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SHORT COMMUNICATION

Effect of surfactants on the porous structure of poly(*N*-isopropylacrylamide) hydrogels prepared by an emulsion templating method

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Abstract Stimuli-sensitive porous hydrogels prepared with an emulsion templating method developed by the authors are potentially applicable in the medical and pharmaceutical fields; thermosensitive *N*-isopropylacrylamide (NIPA) hydrogels having randomly distributed sphere-like cavities have been prepared by the polymerization in an aqueous phase in an oil-in-water (O/W) emulsion, followed by the washing of oil (oleyl alcohol) microdroplets. The surfactant plays a dominant role in the preparation of porous hydrogels and the pore size. This study concerns with the surfactant effects on the stability of pre-gel O/W emulsions. The porous NIPA hydrogels were successfully prepared using the surfactants forming the stable emulsion and their internal structures and swelling properties were characterized. The O/W emulsions and the porous hydrogels prepared using various amounts of oil and surfactant were characterized. The information obtained serves for preparation of porous hydrogels having suitable porous structure for their applications.

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Introduction

Stimuli-sensitive hydrogels have recently attracted considerable attention in the medical and pharmaceutical fields. These hydrogels change their physical properties and network structures abruptly in response to external stimuli such as temperature, pH, specific ions, light, and electric fields. An *N*-isopropylacrylamide (NIPA) hydrogel is a typical thermosensitive hydrogel and possesses a lower critical solution temperature (LCST) of around 33°C [1]; the NIPA hydrogel swells in water below the LCST and it shrinks as the temperature increases. The NIPA hydrogel and its derivatives have been extensively studied on their potential applications in controlled-release drug delivery systems [2–4], biosensors [4, 5], separation operations [6, 7], and so on.

In our previous study [8], a novel emulsion templating method, which is simple and inexpensive, has been developed to prepare porous hydrogels having a unique structure. Porous NIPA hydrogels having sphere-like micron sized cavities randomly distributed and a homogeneous network in the gel phase were prepared as follows; the synthesis of NIPA gels in an aqueous phase in an oil-in-water (O/W) emulsion by free radical copolymerization with a cross-linker, followed by the washing (removal) of the dispersed oil microdroplets as a pore template (porogen). The shrinking rate of the porous NIPA hydrogels is considerably high by the increase in temperature jump across the LCST, while that of the conventional non-porous NIPA hydrogels is low as a result of the formation of a dense shrunken network on the surface, the so-called skin layer [9, 10]. The fast response of hydrogels to external stimuli is advantageous to their applications. The emulsion templating method (or the method without removal of oil microdroplets) can yield potentially intelligent gels in which pores (or oil microdroplets contained) function as spaces for reaction, separation, and storage dealing with macromolecular active agents; we have developed novel NIPA emulsion gels for controlled drug release [11].

It is important to control the size and volume fraction (porosity) of pore in porous hydrogels for their applications. The pore size and porosity can be controlled by varying the volume fraction of oil phase and the amount of added surfactant. The purpose of this study is to elucidate the effect of property and amount of surfactant on the oil microdroplet size in pre-gel O/W emulsions and the pore size in the resulting porous hydrogels and to obtain the keys for preparing hydrogels having porous structure suitable for each application. The candidate is the porous hydrogels consisting of NIPA hydrogels and microdroplets of oleyl alcohol. The stability of the O/W emulsions prepared using the 15 different polyoxyethylene-type surfactants shown in Table 1 was investigated and discussed in relation to their molar masses and hydrophile-lipophili balance (HLB) numbers. The porous NIPA hydrogels were prepared using the surfactants forming the stable emulsions and their internal structures and swelling properties were investigated. In addition, the O/W emulsions and the porous NIPA hydrogels were prepared under a wide range of volume fractions of oil phase in emulsion, ϕ_{oil}, and the weight fractions of surfactant in oil phase, X, and they were characterized.

Experimental

Preparation and characterization of O/W emulsions

Two kinds of solutions were prepared: 4cm^3 water containing NIPA (1,000mol/m^3 water) and 2cm^3 oleyl alcohol containing a surfactant (0.1g/cm^3 oil). The O/W emulsion was formed by mixing the solutions for 30s with a tube mixer and maintained at 10°C before and after the mixing. The stability of the emulsions was monitored by the naked eye and a digital camera. The oil microdroplets were observed with a stereomicroscope, where an extremely small amount of the emulsion was put on the water in a petri dish at 10°C to attain a better viewing.

