Sonoresponsive Volume Phase-transition Behavior of Crosslinked Poly(*N*-isopropylacrylamide-*co*-acrylic acid) Microgel

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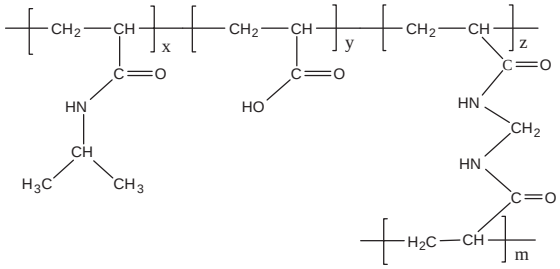
We presented that ultrasound, as a novel environmentally stimuli technique, was used controlling the volume phase-transition temperature of high crosslinked poly(*N*-isopropylacrylamide-*co*-acrylic acid) microgels.

Environmentally sensitive microgels have attracted much attention in recent years. To control their swelling/deswelling behavior is of technical interest for various applications in the fields of engineering and biotechnology. Poly(*N*-isopropylacrylamide) (PNIPAM) is a well-studied polymer for the gels.[1] There are many reports on modifying the volume phase-transition temperature (VPTT) of microgels by incorporation of functional monomers.[2] In the present sudy, we focused on the ultrasound (US) as the external stimuli on the swelling/deswelling behavior of microgel. US technique has been using widely to mix or disperse the microgel particles.[3] In very recent years, it was used in the preparation of poly(*N*-isopropylacrylamide-*co*-acrylic acid) (PNIPAM/AAc) gels because of the mass-transfer acceleration and cavitation effects caused by US. For PNIPAM/AAc microgels prepared by employing sonication,[4] it was found that the microgel showed a significantly different swelling/deswelling behavior from that of the PNIPAM microgel. Two-step volume phase transitions were uniquely observed owing to the hydrophobic attraction of NIPAM and the hydrogen-bonding interaction between NIPAM and AAc. In addition, PNIPAM/AAc hydrogels synthesized under US showed thermoresponsive swelling behavior with a large hysteresis over a wide range of temperatures around its phase-transition temperature.[5] Although US technique plays an important role in the preparation of microgels, so far, there is no report on the US control on the swelling/deswelling behavior of microgels. Because of application in drug delivery system using microgels, to advance US technique to the environmental control of microgels shows huge advantages in several fields. Here, we describe as first report that US alters volume phase transition of high crosslinked PNIPAM/AAc microgel (Scheme 1). The microgel having 15 wt % acrylic acid (AAc) and 15 wt % *N*,*N*′-methylenebisacrylamide (MBAAm) crosslinker to the amount of NIPAM was synthesized by the surfactant-free emulsion polymerization (Supporting Information). The pH of the microgel was fixed at pH 5.0 by adjusting with 0.01 M HCl/NaOH. Then, the microgel was divided into two groups. One group played as control group without further treatment except incubation in a 20 °C water bath in the absence of US (AU microgel). Another group was irradiated by 100 kHz US (300 W) for 60 min. During the US irradiation, the bulk water bath was kept at 20 °C. After the US irradiation, the swelling/deswelling behavior of the microgel (US microgel) was measured immediately. Then, after subsequent incubation in 20 °C water bath for 6 h (US-6h microgel) and 12 h (US-12h microgel), the behavior was also measured similarly.



Scheme 1. Chemical structure of PNIPAM/AAc.

The US influence on the swelling/deswelling behavior of microgel was determined by measuring the particle size as a function of temperature. Figure 1 shows the hydrodynamic diameter of the microgel particles at different temperature. For PNIPAM microgel containing 15 wt % MBAAm but without AAc (Figure 1b), the VPTT was around 35 °C. In addition, there was no difference in the swelling behavior between the PNIPAM microgel with and without US treatment.

Interestingly, after incorporation of AAc segments, PNIPAM/AAc microgel displayed two-step volume phase transition (Figure 1a). As far as AU microgel was concerned, the first volume phase-transition temperature was around 23 °C and the second transition temperature was at 33 °C. At pH 5.0, the AAc segments were not in complete dissociation. The hydrogen bonding between carboxylate group of AAc and amide group of NIPAM induced the initial shrinking of microgel. The second-step shrinking was mainly caused by the hydrophobic interactions of PNIPAM at high temperature.

As particularly noted, the volume phase-transition temperature of the US microgel elevated to higher temperature significantly. The first-step shrinking temperature was 27 °C which was about 4 °C higher than that of the AU microgel. Also, the second step was raised to around 35 °C. This hysteresis was mainly because that the US treatment could restrain the formation of hydrogen bonding. As shown in IR spectra of AU and US microgel (Figure 2), the change in O–H absorption near 3000 cm^{-1} was a measure of the strength of the hydrogen bonding.[6] The intensity and the width of the broad O–H stretch of US microgel decreased comparing to the AU microgel. This result illustrated that hydrogen-bonding interaction in US microgel was much lower than that of AU microgel. As a result, the first volume phase-transition temperature was on the hysteresis. The restraint in the formation of hydrogen bonding delayed the collapse of the microgel as the temperature increased, and the second-step shrinking temperature was shifted to higher temperature side.

