pH and Temperature-sensitive Behaviors of Poly(4-vinyl pyridine-co-*N*-isopropyl acrylamide) Microgels

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ABSTRACT: Poly(4VP-co-NIPAM) microgels were prepared from 4-vinyl pyridine (4VP) and *N*-isopropyl acrylamide (NIPAM) with methylene-bis-acrylamide (MBAm) as a cross-linking agent using partially quarternized poly(4-vinyl pyridine) as emulsifier, which is a special emulsion polymerization method.
   The morphology and hydrodynamic diameter of the microgel particles were characterized by TEM and photon correlation spectroscopy (PCS). The dependence of pH and temperature of the copolymer microgel particles were investigated and the influence of the KCl concentration in the microgel dispersion was observed.
   Hydrodynamic diameters of the microgel particles were drastically increased below pH 5 and those of the microgel particles were depended on temperature and KCl concentration in the microgel dispersion. The dependence of pH and temperature on the microgel particles were affected by molar ratio of 4VP/NIPAM. The cross-linked copolymer microgels composed of 4VP/NIPAM ratio of 1/9, exhibited broad shrinking transition. The swelling behavior for the microgel dispersion was much sensitive to the KCl concentration in the microgel dispersion at elevated temperature.
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Polymer hydrogels and microgels have a wide range of potential application in biotechnology and biomedical field. Therefore, various polymer hydrogels and microgels have been characterized where the volume change can be induced by pH, temperature, ionic strength, and electric field of the polymer matrix.[1–5]

In recent years, colloidal microgel particles have attracted a lot of attention because of their rather fast kinetic response to external stimuli, which is of advantage compared to macroscopic gel particles. Thermo-sensitive hydrogels and microgels can be prepared from *N*-isopropyl acrylamide that has lower critical solution temperature (LCST) at 32 °C.[6–9] It was found that the phase transition occurs at LCST being accompanied with the coil-globule transition of single polymer chain of PNIPAM molecule in water.[10] The microgels based on homopolymer poly(*N*-isopropyl acrylamide, PNIPAM) are limited in their applications due to thermally induced conformational change taking place at a fixed temperature. pH or temperature-sensitive copolymer microgels with other cationic charge such as poly(2-vinyl pyridine-co-styrene) and poly(*N*-isopropyl acrylamide-co-amino ethyl methacrylate) have been reported.[11,12]

A number of studies has been carried out on the temperature-sensitive microgel particles based on PNIPAM, which is cross-linked with methylene-bis-acrylamide containing acrylic acid comonomer.[13–15]

Otherwise, pH sensitive copolymer microgels based on poly(methyl methacrylate), polystyrene, containing poly(methacrylic acid), poly(2-vinyl pyridine) have also been studied.[16–18] However, pH and thermo-sensitive microgels based on poly(4-vinyl pyridine, P4VP) have not been synthesized and studied.

pH sensitive microgels could be prepared by co-polymerization of monomer containing acidic and basic groups. For example, 4-vinyl pyridine is one of the monomer that process desired chemical properties such as acidity, basicity, hydrophilicity, and hydrophobicity. P4VP also can be easily cross-linked both intra and inter microgels. Therefore, the preparation method that is often used for styrene or *N*-isopropyl acrylamide based microgels cannot be applied to the case of 4-vinyl pyridine. This is probably due to the fact that the micelle nucleus cannot be formed as the polymerization progressed. Fukutomi and co-workers[19] have been used the partially quarternized P4VP as an emulsifier for the preparation of cross-linked P4VP microgels.

In this study, we carried out the combination of both properties by synthesizing pH and temperature-sensitive microgels. Synthesis and colloidal properties of poly(4VP-co-NIPAM) microgels were investigated. Especially, the hydrodynamic particle size, and the influence of KCl concentration as function of pH and temperature were also carried out.

