Impact of the State of Water on the Dispersion Stability of a Skin Cream Formulation Elucidated by Magnetic Resonance Techniques

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This study investigated the relationship between the state of water and the dispersion stability of a skin cream formulation. Hydrophilic ointments treated with a high-pressure wet-type jet mill were used as model formulations. Spin–lattice relaxation times (T_1) were measured by magnetic resonance techniques to estimate the state of water in samples. A shorter T_1 relaxation time was obtained from samples with higher surfactant content, whereas the processing pressure of the jet mill and 1-week storage at 40 °C did not influence the T_1 relaxation time. Observations using scanning electron microscopy (SEM) showed that coalescence occurred in samples with lower surfactant contents (1.0% by weight) following 1-week storage at 40 °C. We also investigated samples prepared using a hydrophilic surfactant with a short polyethylene glycol (PEG) chain and with PEG-4000. From the change in T_1 relaxation times after removing the oil phase from samples by centrifugation, it was clarified that most of the surfactant was located on the surface of oil droplets. Furthermore, SEM observations showed that phase separation was facilitated as the PEG chain length of the surfactant shortened. Thus, a thin water layer over oil droplets is the most important factor for stabilizing their dispersion. This study provides proof-of-principle results on the contribution of the state of water to the dispersion stability of a skin cream formulation.

Key words skin cream formulation; dispersion stability; magnetic resonance imaging; T_1 relaxation time; bound water; scanning electron microscopy

A high-pressure wet-type jet mill is a powerful tool for dispersion and emulsification. The internal structure of such a mill is schematized in Fig. 1. Fluids (*e.g.*, slurry and emulsion) fed into the mill are pressurized by a hydraulic plunger pump. The pressurized fluids are jetted into a chamber from two branched channels and are then collided head-on at an extremely high speed. The important aspect of the jet mill is that its processing pressure can be increased to a maximum of 245 MPa. Thus, fine dispersion and emulsification can be achieved.[1—3] The wet-type jet mill is suitable for industrial manufacturing, because it can process a large volume of fluid in a short time and can be integrated easily into a one-pass operation system.

We expect the wet-type jet mill to be an effective tool for preparing pharmaceuticals and we have investigated its usefulness in preparing skin cream formulations.[4] Hydrophilic ointments—among the most popular skin cream bases—are oil-in-water(o/w)-type emulsions. In such formulae, the droplet size is one crucial factor for determining the rheological characteristics; thus, an emulsion with smaller droplets has more viscous properties than that with larger droplets.[5—8] By treating the emulsion with a jet mill, we hoped to improve the rheological properties of a skin cream formulation by decreasing the oil droplet size. Observations using scanning electron microscopy (SEM) confirmed that the oil droplet size was reduced by treatment with the jet mill.[4] As the size decreased, the rheological properties became much more viscous with increased viscosity, hysteresis area and yield value. These changes in the rheological properties depended on the processing pressure of the jet mill, and the results suggest that such treatment offers great benefits for preparing skin cream formulations. For one thing, the jet mill treatment would provide a sensible solution for incorporating a large amount of water into skin cream formulations without interfering with its proper rheological properties. However, it is still difficult to sustain improved rheological properties for a long time after preparation. We addressed this issue in aiming for the practical use of jet mill treatment in preparing