Preparation of porous NIPA hydrogels

The details of the preparation of porous NIPA hydrogels are provided in our previous paper [8] and a brief mention is sufficient here. The NIPA gels were synthesized by the free radical polymerization using *N*,*N'*-methylenebisacrylamide (MBAA) as a cross-linker, *N*,*N*,*N'*,*N'*-tetramethylethylenediamine (TEMED) as an accelerator and ammonium peroxodisulfate (APS) as an initiator. Three kinds of solutions were prepared: the pre-gel aqueous solution containing NIPA, MBAA and TEMED, the aqueous solution containing initiator APS, and oleyl alcohol containing a surfactant. The concentrations were NIPA–MBAA–TEMED–APS = 1,000:50:10:1mol/m^3 in water. The O/W emulsion (12cm^3) was formed by mixing the solutions for 30s with the tube mixer and the mixtures were allowed to stand for a day. The solutions were maintained at 10°C

Table 1 Molar mass M_W and HLB of surfactants used

No.	Surfactant, (abbreviation)	M_W [g/mol]	HLB [-]
1	Polyoxyethylene sorbitan monolaurate, (Tween20)	1,228	16.7
2	Polyoxyethylene sorbitan monooleate, (Tween80)	1,310	15.0
3	Polyoxyethylene laurylether (n=2)	274	7.7
4	Polyoxyethylene tridecylether (n=3)	332	8.0
5	Polyoxyethylene oleylether (n=2)	356	4.9
6	Polyoxyethylene oleylether (n=4), (POOE4)	447	7.9
7	Polyoxyethylene oleylether (n=8), (POOE8)	620	11.3
8	Polyoxyethylene sorbitan monooleate, (D-945)	ca. 1,310	15.0
9	Polyoxyethylene 2-butyl-2-ethyl-1,3-propanediol	ca. 336	10.5
10	PEO-PPO-PEO triblock copolymer	ca. 5,000	10.0
11	Polyoxyethylene nonylphenyl ether (n=5)	440	10.0
12	Polyoxyethylene nonylphenyl ether (n=7.5), (PONPE7.5)	550	12.0
13	Polyoxyethylene nonylphenyl ether (n=10), (PONPE10)	660	13.3
14	Polyoxyethylene nonylphenyl ether (n=15), (PONPE15)	881	15.0
15	Polyoxyethylene nonylphenyl ether (n=20), (PONPE20)	1,101	16.2

Supplier: Wako Pure Chemical Industries (No. 1 and 2), Takemoto Oil & Fat (No. 3–10), and Tokyo Chemical Industry (No. 11–15), HLB number: from catalogue

n Means the number of polyoxyethylene, *PEO* and *PPO* denote poly(ethylene oxide) and poly(propylene oxide), respectively

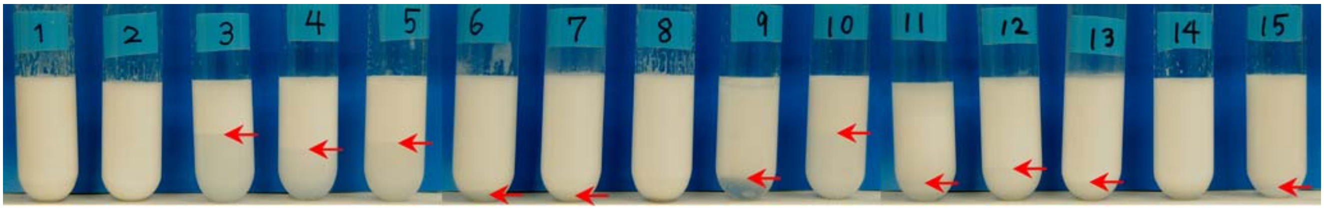

Fig. 1 Photographs of O/W emulsion consisting of 4 cm^3 water containing NIPA (1,000 mol/m^3-water) and 2 cm^3 oleyl alcohol containing a surfactant (0.1 g/cm^3-oil) at 10 °C after 4 h. The number corresponds to that shown in Table 1. The *arrow* represents the phase interface

under a nitrogen atmosphere before and after the mixing. The resulting gels were first washed with methanol, then with water. The porous NIPA hydrogels were prepared under various conditions of ϕ_{oil} and X.

