Temperature-Triggered Disintegrable Poly(*N*-isopropylacrylamide) Nanoparticles via Heterophase Polymerization in the Presence of Tetramethylethylenediamine and Sodium Dodecyl Sulfate

Yan Chen,[1] Shahriar Sajjadi[2]

[1]Tianjin Key Laboratory on Technologies Enabling Development of Clinical Therapeutics and Diagnostics (Theranostics), School of Pharmacy, Tianjin Medical University, Tianjin 300070, China
[2]Department of Physics, King's College London, Strand London, WC2R 2LS, United Kingdom
Correspondence to: S. Sajjadi (E-mail: shahriar.sajjadi-emami@kcl.ac.uk)

ABSTRACT: In this work, polymerization of *N*-isopropylacrylamide (NIPAM) in the presence of *N*,*N*,*N'*,*N'*-tetramethylethylenediamine (TEMED) and sodium dodecyl sulfate (SDS) has been studied. The ability to control the characteristics of resulting particles was investigated via varying the concentrations of monomer, SDS, and TEMED used in the polymerization. Particles formed in the absence of TEMED were not completely soluble in water below lower critical solution temperature (LCST) but were quite stable. With the help of TEMED, fully disintegrable particles in water below LCST could be produced but at the cost of low stability. Electrophoretic measurements showed a substantial decrease in zeta potential of resulting colloids due to many neutral radicals generated by TEMED. With the aid of a small amount of SDS, stable temperature-triggered water-disintegrable polyNIPAM particles as small as 70 nm could be obtained. However, excessive use of SDS caused the particles to swell in the course of reaction and therefore adversely affected particles size and properties. © 2014 Wiley Periodicals, Inc. J. Appl. Polym. Sci. **2014**, *131*, 40781.

INTRODUCTION

Poly(*N*-isopropylacrylamide) (NIPAM) is a typical thermoresponsive polymer, which has hydrophobic and hydrophilic domains below and above the lower critical solution temperature (LCST). NIPAM homopolymers have been applied in a wide range of applications including thermal sensitive micelles for drug delivery, controllable flocculants, well-defined environmentally responsive polymer brushes, matrix for producing high-molecular-weight polymers, and core materials for the preparation of hollow particles.[1–5] Hollow particles have significant potential for emerging applications in drug delivery. Disintegrable polyNIPAM particles, as a core template for hollow structures, offer simplicity, and ease of removal in the water medium, in comparison to other core templates.[5–7] For some applications such as that in drug or DNA delivery across the blood–brain barrier and cell membrane, the size of hollow particles has to be smaller than 200 nm,[8,9] suggesting that control of the size of core templates is crucial.

PolyNIPAM particles produced via conventional heterophase polymerization are not fully disintegrable in water below LCST even in the absence of crosslinker, especially at high monomer concentrations, due to the limited water solubility of polyNIPAM chains.[10–12] The formation of polymer matrix that cannot be dissolved in water has been attributed to physical entanglements of the chains[10] or network formation due to chain transfer to polymer.[11] Such networks can hinder the use of polyNIPAM particles in potential applications that require fast disintegration below LCST. One way around this is to reduce the molecular weight of the polymer using a low monomer concentration in the conventional batch polymerization.[12] But this method is limited to low solid content latexes. A superior method is to use semicontinuous heterophase polymerization in which the monomer concentration at the reaction locus is maintained at low level by adding monomer at a low rate. This method produces polymers with low molecular weight and enhanced water solubility below LCST.[7,12] Another approach is to reduce the polymer chain length of polyNIPAM by introducing *N*,*N*,*N'*,*N'*-tetramethylethylenediamine (TEMED) as an initiator accelerator to the reactor.[11] However, TEMED produces an adverse effect on particles stability.[13,14] This means that a surfactant is probably required to produce fine and stable particles.

In this work, polymerization of NIPAM in the presence of TEMED and sodium dodecyl sulfate (SDS), as surfactant, has been studied. Readers should note that potassium persulfate (KPS) can be used alone as initiator at temperatures higher than 40°C. At lower temperatures around room temperature, an accelerator is also required to reduce the activation energy of KPS for radical generation. However, in this research to be able to compare KPS and KPS/TEMED systems, we carried out the reactions at a temperature (60°C) high enough to allow radicals to be generated by KPS. The monomer concentration, which is usually considered as one of the most influential parameters in the kinetics of NIPAM polymerization,[12] was also altered to investigate its effects on particle size and stability.

EXPERIMENTAL

Chemicals and Procedure

The details of the synthesis of crosslinker-free polyNIPAM particles have been given in another work.[12] Briefly, the reactor was initially charged with most of deionized water (130 mL), SDS (Aldrich, if used) and buffer (0.0672 g, 4×10^{-3} mol L_{aq}^{-1}) and heated up to 60°C while being purged with nitrogen. A given quantity of NIPAM (99%, ACROS), defined as the weight percentage of the overall aqueous phase, was first dissolved in deionized water (40 mL) and then added into the reactor. After another 5 min purging with nitrogen, the initiator solution, 30 mL of deionized water containing KPS (Aldrich) (0.2163 g, 4×10^{-3} mol L_{aq}^{-1}) and TEMED (99%, Aldrich) at a given concentration, if used, was then added to the vessel. The recipes are given in Table I.