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Table I. Preparation of the Poly(4VP-co-NIPAM) Microgels

Sample code	4VP/NIPAM (mole ratio)	(wt ratio)	MBAm (wt %)	P4VP emulsifier (unit mol %)	Particle size (nm) $R_h{}^a$	$D_h{}^b$	Swelling degree[c] (%)
VN-1	9/1	4.47/0.53			194	492.6	154
VN-2	7/3	3.42/1.58			—	430.0	—
VN-3	5/5	2.40/2.60	7.2	5.0	171	635.9	265
VN-4	3/7	1.42/3.58			—	514.2	—
VN-5	1/9	0.47/4.53			157	341.5	118
VN-6	1/9	0.47/4.53	5.0	5.0	207	498.4	141
VN-7	1/9	0.47/4.53	2.5		214	527.0	146

[a]Measured on transmission electron microscopy [b]Measured by photon correlation spectroscopy at pH 7 and 20 °C [c]Calculated from equation $(D_h–R_h)/R_h \times 100$.

EXPERIMENTAL

Materials

4-vinyl pyridine (4VP, Aldrich 99%) and chloromethyl styrene (CMS, Aldrich 99%) were distilled under reduced pressure, and stored at -20 °C. N-isopropyl acrylamide (NIPAM, Kohjin) was recrystallized from 60:40 (v/v) mixture of hexane and toluene. Methylene-bis-acrylamide (MBAm, Aldrich) as a cross-linking agent was recrystallized from ethanol. 1,4-Diiodomethane was used as received.

2,2′-Azobis(2-methylpropane nitrile) (AIBN, Wako 99%) and 2,2′-azobis(2-amidino propane) dihydrochloride (V-50, Wako 99%) were used as initiators. Partially quarternized P4VP was used as an emulsifier. Buffer solutions were prepared from mixture of KH_2PO_4 (Aldrich, 99.8%), K_2HPO_4 (Aldrich, 99.8%) and distilled deionized Milli-Q water.

Preparation of Polymer Emulsifier

Partially guarternized P4VP emulsifier prepared using synthetic method, which was described by Fukitomi and co-workers[11] elsewhere as follows: P4VP was synthesized from radical polymerization of 4VP in methanol using as an AIBN initiator. After 10 g of P4VP was dissolved in 50 mL methanol, 3.5 mL of CMS (26.5 mol % for 4VP units) was added while stirring for 24 h at room temperature. Then 3 mL (50.8 mol % for 4VP units) of iodometane was added into the reaction mixture and stirred at room temperature for 24 h. The solution was diluted with 200 mL of distilled water and stored in a refrigerator at 4 °C.

Synthesis of Copolymer Microgels

Poly(4VP-co-NIPAM) microgel particles were prepared using partially quarternized P4VP emulsifier by emulsion polymerization at 70 °C for 8 h. In this polymerization, molar ratio of 4VP/NIPAM was varied to 10/0, 9/1, 7/3, 5/5, 3/7 and 1/9 with 7.2 wt %

MBAm, and also the copolymer microgels composed of 4VP/NIPAM ratio of 1/9 with 2.5 and 5.0 wt % MBAm were prepared, respectively. The detail feed compositions in polymerization are listed in Table I. Emulsion polymerization was carried out in a 500 mL three-necked, round bottomed flask equipped with a nitrogen inlet, condenser and teflon paddle stirrer.

Different molar ratio of 4VP/NIPAM and given amount of MBAm were dispersed into 200 mL distilled water. 5 min later, 5 unit mol % P4VP emulsifier to 4VP monomer (emulsifier/4VP unit) and V-50 as an initiator were added. The reaction mixture was deoxygenated by stirring at 300 rpm under a nitrogen flow for 30 min, and then the reaction mixture was stirred at 70 °C for 6 h. All microgel particles were cleaned by repetitive centrifugation and redispersion in Milli-Q water several times.

Characterization

The morphology of the copolymer microgels were observed using transmission electron microscope (TEM, Joel JEM-100CX). Small amount of the copolymer microgel dispersion was infinitely diluted with distilled water. The diluted samples were supported on carbon-coated copper grids.

Hydrodynamic diameters of the microgel particles were determined by photo correlation spectroscopy (PCS) using a Zeta Plus dynamic light scattering apparatus (Brookhaven Instruments) fitted with a 635 nm He–Ne laser and detector at 90°. Samples for these experiments were prepared in the buffer solution made by mixing appropriate volumes of 1×10^{-3} M KH_2PO_4 and 1×10^3 M K_2HPO_4, and followed by 100-fold volumetric dilution, giving a final microgel concentration of 5×10^3 wt %.