Observation of porous structure by SEM

The internal structure of porous hydrogels was observed by a scanning electron microscope (SEM). The specimens were prepared as follows; the swollen hydrogels at 10°C were frozen using liquid nitrogen and the resulting frozen gels were dried under reduced pressure.

Measurement of swelling diameter

The cylinder-shaped porous NIPA hydrogels used here were synthesized in a glass tube with an inner diameter 6.0mm and the ratio of the diameter to the length of the gel was 1:1. The hydrogels were initially immersed in water at 10°C. The swelling diameter at equilibrium was measured with a microscope; the central point was used as the measuring point. The temperature was then increased in increments and the diameter was measured at each temperature. The kinetics for the swelling/shrinking of the hydrogels by the temperature jump between 10°C and 50°C

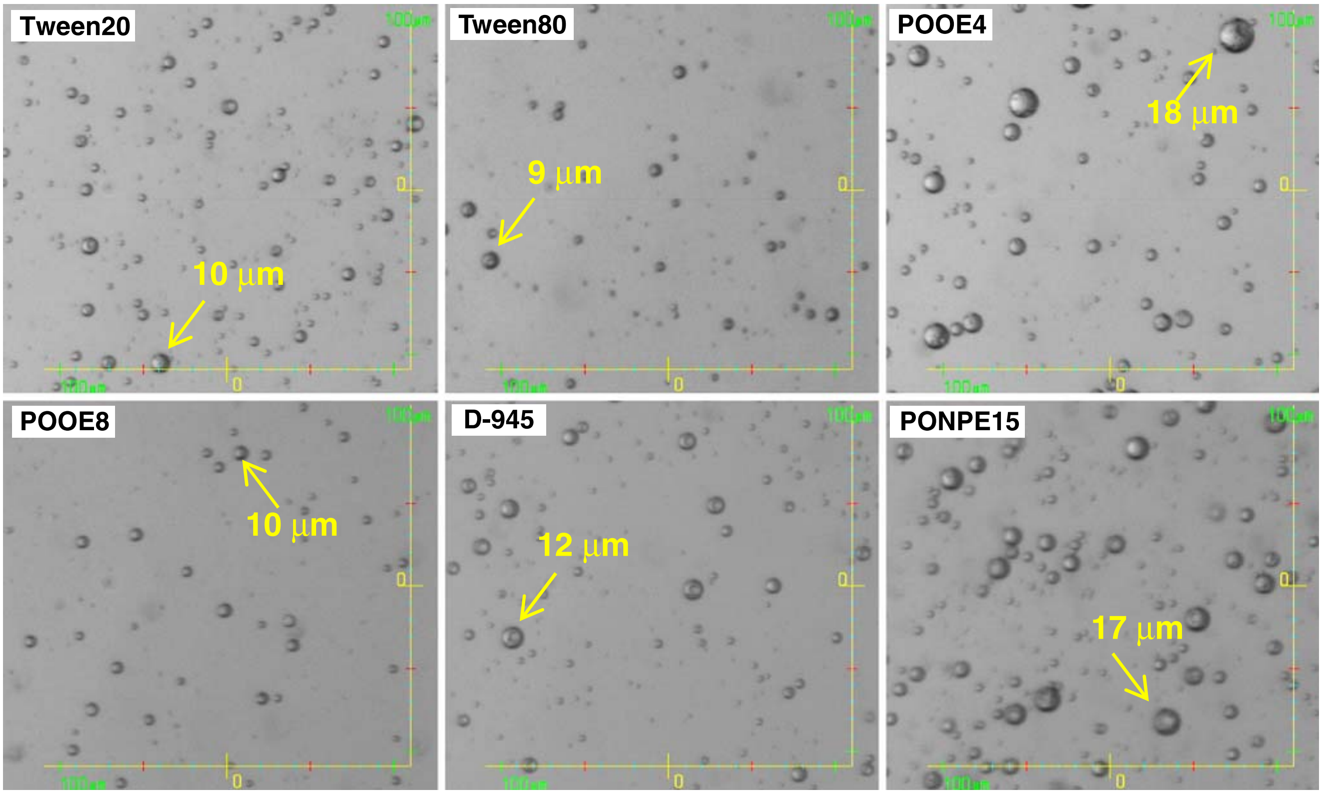

Fig. 2 Photographs of the oil microdroplets spreading on the water surface when a small amount of O/W emulsion was put on water. The maximum diameter of the oil microdroplets observed is shown in each photograph

was investigated; the diameter was measured as a function of time using the digital camera.

