.5 wt.%. The retinol emulsions co-stabilised by 1 wt.% triblock copolymers with different PCL block lengths exhibited the average sizes around 29.5 nm. The reduction in the emulsion size can be explained as follows: the required HLB value for retinol is known as six, while the HLB value of Tween20 is 16.7 ± 1 (Hahn and Sucker, 1989). Therefore, triblock copolymers with a lower HLB value and a higher molecular weight can stabilise the retinol emulsion more efficiently than Tween20. Although we have not yet studied on the molecular interaction between the copolymer and

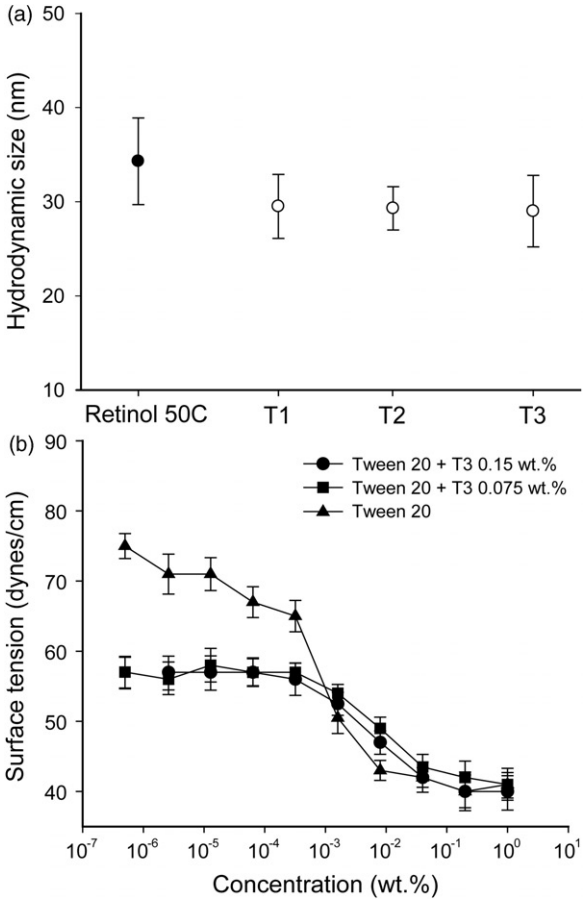

Figure 1. (a) The average hydrodynamic sizes of the Retinol 50C® emulsion and the retinol emulsions co-stabilised by 1 wt.% triblock copolymers (T1, T2 and T3). The concentration of retinol was kept as 0.5 wt.% in all samples. (b) Surface tension plots for Tween20 and Tween20/T3 block copolymer in an aqueous phase at 25°C.

Tween20, the surface tension data (Figure 1b) suggest that T3 block copolymer is more hydrophobic than Tween20, being capable of sufficiently decreasing the surface tension of water even at a very low concentration ($<10^{-3}$ wt.%).

Figure 2 shows the TEM images of the retinol emulsions. The difference in particle size of retinol emulsion is attributed to the physical state of the samples; TEM image shows particles in a dried state, whereas CHDF shows a hydrodynamic size of particles in a wet state. The particle size of the Retinol 50C® emulsion in dried state was relatively big and its morphology was non-spherical (Figure 2A), and which might be due to the aggregation of small retinol emulsions during sample drying. By contrast, the retinol emulsions co-stabilised by triblock copolymers exhibited spherical morphologies without a significant aggregation (Figure 2B–D). It was clearly observed that the average particle size of the retinol emulsion decreased with co-stabilisation of Tween20 and triblock copolymers. Unlike the CHDF data, the TEM images of Figure 2B–D show that the emulsion size slightly decreases and the number of the emulsion increases as the PCL block length increases from T1 to T3. This can be explained by the different solubilisation ability of triblock copolymers for retinol.