Transmittance measurements for the microgel dispersions at a wavelength of 500 nm were performed as a function of temperature in the different KCl concentration using UV/Vis. spectrophotometer (Perkin-Elmer Lambda 5).
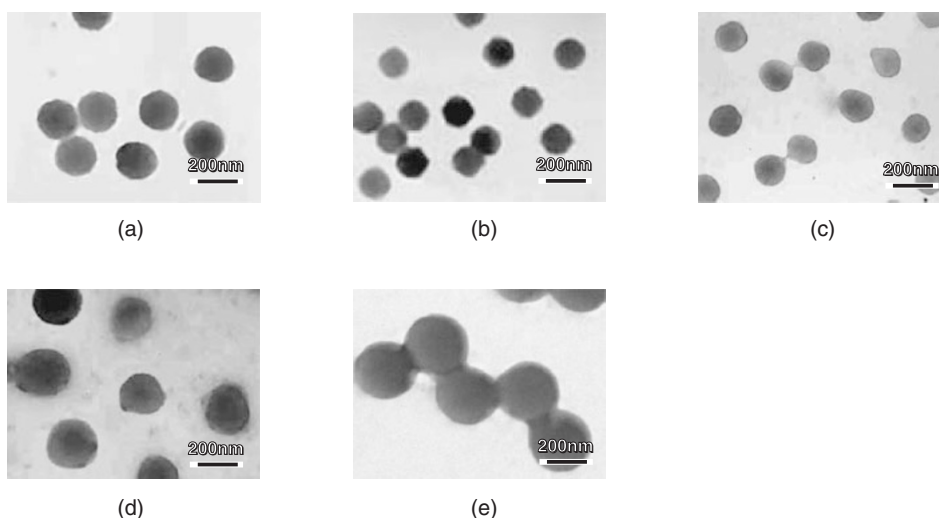
Figure 1. Transmission electron micrographs of the poly(4VP-co-NIPAM) microgels; Molar ratio of 4VP/NIPAM: (a) 9/1 (7.2 wt % MBAm) (b) 5/5 (7.2 wt % MBAm) (c) 1/9 (7.2 wt % MBAm) (d) 1/9 (5.0 wt % MBAm) (e) 1/9 (2.5 wt % MBAm).

RESULTS AND DISCUSSION

Poly(4VP-co-NIPAM) microgels were prepared from the different molar ratio of 4VP/NIPAM and different wt % of MBAm as cross-linking agent by a special emulsion polymerization using partially guarternized P4VP emulsifier.

Particle size of the microgels was distributed in the range of 157–214 nm from TEM measurement. TEM micrographs of the microgel particles are shown in Figure 1. The particle size of microgels was increased with increasing molar ratio of 4VP/NIPAM and the change in particle morphology was irregular spheres with different molar ratio of 4VP/NIPAM. This could be caused by the phase separation of incompatible domains with the microgel particles. The particle size of the microgels composed of 4VP/NIPAM ratio of 1/9 was decreased as expected for more highly cross-linked microgel particles.

The hydrodynamic diameters for the microgel particles as function of pH at 20 °C are shown in Figures 2a and 2b. In these measurement 1×10^{-3} M phosphate buffer was used and hydrodynamic diameter of the microgel particles was represented the mean of measuring value of each samples. The hydrodynamic diameter of the microgel particles was drastically increased below pH 5 and was nearly not changed in the range of pH 5–7. Under alkaline conditions, however, the microgel particles were flocculated.

The pKa_1 and pKa_2 of P4VP is around 3 and 5, respectively. Under acidic conditions the pyridine groups get protonated and the increased charge density on the microgel particles should enhance degree of swelling. It was indicated that pH dependent on swelling behavior for the microgel particles was increased with introduction of cationic charged P4VP into the network.

The hydrodynamic diameters as a function of pH for the microgel particles composed of 4VP/NIPAM ratio of 1/9 with different cross-linking degree at 20 °C are shown in Figure 2c. The hydrodynamic diameter for the microgel particles were decreased with increasing the cross-linking degree and the pH dependence of the microgel particles with 7.2 wt % of MBSA was relatively lower.