Results and discussion

Stability of O/W emulsions prepared using various sorts of surfactants

The O/W emulsion stable for a few hours is indispensable for preparing porous hydrogels by the emulsion templating method. The photographs in Fig. 1 show the stability of the O/W emulsions consisting of NIPA aqueous solution, oleyl alcohol, and 15 different surfactants. Tween20, Tween80, POOE4, POOE8, D-945, and PONPE15 form the stable O/W emulsions after 4h; the surfactants except PONPE15 formed the stable O/W emulsions after 100h. Although POOE4 and POOE8 keep possession of an extremely small amount of phase-separated layer, the majority of their emulsions are stable. The surfactants having the larger values of the molar mass and HLB tend to form the stable O/W emulsions. In general, the surfactants more soluble in water and having higher HLB tend to form O/W emulsions and the surfactants more soluble in oil and having lower HLB tend to form water-in-oil (W/O) emulsions. In addition, the similarity in the chemical structure between surfactant and oil is required for the formation of the stable emulsion; the stability of the emulsion of PONPE10 and PONPE20 having benzene ring in their structure is relatively low in spite of their large values of the molar mass and HLB (it is still unclear why the emulsion using PONPE15 is relatively stable). Although the data are omitted, PONPE7.5 made the emulsion constituting of NIPA aqueous solution and toluene as an oil phase stable and the porous NIPA hydrogel was successfully prepared. Consideration of these points has led us to choose successfully the surfactants to form stable O/W emulsions.

The effect of surfactant on the oil microdroplet size in O/W emulsions was investigated. The six sorts of surfactants forming stable emulsions mentioned above were tested; the photographs of the oil microdroplets are shown in Fig. 2. Our attention is focused on the maximum diameter of the oil microdroplets since the microdroplet diameters are distributed. The maximum diameter is about 18μm for POOE4 and PONPE15, and about 10μm for the