Measurements

Conversions were estimated gravimetrically. Around 1 g of polymer latexes was removed from the reactor and placed in a weighed aluminum foil plate. The polymerization was stopped by adding a small amount of methanol and hydroquinone to the sample. The polymer precipitated, and then the mixture was dried in an oven at an elevated temperature (80°C) to a constant weight (for 48 h). NIPAM monomer was found to sublime under such conditions.[7] Z-average diameters of particles were measured at desired temperature using dynamic light scattering (DLS; Zetasizer Nano; Malvern, UK). By examination of selected polyNIPAM latexes hardened by using a small amount of a crosslinker, with scanning electron microscopy (SEM; Hitachi S4000), a conversion factor of $C_f = 0.90$ was obtained, which used for converting D_z data from DLS to the volume-average diameter of particles (D_v) obtained from SEM. For SEM study, a drop of latexes was placed on a small piece of glass substrate, dried, and then coated with a layer of gold. The number of particles (N_p) was calculated using the equation $N_p = 6m_p/\pi D_v^3 \rho_p$, where m_p gives the mass of polymer in the system at any given time and ρ_p is the density of polyNIPAM which is 1.269 g mL^{-1}.[15] A correction has been made in the calculation of N_p, so that $N_{p,corrected} = 1.4 N_p$. This is based on the assumption that 32 wt % of polyNIPAM phase above LCST is water.[16]

The weight-average molecular weight ($\bar{M}_w$) of polymer was measured via static light scattering (SLS, Zetasizer Nano, Malvern, UK) using toluene and water as standard and solvent, respectively. Samples removed from the reactor were stored in

Table I. Recipes for Synthesis of polyNIPAM Particles

Description	[NIPAM] (wt %)	[SDS] (g L_{aq}^{-1})	[TEMED] (mmol L_{aq}^{-1})
Set A: Effect of [NIPAM]	0.25	0.5	0
	1.0	0.5	0
	4.0	0.5	0
	8.0	0.5	0
	16.0	0.5	0
Set B: Effect of [SDS]	8.00	0.125	0
	8.00	0.25	0
	8.00	0.5	0
	8.00	1	0
	8.00	2	0
	8.00	4	0
	8.00	8	0
Set C: Effect of [TEMED]	1.0	0	5
	1.0	0	10
	1.0	0	15
	1.0	0	20
Set D: Effect of [NIPAM] in the presence of TEMED and SDS	0.25	0.5	10
	0.5	0.5	10
	1.0	0.5	10
	2.0	0.5	10
	4.0	0.5	10
	8.0	0.5	10

$T = 60°C$; $C_{KPS} = C_{buffer} = 4.0$ mmol L^{-1}; 200 mL water.

stirred sealed glass bottles at room temperature for a week. The polymer chains dissolved in water (sol) were then separated via centrifugation from the gels, if any. The serum was first dried in an oven, weighed, and then redissolved in the deionized water at room temperature to obtain polymer solutions with a range of concentrations from 0.25 to 1.0 g L_{aq}^{-1}. For each sample, the scattering intensity of four concentrations of the polymer solution was measured and used to construct a Debye plot, from which the weight-average molecular weight, $\bar{M}_w$, could be obtained. The temperature dependence of phase transition of polyNIPAM was determined using ultraviolet-visible spectroscopy (PerkinElmer, USA). The transmittance was measured as a function of temperature (°C) at the wavelength of 600 nm. Samples taken from the reactor (after full conversion) were not allowed to cool down and directly used for measurements after dilution with preheated water (60°C) to reach a constant polymer concentration. Particles morphology was visualized by SEM. The micrographs of the nanoparticles only showed polymer film due to their lack of crosslinking (not shown).

RESULTS AND DISCUSSIONS

Heterophase Polymerization of NIPAM with Varying Monomer Concentration in the Presence of a Low Amount of SDS (0.5 g L_{aq}^{-1}) (Set A)

It has been shown that surfactant-free polymerization of NIPAM produces large particles even at a low monomer concentration.[12,17] Particles formed in the absence of surfactant were in the range of 160–923 nm for monomer concentration range of 0.25–3.0 wt %, respectively.[12] It has been shown that polyNIPAM particles size, stability, and their polydispersity can be improved with the help of SDS during reaction.[10] A set of polymerizations was conducted with various monomer concentrations in the presence of 0.5 g L_{aq}^{-1} of SDS.

Figure 1 shows the amount of polymer produced, the volume-average diameter and number of particles versus reaction time for various monomer concentrations. The rate of polymerization as well as the rate of particle growth increased with monomer concentration. Stable polyNIPAM latexes could be produced using monomer concentrations up to 8.0 wt % with the aid of SDS. A massive coagulation was observed at high conversions for monomer concentration of 16.0 wt %.