The swelling behavior of the microgel particles composed of different molar ratio of 4VP/NIPAM with 7.2 wt % MBAm as function of temperature at pH 3 and pH 6 is shown in Figures 3a and 3b. Hydrodynamic diameter of the microgel particles composed of 4VP/NIPAM ratio of 3/7, 1/9 was slightly decreased up to 30 and 35 °C, respectively. However, that of the microgel particles was sharply increased up to 50 °C, indicating that aggregation of the colloidal particles occurred at elevated temperature. Whereas, hydrodynamic diameter of the microgel particles composed of 4VP/NIPAM ratio of 5/5 was continuously increased with increasing temperature.

At pH 3, the shrinking transition and LCSTs by PNIPAM of the microgel particles composed of 4VP/NIPAM were not represented. The increase in the molar ratio of 4VP/NIPAM allows protonation of pyridine groups, which seems to prefer swelling at lower pH range. At pH 6 hydrodynamic diameter of the microgel particles composed of 4VP/NIPAM ratio of 1/9 was decreased with increasing temperature and that of the microgel particles composed of 4VP/NIPAM ratio of 3/7 was not nearly changed up to 35 °C but continuously increased above 35 °C. On the other hand, the microgel particles composed of 4VP/NIPAM ratio of 5/5 was continuously
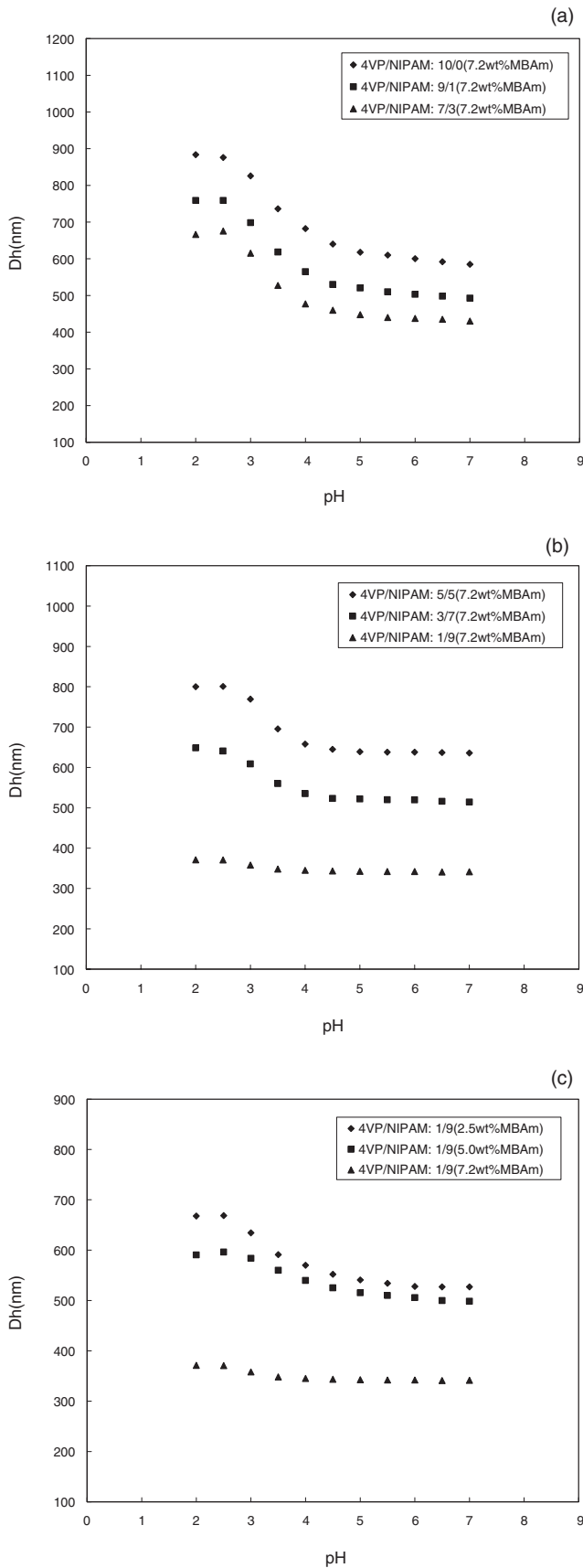
(a)

(b)

(c)