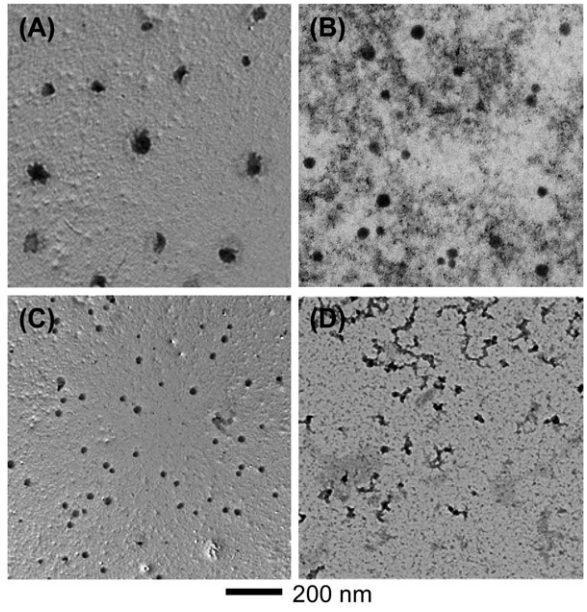

Figure 2. TEM micrographs of (A) the Retinol 50C® emulsion and (B)–(D) the retinol emulsions co-stabilised by 1 wt.% triblock copolymers, T1, T2 and T3, respectively.

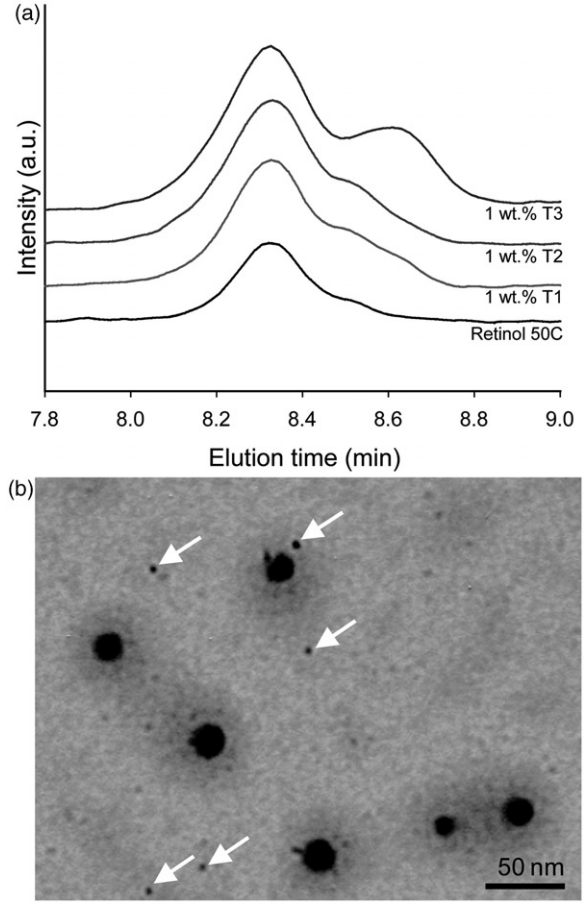

Figure 3. (a) CHDF elution curves of the Retinol 50C® emulsion and the retinol emulsions co-stabilised by 1 wt.% triblock copolymers (the legends are listed in order of the elution curves) and (b) the TEM micrograph for the retinol emulsion stabilised by 1 wt.% T3 triblock copolymer.

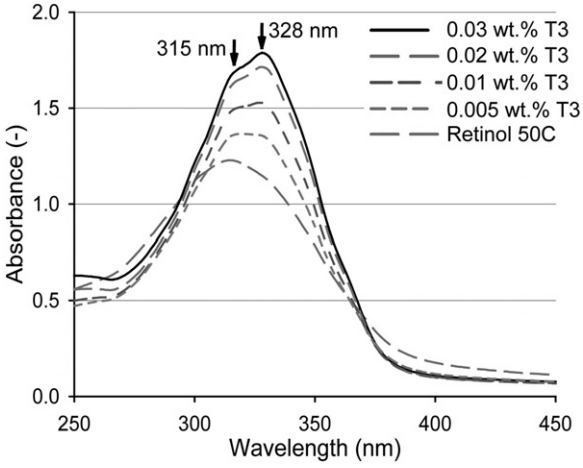

Figure 4. UV-vis absorption spectra of the Retinol 50C® emulsion (0.002 wt.%) and the retinol emulsions co-stabilised with a T3 triblock copolymer at its different concentrations.

