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Preparation and characterization of poly (*N*-isopropylacrylamide-*co*-dimethylaminoethyl methacrylate) microgel latexes

Received: 29 March 2001
Accepted: 2 July 2001

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Abstract Monodisperse cationic thermosensitive latex microgels have been prepared by radical-initiated precipitation polymerization of *N*-isopropylacrylamide, methylene bisacrylamide using 2,2'-azobis(2-amidinopropane hydrochloride) as an initiator and dimethylaminoethyl methacrylate (DMAEMA) as a cationic monomer. The final microgel latexes were characterized with respect to water-soluble polymer formation, particle size and size distribution. Adding cationic monomer (DMAEMA) was found to drastically affect the particle size, but not the size distribution as observed both by transmission electron microscopy and quasielastic light scattering (QELS). However, too high a DMAEMA concentration in the

feed composition led to enhanced formation of water-soluble polymer. The volume phase-transition temperature of cleaned microgels examined by QELS (particle size versus temperature) was found to be around 32 °C and was slightly dependent on the concentration of the cationic monomer. The volume phase-transition temperature range becomes broader with increasing cationic monomer concentration. In addition, the pH of the polymerization medium was found to affect the final particle size and amount of water-soluble polymer formed.

Keywords Cationic microgel · Thermosensitivity · *N*-Isopropylacrylamide · Dimethylaminoethyl methacrylate

Introduction

For many years, thermally sensitive microgel particles have attracted much attention from both scientific and technical viewpoints. Such stimuli-responsive microgels based on *N*-isopropylacrylamide (NIPAM) have been prepared and characterized in several studies [1–6]. They have been shown to exhibit many versatile applications [7, 8], especially in the biomedical field, such as diagnostic tests [9], biomolecule separation [10, 11], drug delivery systems [12], etc.

It is well known that the colloidal stability and surface charge density of thermosensitive microgels are dramatically improved when a small amount of ionic monomer is copolymerized with NIPAM by precipitation polymerization. Acrylic acid or methacrylic acid is

frequently used as the ionic monomer [13, 14], which confers negative charge to the microgel particles and pH sensitivity. However, cationic microgels, which are suitable for the adsorption of nucleic acids (DNA, RNA), have been used less [15, 16]. In fact, the first work was reported by Meunier et al. [15] on the preparation and characterization of cationic polyNIPAM microgel latexes based on 2-aminoethyl methacrylate hydrochloride (AEMH) as a functional monomer. They pointed out that the AEM concentration plays a major role in the polymerization kinetics and particle nucleation. Recently, they [16] prepared another cationic polyNIPAM microgel based on vinylbenzylisothiuronium(VBIC) as a cationic monomer, and particular attention was paid to the effect of VBIC concentration on the polymerization process and colloidal properties

of the resulting microgel latexes. It has been found that both AEMH and VBIC act as a transferring agents but the influence of the pH of the reaction medium has not been investigated.

Dimethylaminoethyl methacrylate (DMAEMA) is a water-soluble monomer containing a tertiary amine group which can be protonized in acidic solution. Recently, Hinrids et al. [17], in order to develop nonviral gene delivery, prepared a DMAEMA/NIPAM copolymer for DNA compacting. The preparation of the cationic microgel latexes based on DMAEMA/NIPAM copolymer has not been reported previously.

The objective of this article is to report the preparation of polyNIPAM-based microgels using methylene bisacrylamide (MBA) as a cross-linker, 2,2'-azobis(2-amidinopropane hydrochloride) (V50) as a cationic initiator and DMAEMA as a cationic monomer. Special attention is paid to the influence of DMAEMA concentration in the feed composition and the pH of polymerization medium on the size of the particles, their swelling ratio and water-soluble polymer of the resulting microgel latexes.