For the lower monomer concentrations ([NIPAM] < 1.0 wt %), the rate of particle formation was slow, but particles were stable and did not coagulate in the course of reaction. Limited particle coagulation, however, occurred during the reactions [Figure 1(c)] if a monomer concentration greater than 1.0 wt % was used. The minimum size of (final) particles was obtained with 0.25 wt % NIPAM monomer concentration, which was around 57 nm, with a population of 2.46×10^{16} L_{aq}^{-1}. In comparison, fewer (6.35×10^{14} L_{aq}^{-1}) and larger (190 nm) particles were obtained for the surfactant-free polymerization using the same amount of NIPAM under similar conditions.[12] Therefore, the colloidal stability of the system significantly improved in the presence of a low amount of SDS.

The calculated final conversions of most experiments, however, exceeded 100% by a slight margin (up to 10 wt %). This discrepancy did not occur for the emulsifier-free NIPAM polymerization.[12] This may be due to the particles gel structure and their capability to incorporate SDS that could lead to dissolution and entrapment of water inside particles[18] and erroneous conversion calculation. This will be further discussed later. The transmittance of latexes at room temperature never reached 100%, which confirms that the resulting polyNIPAM particles contained gel and they were not fully water disintegrable.

Heterophase Polymerization of NIPAM with Varying Concentration of SDS in the Presence of a High Concentration of Monomer (Set B)

To study the interaction of SDS with polyNIPAM during the polymerization, a set of experiments with 8 wt % NIPAM concentration and a range of surfactant concentrations starting from 0.125 to 8.0 g L_{aq}^{-1} was carried out. In most cases, the use of SDS was maintained below the critical micelle concentration (CMC) of SDS in water in the presence of KPS (ca. 1.0 g L_{aq}^{-1} at room temperature).[19] A rather high concentration of NIPAM, 8.0 wt %, was used to be able to study particle stability within a wide size range.
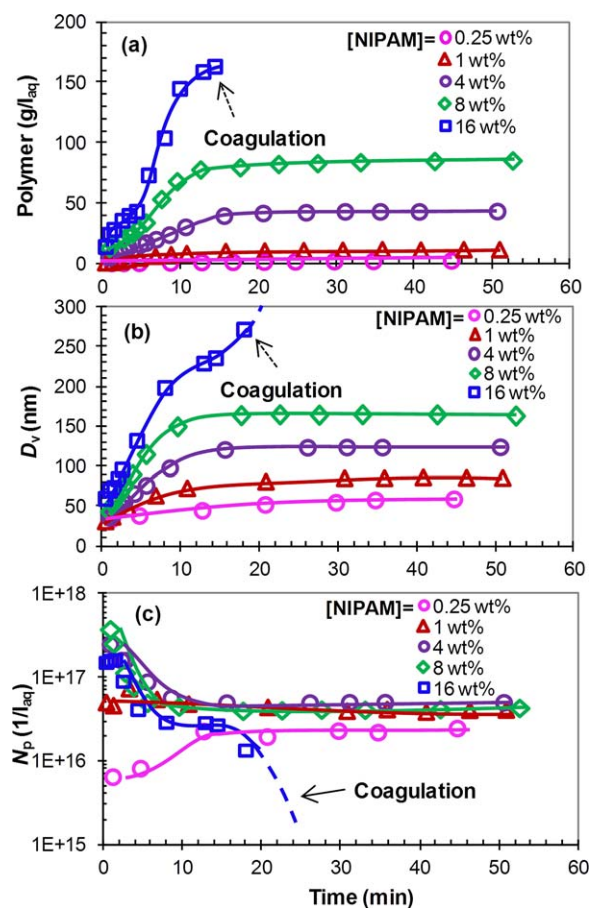

Figure 1. The time evolution of (a) polymer produced, (b) volume-average size, and (c) number of particles for different monomer concentrations ([KPS] = 4.0 mM, [SDS] = 0.5 g L_{aq}^{-1}). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Figure 2 shows the amount of polymer produced and the average size of particles versus time for different surfactant concentrations. The rates of polymerization for all experiments are almost the same. A severe coagulation is observed at high conversions for 0.125 g L_{aq}^{-1} SDS due to the lack of colloidal stability. It can be found, from Figure 2(b), that the initial size of particles, as well as their number, appears to be similar for different surfactant concentrations. However, the rates at which particles grew were quite different. The final size of particles as well as the rate of particle growth decreased with increasing surfactant concentration from 0.125 to 4.0 g L_{aq}^{-1}. One should notice that CMC is an important threshold in conventional emulsion polymerization in which micelles can be locus of nucleation. However, in a typical precipitation polymerization, such as NIPAM, CMC will not bear similar importance because NIPAM is a water-soluble monomer that cannot be accumulated or solubilized inside micelles and as a result nucleation usually occurs in the continuous phase. However, micelles can improve stability of growing particles by disintegration and adsorption on the surface of growing particles. This can explain the decreased rate of particle growth for higher SDS concentrations. However, larger particles were produced with 8.0 g L_{aq}^{-1}
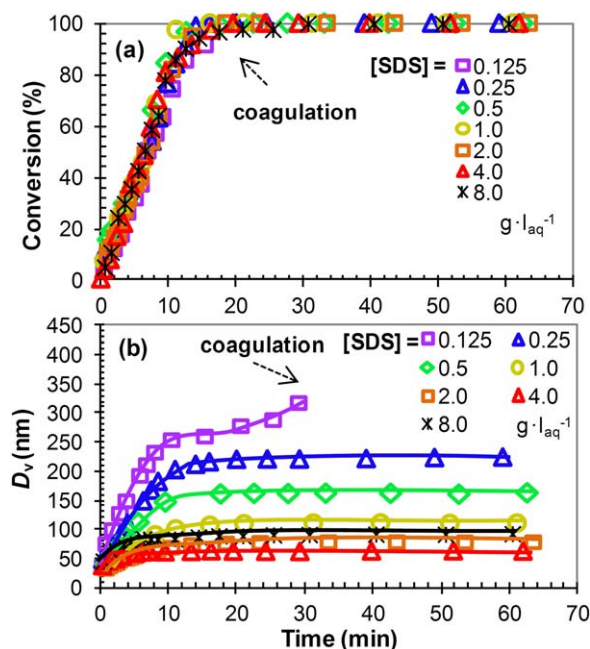
Figure 2. The time evolution of (a) polymer produced and (b) average size of particles for different monomer concentrations ([KPS] = 4.0 mM, [NIPAM] = 8.0 wt %). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