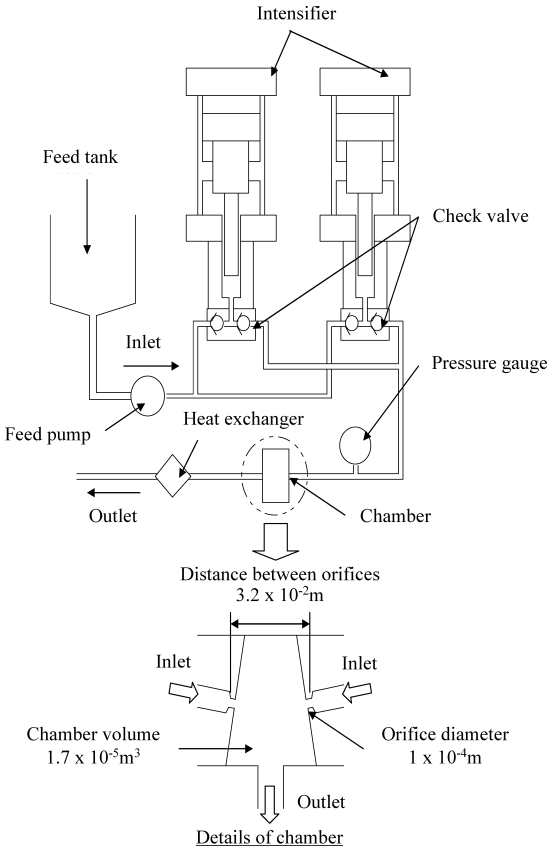

Fig. 1. A Schematic Diagram of the High-Pressure Wet-Type Jet Mill

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skin cream formulations.

To stabilize the dispersion of oil droplets in an o/w-type emulsion, the interaction between surfactant and water is very important. In the JP XV hydrophilic ointment, poly(ethylene glycol)-60 (PEG-60)–hydrogenated castor oil and glycerol monostearate are incorporated as hydrophilic and hydrophobic surfactants, respectively. The surfactants localize at the interface of the oil droplets and aqueous phase and then interact with water, resulting in the formation of a thin layer of water surrounding the droplet surface. The water layer is thought to prevent the oil droplets from coalescing. In addition, part of the hydrophilic surfactant diffuses throughout the aqueous phase, which increases the viscosity by interacting with water. Increasing the viscosity of the continuous phase might contribute to the dispersion stability. Considering these aspects, this study focused on the relationship between the state of water in the skin cream formulation and its dispersion stability.

As test samples, skin cream formulations containing different amounts of surfactants were treated with the jet mill at different processing pressures. To evaluate the state of water, we used magnetic resonance (MR) techniques, nuclear magnetic resonance (NMR) and magnetic resonance imaging (MRI). Based on changes in water proton spin–lattice relaxation times (T_1), we estimated the amount of bound water in each sample. We also observed the oil droplets using SEM immediately after the jet mill treatment and after storage for 1 week at 40 °C. We found that bound water generated by the interaction with surfactants contributed significantly to the dispersion stability of tiny oil droplets in a skin cream formulation.

Experimental

Materials White petrolatum, stearyl alcohol, propylene glycol, glycerol monostearate, methyl parahydroxybenzoate, PEG-4000 and propyl parahydroxybenzoate were purchased from Wako (Osaka, Japan). PEG-60–hydrogenated castor oil (HCO-60) and PEG-40–hydrogenated castor oil (HCO-40) were purchased from Nikko Chemicals (Tokyo, Japan). All other reagents were of chemical grade.

Preparation of the Skin Cream Formulation As a model skin cream formulation, hydrophilic ointments were prepared according to JP XV. The formulation used in this study is listed in Table 1. In brief, white petrolatum, stearyl alcohol, HCO-60 and glycerol monostearate were fused in a water bath at 75 °C and the mixture was stirred until it became homogeneous. This liquid was used as the oil phase. For the aqueous phase, propylene glycol, methyl parahydroxybenzoate and propyl parahydroxybenzoate were added to water and then stirred in a water bath at 75 °C. The two phases were then mixed in a water bath at 75 °C to form an o/w-type emulsion. The emulsion was stirred gently until it cooled to room temperature. The water content was fixed at 75% and the surfactant contents were changed from 1.0 to 3.6% of total weight. The skin cream formulations prepared were then treated with a high-pressure wet-type jet mill (HJP25003; Sugino Machine Ltd., Toyama, Japan). For evaluating changes in their characteristics with aging, the samples were stored at 40 °C for 1 week.