Experimental

Materials

NIPAM (Tokyo Kasei Kogyo) and MBA (Fluka) were purified from 60/40 hexane/toluene mixtures and methanol, respectively. V50 (Aldrich) was recrystallized from a 50/50 acetone/water mixture. DMAEMA (Tokyo Kasei Kogyo) was purified by passing it through an alkaline Al_2O_3 column. HCl and NaCl were of reagent grade and were used as received. Water was deionized before use.

Preparation of microgel latexes

The polymerization experiments were carried out in a 250-ml round-bottomed four-necked flask equipped with a poly(tetrafluoroethylene) anchor-shaped stirrer, a condenser, a thermometer and a nitrogen inlet and outlet. The pH of the water solution of NIPAM, MBA and DMAEMA was adjusted to a given value by adding 0.1 N HCl. (In this case DMAEMA was in its hydrochloride salt form, i.e., $DMAEMAH^+Cl^-$. For convenience, the simple

nomenclature of DMAEMA is still used in the following discussion.) The solution was stirred at 200 rpm for 30 min with a nitrogen purge to remove oxygen, the temperature was raised to 70 °C using a oil bath with a thermostat, then, V50 dissolved in water was added, which marked the beginning of the polymerization reaction, and an inert atmosphere was maintained throughout the experiment. One or two minutes later, opalescence appeared. The stirring speed was lowered to about 100 rpm to prevent flocculation and the reaction was continued for up to 4 h.

Purification of microgels

All the microgel particles were cleaned via repetitive centrifugation and redispersion cycles using deionized water. The supernatant collected from the first separation step was analyzed so as to determine the water-soluble polymer content and their molecular weight.

Characterization

The particle size and the size distribution were determined by quasielastic light scattering (QELS) (Malvern Autosizer 4700) or by transmission electron microscopy (TEM) (Hitachi, H-600). The molecular weight of the water-soluble polymer was determined by gel permeation chromatography (Hewlett-Packard, HP1100) [methacrylate column, poly(ethylene oxide) as standards, H_2O flow rate: 0.5 ml/min].

Results and discussion

Influence of the amount of DMAEMA monomer on the particle size and the size distribution

The effect of the amount of DMAEMA on the precipitation polymerization of NIPAM was examined at constant initiator and cross-linker concentrations according to the recipe given in Table 1. As illustrated in Fig. 1, the poly(NIPAM-co-DMAEMA) microgels have a spherical structure and exhibit a very narrow size distribution (i.e., low polydispersity) whatever the amount of the functional monomer, which suggests an extremely short nucleation step involving a self-aggregation mechanism of NIPAM/DMAEMA copolymers originating from water. The trend is reflected through the examination of the particle size evolution versus

Table 1 Composition of monomer solutions and their pH. All of the monomer solutions contain 100 g water and 0.04 g 2,2'-azobis(2-amidinopropane hydrochloride)

Microgel code	<i>N</i> -Isopropylacrylamide (g)	Methylene bisacrylamide (g)	Dimethylaminoethyl methacrylate (mg)	pH
MG400	2.2	0.19	0	4.0
MG405	2.2	0.19	5	4.0
MG410	2.2	0.19	10	4.0
MG420	2.2	0.19	20	4.0
MG440	2.2	0.19	40	4.0
MG480	2.2	0.19	80	4.0
MG220	2.2	0.19	20	2.0
MG320	2.2	0.19	20	3.0
MG520	2.2	0.19	20	5.0
MG620	2.2	0.19	20	6.0