SDS. This is against what is understood from conventional heterophase polymerizations in which the average size of particles is reduced with increasing surfactant concentration. This may be due to the fact that SDS molecules can interact with polyNIPAM chains,[18,20–23] as explained later. The associations of SDS molecules with polymer chains can promote both intermolecular and intramolecular solubility so that the phase transition temperature increases with surfactant concentration. In most investigations carried out so far, the interaction of SDS was investigated with preformed polyNIPAM.[24] Therefore, a systematic study of the interaction of SDS during the synthesis of polyNIPAM particles is lacking.

It has been reported that SDS molecules can penetrate into the network of polyNIPAM microgels at room temperature and cause the particles to swell.[18] We attribute the inaccuracy in NIPAM conversions for runs with SDS to this phenomenon. However, no data has been reported to date that the absorption of SDS within the polyNIPAM chains can take place during polymerization at temperatures well above LCST. To verify it, a simple experiment was carried out. Crosslinker-free polyNIPAM particles were first produced via surfactant-free heterophase polymerization at 60°C with 1 wt % monomer. The latex was then incubated at the reaction temperature while an aqueous solution of SDS was added dropwise, and size measurements were conducted at the same temperature. The DLS readings did not show any significant change when SDS concentration was below 4.0 g L$_{aq}^{-1}$. However, at higher SDS concentrations (>4.0 g L$_{aq}^{-1}$), particles instantaneously started to swell with water (Figure 3). SDS molecules bear long hydrophobic chains and a small ionic group. At low concentration of SDS, long alkyl chains affect both solubility and LCST of polyNIPAM
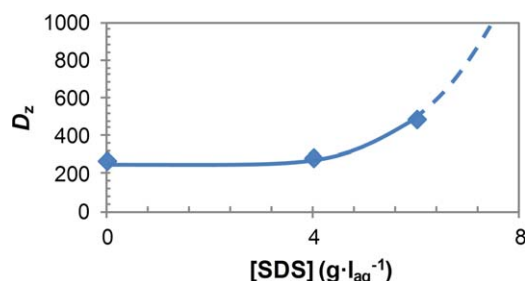

Figure 3. Variations in the z-average diameter (nm) of final particles produced with 1.0 wt % NIPAM in the presence of different amounts of SDS. $T = 60°$C. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

chains. With increasing concentration above a critical value, when the repulsive forces between the ionic groups exceed the hydrophobic interactions between dodecyl groups, particles start to swell.[25] Such particles can adversely affect latex stability by removing SDS from the continuous phase via inclusion within them, and also by adsorbing excess SDS at their expanding surface. Therefore, the larger particles produced at the highest SDS concentration used (8.0 g L$_{aq}^{-1}$) could be attributed to the interaction of SDS with polyNIPAM chains in the course of reaction. The enhanced swelling of SDS-encapsulated polyNIPAM particles with moieties such as drugs suggests that they can have good potential for enhanced drug delivery applications.

Figure 4 shows that the final size of particles tends to decrease with increasing SDS concentration until the threshold of 4.0 g L$_{aq}^{-1}$ was reached, beyond which the size of particles showed an increase. The number of particles showed an opposite trend with increasing SDS concentration.

