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ORIGINAL PAPER

Salt-responsive monoolein cubic phase containing polyethyleneimine gel

Danbi Park[1] · Madhusudhan Alle[2] · Seung-Jun Lee[3] · Seung-Hwan Lee[2] · Jin-Chul Kim[1]

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Abstract

Monoolein (MO) cubic phases responsive to salt ions were prepared by immobilizing polyethyleneimine (PEI) in its water channel through its electrostatic attraction with octanoic acid (OA) intercalated in MO bilayer and ionically gelling PEI using tripolyphosphoric acid (TPPA). The interfacial tension of PEI/OA solution markedly decreased with increasing concentration and it was typical of the interfacial tension profile of a surfactant solution. TPPA remarkably lowered the transition temperature of MO cubic phase from about 63 °C to below 46 °C, possibly because the hydroxyl groups of TPPA participated in hydrogen bonding with the glycerol residue of MO. The cubic phases showed finger print–like patterns on TEM micrographs and neither OA, nor PEI, nor TPPA affected the structure of the cubic phases. When PBS was used as a release medium, the release degree of a dye (i.e. Rhodamine B) loaded in the cubic phase was more than two times higher than that obtained using distilled water. The salt ions contained in the buffer solution would be able to dissolve PEI gel via ion exchange and promote the release of dye out of the cubic phase.

Keywords Cubic phase · Polyethyleneimine · Tripolyphosphoric acid · Gel · Salt ions-induced release

Introduction

2-Monoolein (2-oleoylglycerol, MO) is an amphiphilic molecule whose packing parameter is slightly greater than 1 and it can be spontaneously built into cubic phase when hydrated with adequate amount of water [1–4]. The name of cubic phase was coined because the crystallographic unit was a cube. The size ranges of cube are about 9.7 to 18.5 nm and two intercrossing water channels whose diameter is about 3–5 nm are passing through the cube with being surrounded by MO bilayers [5, 6]. The water content, based on the mass of cubic phase (i.e. the mass of MO plus water), is about 28 to 32% for gyroid type and 32–40% for diamond type [7, 8]. The water channels can envelope polar compounds and MO bilayers can intercalate nonpolar ones. Several kinds of stimuli-sensitive polymers were introduced in the water channel to render MO cubic phase responsive, in terms of release, to stimuli such as temperature change, pH change, light, redox, glucose concentration, and electric field [9–15]. When exposed to the stimuli, the polymer chains could change their conformation or their crosslinking density, thus the release took place in a stimuli-responsive manner [16–18].

In this study, MO cubic phase including ionically-gelled polyethyleneimine (PEI) in its water channel was prepared to render the cubic phase responsive to salt ions in terms of release. The cationic polymer (i.e. PEI) was reported to be cross-linked and gelled by tripolyphosphoric acid (TPPA) through salt bridging [19]. First, MO melt was hydrated with PEI solution to obtain a cubic phase containing the polymer chains in its water channel. Then, the cubic phase was additionally hydrated with TPPA solution for the gelation of PEI chains contained in the water channel. If the cubic phase is placed in a medium whose salt concentration is null or low, PEI gel would maintain its integrity and the diffusivity of a

✉ Seung-Hwan Lee
lshyhk@kangwon.ac.kr

✉ Jin-Chul Kim
jinkim@kangwon.ac.kr

[1] Department of Medical Biomaterials Engineering, College of Biomedical Science and Institute of Bioscience and Biotechnology, Kangwon National University, 192-1, Hyoja 2 dong, Chunchon, Kangwon-do 200-701, Republic of Korea

[2] Institute of Forest Science, Kangwon National University, Chuncheon 24341, Republic of Korea

[3] Department of Pharmaceutical Science and Engineering, School of Convergence Bioscience and Technology, Seowon University, Cheongju 28674, Chungbuk, Republic of Korea

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payload through the water channel would be low, leading to a suppressed release. Meanwhile, if the cubic phase comes in contact with a medium of high salt concentration, salt ions can be attached to the amino group of PEI, they would be able to interfere with the electrostatic interaction between the amino group of PEI and the phosphoric group of TPPA, thus PEI gel would be dissolved to become sol, giving a rise to a promoted release (Fig. 1).

Material and methods

Materials

Monomuls 90-O18 (monoolein, MO) was gifted from BASF Korea Ltd. (Seoul, Korea). (monoglyceride content is about 94% (*w*/w)). Phosphotungstic acid, octanoic acid (OA), and tripolyphosphoric acid (TPPA) were purchased from Sigma-Aldrich Co. (St. Louis, USA). Polyethyleneimine (M.W. 10,000, PEI) was purchased from Thermo Fisher Scientific (Waltham, USA). Rhodamine B was purchased from Tokyo Chemical Industry Co., Ltd. (Tokyo, Japan).

Air/water interfacial activity of PEI/OA mixture

PEI and OA were co-dissolved in distilled water so that the molar ratio of amino to carboxyl group was 1:0, 1:0.1, 1:0.5, 1:0.8, 1:1, and 0:1 with the concentration of PEI plus OA being kept to 1 mg/mL. Each of solutions was 1.4 times diluted with distilled water in series to obtain solutions of lower concentrations (0.00375 to 0.714 mg/mL). The air/water interfacial tensions of diluted solutions were measured by an O-ring method on a surface tensiometer (DST 60, SEO Co., Korea). PEI/OA mixture solution whose amino to carboxylic group molar ratio was a/b was named as PEI/OA(a/b) solution.