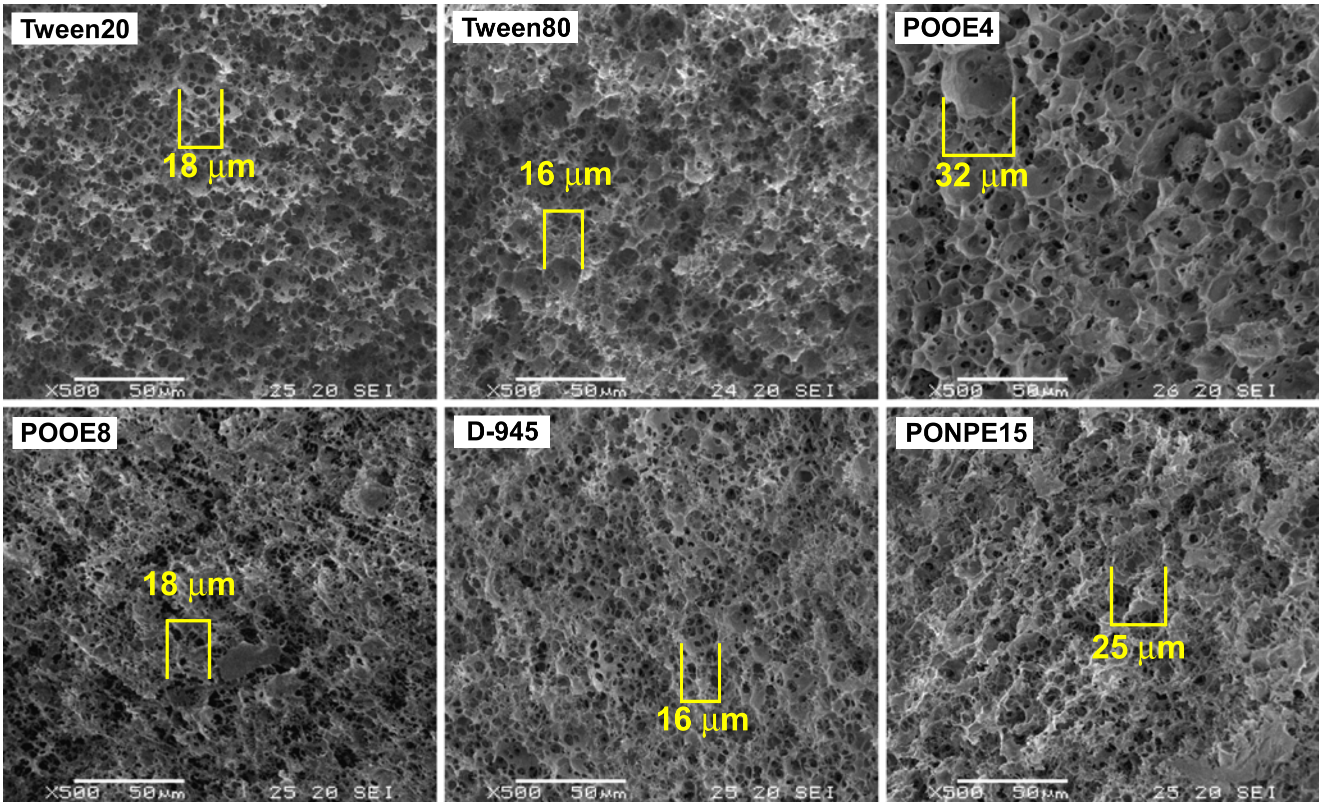

Fig. 3 SEM micrographs of the freeze-dried specimens of the porous NIPA hydrogels. The gels were prepared using six sorts of surfactants under the conditions of 8 cm^3 water containing monomers and 4 cm^3 oleyl alcohol containing a surfactant (0.1 g/cm^3-oil) The maximum diameter of spherical pore observed is shown in each photograph

others. PONPE15 has a benzene ring in its structure and the emulsion is phase-separated after 100h as already mentioned above. POOE4 has the smallest values of molar mass and HLB among the surfactants tested. Therefore, the stability of the emulsions of POOE4 and PONPE15 is somewhat lower compared to the others. The surfactants forming more stable O/W emulsion generate smaller oil microdroplets. The stability of O/W emulsions and the diameter of dispersed oil microdroplets can be interpreted in terms of the interfacial energy and interfacial tension which are the subject of our future study.

Internal structure of porous NIPA hydrogels prepared using various sorts of surfactants

The porous NIPA hydrogels were successfully prepared by the emulsion templating method using six sorts of surfactants forming the stable emulsions under the condition of the same oil volume fraction and surfactant concentration as mentioned in Figs. 1 and 2. The size consistency of the pore in the porous NIPA hydrogels and the oil microdroplets shown in Fig. 2 was examined. The SEM micrographs of the porous NIPA hydrogels are shown in Fig. 3. The porous structure is clearly observed and the pore diameters are also distributed. POOE4 and PONPE15 possess the larger pores in their hydrogels than the others, as well as possessing the larger oil microdroplets in their emulsions. Therefore the pore size in the porous hydrogels corresponds to the oil microdroplet size in the O/W emulsion. The pore diameter is somewhat larger than the oil microdroplet diameter shown in Fig. 2 in each surfactant because the swollen hydrogel at 10°C (specimen) has a larger size than that of the as-synthesized gel (see Fig. 4) and the polymer aggregates caused by freeze-drying expand pore. We can control the pore size in the porous hydrogel to some extent by choosing the surfactants.

Swelling properties of porous NIPA hydrogels prepared using various sorts of surfactants

Figure 4 shows the swelling properties of the cylinder-shaped porous NIPA hydrogels prepared using six different surfactants: (1) swelling diameter as a function of temperature, (2) shrinking rate for the temperature jump from 10°C to 50°C, and (3) swelling rate for the temperature drop from 50°C to 10°C. In Fig. 4a, every porous hydrogel shows similar in thermosensitive swelling pattern to the non-porous hydrogel [8]. The diameters for POOE4, POOE8, and PONPE15 are somewhat smaller than those for the others at 50°C. This behavior may be related to that the stability of the emulsions of POOE4, POOE8, and PONPE15 is somewhat lower as mentioned above, but details are still unclear.