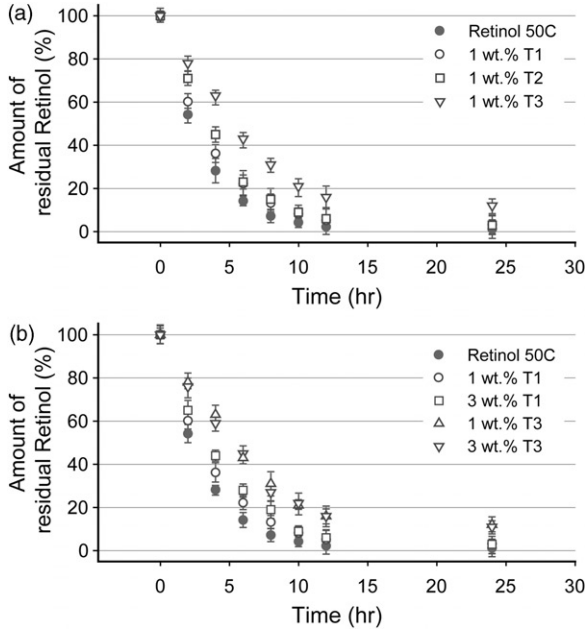

Figure 5. UV stability of the Retinol 50C® emulsion and the retinol emulsions co-stabilised by triblock copolymers at 20°C. (a) the effect of PCL block length at 1 wt.% triblock copolymers and (b) the effect of concentration for T1 and T3 triblock copolymers.

Figure 3(a) shows the CHDF elution curves of the Retinol 50C® emulsion and the retinol emulsions co-stabilised by the three different triblock copolymers. In all cases, the elution times for the maximum peak were around 8.3–8.4 min. Compared with the pristine Retinol 50C® emulsion, the elution curves became broadened in the presence of the triblock copolymers. It was notable that a shoulder peak of the retinol emulsion co-stabilised by a T3 triblock copolymer was observed at *ca.* 8.6 min, indicating the existence of small retinol emulsions or mixed micelles stabilising retinol molecules (the particle size could not be calculated due to the lower size limit of commercialised standard samples). In addition, the TEM image of the retinol emulsion for T3 also proves the existence of the small and individual retinol emulsions (indicated by the arrows in Figure 3b) together with large retinol emulsions. This enhanced solubilisation of retinol in terms of PCL block length can be corroborated by CHDF, TEM and UV spectroscopic data. As shown in the CHDF elution curves for T1 and T2, the small individual particles were rarely observed in TEM images of the retinol emulsion co-stabilised by T1 or T2 triblock copolymers. In CHDF a UV light is generally used as a source of detection, so UV absorbing species (i.e. retinol) can only be detected (Dos Ramos and Silebi, 1993). Therefore, the secondary peak (*ca.* 8.6 min) in the elution curve of T3 confirms that the formation of smaller retinol emulsion is predominant as compared to T1 or T2.

Solubilisation of retinol

Figure 4 shows the UV-vis absorption spectra of the Retinol 50C® (0.002 wt.%) emulsion and the retinol emulsions costabilised by a T3 triblock copolymer at different concentrations. Retinol can be solubilised as a monomeric unit in good solvents (e.g. ethanol or methanol), and which generally gives the maximum absorption wavelength (λ_{max}) of π–π^* electron transition at 325–329 nm (Morgareidge, 1942; Destree et al., 2008). As shown in Figure 4, small peak shoulders for the J-aggregate of retinol were found at 360 nm wavelength in all samples and the Retinol 50C® emulsion exhibited a broad UV absorption spectrum due to the emulsion state. The λ_{max} of the Retinol 50C® emulsion was found at 315 nm, which is attributed to hydrophilic environment of Tween20. As the concentration of T3 increased, the λ_{max} shifted from 315 to 328 nm, implying that the surrounding of the retinol was changed from hydrophilic to lipophilic character. This red shift is resulted from the attractive polarisation forces between the triblock copolymer and retinol, and which lower the electron energy levels of both π and π^* states. However, this effect is greater for the π^* state, eventually leading to the red shift. Note that both intensities at 315 and 328 nm wavelengths increased with an increase in the concentration of T3. As shown in Table 1, the triblock copolymers are more hydrophobic and longer than Tween20. Therefore, the more and smaller (namely, non-aggregated) retinol emulsions are formed by the co-stabilisation with triblock copolymers after the ultrasonication. Co-existence of the two different absorption peaks in Figure 4 is due to the slow exchange rate of a T3 triblock copolymer, because the hydrophobic core of block copolymer micelles is generally considered as 'frozen' state (Johnson and Prud'homme, 2003; Letchford and Burt, 2007; Cho et al., 2010).