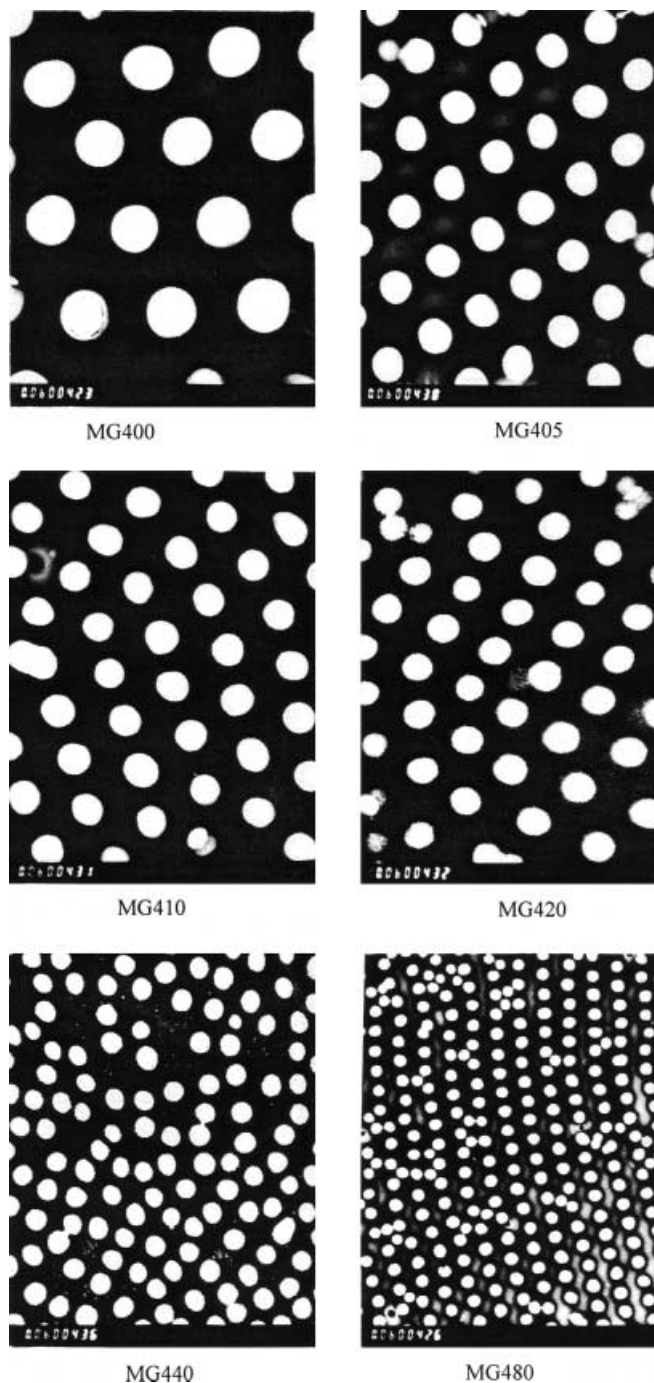


Fig. 1 Transmission electron microscopy (TEM) micrographs of cleaned copolymer *N*-isopropylacrylamide (NIPAM) and dimethylaminoethyl methacrylate (DMAEMA) microgels

polymerization time as measured by QELS and reported in Fig. 2. In all cases, the particle size reached its maximum within 10 min, which can be explained by the high NIPAM propagation rate constant [2] similar to that of any acrylamide derivatives associated with the

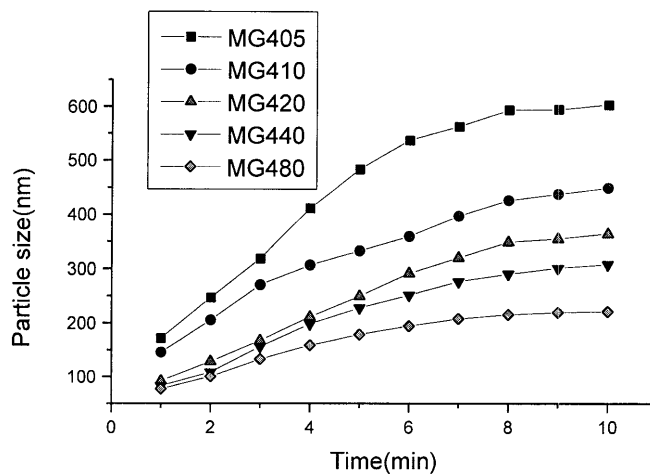


Fig. 2 Influence of DMAEMA concentration on microgel size as a function of time (20 °C, 0.001M NaCl, pH 3)

heterogeneous character of the polymerization mechanism.