Preparation of cubic phases containing polyethyleneimine gel

A melt-hydration method was exploited for the preparation of MO cubic phase containing PEI gel. MO (1.4 g) contained in a 10 mL vial was melted in a water bath (50 °C) and, when necessary, OA (0.04 mg) was dissolved in the MO melt. Each of PEI solution (0.5 mL, 1.2% (*w*/*v*), in distilled water) and distilled water was heated to the same temperature and it was put on the lipid melt. When dye-loaded cubic phase was prepared for the release experiment, Rhodamine B was dissolved in each of PEI solution and distilled water, used for the hydration of the lipid melt, so that the concentration was 3 mM. After being tightly sealed, the vial was kept at room temperature under a dark condition to allow the aqueous solution to be absorbed into the lipid melt. TPPA solution (0.1 mL, 0.3% (*w*/*v*)) or distilled water was additionally added to the hydrated lipid and it was left at room temperature for the complete absorption into the lipid layer. Cubic phase

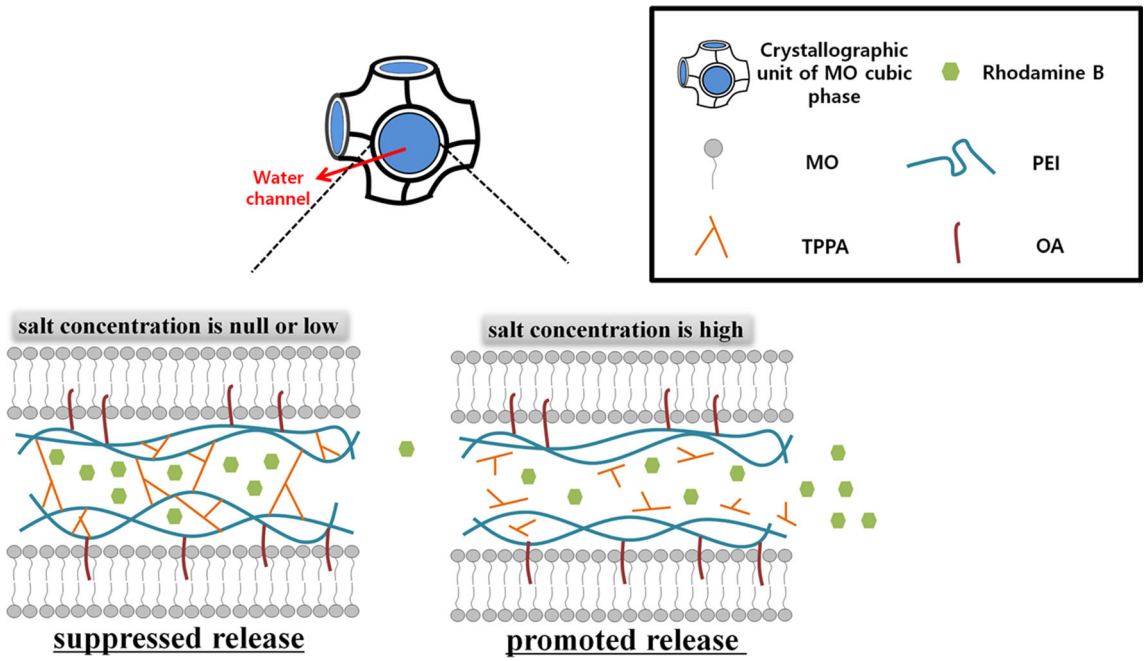

Fig. 1 Illustration of MO cubic phase responsive to salt concentration. TPPA-crosslinked PEI gel is contained in the water channel of the cubic phase. If placed in a medium whose salt concentration is null or low, the diffusivity of a payload through the water channel filled with PEI gel would be low, leading to a suppressed release. If placed in a medium of high salt concentration, salt ions can interfere with the electrostatic interaction between PEI and TPPA, thus PEI gel would be dissolved to become sol, giving a rise to a promoted release (Fig. 1)

containing additives was abbreviated to CP (additive names) and cubic phase without additive was termed as CP (nothing).

Determination of phase transition temperature

Polarized optical microscopy: the phase transition temperature of cubic phase was determined by a method described elsewhere [12, 20]. Each of cubic phases was put in a cell prepared by spacing two parallel cover glasses using an O ring (6 mm in inner diameter and 0.1 mm in thickness). The cell containing cubic phase was put in a temperature controller (HS81, Mettler Toledo, USA) and it was placed on a polarized optical microscope (CX31, OLYMPUS, Japan). The texture of cubic phase was investigated in 30–70 °C at heating rate of 2 °C/min. Differential scanning calorimetry: 5–6 mg each of cubic phases was put in an aluminum pan, capped, pressed for sealing, and thermally scanned on a differential scanning calorimeter (DSC Q2000, TA Instruments, USA, in the Central Laboratory of Kangwon National University). An empty aluminum pan was used as a reference and the cubic phase was heated in 30–70 °C at heating rate of 2 °C/min.

Transmission electron microscopy

The structure of cubosomes was investigated by transmission electron microscopy using a negative staining technique [21–23]. Cubosomes were stained by mixing cubosome suspensions and phosphotungstic acid solution (2% (*w*/*v*), pH 6.8) in equi-volumetric ratio and standing the mixture at room temperature overnight. A drop of the stained cubosome suspension was put on a formvar/copper-coated grid (200 mesh), an excess of suspension was soaked by a filter paper, and the wet grid was air-dried at room temperature overnight. The structure of cubosomes was observed on a transmission electron microscope (LEO 912AB, OMEGA, Germany, located at Korea Basic Science and Institute (Chuncheon, Korea)).