Table 1. Formulation of Skin Cream

Component	Composition (%)
White petrolatum	10.6—9.2
Stearyl alcohol	8.5—7.3
PEG-60–hydrogenated castor oil	0.8—2.9
Glycerol monostearate	0.2—0.7
Propylene glycol	4.8
Methyl parahydroxybenzoate	0.04
Propyl parahydroxybenzoate	0.04
Water	75

We also prepared a skin cream formulation using HCO-40, having a shorter PEG chain than HCO-60, to examine the effect of PEG chain length on dispersion stability. For sample preparation, 1.2% of HCO-40 (4.7 mmol/l) was incorporated. This was the same molar concentration as HCO-60 in the sample with 2.0% surfactants shown in Table 1. In addition, PEG-4000 (5.33 mg/ml of aqueous phase) was incorporated into the aqueous phase to compensate for the difference in the PEG amount between HCO-40 and HCO-60.

^{1}H-NMR Relaxation and MRI Experiments The T_1 relaxation time was measured and MRI performed using a Varian NMR system (Varian Technologies Japan Ltd., Tokyo, Japan) at 9.4 T at room temperature. The T_1 relaxation time was measured using the inversion-recovery (IR) sequence (180°–τ–90°-acquisition) and a spin–echo (SE) sequence. Such IR-SE mixed sequences are used frequently for T_1 measurements.[9—11] T_1-weighted images were acquired using an SE pulse sequence with an effective echo time (TE) of 14.54 ms and a repetition time (TR) of 300 ms. The spatial resolution was 0.234×0.234 mm (matrix size=128×128 pixels; field of view=30×30 mm). Quantitative T_1 maps were acquired with a gradient echo pulse sequence with a TE of 1.54 ms and six different inversion times (TIs) (200, 400, 800, 1400, 2000, 3000 ms) and a flip angle of 10°. The spatial resolution was 0.469×0.469 mm (matrix size=64×64, field of view=30×30 mm). Final analysis was performed using ImageJ® software (http://rsbweb.nih.gov/ij/; U.S. National Institutes of Health, Bethesda, MD, U.S.A.).

SEM Observation of Oil Droplets in a Skin Cream Base Immediately after the jet mill treatment or after storage for 1 week at 40 °C, the oil droplets were monitored using SEM (JSM-5600LV; Jeol Co., Ltd., Tokyo, Japan) as described.[4] For sample preparation, skin cream formulations (15 μl) were set in a wet SEM capsule (QX102-capsules; QuantomiX, Nes Ziona, Israel). These contain an ultrathin membrane that is transparent to the electron beam but is impervious to water. The mechanical strength of the membrane is high enough to resist a 1-atmosphere pressure difference. Therefore, because the sample in the capsule was completely isolated from the vacuum in the microscope chamber, samples could be monitored directly in their native wet environment using SEM. Feret diameters of oil droplets were measured (n=100).

Results

Changes in T_1 Relaxation Time of Skin Cream Formulations with Different Preparation Conditions We first acquired T_1-weighted images and quantitative T_1 maps of the skin cream formulations containing different amounts of surfactants (Fig. 2). Although T_1-weighted images showed similar aspects of the samples, their T_1 maps were quite different. A red spot in Fig. 2 indicates a longer T_1 relaxation time of water in the samples and blue spots represent shorter times. The T_1 map of the sample containing 1.0% surfactants showed some red and orange spots, whereas most parts of the sample containing 3.6% surfactants appeared to be blue. This suggests that the T_1 relaxation time is shortened by increasing the surfactant content.

To understand fully the change in T_1 relaxation times, the values for different samples were measured from ^{1}H-NMR spectra (Fig. 3, Table 2). For reference, we acquired the T_1 relaxation time of purified water. The value of about 2.8 s is consistent with other reports,[12—15] indicating the validity of this experimental approach. As shown in Table 2, the T_1 relaxation times were noticeably shorter for skin cream formulations than for purified water, indicating that the state of water in the skin cream formulations differed. The T_1 relaxation times shortened progressively with increasing surfactant content: the values of samples containing 1.0% and 3.6% surfactants were about 2.2 s and 1.8 s, respectively (Fig. 3a). However, the T_1 relaxation time of samples treated with the jet mill at different processing pressures changed little (Fig. 3b).