Emulsifier-Free Heterophase Polymerization of NIPAM with Varying Concentrations of TEMED (Set C)
To investigate the effect of TEMED, surfactant-free polymerizations were carried out in the presence of various concentrations of TEMED, from 5.0 to 20.0 mmol L$_{aq}^{-1}$ and with 1.0 wt % NIPAM monomer. A low monomer concentration was used to limit particle growth because of the extreme instability of particles in emulsifier-free heterophase polymerization.[26] The minimum concentration of TEMED used was 5.0 mmol L$_{aq}^{-1}$, which is larger than 4.0 mmol L$_{aq}^{-1}$ used for the initiator. According to the redox chemical reaction scheme for TEMED
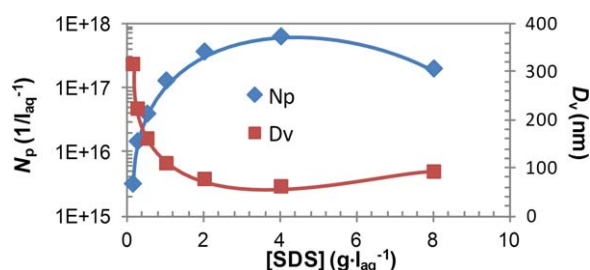

Figure 4. Variations in the final number and volume-average size of particles as a function of SDS concentrations. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]
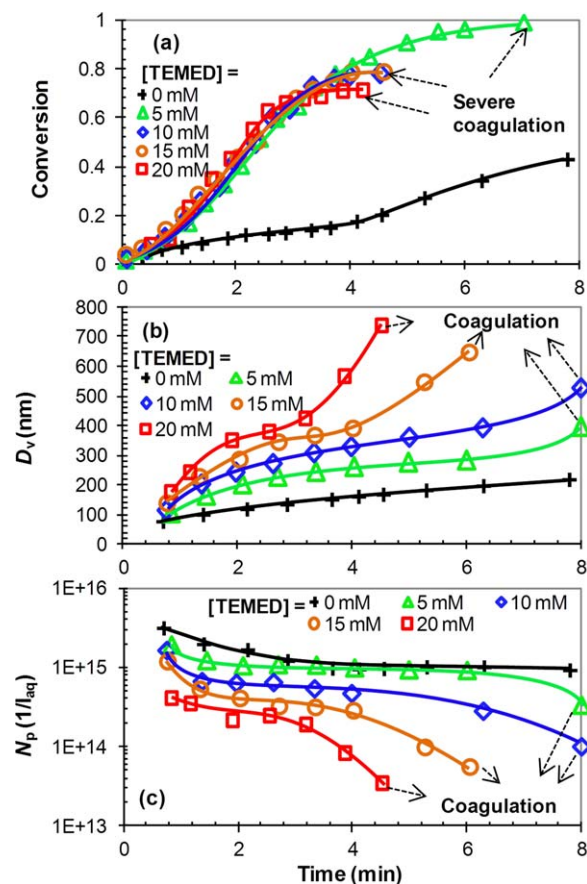
Figure 5. The time evolution of (a) polymer produced, (b) volume-average diameter of particles, and (c) the number of particles for different TEMED concentrations ([KPS] = 4.0 mM, [NIPAM] = 1.0 wt %). [Color figure can be viewed in the online issue, which is available at wileyonline-library.com.]

Table II. Zeta Potential of Particles Produced with Different Amounts of TEMED, 1.0 wt % NIPAM, $T = 60°C$

TEMED (mmol L_{aq}^{-1})	Zeta potential (mV)	pH
0	−28.1	7.0
10	−1.48	7.0
20	−1.40	7.0

tration, suggesting that TEMED served to destabilize the particles.

Table II shows the zeta potential of particles produced with different amounts of TEMED. As coagulation proceeds during polymerization, the zeta potential of particles might change due to the subsequent particle growth. Therefore, to have a better estimation of the effect of TEMED on the stability of newly nucleated particles, samples for analysis were taken during the early stage of polymerization. The particles produced with KPS had negative zeta potentials, due to the presence of persulfate groups on their surface. A potential of around −30 mV is within the range of zeta potential that is usually required to produce a relatively stable colloidal system. Comparatively, the particles produced with TEMED (and KPS) had a quite low absolute value of zeta potential, around −1.40 mV, indicating that these particles were extremely unstable and prone to coagulation, as seen in Figure 5(c). Such a behavior probably suggests that the radicals generated from TEMED ((CH_3)$_2$NCH$_2$CH$_2$ NCH$_3$CH$_2$) are hydrophilic and, cannot contribute to the colloidal stabilization of latexes. As a result, the presence of TEMED would depress the stability of particles. However, the rate of radical generation by redox initiation system does not appear to increase with TEMED for concentration above 5.0 mmol L_{aq}^{-1}, as explained before. But there is another reaction, the thermal decomposition of KPS, which occurs in parallel with that of redox initiation system at the reaction temperature (60°C). Therefore, with further addition of TEMED to the reaction medium, the redox initiation becomes more favorable, at a constant overall rate, and more hydrophilic radicals will be produced, causing further suppression of the colloidal stability of latexes, as shown in Figure 5(b,c).

As expected, the resulting latex transformed into transparent solution at room temperature, indicating that water solubility of polyNIPAM has been significantly improved with the aid of TEMED. However, the data clearly show that stable small particles could not easily be produced via surfactant-free polymerization.