Observation of salt–responsive release

Rhodamine is a water-soluble dye and it was reported to be included in the water channel of cubic phase [24]. Free dye should be removed to avoid the erroneous results of release experiments. The surface of a cubic phase and the inside wall of a 10 mL vial containing the cubic phase were washed with distilled water to remove free Rhodamine B on the surfaces. Release medium (5 mL), either distilled water (pH 5.8) or PBS (135 mM NaCl, 2.7 mM KCl, 4.3 mM Na_2HPO_4, 1.4 mM KH_2PO_4, pH 5.8), was put over the cubic phase and it was gently shaken at room temperature. Release medium (1 mL) was taken at a given time, the fluorescence intensity was determined at 582 nm using the excitation wavelength of 555 nm on a fluorescence spectrophotometer (Hitachi F2500, Hitachi, Japan), and the dye concentration was calculated using a calibration curve. The release medium used for the measurement of fluorescence intensity was put back to the vial containing cubic phase. The release degree of dye was expressed as the percent of the cumulative amount of dye released during a certain period based on the initial amount of dye loaded in cubic phase [25, 26]. MO cubic phase containing ionically gelled PEI in their water channel (i.e. a salt ions-responsive cubic phase) were designed for its use as a transdermal delivery carrier. Once the cubic phase is applied onto human skin, it gets to be put under the skin biological conditions (ca. 150 mM NaCl and pH 5–6). This was a reason why NaCl solution (i.e. PBS) whose NaCl concentration was 135 mM and pH value was 5.8 was used as a release medium.

Observation of interaction of PEI, TPPA, and salt ions through light scattering

In order to investigate whether TPPA could crosslink PEI chains to form insoluble particles, PEI/TPPA mixture solutions were subjected to the measurement of light scattering intensity. TPPA solution (0.25 to 1.25 mL, 3.98 mg/mL, in distilled water) was added to PEI solution (1 mL, 1 mg/mL, in distilled water) contained in a 10 mL vial so that amino/phosphoric group molar ratio was 1:0.5 to 1:3. Distilled water was added to the mixture solutions to make up to 3 mL and the vials were rolled on a roller mixer at room temperature overnight. The light scattering intensity of the mixture solutions were measured on light scattering equipment (Plus 90, Brookhaven Instrument, USA). In order to investigate whether salt ions could dissolve TPPA-crosslinked PEI gel, PBS (135 mM NaCl, 2.7 mM KCl, 4.3 mM Na_2HPO_4, 1.4 mM KH_2PO_4, pH 7.4) was mixed with PEI/TPPA mixture solution and it underwent the measurement of light scattering intensity. TPPA solution (1 mL, 39.8 mg/mL, in distilled water) was added to PEI solution (1 mL, 10 mg/mL, in distilled water) contained in a 10 mL vial so that amino/phosphoric group molar ratio was 1:2. Distilled water (3 mL) was added to the mixture solutions and it was agitated on a roller mixer at room temperature overnight. PEI/TPPA mixture solution (5 mL) was added to the same amount of distilled water (pH 5.8) and PBS (135 mM NaCl, 2.7 mM KCl, 4.3 mM Na_2HPO_4, 1.4 mM KH_2PO_4, pH 5.8), each contained in a 10 mL vial. The light scattering intensity of the mixture solutions was determined at a given time for 24 h.

Results and discussion

Air/water interfacial activity of PEI/OA mixture

Figure 2 shows the air/water interfacial tensions of PEI solution, PEI/OA mixture solutions, and OA solution.

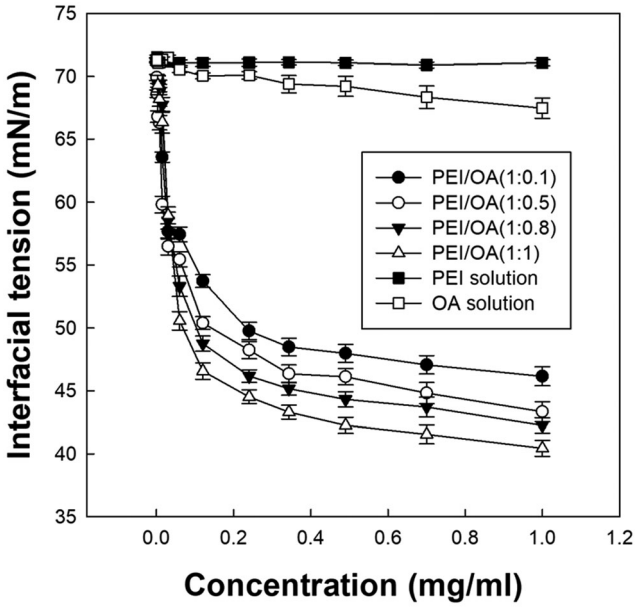

Fig. 2 Air/water interfacial tensions of PEI solution, PEI/OA (1:0.1) mixture solution, PEI/OA (1:0.5) mixture solution, PEI/OA (1:0.8) mixture solution, PEI/OA (1:1) mixture solution, and OA solution