The data were analyzed by two-way analysis of variance

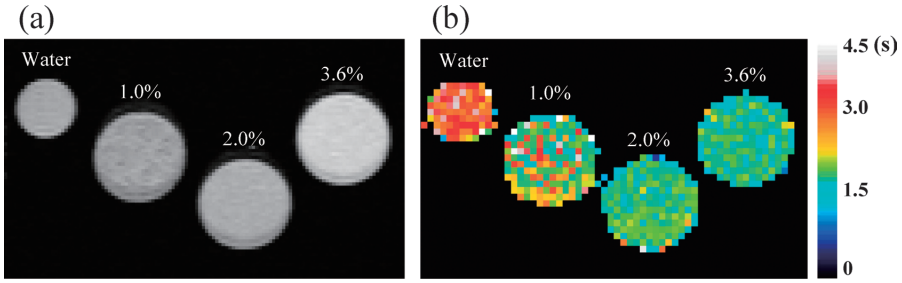

Fig. 2. Spin–Lattice Relaxation Times (T_1)-Weighted Image (a) and Quantitative T_1 Map (b) of Skin Cream Formulations Just after Treatment with the Jet Mill

(a) Spin–echo sequence of effective echo time (TE) and repetition time (TR) gave TR/TE=300/14.54 ms, field of view of 30×30 mm, matrix size of 128×128 pixels and 1 mm axial slice thickness. (b) T_1 map of fresh samples. Gradient echo pulse sequence with TE=1.54 ms and six different inversion times (TIs) (200, 400, 800, 1400, 2000, 3000 ms), field of view of 30×30 mm, matrix size of 64×64 pixels and 1 mm axial slice thickness. Red spots represent longer T_1 relaxation times, whereas blue spots represent shorter T_1 relaxation times. The samples were purified water and skin cream formulations containing 1.0%, 2.0%, or 3.6% surfactant.

Table 2. T_1 Relaxation Times (s) of Water Protons (H^+) in Skin Cream Formulations after Treatment with the Wet-Type Jet Mill as a Function of Processing Pressure

	Processing pressure (MPa)	Delay in measuring T_1 value[a)]	Surfactant concentration[b)] (%)		
			1.0	2.0	3.6
Skin cream formulation	0	Immediately after processing	2.25±0.09	2.08±0.12	1.86±0.12
		After 1 week at 40 °C	2.30±0.13	2.07±0.03	1.85±0.08
	150	Immediately after processing	2.22±0.04	2.00±0.10	1.81±0.04
		After 1 week at 40 °C	2.25±0.05	2.08±0.05	1.82±0.07
	245	Immediately after processing	—	2.04±0.16	—
Purified water			2.87±0.37		

a) T_1 relaxation time of the samples was measured just after the jet mill treatment or after 1-week storage at 40 °C. *b*) Total concentrations of HCO-60 and glycerol monostearate in the samples. Each value represents the mean±S.D. (n=3 or 6).

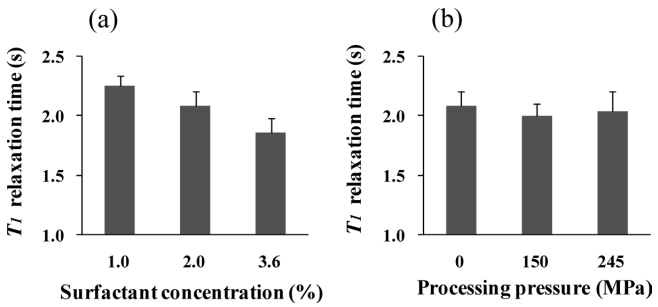

Fig. 3. Changes in T_1 Relaxation Times of Skin Cream Formulations as a Function of Surfactant Concentration (a) and Processing Pressure of the Jet Mill (b)

The processing pressure of the jet mill used for treating the samples shown in (a) was 150 MPa and total concentrations of HCO-60 and glycerol monostearate shown in (b) were fixed at 2.0%. Each value represents the mean±S.D. (n=6).