Heterophase Polymerization of NIPAM with Varying Monomer Concentrations in the Presence of TEMED and SDS (0.5 g L_{aq}^{-1}) (Set D)

It follows from the previous section, that a surfactant is required to improve the colloidal stability of particles, if TEMED is to be used. Several experiments were carried out with various monomer concentrations in the presence of 10.0 mmol L_{aq}^{-1} of TEMED and a small amount of SDS (0.5 g L_{aq}^{-1}). Results are shown in Figure 6. The reactions occurred quickly and almost completed within a few minutes for most

with a persulfate, KPS, the stoichiometric ratio between them is 1 : 1.[27] This means an increase in TEMED concentration above 4.0 mmol L_{aq}^{-1}, the concentration used for the persulfate initiator, should have little effect on radical generation. However, a concentration larger than 4.0 mmol L_{aq}^{-1} ensures that the rate of radical generation does not change with TEMED concentration. The results are shown in Figure 5. With the help of TEMED, the rate of polymerization increased significantly. This implies an enhanced rate of radical generation in the presence of TEMED. However, the rate of reaction did not change with the amount of TEMED used, as expected.

Furthermore, the final conversion of around 100% was achieved for 5 mmol L_{aq}^{-1} TEMED, but decreased with further increase in TEMED concentration due to coagulation, as shown in Figure 5(b,c). The size of particles increased from around 200 nm, for TEMED-free polymerization, to above 400 nm, depending on TEMED concentration. Particles were found to be quite unstable and underwent significant coagulation in the course of reactions. This is clearly inferred from Figure 5(c), which shows the difference between the initial and final number of particles. The difference became wider with increasing TEMED concen-
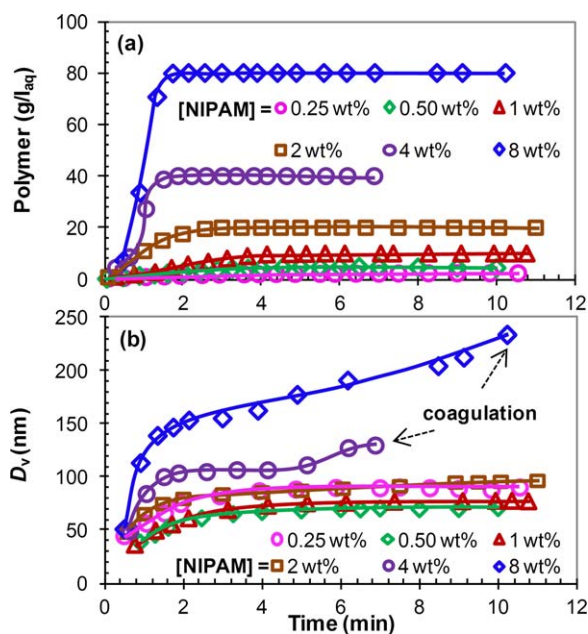
Figure 6. The time evolution of (a) polymer produced and (b) average size of particles for different monomer concentrations ([KPS] = 4.0 mM, [TEMED] = 10.0 mmol L_{aq}^{-1}, [SDS] = 0.5 g L_{aq}^{-1}). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

runs. The rate of growth of particles, due to coagulation, was damped using SDS, leading to the formation of stable latexes. A low concentration of surfactant was used, however, there was still significant coagulation during the course of reaction.

The minimum size of particles that could be produced is around 70 nm when monomer concentration was 0.5 wt % [Figure 6(b)]. One thing to be noticed is that particle coagulation continued even after full completion (100% conversion) of the reactions using monomer concentration equal or greater than 4.0 wt %, showing vulnerability of particles to coagulation (Figure 6).

Figure 8 shows that the weight-average molecular weight (M_w) of the polymer increased with monomer concentration. It appears that the presence of TEMED has led to a significant drop in the molecular weight of polymer in particular at low monomer concentrations. This point is supported by the fact that $\bar{M}_w$ of the polymer produced with 1.0 wt % NIPAM, which is 105 kDa, is
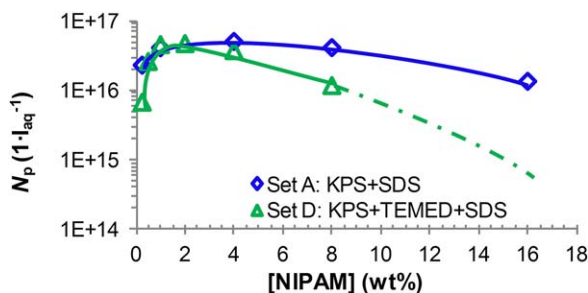

Figure 7. Comparison of final N_p versus monomer concentration for Set A ([KPS] = 4.0 mM, [SDS] = 0.5 g L_{aq}^{-1}) and Set D ([KPS] = 4.0 mM, [TEMED] = 10.0 mmol L_{aq}^{-1}, [SDS] = 0.5 g L_{aq}^{-1}). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]
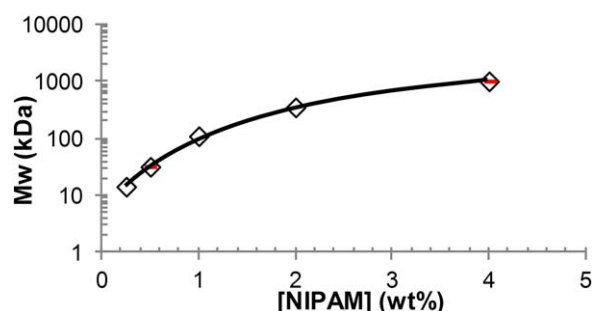