The interfacial tension of PEI solution was almost constant, about 72 dyne/cm, in the full range of concentration (0–1 mg/mL). PEI is a water-soluble cationic polymer and known to be surface-inactive. The interfacial tension of OA solution slightly decreased from about 71 to 67 dyne/cm when the concentration increased up to 1.0 mg/mL. OA is a saturated medium-chain fatty acid with an 8-carbon backbone and it may exhibit a surface activity because of its amphiphilicity. The interfacial tension of PEI/OA(1/0.1) solution markedly decreased from 70 to 46 dyne/cm in a saturation manner in the same concentration range and the interfacial tension profile was typical of that of a surfactant. OA molecules would be able to be conjugated with PEI chains through salt bridges because the carboxylic group of the fatty acid can electrostatically attract with the amino group of the polymer. Since the carbon backbone of OA is lipophilic and PEI chain is hydrophilic, PEI/OA conjugate was likely to be amphiphilic and surface-active. The interfacial tension profile of the other PEI/OA mixture solutions resembled that of PEI/OA(1/0.1) solution. The interfacial tension was slightly but definitely lower as PEI/OA ratio was higher. For example, the minimum interfacial tension of PEI/OA(1/0.1), PEI/OA(1/0.5), PEI/OA(1/0.8), and PEI/OA(1/1) solution were about 46, 43, 42, and 40 dyne/cm, respectively. OA would provide amphiphilic property to PEI through an electrostatic conjugation, thus, as the amount of the fatty acid increases, the amphiphilicity is likely to become prominent, resulting in a marked reduction in the interfacial tension.

Determination of phase transition temperature

Figure 3 shows the polarized optical micrographs of CP(nothing), CP(PEI), CP(OA/PEI), CP(PEI/TPPA), and CP(OA/PEI/TPPA). CP(nothing) exhibited no patterns in 30–38 °C but showed patterns in 39–65 °C. MO cubic phase is an optically isotropic gel and presents no birefringence under the irradiation of a polarized light. While being heated, the cubic phase is subjected, at a certain temperature, to phase transition to a hexagonal phase that is optically anisotropic and shows birefringence [27, 28]. Thus, it was concluded that the cubic-to-hexagonal phase transition occurred at 63.1 °C where birefringence emerged. The phase transition temperature of CP(PEI) and CP(OA/PEI) were 63.7 °C and 63.6 °C, respectively, and they were close to that of CP(nothing), indicating that PEI and OA had little effect on the phase transition temperature of MO cubic phase. PEI is water-soluble and surface-inactive, thus it would be in the water channel and hardly be partitioned into the lipid bilayer, resulting in little effect on the phase transition temperature. Whereas, OA is oil-soluble, it would be able to be intercalated into the lipid bilayer, and it was likely to affect the phase transition temperature. However, the content of OA in cubic phase, based on the mass of MO, was only 0.003% and it seemed to be too small to alter the transition temperature. On the other hand, the phase transition temperature of CP(PEI/TPPA) was about 39 °C. The phase transition temperature was much lower than that of CP(PEI) (63.7 °C), suggesting that TPPA remarkably lowered the transition temperature. The hydroxyl groups of TPPA were thought to participate in hydrogen bonding with the glycerol residue of MO. Thus, TPPA would interfere with the intermolecular hydrogen bonding among the glycerol residues thus weaken the intermolecular attractive force among MO molecules. This could explain why TPPA markedly lowered the phase transition temperature of MO cubic phase. The phase transition temperature of CP(OA/PEI/TPPA) was about 46 °C. It was far lower than that of CP(OA/PEI) (63.6 °C), also indicating that TPPA could lower the transition temperature noticeably.

By the way, TPPA could not lower the phase transition temperature of CP(OA/PEI) as much as that of CP(PEI). OA would be intercalated into the lipid bilayers of MO cubic phase and would be capable of immobilizing PEI chains on the surface of the water channels through an electrostatic attraction. Since the immobilized PEI chains were likely to be closer to one another than free ones, they would be crosslinked by TPPA more efficiently thus consume more the cross-linker. Hence, the amount of free TPPA in CP(OA/PEI) might be less than in CP(PEI), accounting for why TPPA lowered the phase transition temperature of CP(OA/PEI) to less than that of CP(PEI). Figure 4 shows the thermograms of CP(nothing), CP(PEI), CP(OA/PEI), CP(PEI/TPPA), and CP(OA/PEI/TPPA). Endothermic peaks were observed in all the