Table 3. ANOVA Table for T_1 Relaxation Time of Water Protons (H^+) in Skin Cream Formulations

Factors	DF	SS	F_o
Processing pressure of the jet mill	1	0.023	2.88
Surfactant concentration of skin cream formulation	2	0.976	60.56**
Aging the samples for 1 week at 40 °C	1	0.000	0.01

Key: DF, degrees of freedom; SS, sum of squares. ** p<0.01.

(ANOVA). In addition to the effects of surfactant contents and processing pressure of the jet mill, we also evaluated the effect of aging on the T_1 values. The F_o value of the surfactant concentration was very high, 60.56, whereas those of the processing pressure and time lag for the measurement were very low, 2.88 and 0.01, respectively (Table 3). This indicates that the surfactant content exerts a dominant influence on the state of water molecules and that the operational conditions of the jet mill and aging the samples have no effects.

We next removed the oily phase from the samples by centrifugation (SRX-201, TOMY Digital Biology Co., Ltd., Tokyo, Japan) at 10000 ***g*** for 30 min at room temperature and then evaluated changes in T_1 relaxation times. For this experiment, we also prepared a skin cream formulation using HCO-40 instead of HCO-60. Because HCO-40 has a shorter PEG chain than HCO-60, we compensated for the difference in PEG amount by adding PEG-4000. The total concentration of surfactants and PEG-4000 were fixed at 2.0% of total weight. Figure 4 shows the change in T_1 relaxation times of pre- and postcentrifugation samples. The T_1 relaxation times became much shorter by removing the oily phase with centrifugation. As for each value of precentrifugation samples, there was no difference between samples prepared with HCO-60 and HCO-40: 2.09±0.04 s for HCO-60 and 2.10±0.06 s for HCO-40. After removing the oily phase by centrifugation, their T_1 relaxation times were quite different: 2.37±0.05 s for HCO-40 was significantly shorter (p<0.01) than 2.57±0.03 s for HCO-60 (Fig. 4). We further measured the T_1 relaxation time of the PEG solution, the aqueous phase of the skin cream formulation with HCO-40. As shown, the T_1 relaxation time of the PEG solution, 2.30±0.10, was similar to that of the postcentrifugation sample using HCO-40.

Monitoring Oil Droplets in Skin Cream Formulations with SEM We used SEM to observe the properties of the

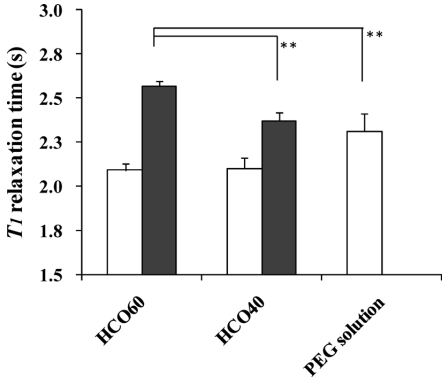

Fig. 4. T_1 Relaxation Times of Skin Cream Formulations Measured before (□) and after (■) Centrifugation

For postcentrifugation sample preparation, the samples were centrifuged and their oily phases were removed. HCO-60, the skin cream formulation shown in Table 1 (the surfactant concentration of 2%); HCO-40, the skin cream formulation prepared using HCO-40 and PEG-4000 instead of HCO-60; PEG solution, the aqueous phase of the skin cream formulation with HCO-40 (the concentrations of PEG and propylene glycol concentrations were 5.33 mg/ml and 64.0 mg/ml, respectively). Each value represents the mean±S.D. ($n=3$) ** $p<0.01$.