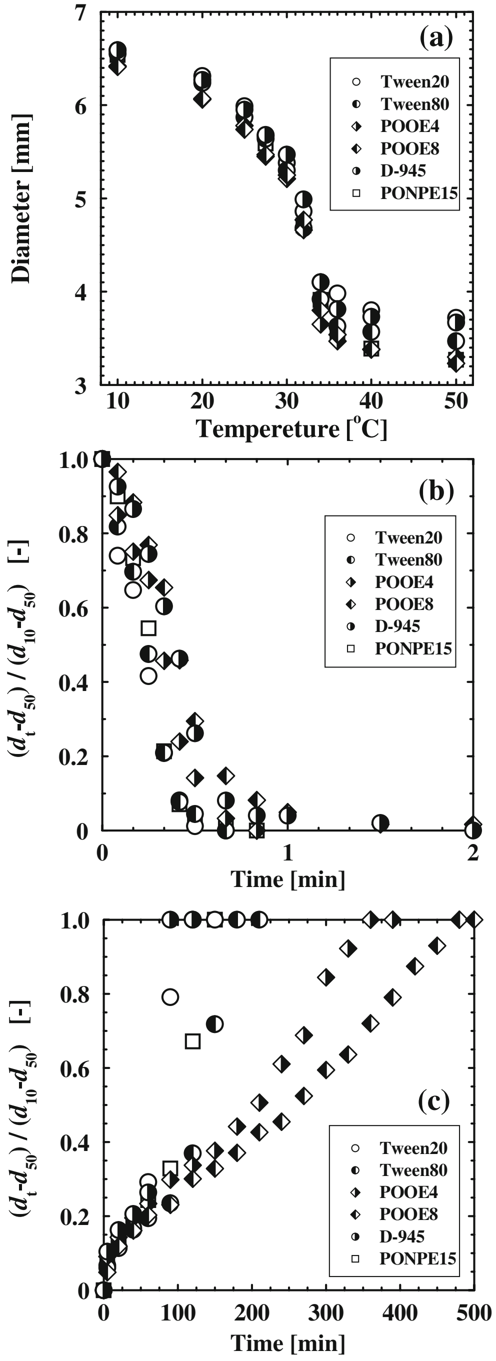

Fig. 4 Swelling properties of the cylinder-shaped porous NIPA hydrogels in water: **a** swelling diameter as a function of temperature, **b** shrinking rate for the temperature jump from 10 °C to 50 °C, and **c** swelling rate for the temperature drop from 50 °C to 10 °C. The gels were prepared under the same condition as mentioned in the caption to Fig. 3

In Fig. 4, the swelling/shrinking rate is represented as time course of the normalized hydrogel diameter: $(d_t - d_{50})/(d_{10} - d_{50})$, where d_t is the hydrogel diameter at time $t = t$ and d_{10} and d_{50} are the equilibrium diameters at 10°C and

Table 2 The maximum diameter of the oil microdroplets distributed in the O/W emulsions consisting of water containing NIPA (1,000 mol/m^3-water) and oleyl alcohol containing Tween20 under a wide range of the volume fraction of oil phase in emulsion, ϕ_{oil}, and the weight fraction of surfactant in oil phase, X

X	0.01	0.05	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
ϕ_{oil}											
0.05	95	29	25	13	23	20	11	10	11	<1	<1
0.1	54	32	27	35	23	21	11	8	9	<1	<1
0.2	33	26	23	27	16	16	7	6	8	<1	<1
0.3	93	26	16	12	15	12	7	6	6	—	—
0.4	73	22	16	15	13	11	4	3	—	—	—
0.5	50	22	14	7	5	4	—	—	—	—	—
0.6	58	17	7	6	—	—	—	—	—	—	—
0.7	42	7	—	—	—	—	—	—	—	—	—
0.8	21	—	—	—	—	—	—	—	—	—	—

— Highly viscous emulsion

50°C, respectively. In Fig. 4b, the swelling equilibrium is attained within about 1min independent of the surfactants; it should be mentioned that the swelling equilibrium of the non-porous hydrogel was attained in approximately a day [8]. The shrinking rates of the porous hydrogels are quite high. In Fig. 4c, the swelling rate of the porous hydrogels is higher than that of the non-porous hydrogel [8], although the swelling rate enhancement is less than that of the shrinking rate. The presence of the pore in the shrunken hydrogel must contribute to faster swelling. In fact, the order of the swelling rate coincides with the order of the swelling diameter at 50°C. A definite relationship between the swelling properties and the porous structure depending on the surfactants, however, is as-yet-unknown.