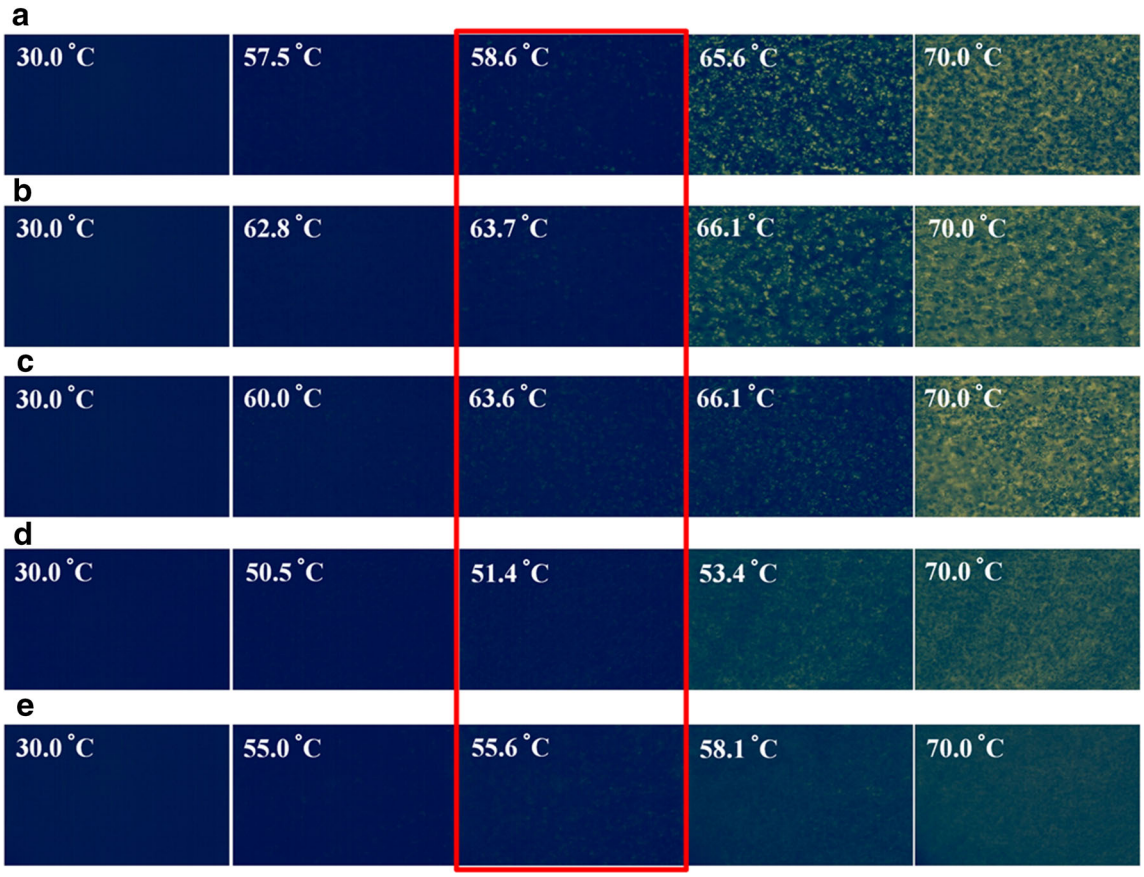

Fig. 3 Polarized optical micrographs of CP(nothing) (**a**), CP(PEI) (**b**), CP(OA/PEI) (**c**), CP(PEI/TPPA) (**d**), and CP(OA/PEI/TPPA) (**e**)

thermograms and they could be attributed to the cubic-to-hexagonal phase transition. The phase transition temperature of CP(nothing), CP(PEI), CP(OA/PEI), CP(PEI/TPPA), and CP(OA/PEI/TPPA) were found at 59.2 °C, 60 °C, 60.9 °C, 37.7 °C, and 43.6 °C, respectively, and the results did not markedly deviate from those observed by polarized optical microscopy.

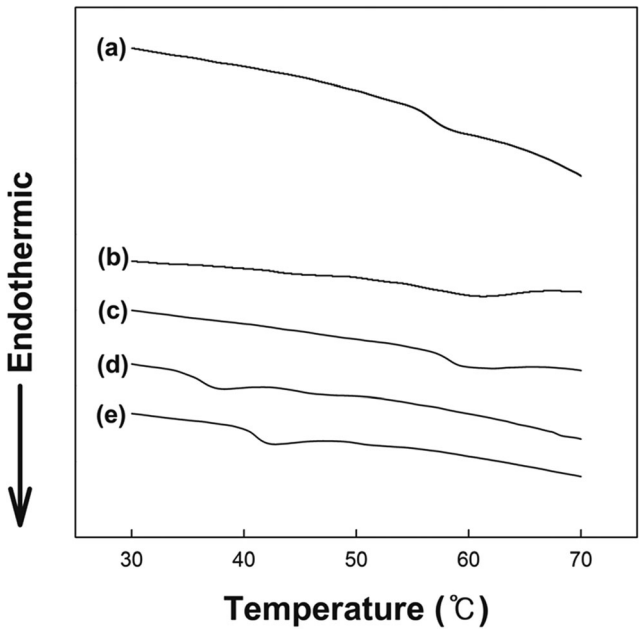

Fig. 4 Thermogram of CP(nothing) (a), CP(PEI) (b), CP(OA/PEI) (c), CP(PEI/TPPA) (d), and CP(OA/PEI/TPPA) (e)

Transmission electron microscopy

Figure 5 shows the TEM micrographs of CS(nothing), CS(PEI), CS(OA/PEI), CS(PEI/TPPA), and CS(OA/PEI/TPPA). All the cubosomes exhibited finger print–like patterns. The water channels could scatter electron beams due to heavy metal ions contained in them thus they were shown as black lines, whereas MO bilayers allow electron beams to pass through them thus they appeared as white ones. No structural difference was found among five kinds of cubosomes. PEI is water-soluble, and hardly portioned into MO bilayers thus would seldomaffect the structure. OA would be intercalated into the lipid bilayers and could affect the pacing integrity. However, the amount of OA included in the cubosomes seemed not to be enough to affect the structure (the content of OA, based on the mass of MO, was only 0.003% (*w*/w)). TPPA would interact mainly with PEI through electrostatic attraction and it would also be able to interact with the glycerol residue of MO through hydrogen bonding. The former