oil droplets in the samples. All samples used here were treated with the jet mill at a processing pressure of 150 MPa and then kept for 1 week at 40 °C. The dark spots shown in Fig. 5 represent oil droplets in the skin cream formulations. SEM images obtained just after the jet mill treatment showed no difference in terms of droplet shape and size regardless of the surfactant contents (Figs. 5a, c, e). The Feret diameters of the fresh samples containing 1.0%, 2.0% and 3.6% of surfactant were 1.76±0.49, 1.73±0.60 and 1.73±0.49 μm, respectively (Table 4). The mean diameter was 5.97±2.78 μm for the pretreatment sample (Table 4); the droplet size was decreased substantially by the treatment with the jet mill. Storage for 1 week at 40 °C tended to increase the droplet size, especially in creams with low surfactant content. The mean diameter for the sample containing 1.0% surfactant was 5.03±2.57 μm: *i.e.*, the oil droplets had increased in size by about three times after storage for 1 week. By contrast, the droplet size changed little in samples with higher surfactant content: 2.16±1.09 μm for 2.0% and 1.79±0.76 μm for 3.6%. We also monitored the oil droplets of samples prepared using HCO-40. Just after the jet mill treatment, the aspects (Fig. 5g) seemed similar to those using HCO-60. After 1 week at 40 °C, the phase separation of oil and water obviously proceeded (Fig. 5h). We note that the 1-week storage hardly affected the sample prepared using HCO-60 at a surfactant content of 2.0% (Fig. 5d).

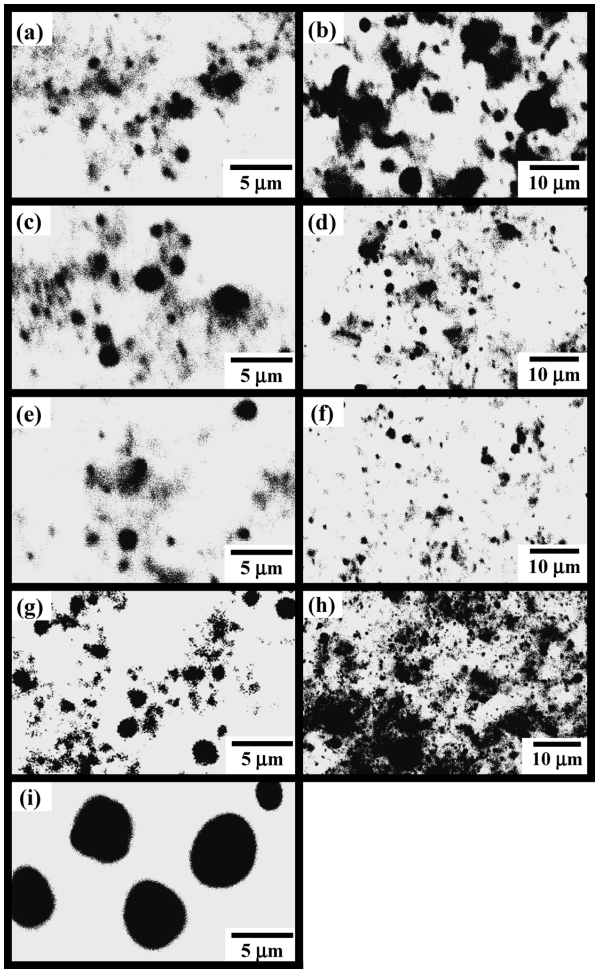

Fig. 5. Scanning Electron Microscopy (SEM) Micrographs of Oil Droplets in the Skin Cream Formulations

Skin cream formulations prepared using HCO-60 (a—f, and i) or HCO-40 and PEG-4000 (g and h) were treated with the jet mill at a processing pressure of 150 MPa. SEM was performed immediately after treatment with the jet mill (a, c, e and g) and after storage for 1 week at 40 °C (b, d, f and h). The surfactant content was 1.0% (a and b), 2.0% (c, d, g and h), or 3.6% (e and f). The pretreatment sample containing 1.0% surfactant (i) is shown as a control.