Figure 8. Weight-average molecular weight of polymer produced as a function of monomer concentration for Set D, ([KPS] = 4.0 mM, [TEMED] = 10.0 mmol L_{aq}^{-1}, [SDS] = 0.5 g L_{aq}^{-1}). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

only half of that produced under similar conditions but in the absence of TEMED (229 kDa).[12] The decrease in $\bar{M}_w$ can be attributed to the higher rate of initiation in the presence of TEMED, as explained before. However, recently, Hu et al. have pointed out that TEMED can also act as a transfer agent in the polymerization of NIPAM. According to them, the propagating polyNIPAM chains would likely undergo transfer with TEMED rather than undergo a chain termination reaction with other propagating chains. As a result, the residual TEMED in the system could hinder the chain branching and thus act to control the molecular weight of resulting polymer chains.[11]

Disintegration of Particles

To verify the temperature-triggered disintegration of latex particles formed in the presence of TEMED and SDS, the latex particles with 1.0 wt % NIPAM monomer from set D were cooled from the reaction temperature (60°C) to room temperature and their z-average diameter and transmittance were carefully monitored against time and temperature. For size measurement, samples were cooled down at a constant rate of 1.0°C min^{-1} [see lower panel in Figure 9(a)]. For turbidity measurement, samples were gradually cooled by heat transfer to the surrounding [see lower panel in Figure 9(b)]. The results are compared with the particles obtained with the same monomer concentration and similar particle size, but in the absence of TEMED [Set A, see Figure 1(b)]. The change in the volume of particles, or volume ratio (V_r) was defined as the cube of the ratio of the instantaneous z-average diameter of particles at any given time to that of particles at collapsed state (above LCST). Therefore, $V_r = 1.0$ indicates that particles are at the collapsed state. $V_r > 1.0$ and $V_r < 1.0$ indicate particle swelling and shrinking, respectively.

The kinetics of polyNIPAM particles disintegration in water below LCST can be inferred from the time variations of transmittance, but the equilibrium water solubility of the particles can be found from transmittance at a later times. As shown in Figure 9(a), particles started to swell from temperature of around 32–34°C. After being swollen to their maximum size, particles shrank with temperature very steeply. The maximum particle swelling ratio was found to be around 5.4, which is lower than that produced in the absence of TEMED ($V_r = 15.8$), indicating that particles produced in the presence of TEMED start to disintegrate while swelling.
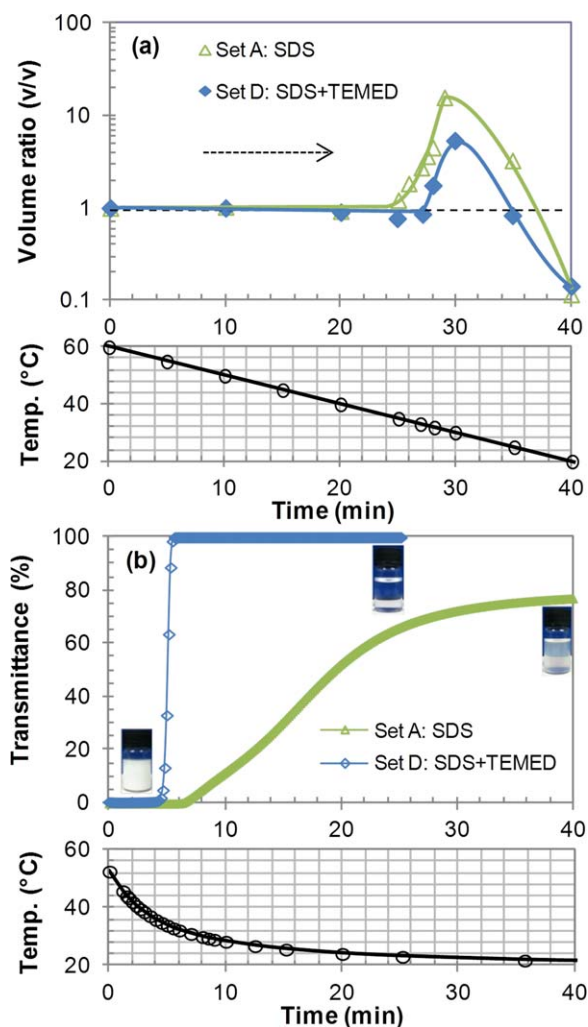
Figure 9. The evolution of *z*-average hydrodynamic size and transmittance of the final latexes from Set A ([SDS] = 0.5 g L_{aq}^{-1}) and Set D ([TEMED] = 10mmol L_{aq}^{-1}, [SDS]=0.5 g L_{aq}^{-1}). [KPS] = 4.0 m*M*, [NIPAM] = 1.0 wt %. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

The transmittance curve, as shown in Figure 9(b), indicates that particles produced in the presence of TEMED were quite responsive to changes in temperature and could be fully disintegrated in the water phase when temperature was below 32°C. Particles formed in the absence of TEMED, however, showed a slow dynamics with temperature and were only partially soluble in water below LCST.