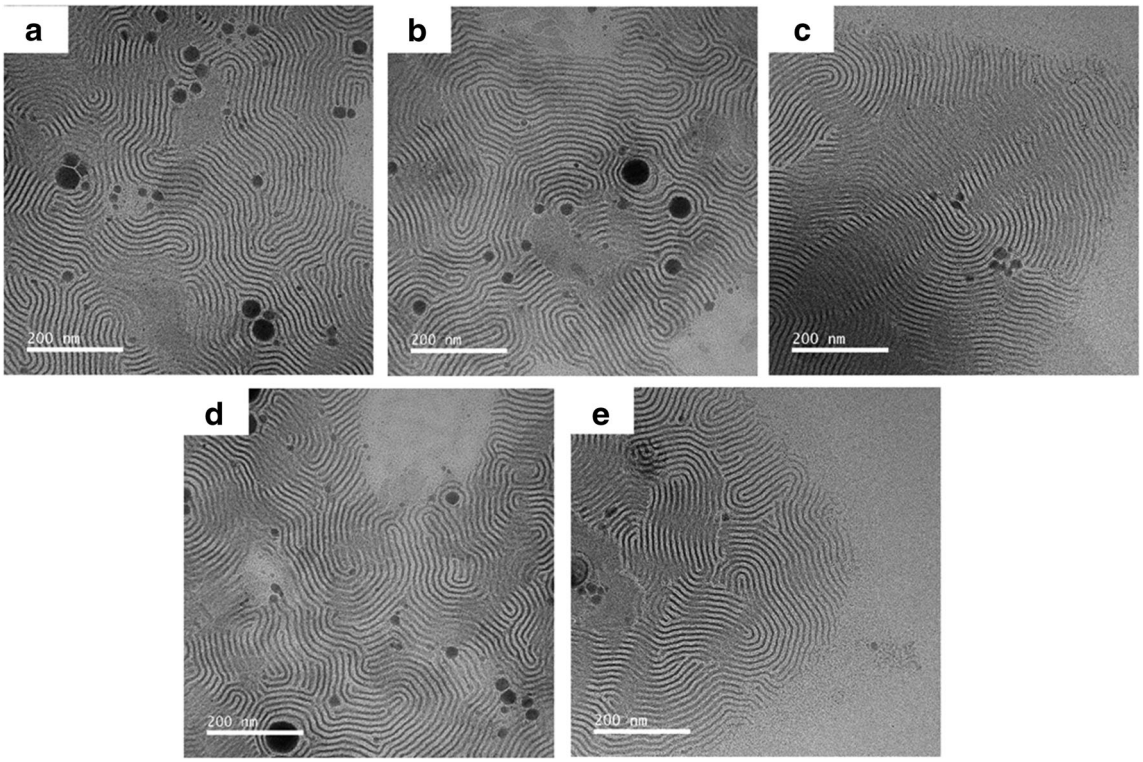

Fig. 5 TEM micrographs of CS(nothing) (**a**), CS(PEI) (**b**), CS(OA/PEI) (**c**), CS(PEI/TPPA) (**d**), and CS(OA/PEI/TPPA) (**e**)

interaction could hardly affect the integrity of the bilayer structure because the electrostatic attraction took place in the water channels. The latter interaction might have an effect on packing state of MO molecules because TPPA could interfere with the intermolecular hydrogen bonding among MO molecules. However, no apparent difference in structure was found between cubosomes with and without TPPA. Instead, there was marked difference in phase transition temperature between them (Figs. 3 and 4).

Observation of salt–responsive release

Figure 6 shows the release profiles of dye loaded in CP(nothing) when the release medium was distilled water (pH 5.8) and PBS (135 mM NaCl, 2.7 mM KCl, 4.3 mM Na_2HPO_4, 1.4 mM KH_2PO_4, pH 5.8). The release degree in distilled water increased along a saturation curve and reached about 50.4% for 24 h. Monolithic types of carriers including MO cubic phase were reported to release their payload in a saturation manner [29–31]. The release profile and the release degree in PBS were almost the same as those in distilled water. Since only difference between PBS and distilled water was that the buffer solution contained salts as much as 137 mM, it could be said that the release degree was little affected by salts. Figure 7 shows the release profiles of dye loaded in CP(OA/PEI(0.5%)/TPPA) and CP(OA/PEI(1.0%)/TPPA) when the release medium was distilled water (pH 5.8) and PBS (135 mM NaCl, 2.7 mM KCl, 4.3 mM Na_2HPO_4, 1.4 mM KH_2PO_4, pH 5.8). The release degree of dye loaded in CP(OA/PEI(0.5%)/TPPA) increased to about 20.2% for 24 h in case distilled water was used as a release medium. The release degree was much lower than that of dye loaded in CP(nothing) (ca. 50.3%). PEI chains can be crosslinked by TPPA through electrostatic attraction between the amino

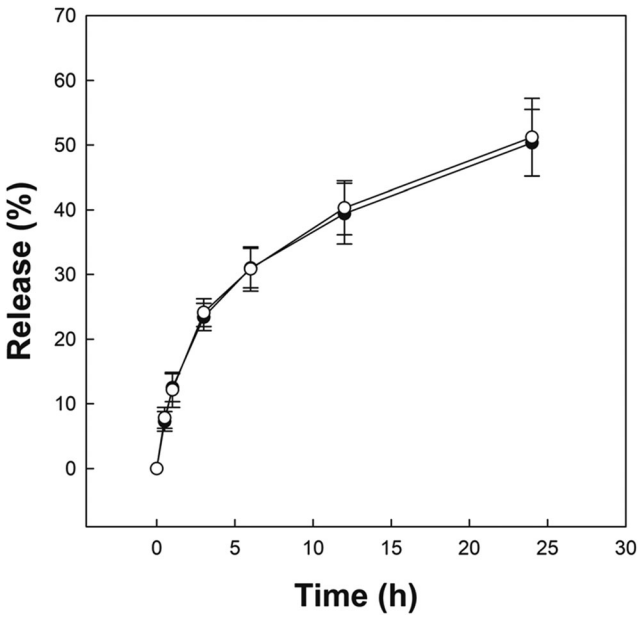

Fig. 6 Release profiles of dye loaded in CP(nothing) when the release medium was distilled water (pH 5.8) (●) and PBS (135 mM NaCl, 2.7 mM KCl, 4.3 mM Na_2HPO_4, 1.4 mM KH_2PO_4, pH 5.8) (○)