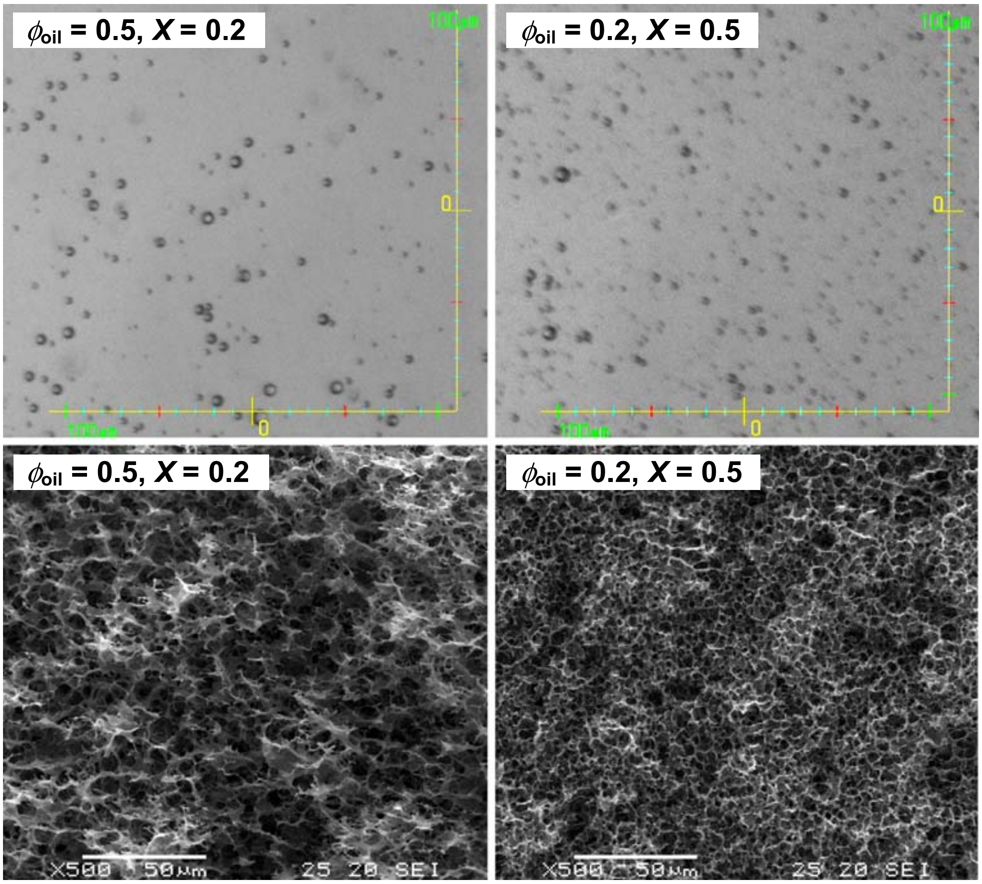

Fig. 5 Photographs of the oil microdroplets in O/W emulsion and SEM micrographs of the freeze-dried specimens of the porous NIPA hydrogels prepared under the conditions of ϕ_{oil}=0.5 and X=0.2, and ϕ_{oil}=0.2 and X=0.5

Effect of oil volume fraction and surfactant concentration on the size of oil microdroplet in O/W emulsions and pore in porous NIPA hydrogels

