Synthesis and characterization of multi-responsive poly (NIPAm-co-AAc) microgels

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Abstract. Two samples of multi-responsive copolymer microgels, poly(N-isopropylacrylamide-co-acrylic acid) [P(NIPAm-co-AAc)], were synthesized by emulsion polymerization using different amounts of emulsifier. The unreacted monomers and surfactant were removed from the microgels by dialysis. Dynamic Laser Light Scattering (DLS) was used to determine the diffusion coefficient and hydrodynamic radius (Rh) of the microgels at different pH values and temperatures. At pH 7 the microgel showed rapid response to temperature and underwent volume phase transition (VPT) as the temperature was raised. At lower temperature the microgels were in the hydrated or swollen state but beyond 38oC, the size was abruptly decreased. Under different conditions of pH and NaCl concentrations, variations in VPTT values were noticed. By increasing pH the VPTT was increased but the addition of salt had an inverse effect. The weight average molar mass (Mw) and radius of gyration (Rg) were measured by Static Laser Light Scattering (SLS). FTIR spectroscopy was used to confirm the chemical structures of microgels.

1. Introduction

A polymer gel consists of an elastic cross-linked polymer network with a fluid filling the interstitial space of the network. Recently microgels have gained tremendous importance in theoretical studies on soft matter [1] and applied fields [2, 3]. In particular, they have proved very useful in the domain of material science owing to their potential applications in drug delivery,[4-6] sensing,[7,8], fabrication of photonic crystals,[9-11] template-based synthesis of inorganic nanoparticles,[10,12], separation and purification technologies[13]. The vast array of applications that microgels are suitable for arises from their stimulus-responsive nature, that is, their ability to undergo reversible volume phase transitions in response to external stimuli such as a change in pH,[14-16] temperature,[17,18] ionic strength of the surrounding medium,[19,20] nature of the solvent,[21,22] and the effect of an external electromagnetic field[23,24]. The swelling and deswelling transitions of stimulus-responsive microgels are governed by the imbalance between the repulsive and attractive forces acting within the molecules.

Several methods have been developed to enhance the response rate of microgels to the surrounding environment. Incorporation of hydrophilic polymers into the P(NIPAm) microgel network by interpenetrating polymer network (IPN) technologies has been reported to be an effective approach [25-27]. Zhang et al. synthesized a thermo-sensitive hydrogel with macroporous structures using a pore-forming strategy and expanded network structures [28]. Okano et al. achieved rapid deswelling volume changes in a comb-type grafted P(NIPAm) hydrogel with freely mobile chains grafted on a backbone network [29,30]. To increase the response rate of dual thermo- and pH-responsive microgel, several distinctive methods have also been reported. For instance, Lee et al. generated a series of rapidly responsive comb-type hydrogels by grafting thermo-responsive P(NIPAm) chains onto the backbone of
alginate networks and chitosan chains [31]. Asoh et al. developed rapidly responsive porous semi-IPNs composed of P(NIPAm) networks and PAAc linear chains [32]. Kishi et al. prepared fast responsive and pH-/thermo-responsive copolymer microgel by creating micro-porous structures with γ-ray irradiation treatment [33]. However, because of their appeal, dual thermo- and pH-sensitive microgels with rapid responsivity continue to increasingly attract attention. Thus, in order to promote new applications, it remains essential to develop multi-responsive microgel with new synthetic strategies.

2. Experimental

Materials: N-Isopropylacrylamide (NIPAm) and Acrylic acid (AAc) were purchased from Sigma-Aldrich. N,N-methylenebis(acrylamide) (BIS) was obtained from ACROS. NIPAm was recrystallized from hexane–toluene (1:1 volume ratio) mixture and dried in an oven. Acrylic acid (AAc) was purified by distillation under reduced pressure to remove hydroquinone inhibitor whereas N, N-methylenebis (acrylamide) (BIS) was used without further purification.

