Development of a new phosphatidylcholine-like surfactant and its application in cosmetics

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Background
Surfactants are crucial components of cosmetic products. We aimed to develop novel surfactants with high safety, such as phospholipids, and excellent stability owing to their low critical micelle concentration and high self-association properties, such as gemini surfactants. Thus, we focused on stearyl behendimonium ethyl phosphate [PCG(P(18)-N(22))], a gemini surfactant with a phosphorylcholine group. Accordingly, a novel surfactant was developed and its functionality was confirmed.

Methods
In previous studies, we reported the strong ability to lower the interfacial tension and high emulsification stability of bis(hydroxyethyl)oleylammonium ethyl phosphate behenyl [PCG(P(22)-N(Et)(18:1))] and bis(hydroxyethyl)behenylammonium ethyl phosphate oleyl [PCG(P(18:1)-N(Et)(22))], which bear unsaturated bonds and hydroxyethyl groups (*1). This paper reports other functional properties and their applications in cosmetics.
In this study, the solubility and emulsification maintenance times of the oil agents were confirmed. Reportedly, [PCG(P(18)-N(22))] forms vesicles, and the synthesized samples may exhibit similar formation; thus, three-phase diagrams were prepared using surfactants, water, and glycol. Subsequently, we used polarizing microscopy, dynamic light scattering measurement, small-angle X-ray scattering measurements, and transmission electron microscopy.

Results and Discussion
[PCG(P(22)-N(Et)(18:1))] exhibited significant solubility and emulsification maintenance time, which is attributable to the unsaturated bond in the lipophilic chain, which binds to the nitrogen atom and the hydroxyethyl group in the hydrophilic site. Furthermore, three-phase diagrams of phospholipids [PCG(P(18)-N(22))] and [PCG(P(22)-N(Et)(18:1))] were prepared, and their compositions were analyzed using Maltese cross confirmation. The results suggest that the regions of [PCG(P(22)-N(Et)(18:1))] that form lamellar structures are enlarged compared to those of the other regions.
Keywords: gemini surfactant, lamellar structure, SAXS, TEM, phosphorylcholine group

Introduction
In recent years, consumers of cosmetics have not only required high quality and functionality, but also a pleasant feeling after use and safety. Therefore, multiple studies have been conducted to develop new ingredients, combinations, and technologies. The ingredients used in cosmetics are broadly classified as water-, oil-, powder-, and surfactant-based ingredients. Surfactants are vital components that significantly contribute not only to the functionality and feeling of use of commodities, but also to their stability.
Conventional surfactants used in cosmetics are monomeric, which indicates a single-chain single hydrophilic group; however, attention has been focused in recent years on gemini-type double chain 2 hydrophilic groups, in which surfactants are tethered to each other in the vicinity of a hydrophilic group by an appropriate linking group. Gemini-type surfactants have extremely low critical micelle concentrations (CMC), high interfacial tension-lowering abilities, and high surfactant abilities, which

are represented by low kraft points. Additionally, they exhibit excellent characteristics, such as high molecular associativity, antibacterial properties, and high foaming and penetration properties, which enable the spontaneous formation of higher-order structures, such as vesicles (*2). Gemini-type surfactants can express a surfactant with a scientific function equivalent to or higher than that of single-chain single hydrophilic group-type surfactants with a small addition amount ; by replacing a conventional surfactant with a gemini-type surfactant, the total amount of surfactant used can be reduced, thereby resulting in a low environmental load.

Phospholipids are constituents of biological membranes; therefore, they are used in many cosmetics as surfactants with high safety. Phosphocholine (PC) groups, which are polar groups of phospholipids that exhibit excellent characteristics, such as biocompatibility and moisture retention, are widely utilized as functional groups.

Therefore, we aimed to develop novel surfactants with high safety and biocompatibility, similar to those of phospholipids and features of gemini-type activators. Therefore, we focused on phosphatidylcholine, a phospholipid, and [PCG(P(18)-N(22))], a gemini-type active agent with a phosphocholine group, to develop a novel surfactant and determine its functionality.

Methods

Raw materials

1.3-Butylene glycol (BG), phospholipids, [PCG(P(18)-N(22))], [PCG(P(22)-N(Et)(18:1))], [PCG(P(18:1)-N(Et)(22))], glyceryl tri-2-ethylhexanoate, liquid paraffin, purified water, carrageenan sucrose mixture, and PEG phytosterol

Sample preparation

The formulation was prepared by heating the active agent and 1, 3-BG at 80 °C, adding purified water and a carrageenan sucrose mixture, heating at 80 °C, and uniformly stirring with a homodisperser. Thereafter, the mixture was cooled to 40 °C in cold water, subjected to high-pressure or high-temperature and high-pressure treatments, and maintained at room temperature for 1 d.

small-angle X-ray scattering measurements (SAXS) : Small-angle X-ray scattering (SAXS) measurements were performed on an SAXS instrument installed at the BL40B2 beamline in SPring-8 (Hyogo, Japan). The X-ray wavelength was 0.7 Å, and the sample-to-detector distance was 2.0 m. The covered q range was 0.1–5 nm−1 (where $q = (4\pi/\lambda) \sin(\theta/2)$, in which λ and θ represent the wavelength and scattering angle, respectively). The exposure time for each sample was 3 minutes.