CONCLUSIONS

Systematic studies were carried out via closely monitoring the kinetics of polymerizations of NIPAM in the presence of TEMED and SDS. The average size of resulting particles, and their water solubility, has been successfully manipulated via varying monomer, SDS, and TEMED concentrations. Particles with average size range from 57 to 800 nm have been produced.

SDS, which is usually used as surfactant, was found to interact with polyNIPAM chains during polymerization in an unusual way; by incorporation into polymer particles and causing them to swell with water at the reaction temperature, especially at high SDS concentrations. This interaction was found to adversely affect particles size in the course of reaction.

TEMED not only fastened the response time for the polymer dissolution in water with temperature but also improved the (equilibrium) water solubility of polyNIPAM below LCST. However, TEMED depressed the colloidal stability of particles during polymerization at the same time. The zeta potential data suggest that the formation of hydrophilic and neutral radicals from TEMED is the main reason for the lack of colloidal stability.

The dissolution of a polymer into solvent involves two steps, which are solvent diffusion (swelling) and chain disentanglement.[28] The results suggest that both enhanced hydrophilicity and reduced length of polymer chains, with the aid of TEMED, can improve the water solubility of polyNIPAM. With the help of both TEMED and SDS, stable temperature-triggered water-disintegrable nanoparticles as small as 70 nm were obtained.

REFERENCES

1. Li, H.; O'Shea, J.; Franks, G. V. *AIChE J.* **2009**, *55*, 2070.
2. Kizhakkedathu, J. N. *Macromolecules* **2004**, *37*, 734.
3. Ishifune, M.; Suzuki, R.; Yamane, M.; Tanabe, H.; Nakagawa, Y.; Uchida, K. *J. Macromol. Sci.* **2008**, *45*, 523.
4. Talelli, M.; Hennink, W. E. *Nanomedicine* **2011**, *6*, 1245.
5. Weda, P.; Trzebicka, B.; Dworak, A.; Tsvetanov, C. B. *Polymer* **2008**, *49*, 1467.
6. Qian, J.; Wu, F. P. *Chem. Mater.* **2007**, *19*, 5839.
7. Chen, Y.; Sajjadi, S. *Polymer* **2013**, *54*, 5467.
8. Kreuter, J.; Alyautdin, R. N.; Kharkevich, D. A.; Ivanov, A. A. *Brain Res.* **1995**, *674*, 171.
9. Prabha, S.; Zhou, W. Z.; Panyam, J.; Labhasetwar, V. *Int. J. Pharm.* **2002**, *244*, 105.
10. Mcphee, W.; Tam, K. C.; Pelton, R. *J. Colloid Interface Sci.* **1993**, *156*, 24.
11. Hu, X. B.; Tong, Z.; Lyon, L. A. *Langmuir* **2011**, *27*, 4142.
12. Chen, Y.; Sajjadi, S. *Colloid. Polym. Sci.* **2014**, to appear, doi:10.1007/s00396-014-3182-3.
13. Xu, Y. J.; Li, G.; Haraguchi, K. *Macromol. Chem. Phys.* **2010**, *211*, 977.
14. Gao, J.; Frisken, B. *J. Langmuir* **2003**, *19*, 5212.
15. Lele, A. K.; Hirve, M. M.; Badiger, M. V.; Mashelkar, R. A. *Macromolecules* **1997**, *30*, 157.
16. Osada, Y.; Rossmurphy, S. B. *Sci. Am.* **1993**, *268*, 82.
17. Pelton, R. H.; Chibante, P. *Colloids Surf.* **1986**, *20*, 247.
18. Andersson, M.; Maunu, S. L. *J. Polym. Sci., Part B: Polym. Phys.* **2006**, *44*, 3305.
19. Chen, Y.; Jahanzad, F.; Sajjadi, S. *Langmuir* **2013**, *19*, 5650.

20. Meewes, M.; Ricka, J.; Silva, M.; Nyffenegger, R.; Binkert, T. *Macromolecules* **1991**, *24*, 5811.

21. Ricka, J.; Meewes, M.; Nyffenegger, R.; Binkert, T. *Phys. Rev. Lett.* **1990**, *65*, 657.

22. Tam, K. C.; Ragaram, S.; Pelton, R. H. *Langmuir* **1994**, *10*, 418.

23. Wu, C.; Zhou, S. Q. *J. Polym. Sci., Part B: Polym. Phys.* **1996**, *34*, 1597.

24. Wu, X. Y.; Pelton, R. H.; Tam, K. C.; Woods, D. R.; Hamielec, A. E. *J. Polym. Sci. Part A: Polym. Chem.* **1993**, *31*, 957.

25. Peng, S. F.; Wu, C. *Macromolecules* **2001**, *34*, 568.

26. Chen, Y.; Sajjadi, S. *Polymer* **2009**, *50*, 357.

27. Feng, X. D.; Guo, X. Q.; Qiu, K. Y. *Macromol. Chem. Phys.* **1988**, *189*, 77.

28. Narasimhan, B.; Peppas, N. A. *Macromolecules* **1996**, *29*, 3283.