Figure 2. Hydrodynamic diameter for the poly(4VP-co-NIPAM) microgels as a function of pH at 20 °C.
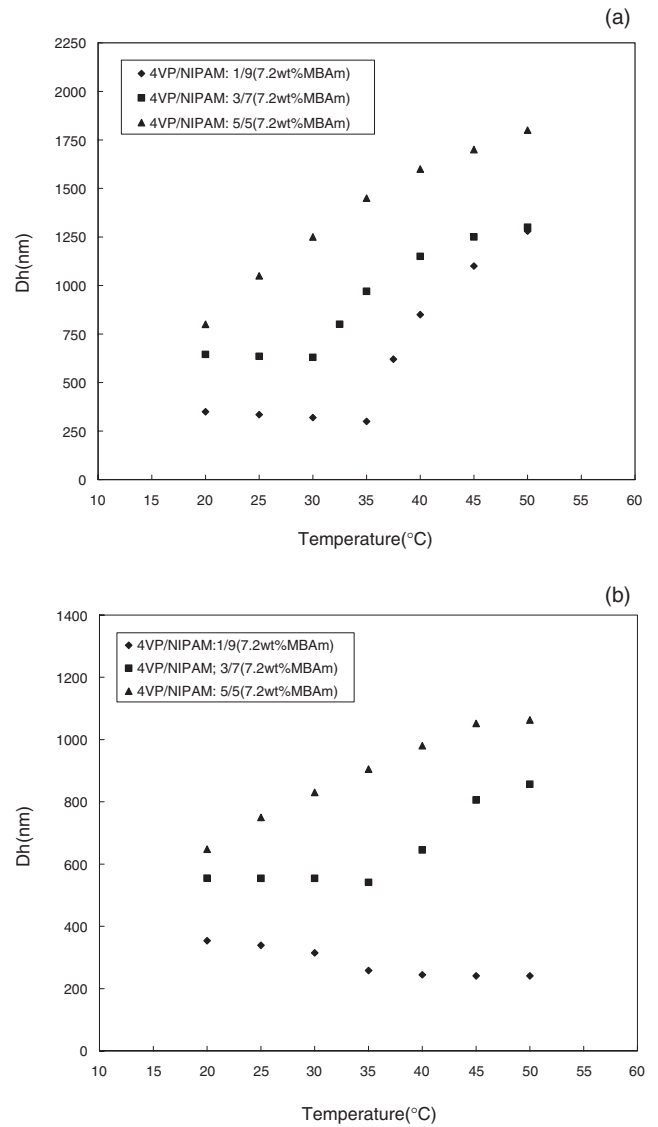

(a)

(b)

Figure 3. Hydrodynamic diameter for the poly(4VP-co-NIPAM) microgels as a function of temperature at pH 3 (a) and pH 6 (b).

increased with increasing temperature. Under acidic conditions, the size of an aggregates with temperature depends on the content of P4VP present in the microgels. A reasonable explanation for this effect is to break the inter-particle hydrogen bonding between nitrogen on pyridine rings of the P4VP side chain and the amide groups of PNIPAM and to aggregate between swollen microgel particles.

The hydrodynamic diameters as a function of temperature for the microgel particles composed of 4VP/NIPAM ratio of 1/9 with different cross-linking degree at pH 6 are shown in Figure 4. The shrinking transition of the microgel particles observed at slightly higher temperature range as to cross-linked PNIPAM. Hydrodynamic diameter of the microgel particles cross-linked with 2.5 wt % MBAm was sharply increased around the critical temperature indicating
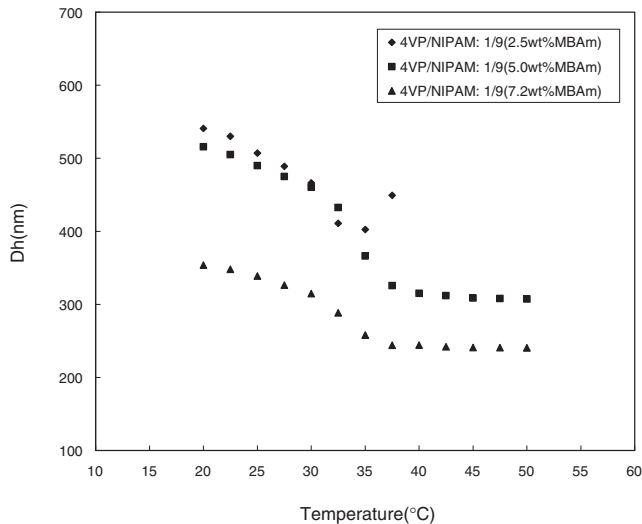
Figure 4. Hydrodynamic diameter as a function of temperature for the copolymer microgels at pH 6.