Table 4. Feret Diameters (μm) of Oil Droplets in Skin Cream Bases Immediately after the Jet Mill Treatment and after 1-Week Storage at 40 °C

	HCO-60			HCO-40
Surfactant concentration (%)	1.0	2.0	3.6	2.0
Pretreatment	5.97±2.78	—	—	—
Immediately after treatment	1.76±0.58	1.73±0.60	1.73±0.49	1.80±0.92
After storage at 40 °C for 1 week	5.03±2.57	2.16±1.09	1.79±0.76	2.61±2.49

The formulations of the samples with HCO-60 are listed in Table 1. The sample with HCO-40 contained 1.2% of HCO-40 and 0.4% of PEG-4000. The molar concentration of HCO-40 was the same as that of HCO-60 in the sample with 2.0% surfactants. The jet mill treatment was performed at the processing pressure of 150 MPa. Each value represents the mean±S.D. ($n=100$).

Discussion

To address the problem of dispersion stability after treatment with a jet mill, we monitored the state of water in skin cream formulations. In general, water is classified into three states: free water, freezing interfacial or intermediate water and nonfreezing or bound water.[16,17] Free water is defined as the water with the same phase transition temperature as bulk water. Freezing interfacial water is water whose phase transition is lower than 0 °C. Nonfreezing water is defined as water with no detectable phase transition from 0 to −100 °C. Freezing water and nonfreezing water—generally defined as bound water—are generated because the water interacts weakly and strongly, respectively, with the polar moieties of hydrophilic polymers.[12,18] In the case of our skin cream formulations, interacting with the long PEG chain of HCO-60 should generate a considerable amount of bound water. We speculate that this bound water plays an important role in the

dispersion stability of the skin cream formulations.

To date, many methods have been used to identify and distinguish the different states of water molecules. The methods used most often are heat analysis (*e.g.*, differential scanning calorimeter, DSC) and MR techniques (*e.g.*, NMR).[19,20] However, using DSC to estimate the state of water in a skin cream formulation is a challenge because one cannot distinguish the endothermic peaks of each state of water from numerous other peaks and noise.

MR techniques are promising for detailed studies of the structure and mobility of hydrogen ion (H^+) protons in the ointment. Because all samples comprised mainly water (75%), most of the obtained MR signal can be regarded as being derived from water. Identifying different states of water from the T_1 relaxation time and water proton spin–spin (T_2) relaxation time[13,21—26] is an established method. When bound water is generated, the motion of water slows and shorter T_1 relaxation times are observed.

As anticipated, the T_1 relaxation times were noticeably shorter for the samples than for purified water (Fig. 3), indicating that bound water restricted by surfactant was present together with free water in the samples. The amount of bound water increased in samples with higher surfactant content, which was reflected in the shorter T_1 relaxation times. Interestingly, the processing pressure of the jet mill treatment exerted no influence on the T_1 relaxation time (Table 3). We have already clarified that this is a dominant factor for decreasing oil droplet size: thus, droplet sizes of skin cream formulations containing 70% water decreased progressively from 3.01 ± 1.58 to $0.78 \pm 0.28\,\mu$m with increasing processing pressures from 0 to 245 MPa.[4] The T_1 relaxation time is sensitive to the amount of surfactant but is insensitive to the shape of the oil droplet. Storage for 1 week at 40 °C also had no effect on the T_1 relaxation time (Table 3). From these findings, we conclude that the T_1 relaxation time can be used as an index to estimate the amount of bound water in a sample.

We next evaluated the change in the oil droplet size following 1-week storage at 40 °C. As shown in Fig. 5, the oil droplet size was noticeably larger for samples with 1.0% surfactant than with 2.0% or 3.6% surfactant. This suggests that the growth behavior of oil droplets is connected intimately to the amount of bound water in the sample. Once skin cream formulations were treated with the jet mill, the droplet size decreased significantly. We note that the droplet sizes just after the jet mill treatment depended on the processing pressure: thus, the droplet sizes treated at 150 MPa were almost the same regardless of the formulation (Fig. 5). By contrast, the amount of bound water in the sample is decided by its surfactant content. Therefore, the samples with lower surfactant content (*e.g.*, 1.0%) were probably unable to maintain the large specific surface area expanded by the jet mill treatment, and then coalescence continued until the droplet size had been adjusted in relation to the stabilizing effect of each sample.