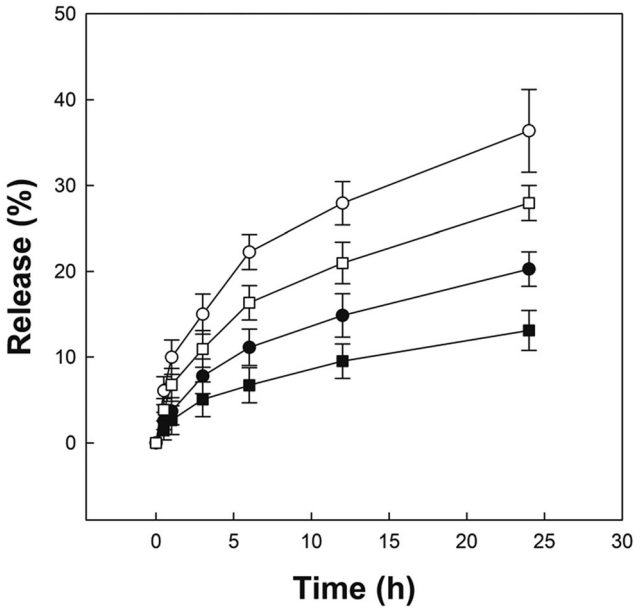

Fig. 7 Release profiles of dye loaded in CP(OA/PEI(0.5%)/TPPA) (●, ○) and CP(OA/PEI(1.0%)/TPPA) (■, □) when the release medium was distilled water (pH 5.8) (●, ■) and PBS (135 mM NaCl, 2.7 mM KCl, 4.3 mM Na_2HPO_4, 1.4 mM KH_2PO_4, pH 5.8) (○, □)

group and the phosphoric acid group. PEI is a water-soluble polymer and it was likely to be included in the water channel of cubic phase. TPPA is a small water-soluble compound (MW 258) thus it would readily penetrate into the water channel and crosslink PEI chains. Accordingly, the water channel of CP(OA/PEI(0.5%)/TPPA) seemed to be filled with PEI gel. The diffusion of dye through the water channel would be hindered by the PEI gel, leading to a suppressed release. This would account for why the release degree of dye loaded in CP(OA/PEI(0.5%)/TPPA) was much lower than that of dye loaded in CP(nothing). When PBS was used as a release medium, the release degree of dye loaded in CP(OA/PEI(0.5%)/TPPA) increased to about 36.3% for 24 h. The release degree was more than two times higher than that obtained using distilled water. The salt concentration of PBS was about 137 mM and the ions would interfere with the electrostatic attraction between PEI and TPPA. For example, sodium ions can be electrostatically attached to the amino groups of PEI and chloride ions can be attracted to the phosphoric acid group of TPPA. In this circumstance, TPPA molecules could hardly crosslink PEI chains and PEI gel would be broken down, accounting for why the release was promoted when PBS was used as a release medium. On the other hand, the release degree of dye loaded in CP(OA/PEI(1.0%)/TPPA) increased to about 13.1% for 24 h when distilled water was used as a release medium. The release degree was somewhat lower than that of dye loaded in CP(OA/PEI(0.5%)/TPPA) (ca. 20.2%). PEI was included in CP(OA/PEI(1.0%)/TPPA) and CP(OA/PEI(0.5%)/TPPA) so that the concentration base on the water amount was 1% and 0.5%, respectively. Thus, the amount of PEI network in the water channel of the former cubic phase would be about 2 times higher than that of the latter one. Accordingly, the release would be more suppressed when PEI concentration was higher. This would be a reason why the release degree of dye loaded in CP(OA/PEI(1.0%)/TPPA) was lower than that of dye loaded in CP(OA/PEI(0.5%)/TPPA). As CP(OA/PEI(0.5%)/TPPA) did, CP(OA/PEI(1.0%)/TPPA) exhibited a promoted release when PBS was used as a release medium. For example, the release degree in 24 h was about 27.9% in PBS and it was about two times higher than that obtained using distilled water. As described previously, ions contained in the buffer solution would be able to dissolve PEI gel via ion exchange and promote the release of dye out of the cubic phase.