Figure 5. Hydrodynamic diameter as a function of temperature for the poly(4VP-co-NIPAM) microgel at pH 3 and 9; Molar ratio of 4VP/NIPAM: 1/9 (7.2 wt % MBAm).

aggregation of the microgel particles above 35 °C. While hydrodynamic diameters of the microgel particles cross-linked with 5.0 and 7.2 wt % MBAm were gradually decreased in the temperature range of 20–40 °C. The hydrodynamic diameter of the microgel particles cross-linked with 7.2 wt % MBAm is smaller than that cross-linked with 2.5 and 5.0 wt % MBAm. However, the hydrodynamic diameter of the microgel particles was not nearly changed above 37.5 °C. It is shown that the continuous variation of hydrodynamic diameter is not due to coagulation, since the microgel particles do not flocculate at any temperature range of 20–50 °C.

The temperature dependence on swelling behavior of the microgel particles composed of 4VP/NIPAM ratio of 1/9 with 7.2 wt % MBAm at pH 3 and pH 9 in Figure 5. The hydrodynamic diameters of the microgel particles as function of temperature at pH 3 were markedly larger than that at pH 9. It becomes clear evidence that the size of the microgel particles as well as the shrinking process depend critically on pH. This is in accord with the fact that P4VP is fully dissociated at lower pH.

The transmittance changes for 0.02 wt % microgel dispersion in the different KCl concentration are shown in Figure 6. The transmittance changes in 0.5 M KCl solution for the microgel dispersions composed of 4VP/NIPAM ratio of 1/9 with 7.2 wt % MBAm were decreased with increasing temperature and a broad shrinking transition takes place around the temperature range of 30–40 °C. However, the microgel dispersions composed of 4VP/NIPAM ratio of 5/5, 9/1 were slightly increased with increasing temperature and disappeared the shrinking transition.

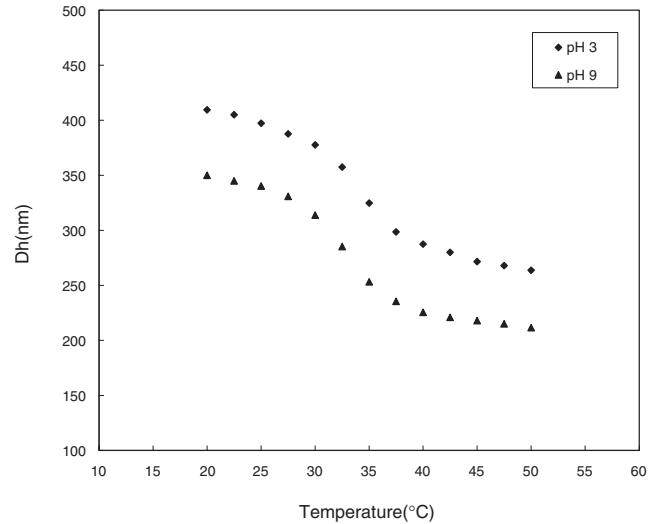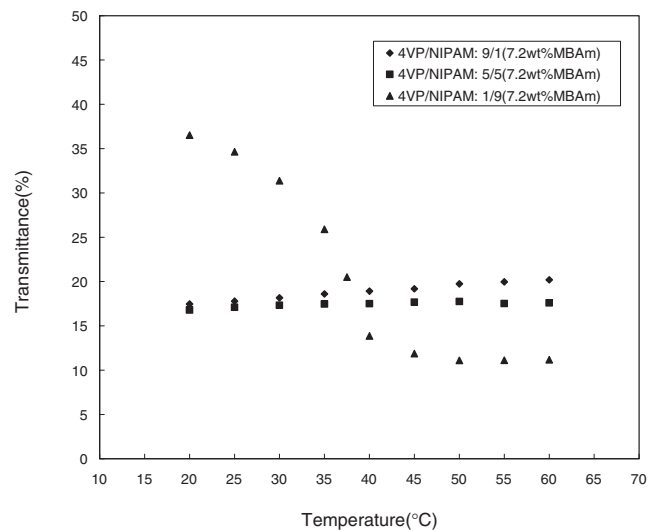In general, an increase in ionic strength diminishes