It can be seen from Fig. 3 that the size of the final microgels decreases with increasing amount of DMAEMA. Detailed data measured by QELS (below and above the lower critical solution temperature, LCST, of polyNIPAM) and TEM are shown in Table 2. The TEM technique gives the lowest size due to the shrinkage of the microgel under vacuum (analysis under drying state). Without DMAEMA monomer, the microgel size is very large and its dispersion is unstable, which confirms that such NIPAM-based latex particles are mainly sterically stabilized and electrostatic stabilization originating from charged groups introduced by the initiator is much less significant. Even though a small amount of DMAEMA is used, the microgel size decreases sharply, as depicted in Fig. 3. This observation shows that the number of

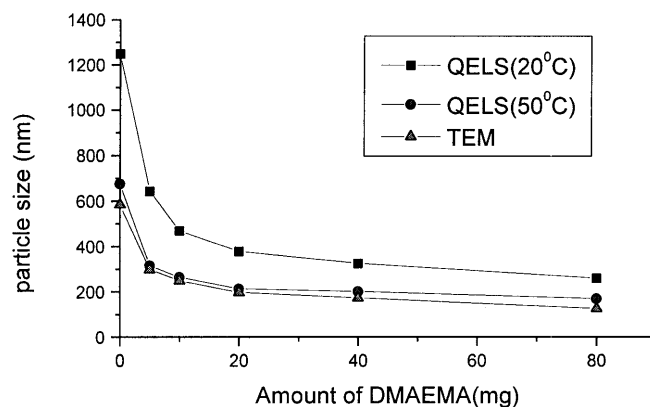


Fig. 3 Influence of DMAEMA concentration on microgel size: comparison of quasielastic light scattering (20 and 50 °C) and TEM data

Table 2 Influence of dimethylaminoethyl methacrylate concentration on the size of the microgels measured by quasielastic light scattering (*QELS*) and transmission electron microscopy (*TEM*) and their swelling ratio

Microgel code	Particle size (nm)			Swelling ratio ($D_{20\text{ }^\circ\text{C}}/D_{50\text{ }^\circ\text{C}}$) ³
	QELS (20°C)	QELS (50°C)	TEM	
MG400	1,249	675	584	6.33
MG405	643	315	298	8.50
MG410	469	264	249	5.63
MG420	378	213	197	5.56
MG440	325	201	173	4.24
MG480	260	170	126	3.58

microgel particles increases when the functional monomer concentration is increased in the polymerization recipe. In fact, introduction of a small amount of DMAEMA monomer enhances the formation of more precursors and increases the colloidal stabilization of the nucleated particles through an electrostatic mechanism. Then, these particles rapidly become the polymerization loci and no new particles are formed.

Effect of DMAEMA on the swelling ratio

As shown in the last column of Table 2, the swelling ratio defined as $(D_{20\text{ }^\circ\text{C}}/D_{50\text{ }^\circ\text{C}})^3$ significantly decreases upon increasing the amount of DMAEMA. Since MBA, which is responsible for the polymer cross-linking density in the particles, was kept constant in the various experiments, the swelling behavior can be attributed to the variation of the MBA distribution in the final particles. It was indeed reported that MBA was more reactive than NIPAM [2], which causes the particles to be more cross-linked at the beginning of the polymerization reaction. This behavior has been already pointed out by Guillermo et al. [6] in their investigation of the internal network structure of cross-linked poly(*N*-isopropyl methacrylamide) versus MBA concentration using the NMR approach (measurements of residual spin-spin interaction resulting from nonisotropic rotations of monomeric units). The results obtained showed that the internal particle structures were looser and looser from the core to the shell. As the amount of DMAEMA is increased in the recipe, it may be postulated that the MBA incorporation in the forming particles could be modified through a copolymerization effect or/and a change in the monomer partitioning. DMAEMA incorporation improves the cross-linking distribution inside the microgel network and then influences its swelling ratio.