Preparation of the porous NIPA hydrogel for which the pore size and the porosity are adequately adjusted has been tried by varying the volume fraction of oil phase in emulsion, ϕ_{oil}, and the weight fraction of surfactant in oil phase, X. First, the oil microdroplets was observed for the O/W emulsions consisting of water containing NIPA (1,000mol/m^3 water) and oleyl alcohol containing Tween20, a representative surfactant, under a wide range of ϕ_{oil} and X; the maximum diameters observed are listed in Table 2. In the cases of higher ϕ_{oil} and/or X, the emulsions were unstable due to the high viscosity; the gel can not be synthesized in the highly viscous emulsions. The oil microdroplet diameters decrease with an increase in ϕ_{oil} and/or X. In the case of X over 0.8, the oil microdroplets were not observed with the stereomicroscope used in this study; for instance, the average diameter of oil microdroplets for $\phi_{\mathrm{oil}} = 0.1$ and $X = 0.9$ is 4.3nm, which was measured by a dynamic light scattering method. The porous NIPA hydrogel having pores in the range from several nanometers to several tens of micrometers can be prepared by the emulsion templating method. A diameter of oil microdroplets different from those shown in Table 2 can be obtained by changing the agitation intensity; however, the dependence of diameter on ϕ_{oil} and X can be the same as that shown in Table 2.

The feasibility of the preparation of the porous hydrogel having the pore size corresponding to the oil microdroplet size was confirmed through the preparation of gels under various conditions of ϕ_{oil} and X. The two cases deserve to mention; $\phi_{\mathrm{oil}} = 0.5$ and $X = 0.2$, and $\phi_{\mathrm{oil}} = 0.2$ and $X = 0.5$. Figure 5 shows the photographs of the oil microdroplets in the O/W emulsions and the SEM micrographs of the porous NIPA hydrogels. The size and distribution of the oil microdroplets is quite similar in both cases (each maximum diameter is 7 μm as shown in Table 2). The pore diameter for ϕ_{oil}=0.5 looks somewhat larger than that for ϕ_{oil}=0.2, where the specimens were prepared by freeze-drying the swollen hydrogels at 10 °C; the both porous hydrogels in the as-synthesized state must have the same pore size corresponding to the oil microdroplet size. The oil droplets (especially for ϕ_{oil}=0.5) may coalesce, but the degree of coalescence can be low considering the fact that Tween20 formed the stable emulsion for several days as mentioned above. Porous hydrogels having the same diameter and the different porosity can be successfully prepared. The information shown in Table 2 serves as the key to prepare porous hydrogels having the pore size and porosity which changes freely with the variation of ϕ_{oil} and X.

Conclusions

In the process of the preparation of porous NIPA hydrogels by the emulsion templating method, the effect of surfactants on the stability of pre-gel O/W emulsions and the porous structure of resulting hydrogels were investigated. The six sorts of surfactants form the stable emulsions among 15 different polyoxyethylene-type surfactants tested. The surfactants having the larger values of the molar mass and HLB form the stable emulsions, where the similarity in the chemical structure between surfactant and oil is required. The porous NIPA hydrogels prepared using the surfactants forming the stable emulsion were characterized; the pore size corresponds to the oil microdroplet size in the emulsion and the swelling/shrinking rate of the porous hydrogels is quite high compared to the conventional non-porous hydrogel. The O/W emulsions and the porous NIPA hydrogels prepared under a wide range of ϕ_{oil} and X were characterized; the information obtained is useful for the preparation of the porous NIPA hydrogels for which both the pore diameter and the porosity are adjusted for their applications.

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References

1. Hirokawa Y, Tanaka T (1984) J Chem Phys 81:6379
2. Yoshida R, Sakai K, Okano T, Sakurai Y (1993) Adv Drug Delivery Rev 11:85
3. Ito T, Yamaguchi T (2006) Langmuir 22:3945
4. Yoshida R (2005) Curr Org Chem 9:1617
5. Suzuki H, Kumagai A, Ogawa K, Kokufuta E (2004) Biomacromolecules 5:486
6. Kikuchi A, Okano T (2002) Prog Polym Sci 27:1165
7. Tokuyama H, Iwama T (2007) Langmuir 23:13104
8. Tokuyama H, Kanehara A (2007) Langmuir 23:11246
9. Kaneko Y, Yoshida R, Sakai K, Sakurai Y, Okano T (1995) J Membr Sci 101:13
10. Tokuyama H, Ishihara N, Sakohara S (2007) Eur Polym J 43:4975
11. Tokuyama H, Kato Y (2008) Colloids Surf, B 67:92