Stability of retinol

Figure 5 shows UV stability of the Retinol 50C® emulsion and the retinol emulsions co-stabilised by triblock copolymers. As shown in Figure 5(a), the amounts of residual (undenatured or pristine) retinol linearly decreased at the

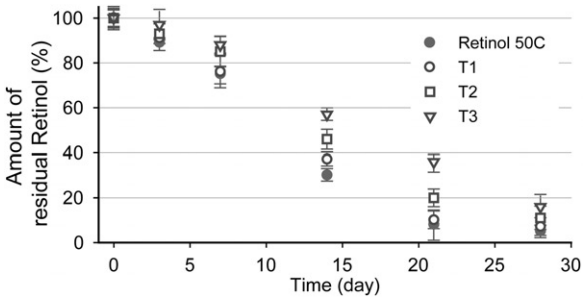

Figure 6. Thermal stability of the Retinol 50C® emulsion and the retinol emulsions co-stabilised by 1 wt.% triblock copolymers at 40°C.

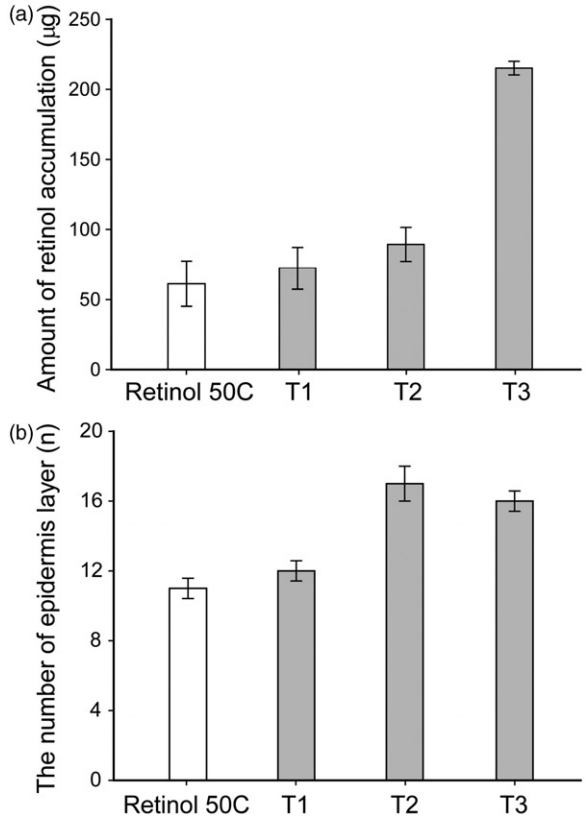

Figure 7. (a) The cumulative amount of retinol after 24 h and (b) the number of epidermis layer after one week. The artificial skin (the number of sample = 3, the initial number of the viable epidermis cell layer ($n = 9 \pm 1$) was treated with the Retinol 50C® emulsion (control) and the retinol emulsions co-stabilised by triblock copolymers at 32°C. The amount of retinol emulsion was 200 μL (*ca.* 3340 IU) for every 24 h. The area of the skin was 0.785 cm^2.