Dynamic light scattering (DLS) : Dynamic light scattering (DLS) measurements were performed on an ALV- 5000E spectrophotometer (Hessen, Deutschland). ALV-5000/E for Windows software was used to compute the particle size distribution (CONTIN analysis).

Transmission electron microscopy (TEM) observation: The structural status of the prepared associates was observed using negative staining and TEM (HI-7600; Hitachi) (100V).

Observed of Maltese cross: The prepared samples observed by polarized light microscopy were used to confirm the Maltese cross via modified electron microscopy (BX53:OLYMPUS).

Results

・Sample selection

Owing to their unsaturated bonds and hydroxyethyl groups, [PCG(P(22)-N(Et)(18:1))] and [PCG(P(18:1)-N(Et)(22))] exhibit high interfacial tension lowering ability and emulsification stability. Therefore, their solubility and emulsification maintenance time in polar and hydrocarbon oils, which are general-purpose raw materials in cosmetics, were confirmed (Table 1). Based on their solubility and emulsification maintenance time, [PCG(P(22)-N(Et)(18:1))] showed excellent solubility and emulsification maintenance time in polar and hydrocarbon oils; thus, [PCG(P(22)-N(Et)(18:1))] was selected for use in this study.

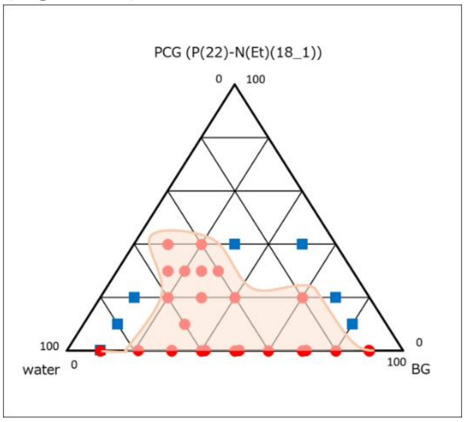
(Table 1)

	Solubility			Emulsification maintenance time	
Surfactant	Polar oil	Hydrocarbon oil	Water	Polar oil	Hydrocarbon oil
PCG(P(18)-N(22))	△	×	×	15 min	×
PCG(P(22)-N(Et)(18:1))	◯	◯	×	60 min	45 min
PCG(P(18:1)-N(Et)(12))	△	×	×	×	Not soluble

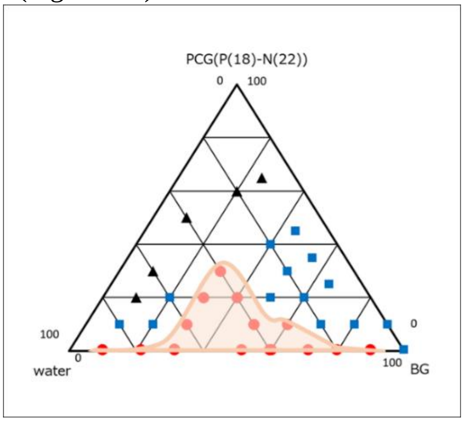
・Fabrication of three-phase diagrams

[PCG(P(18)-N(22))] Based on vesicle formation, [PCG(P(22)-N(Et)(18:1))] may form associates as well. Therefore, we confirmed the changes in the regions of each phospholipid, [PCG(P(18)-N(22))] and [PCG(P(22)-N(Et)(18:1))], which can confirm their association with optical anisotropy (Maltese cross confirmation). which was confirmed by fabricating three-phase diagrams using 1, 3-BG, water, and various surfactants (Figures 1-1–1-3). Each site (plot) was color-coded according to the Maltese cross confirmation and the appearance of the samples (Table 2). The results showed that the regions where liquid and Maltese crosses were identified were larger in [PCG(P(22)-N(Et)(18:1))] than in the phospholipids and [PCG(P(18)-N(22))]. Moreover, [PCG(P(22)-N(Et)(18:1))] confirmed the Maltese cross in the low-concentration region, where the Maltese cross cannot be confirmed with phospholipids and [PCG(P(18)-N(22))]. This reveals that compared to phospholipids and [PCG(P(18)-N(22))], [PCG(P(22)-N(Et)(18:1))] has a wider region that is associated with optical anisotropy.