Figure 6. Transmittance at 550 nm for the poly(4VP-co-NIPAM) microgels as a function of temperature in 0.5 M KCl solution at pH 6; Conc. of microgel: 0.02 wt %.

the repulsive electrostatic forces between the protonated pyridine residues on the particle surface. Moreover, changes of the osmotic pressure and the shielding effect caused by the counter ions under higher ionic strength.[13] Therefore, it is expected that addition of KCl solution would have a strong effect on the swelling behavior of the microgels.

The transmittance changes for the microgel dispersions in the different KCl concentration are shown in Figure 7. The transmittance changes for the microgel dispersion composed of 4VP/NIPAM ratio of 1/9 with 5.0 wt % MBAm in 0.05 and 0.1 M KCl solution decreased in the temperature range of 30–35 °C, 30–40 °C, respectively. The transmittance for the micro-
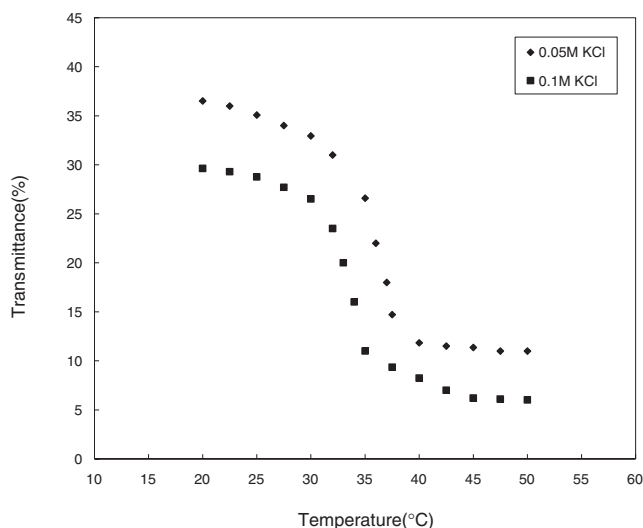
Figure 7. Transmittance at 550 nm for the poly(4VP-co-NIPAM) microgel as a function of temperature in different concentration of KCl solution at pH 6; Molar ratio of 4VP/NIPAM: 1/9 (5.0 wt % MBAm); Conc. of microgel: 0.02 wt %.

gel dispersion in 0.1 M KCl solution was lower than that in 0.05 M KCl solution. It indicates that the transmittance decrease is due to the shrinking of microgel particles. Therefore, the volume transition by the shrinking of microgel particles also shifted to lower temperature. This effect can be attributed to reduce osmotic swelling pressure, because a high KCl concentration in the microgel dispersion has a consequence that the concentration gradient between the KCl concentration in the microgel dispersion inside and outside of the microgel particles.

CONCLUSIONS

Poly(4VP-co-NIPAM) microgels were prepared from 4VP and NIPAM with MBAm as cross-linking agent by a special emulsion polymerization method using partially quarternized P4VP as an emulsifier.

The morphology of the microgel particles exhibited the spherical particles with hydrophilic PNIPAM hydrogel layer and the particle size of the microgels was in the range of 157–214 nm.

The microgel particles were exhibited pH and temperature response behaviors. Their swelling behaviors as a function of pH and temperature were depended on molar ratio of 4VP/NIPAM and wt % of MBAm for total monomers. pH dependence on swelling behavior of the microgel particles was significantly affected

with introduction of cationic charged 4VP, but shrinking transition by the PNIPAM was disappeared and aggregated with increasing temperature. Particularly, the cross-linked microgel particles composed of 4VP/NIPAM ratio of 1/9 exhibited broad shrinking transition around 30–37.5 °C.

The KCl concentration in the microgel dispersion was shown a drastic influence on shrinking of the cross-linked microgel particles composed of 4VP/NIPAM ratio of 1/9. The swelling behavior for the microgel particles was decreased with increasing KCl concentration as temperature increase.

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