Effect of amount of DMAEMA on the water-soluble polymer

Several studies [15, 16] have shown that the incorporation of ionic comonomer into polyNIPAM microgels led

to an increase in the amount of water-soluble polymer. It is worthy analyzing the water-soluble oligomer produced during the formation of the microgels in order to clarify the nucleation mechanism of cationic polyNIPAM microgels. Table 3 exhibits a drastic increase in the amount of water-soluble polymer as the DMAEMA concentration is increased. This is an indication that some NIPAM/DMAEMA copolymers which were not captured by the particles were formed owing to complete consumption of MBA and/or low-molecular-weight chains produced by some transfer reaction during the particle formation. Additionally, the molecular weight of the water-soluble polymer based on DMAEMA/NIPAM copolymer is much larger than that of the water-soluble polymer consisting of pure NIPAM. The former is polyelectrolyte in character, whereas the latter is homopolyNIPAM which is water-soluble at the polymerization temperature (above the LCST of polyNIPAM) when its molecular weight is very low. On increasing the amount of DMAEMA in the recipe, the molecular weight of the water-soluble polymer increases. This may be due to the formation of more hydrophilic linear DMAEMA-rich copolymers which were not thermally sensitive. This indicates that the functional monomer plays a major role in the formation of the water-soluble oligomer.

Effect of the pH of the polymerization medium

Owing to the basic nature of DMAEMA and knowing the drastic sensitivity of particle formation to the hydrophilicity of the functional monomer, the influence of the pH of the polymerization medium was examined.

Table 3 Effect of dimethylaminoethyl methacrylate concentration on the amount of water-soluble polymer

Microgel code	Amount of water-soluble polymer	Molecular weights (M_w)
MG400	6.4	528
MG405	5.2	53,500
MG410	7.1	57,600
MG420	10.3	63,800
MG440	17.8	—

The results obtained are illustrated in Table 4, which shows the final particle sizes and the amounts of water-soluble polymer for different microgel syntheses upon changing the pH of the reaction medium and keeping constant the amounts of DMAEMA and initiator (as shown in Table 1).

It is worth noting the marked size increase as the pH is increased. An upper pH limit is reached, otherwise the latex was found to be partially or totally flocculated above pH 6. This reveals that the pH of the polymerization reaction medium has an effect on the nucleation step and the microgel latex stability. From our titration experiments, the pK_b of DMAEMA at 15 °C is 8.1. When DMAEMA is copolymerized with a thermosensitive monomer (such as NIPAM), its pK_b in the copolymer should decrease as shown in the study of Feil et al. [18]. If the pH of the polymerization medium is lower than the pK_b of DMAEMA in the copolymer at the reaction temperature, DMAEMA is charged and the microgel latexes formed are stable owing to strong electrostatic repulsion. In contrast, DMAEMA is uncharged at a pH above its pK_b and the microgel latexes are unstable owing to the low charge density on their surfaces. Concerning the swelling ratio, it seems that no significant change appears within experimental uncertainty. The same is true as regards the amount of water-soluble polymer recovered from the final latexes since approximately 10 wt% is found regardless of the pH.

Influence of the amount of DMAEMA on the thermosensitive volume phase transition

Generally, incorporation of small amounts of ionic comonomers results in a strong increase or disappearance of the collapse temperature of polyNIPAM gel [19–21]. The temperature dependence of the size of the poly(NIPAM-*co*-DMAEMA) microgel at pH 3 in 0.001 M NaCl solutions is shown in Fig. 4. The transition temperature was found to be around 32 °C and was slightly dependent on the concentration of the cationic monomer. On increasing the amount of DMAEMA, the extent of shrinkage of the microgels was reduced and the transition region become broader and broader. Finally, incorporation of a large amount of the cationic monomer results in the disappearance of the