Although US irradiation can restrain the formation of hydrogen bonding, this effect is temporary. The data of Figure 1a presented that hydrogen bonding formed again after the US irradi-

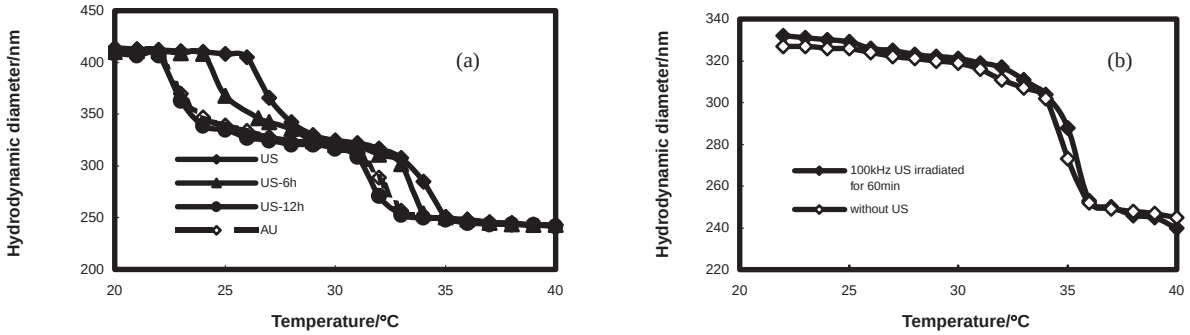


Figure 1. Influence of US on the volume phase-transition behavior of (a) PNIPAM/AAc microgels [(◆) US microgel, (▲) US-6h microgel, (●) US-12h microgel, and (◇) AU microgel] and (b) PNIPAM microgels [(◆) microgel with 100 kHz US irradiation for 60 min and (◇) microgel without US irradiation] at pH 5.0. The concentration of the microgel suspension was 0.053 mg/mL.

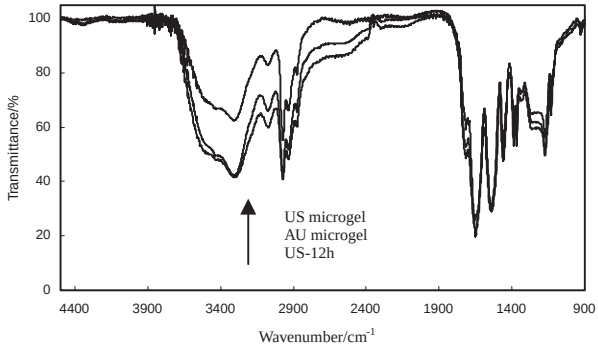


Figure 2. IR spectra of PNIPAM/AAc microgels without and with US irradiation at 25 °C.

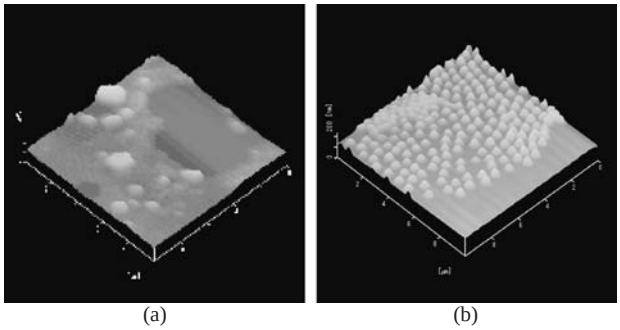


Figure 3. AFM images of the PNIPAM/AAc microgels at pH 5 and 25 °C (a) without US and (b) with 100 kHz US irradiation for 60 min.

ation. The VPTT shifted to the lower temperature side gradually with time after the US irradiation. Interestingly, the hydrodynamic diameter–temperature curve of the US-12h microgel was almost the same as that of AU microgel. Namely, the volume phase-transition behavior was back to the original transition within 12 h. The IR spectrum of the US-12h microgel (Figure 2) also shows strong and broadened O–H stretch at 3300–2500 cm^{-1}. The spectrum shape was almost the same as that of the AU microgel. This revealed the occurrence of hydrogen bonding after the US treatment.

As shown in Figure 1a, the first-step shrinkage of AU microgel had occurred at 25 °C, whereas there was no volume phase transition happening at this temperature for US microgel. Hence, we observed the difference in the shape of microgel particles at 25 °C by AFM. Herein, we traced the dilute microgel suspension (0.053 mg/mL) before and after the US treatment on glass plate at 25 °C. Then, the glass plate coating with the suspension was quickly frozen-dried. Figure 3 shows the particle morphologies for (a) AU microgel and (b) US microgel. It is clear that the microgel without US treatment had a strong tendency to aggregate due to the interaction of the inter-hydrogen bonding between the particles. To contrast, after US irradiation the interhydrogen bonding between the microgel particles was broken, and the microgel particles were dispersed separately.

In conclusion, we firstly explored sonoresponsive swelling/deswelling behavior of high crosslinked PNIPAM/AAc microgel. Our results suggested that hydrophobic interaction and hydrogen bonding dominated the VPTT of microgel at pH 5.0. The volume phase transition of the microgel could be modulated by US technique through the controlling the formation of the hydrogen bonding. This unique technique for alternation of swelling/deswelling behavior of microgel can undoubtedly extend US as a novel stimulation in the drug delivery system, biomaterials separation, and so on.

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