Co-Polymer Microgel Synthesis: Poly(NIPAm-Co-AAc) microgel was prepared by free radical emulsion polymerization. SDS was used as emulsifying agent. 1.4 g NIPAm, 0.033 g BIS and 0.095 mL of AAc were dissolved in 100 mL of deionized water in a three-necked round bottom flask equipped with a condenser and nitrogen inlet. The reaction mixture was heated at 70°C under a gentle stream of nitrogen. After the passage of one hour polymerization was started with 5 mL Ammonium per sulphate (APS) (0.0108g dissolved in 5mL of aqueous solution) at 70°C under constant stirring and continued supply of nitrogen for 5 hours. The resulting polymer microgel was refined by dialysis for 14-21 days (Spectra/Por molecular porous membrane tubing, cutoff, 12000-14000) with very frequently changed water at room temperature to remove unreacted monomers followed by centrifugation. Finally the microgel was dispersed in 100 mL of deionized water and labelled as G-1. Another microgel sample was synthesized using the same procedure but different amount of the emulsifier. This sample was labeled as G-2. The polymer microgel synthesis is shown by the equation in Figure 1 and chemical composition of both samples synthesized is shown in Table 1.

| Sample Code | NIPAm  | AAc | BIS  | SDS  | APS (0.06M) | H2O   |
|-------------|-------|-----|------|------|------------|-------|
| G-1         | 1.4 g | 0.095 mL | 0.033 g | 0.057 g | 5 mL | 100 mL |
| G-2         | 1.4 g | 0.095 mL | 0.033 g | 0.114 g | 5 mL | 100 mL |
Characterization: FTIR spectroscopy was used to identify different functional groups present in the microgels. By interpreting the infrared absorption spectrum, the chemical bonds in a molecule can be determined. FTIR spectroscopy confirmed the chemical structure of product microgel P(NIPAm-co-AAc) and helped to estimate the completeness of polymerization reaction. Light scattering was used to study the solution behavior of microgels. The static and dynamic light scattering were performed using a standard laser light scattering spectrometer BI-200SM motor-driven goniometer equipped with BI-9000AT digital autocorrelator and a cylindrical 22mW uniphase He–Ne laser (wave length = 637nm) and BI-ISTW software. Dynamic light scattering experiments were carried out at different temperatures ranging from 15-70 °C and at different pH values ranging from 2-9 at angle 90o. DLS of the microgel was also conducted in the presence of different concentrations of NaCl in order to study the effect of electrolyte on the polyelectrolyte i.e. P(NIPAm-co-AAc) microgel. The experiment duration was 5 min. Each experiment was repeated two or more times. In DLS, $\Gamma$ is related to the translational diffusion coefficient $D$ by $(\Gamma/q^2)C\rightarrow0,q\rightarrow0 = D$, where $q = (4\pi/\lambda) \sin(\theta/2)$ with $\lambda$, $\theta$, and $\eta$ being the solvent refractive index, the wavelength of the incident light in vacuum, and the scattering angle, respectively. $D$ was converted to a hydrodynamic radius ($R_h$) distribution by using the Stokes-Einstein equation, $R_h = (kT/6\pi\eta)D^{-1}$, where $T$, $k_B$, and $\eta$ are the absolute temperature, the Boltzmann constant, and the solvent viscosity, respectively. The Static Laser Light Scattering experiment was carried out at 25°C. Dilute solution (concentration approaches to zero) of microgel was used to find the molar mass and radius of gyration according to Zimm equation.

3. Results and discussions
Multi-responsive copolymer microgels, poly[N-isopropylacrylamide-co-acrylic acid] [P(NIPAm-co-AAc)], were synthesized by using different amounts of emulsifier through emulsion polymerization. The FTIR spectra of crosslinked copolymer microgels G-1 and G-2 are shown in Figures 2 and 3.
respectively. All the absorption peaks observed in the spectra of the microgel samples are given in table 2. The FTIR spectra, depicts bands for –CH2 (b) near1550 cm -1 and for C=O near 1620 cm -1 but no peak for C=C. The details of absorption ranges are also shown in table 2, which shows that polymerized microgels contain all the main functional groups required to confirm the chemical structure. The observed absorption bands are in good agreement with the reported range shown in Table 2. Both the spectra show similarity in absorption bands i.e. close values are observed for peaks of the same functional groups.