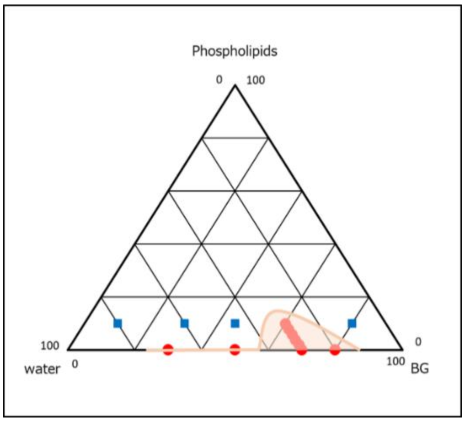
(Figure 1-1)



(Figure 1-2)



(Figure 1-3)



(Table 2)

	Condition
▲	Not soluble
■	Solid state
●	Liquid state

・Analysis of associates

[PCG(P(22)-N(Et)(18:1))] To analyze the physicochemical properties of the formed associates, samples according to the following formulations (Tables 3-1, 3-2) were prepared and analyzed by DLS, SAXS, and TEM. The DLS and SAXS results of the prepared samples are shown below (Figures 2-1 and 2-2). To confirm the effects of other factors on the associates, samples were prepared by mixing water-soluble polymers and high-pressure treatment. The samples were also analyzed by DLS and SAXS (Figures 3-1, 3-2). Additional TEM observations were conducted, and multilayered associates were observed (Figure 4). These results suggested that the associate formed by [PCG(P(22)-N(Et)(18:1))] was a vesicle.

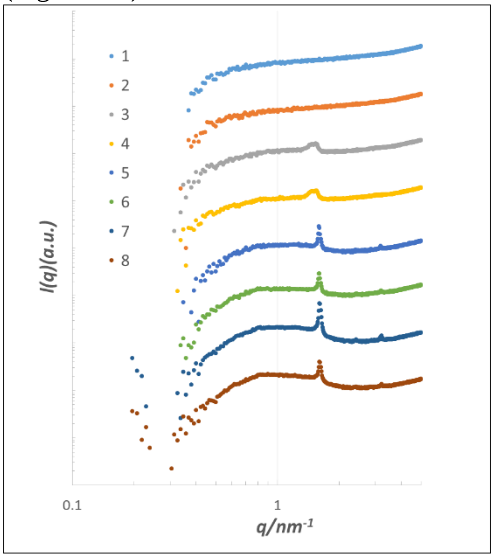
(Table 3-1)

	1	2	3	4	5	6	7	8
PCG(P(22)-N(Et)(18:1))	0.01	0.01	0.1	0.1	1	1	0.5	0.5
1, 3-BG	31	31	31	31	31	31	31	31
Water	68.99	68.99	68.8	68.8	67	67	68	68
PEG Phytosterol	—	—	0.1	0.1	1	1	0.5	0.5
Water solubility High polymer	—	—	—	—	—	—	—	—
High-pressure treatment	—	2	—	2	—	2	—	2

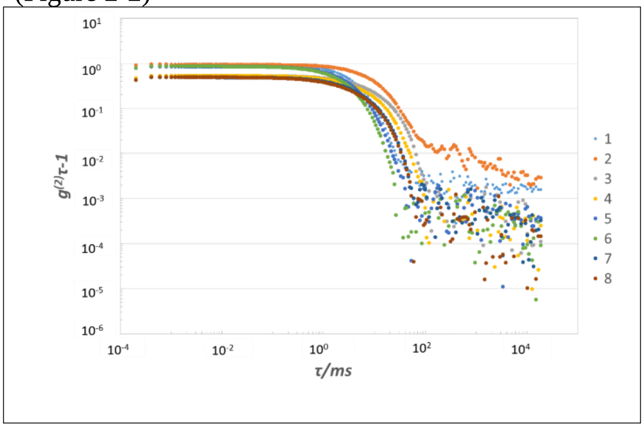
(Table 3-2)

	9	10	11
PCG(P(22)-N(Et)(18:1))	0.5	1	2
1, 3-BG	36	36	36
Water	61.75	61.75	61.75
PEG Phytosterol	0.5	1	2
Water solubility High polymer	0.25	0.25	0.25
Warming High-pressure treatment	2	2	2