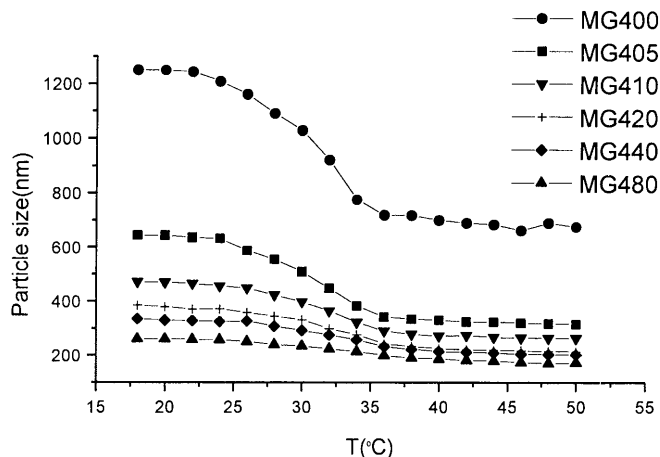


Fig. 4 Effect of DMAEMA concentration on the volume phase transition of microgels (0.001 M NaCl, pH 3)

thermosensitive property. An increase in the relative DMAEMA content reduced the content (and the chain length) of the thermosensitive polyNIPAM chains inside the copolymer microgels, thus reducing the extent of shrinkage by the microgels. Additionally, the increase in the amount of water-soluble polymer, which is mainly composed of NIPAM and DMAEMA, led to an increase in the relative content of MBA inside the microgel network upon raising the DMAEMA proportion in the monomer mixture, and the increase in the cross-linking might also contribute to the reduction in the extent of microgel shrinkage as the temperature is increased above the LCST. The broader transition might be attributed to the polyNIPAM segment inhomogeneity and distribution in the microgel network. It is known that for a given polymer concentration polymer chains with different lengths undergo a phase transition at different temperatures [22]. For the DMAEMA/NIPAM random copolymer microgels, the polyNIPAM segments inside the microgel network have a broad molecular-weight (length) distribution. With increasing DMAEMA content, the molecular-weight (segment length) distribution of the thermosensitive polyNIPAM segments that have been copolymerized randomly inside the microgel are broadened. The higher the DMAEMA/NIPAM weight ratio in the feed composition, the larger the polyNIPAM segment length difference inside the micro-

Table 4 Influence of solution pH on the particle size and the amount of water-soluble polymer

Microgel code	Particle size (nm)		Swelling ratio ($D_{20\text{ °C}}/D_{50\text{ °C}}$) ³	Water-soluble polymer (wt%)
	$D_{20\text{ °C}}$	$D_{50\text{ °C}}$		
MG220	277	158	5.39	11.4
MG320	289	167	5.18	11.7
MG420	378	213	5.56	10.3
MG520	405	231	5.37	9.8
MG620	449	250	5.79	10.1

gels, and thus the broader the phase-transition temperature range, until the polyNIPAM segment inhomogeneity reaches a maximum at a certain DMAEMA/NIPAM weight ratio.

Conclusion

Monodisperse and stable microgel latexes were obtained through a control of the DMAEMA concentration in the polymerization recipe and the pH of reaction medium. Raising the DMAEMA concentration causes the water-soluble polymers to increase, whereas microgel size decreases, which explains the dramatic effect of the ionic

monomer on the particle formation as in emulsifier-free emulsion polymerization. Additionally, the molecular weight of the water-soluble polymer revealed an increase upon increasing DMAEMA concentration. Since the cationic monomer is a weak base, the pH of the reaction medium has an effect on the nucleation step and on raising the pH the particle size increases. On increasing the DMAEMA concentration, the temperature dependence of the particle size become less and less dramatic.

Acknowledgements The authors are grateful to the National Natural Science Foundation of China (no. 29874010) and The Key Laboratory of Molecular Engineering of Polymers of the Educational Ministry for their financial support.

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