We further investigated the role of surfactants in stabilizing oil droplet dispersion. We assumed that most of the surfactant is located on the surface of oil droplets and then forms a thin layer over oil droplets by interacting with the surrounding water. This layer is supposed to prevent oil droplets from coalescence. In addition, some of the surfactants are also distributed in the aqueous phase. Because the surfactant can increase the viscosity of the aqueous phase, it might also contribute to stabilizing the dispersion of oil droplets. To confirm the mechanism responsible for the dispersion stability, we prepared a skin cream formulation using HCO-40 instead of HCO-60. Because we speculate that the PEG chain of a hydrophilic surfactant is the most important element to generate bound water, we compensated for the difference in PEG contents between HCO-40 and HCO-60 by adding PEG-4000. As anticipated, by adding PEG-4000 the T_1 relaxation time of the sample using HCO-40 was adjusted to be similar to that of HCO-60 (Fig. 4). We also expected the experiment to clarify the localization of surfactant in the sample. As a result, the T_1 relaxation time became longer by removing the oily phase from the samples, indicating that much of the surfactant was removed with the oily phase by centrifugation. Furthermore, when comparing the postcentrifugation T_1 relaxation times, the value of the sample with HCO-40 was shorten than that with HCO-60 and similar to that of its aqueous phase (PEG solution). This suggests that, unlike surfactant, PEG-4000 added with HCO-40 prefers to disperse in the aqueous phase. From the findings, surfactants are thought to concentrate on the surface of oil droplets, generating a thin water layer.

We also monitored the growth behavior of oil droplets of the sample prepared using HCO-40. By adding PEG-4000, the sample with HCO-40 was more viscous than that with HCO-60; 24.0 ± 0.3 mPa·s for HCO-40 and 11.7 ± 0.1 mPa·s for HCO-60 at a shear rate of 191.5 s^{-1} (data not shown). Thus, in terms of the viscosity, the sample with HCO-40 should have had an advantage in stable dispersion over that with HCO-60. However, the sample with HCO-40 underwent phase separation more easily than that with HCO-60 (Fig. 5). A thinner water layer generated by HCO-40 could have caused this. The PEG chain length of HCO-40 is shorter than that of HCO-60; also, PEG-4000 added with HCO-40 was mostly dispersed in the aqueous phase and not on the surface of the oil droplets. Thus, the water layer of the sample with HCO-40 was probably thinner than that with HCO-60. From the findings, we conclude that the water layer over an oil droplet is the dominant role of surfactants in stabilizing dispersion of skin cream formulations.

Based on our MR results, we confirmed the significant relationships between the state of water and the dispersion stability of a skin cream formulation. MRI has become a powerful tool for designing and characterizing pharmaceutics.[27—31] In addition to the ability to image a chosen slice of samples noninvasively, MRI provides valuable information about the state of water in terms of swelling or erosion. Furthermore, MRI is well suited for longitudinal imaging (*e.g.*, the monitoring of drug release from formulations and implanted devices intended for long-term treatment protocols). This is because, unlike the innately short half-life of radionuclide imaging, there is no limitation on the effective measurement period. In the future, MRI will become an invaluable tool in the development of pharmaceutics.

This is the first technical report on the application of MRI to investigating the state of water in a skin cream formulation. These findings will be useful for improving the dispersion stability of skin cream formulations after treatment with a jet mill.

Conclusion

MRI and NMR, provide powerful tools to estimate the amount of bound water in complicated systems. They enabled us to visualize and quantify the state of water in a skin cream formulation of various components. By taking advantage of MR techniques, we could confirm that a thin water layer over the oil droplets generated by the interaction between the surfactant and water is an essential element for stabilizing the fine dispersion of oil droplets in an aqueous phase. This study provides insight into the dispersion stability of skin cream formulations after treatment with a jet mill.

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