Observation of interaction of PEI, TPPA, and salt ions through light scattering

Figure 8 shows the light scattering intensity of PEI/TPPA mixture solutions with changing amino/phosphoric group molar ratio. The light scattering intensity increased from 160 to 281 Kcps when amino/phosphoric group molar ratio increased from 1:0.5 to 1:3. As described previously, TPPA is capable of crosslinking PEI chains to form gel through the electrostatic interaction between the phosphoric group and the amino group. The light would be scattered by PEI gel particles and the light scattering intensity could be used as a measure of the crosslinking degree. Assuming that TPPA and PEI were completely ionized, maximum crosslinking would take place at amino/phosphoric group molar ratio of 1:1. However, the light scatter intensity increased with increasing the molar ratio even after equimolar ratio. This was possibly because all the phosphoric groups would not be able to participate in electrostatic attract with the amino groups due to the steric hindrance and the restricted rotational flexibility of TPPA back bone. Since CP(OA/PEI/TPPA) was prepared so that amino/

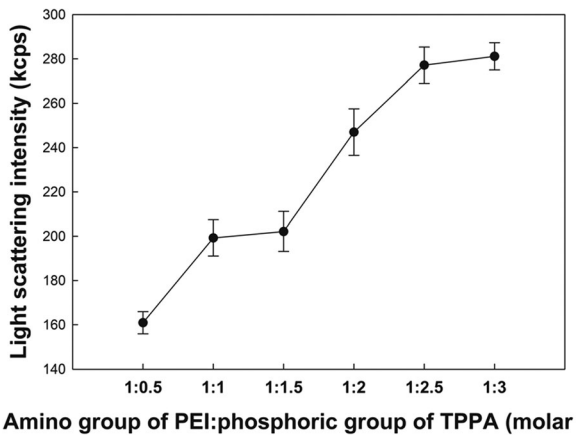

Fig. 8 Light scattering intensity of PEI/TPPA mixture solutions with changing amino/phosphoric group molar ratio

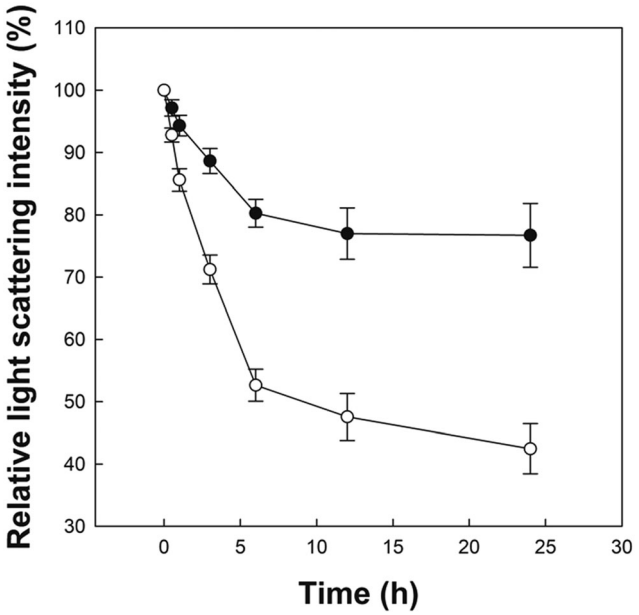

Fig. 9 Change of light scattering intensity of PEI/TPPA mixture solution with time lapse when distilled water (pH 5.8) (●) and PBS(135 mM NaCl, 2.7 mM KCl, 4.3 mM Na_2HPO_4, 1.4 mM KH_2PO_4, pH 5.8) (○) was added to the mixture solution at time 0

phosphoric group molar ratio was 1:1, it was thought that gel particles of TPPA-crosslinked PEI chains were included in the water channel of the cubic phase. Figure 9 shows the change of light scattering intensity of PEI/TPPA mixture solution with time lapse when distilled water (pH 5.8) and PBS (135 mM NaCl, 2.7 mM KCl, 4.3 mM Na_2HPO_4, 1.4 mM KH_2PO_4, pH 5.8) was added to the mixture solution at time 0. The light scattering intensity decreased to 76% for 24 h in a saturation manner when distilled water was added to the mixture solution. Upon the addition of distilled water, equilibrium between TPPA trapped in PEI gel (i.e. PEI-bound TPPA) and free TPPA was thought to be broken and the bound TPPA would be released out of PEI gel to reach a new equilibrium, leading to a decrease in the light scattering intensity. On the other hand, the light scattering intensity decreased to 42% for 24 h when PBS was added to the PEI/TPPA mixture solution. PBS could decrease the light scattering intensity over two times more than distilled water. Besides the dilution effect described above, salt ions included in PBS would be able to interrupt the electrostatic attraction between PEI and TPPA because sodium ions could be electrostatically attached to the amino groups of PEI and chloride ions could be attracted to the phosphoric group of TPPA. Accordingly, PEI chains could hardly be crosslinked by TPPA molecules and PEI gel would be dissolved, accounting for why PBS decreased the light scattering intensity much more than distilled water. The promoted release of dye loaded in CP(OA/PEI/TPPA), observed using PBS as a release medium (Fig. 7), could be ascribed to the ions-induced dissolution of PEI gel.

Conclusions

MO cubic phases containing ionically gelled PEI in their water channel were prepared as a salt ions-responsive vehicle. The interfacial tension profile of PEI/OA solutions were typical of a surfactant solution, suggesting that PEI could be immobilized in water channel due to the surface-active property. The phase transition temperature of MO cubic phase was about 63 °C and it was remarkably lowered to below 40 °C by TPPA, possibly because TPPA interfered with the intermolecular hydrogen bonding among MO molecules. On the TEM micrographs, the structure of the cubic phase was little affected by additives (i.e. OA, PEI, and TPPA). When placed in PBS, the release degree of Rhodamine B loaded in cubic phase containing PEI gel (i.e. CP(OA/PEI/TPPA)) was more than two times higher than that observed when placed in distilled water. The promoted release of the dye loaded in CP(OA/PEI/TPPA), observed using PBS as a release medium, could be ascribed to the salt ions-induced dissolution of PEI gel.

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