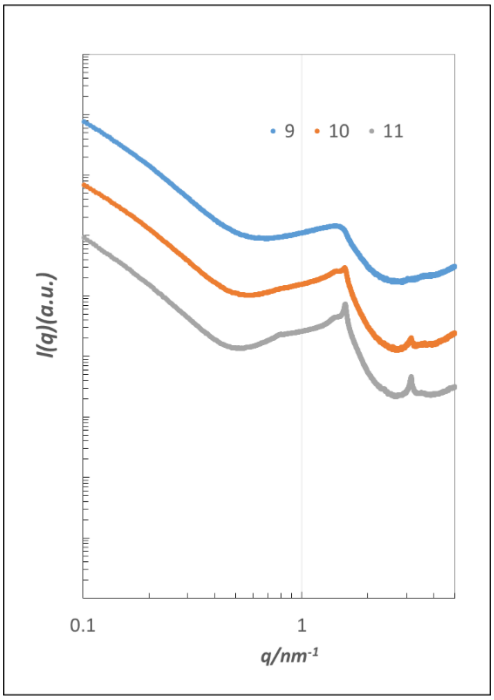
(Figure 2-1)



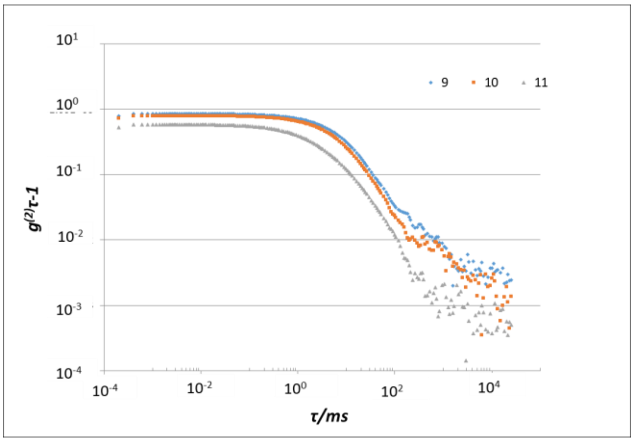
(Figure 2-2)



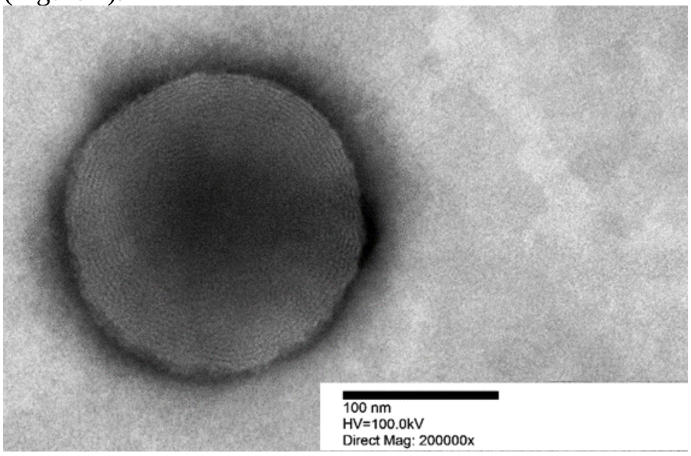
(Figure 3-1)



(Figure 3-2)



(Figure 4).



Discussion

The ability of [PCG(P(22)-N(Et)(18:1))] to form associates was greater than that of phospholipids [PCG(P(18)-N(22))]. This superior ability can be attributed to the critical packing parameter (R) of [PCG(P(22)-N(Et)(18:1))], which indicates that it is more likely to form an association. Moreover, DLS measurements of the sample were performed by compounding the water-soluble polymer, and the SAXS results proved that the SAXS profile changed in the sample blended with the water-soluble polymer. This result can be attributed to a change in the structure of the associate contained within the original sample caused by the addition of the water-soluble polymer. Thus, the combination of the water-soluble polymer and [PCG(P(22)-N(Et)(18:1))] is likely to have formed a new associate that was different from the original associate.

Conclusion

A new gemini-type surfactant was developed, and its functionality was determined. The association formed by [PCG(P(22)–N(Et)(18:1))] was confirmed to be a vesicle. Moreover, the new surfactant exhibited improved vesicle formation ability compared to those of phospholipids and [PCG(P(18)-N(22))]. Because the vesicles formed by [PCG(P(22)-N(Et)(18:1))] are expected to be highly effective in transepidermal water transpiration and stratum corneum water content, cosmetics prepared using [PCG(P(22)-N(Et)(18:1))] are considered to have high functionality. Detailed analysis of vesicles and their usefulness in the skin will be conducted in future studies.

Reference.

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(*2) H. Okawa, K. Hanabusa, M. Suzuki, H. Fukui, Efficacies of a novel Gemini Compound "2-(Dimethyldocosylammonio)ethyl octadecyl ethyl phosphate" as a Cosmetic ingredient, International Journal of Research in Cosmetic Science, 3(2) (2013) 19-24.