early stage of UV irradiation but their slopes gradually decreased after 5 h. It was observed that the T3 triblock copolymer exhibited a better UV stability than Tween20 (Retinol 50C®) and the other triblock copolymers. The degradation slope was reduced in order of Retinol 50C® > T1 > T2 > T3. Figure 5(b) shows the effect of concentration of the triblock copolymers (T1 and T3) on the UV stability of retinol. The amounts of residual retinol decreased in the same pattern as observed in Figure 5(a). However, a higher concentration (3 wt.%) of triblock copolymers could not further enhance the UV stability of retinol, implying that the protective effect was not related to the concentration of triblock copolymers. It may be due to the fact that the retinol was sufficiently surrounded by the triblock copolymers at above 1 wt.% concentration. The results suggest that the UV stability of retinol can be enhanced by employing triblock copolymer with a long PCL block length at a high concentration. In general, the degradation of retinol by UV light is significantly much faster than that by heat. The first order degradation constant (K) of retinol by heat is ranged from 0.001 to 0.02 h^{-1}, whereas 50% of all-*trans* retinol can be decomposed within 6 h under the UV light ($K = 0.12\ h^{-1}$) (Eskandar et al., 2009). Besides UV stability, thermal stability of the retinol emulsions was also improved by employing triblock copolymers with a long PCL block length due to the protective effect (Figure 6). In this analysis, the amounts of residual retinol linearly decreased until 20 days, and the degradation slope was reduced in the same order of Retinol 50C® > T1 > T2 > T3.

Topical delivery of retinol

Stratum corneum consists of hydrophilic bundles of keratins and hydrophobic mixed lamellar structure. Therefore, amphiphilic feature is required for effective transdermal permeation through the stratum corneum. In this work, an intercellular route of the mortar is more favorable than a transcellular route of the bricks because the molecular weights of triblock copolymers are higher than 500 Da (Elias et al., 1987; Barbero Ana and Frasch, 2005; Chen et al., 2010). Therefore, the diffusion of retinol through the interface between the emulsion phase and the stratum corneum can be a major pathway for transport over the intercellular routes. To investigate the effect of triblock copolymer on the permeation of retinol, FDC analysis was carried out with artificial skins treated with the Retinol 50C® emulsion and the three kinds of the retinol emulsions co-stabilised by triblock copolymers (T1, T2 and T3) for 24 h at 32°C. As shown in Figure 7(a), the amount of accumulated retinol in the stratum corneum and viable epidermis tended to increase as PCL block length increased from T1 to T3. The added amount of retinol was 3340 IU (1 IU = 0.3 μg) for each skin sample, but the cumulative amounts of retinol were 204, 241, 298 and 717 IU for Retinol 50C®, T1, T2 and T3, respectively. Therefore, the permeation efficiency of retinol could be calculated as 6.1, 7.2, 8.9 and 21.5%, respectively. Note that a significantly large amount of retinol was penetrated and accumulated in the artificial skin when the retinol emulsion co-stabilised with T3 triblock copolymer was applied. These results are ascribed to the HLB value and solubilisation ability of T3 block copolymer.

Figure 7(b) shows the effects of PCL block length of triblock copolymers on the proliferation of epidermis layer (see Figure S1 for the optical images of the cross-section of the artificial skins). Unlike the result of the amount of accumulated retinol, the number of epidermis

cell layer increased from T1 to T2 and reached a plateau in the case of T3. This result might be due to the tolerable upper intake level of retinol (UL), although we could not estimate the cumulative amounts of retinol in this analysis because of large discrepancies in contact area, nature of artificial skin, and different administrative conditions. By considering the UL of retinol for a 25-year old male is about 10 000 IU (Nohynek et al., 2006), the excessive amounts of retinol might be penetrated into the artificial skin for T3 block copolymer.

Conclusion

We have successfully prepared the retinol emulsions co-stabilised by PEO-PCL-PEO triblock copolymers with different PCL block lengths using Retinol 50C® as a retinol source. This work demonstrated not only the enhanced UV and thermal stabilities of retinol by employing the triblock copolymers but also excellent permeation of retinol into an artificial skin. These results can be rationalised by superior solubilisation ability of the triblock copolymers with large molecular weights and hydrophobic properties. Besides improved solubilisation ability, size reduction of retinol emulsions promoted the permeation of retinol into the skin through the amphiphilic intercellular route of stratum corneum. These results suggest that the control of HLB and molecular weight of the triblock copolymers are important factors for the topical delivery of retinol into the skin. In addition, the triblock copolymers explored in this work are biocompatible and biodegradable, so they will find a variety of formulations where non-toxic vehicles should be utilised. Although our investigation was focused on topical delivery, the results can be expanded into the stabilisation and administration of other hydrophobic ingredients for pharmaceutics, cosmetics, and food industries.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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