Table 2. Summary of FT-IR absorption bands of different chemical bonds of P(NIPAm-co-AAc) microgels G-1 and G-2.

| Chemical Bond /Functional Group | Observed Peaks for G-1 (cm-1) | Observed Peaks for G-2 (cm-1) | Range of Peaks (cm-1) |
|---------------------------------|-------------------------------|-------------------------------|----------------------|
| C-N                             | 1150.00                       | 1153.10                       | 1100-1200            |
| CH2 (b)                         | 1550.34                       | 1533.79                       | 1460-1550            |
| C=O (amide)                     | 1616.55                       | 1624.83                       | 1600-1750            |
| C-H (s) sp3                     | 2973.79                       | 2965.52                       | 2900-3000            |
| N-H (s)                         | 3305.00                       | 3310.50                       | 3300-3500            |

4. Thermo-responsive behavior of poly(NIPAm-co-AAc) microgels

Figure 4 shows the thermo-responsive behavior of microgel. The polt shows the decrease in hydrodynamic radius of poly(NIPAm-co-AAc) microgel with temperature (15-60°C) at constant pH. At lower temperature, it is observed that the size of the microgel is large but as the temperature is increased, the size of the microgel is slightly decreased up to 38°C. After 38°C there occurs a dramatic decrease in the size of the microgel and this transition in size is called volume phase transition while the temperature at which this transition takes place is named as volume phase transition temperature (VPTT). Actually at low temperatures, microgel is highly solvated due to hydrogen bonding between the amide residues on the polymer chain and the water molecules. Hence at low temperature, the polymer-solvent interactions are stronger than the polymer-polymer interactions and poly(NIPAm-co-
AAc) exists in a swollen state. At elevated temperature, the hydrogen bonds between the polymer and the water molecules are broken, leading to an entropically favored expulsion of water from the polymer network. Consequently, the polymer-polymer interactions become stronger than the polymer-solvent interactions, resulting in phase separation as the polymer assumes a collapsed (shrunken) state. Hence, at $T < VPTT$ the microgels are individually swollen with water and at $T > VPTT$ the microgels deswell due to expulsion of water from the microgel interior. It is reported that $VPTT$ of homopolymer microgel P(NIPAm) occurs at 32°C in water [34]. But our copolymer microgel is composed of N-isopropylacrylamide and Acrylic acid for which $VPTT$ was observed at 38°C at pH 7. It shows the $VPTT$ of our poly(NIPAm-co-AAc) microgel system is higher than the $VPTT$ of poly(NIPAm) microgel. This increase in transition temperature is observed because of the increase in hydrophilic nature of the microgel particles because of presence of AAc.

5. Thermo-responsive behavior of the microgels at different pH values
The swelling and deswelling behavior of the microgels G1 and G2 as a function of temperature at different pH values ranging from 3 to 9 is shown in figures 6 and 7. There is a continuous decrease in the $VPTT$ and hydrodynamic radius (Rh) as we go on decreasing the pH. In swollen state maximum size of gel is observed at pH 9, but the transition is less pronounced and after transition there is less reduction in hydrodynamic radius (Rh) of microgel. This is because in basic media, the microgel is in hydrophilic state and the pH effect is dominant over the thermosensitivity of microgel. Minimum size is observed at pH 3 in swollen state i.e.; at low temperature (below $VPTT$) but thereafter the $VPTT$ instead of going into collapsed state by showing reduction in size, Rh increases abruptly indicating the aggregation of colloidal particles at elevated temperature. A reasonable explanation for this different phenomenon of microgel is inter-particle hydrogen bonding interactions between the carboxyl group of the acrylic acid side chain and the amide group of NIPAm which seems to favor larger aggregates. The decrease in size and $VPTT$ of microgel with decrease in pH means that our microgel is more temperature sensitive at lower pH because it undergoes transition at lower temperature. The observed $VPTT$ is higher at high pH because P(NIPAm-co-AAc) becomes more pH sensitive at high pH as acrylic acid deprotonates its carboxyl moieties in alkaline solution, due to which repulsion between these groups increases.

6. Effect of Emulsifier (Surfactant)
Figure 5 shows that both samples of microgel (G-1 and G-2) underwent phase transition on changing temperature from 15°C to 60°C at pH 7. But difference in Rh size was observed between two synthesized microgel samples. Different amounts of SDS were used as emulsifier during emulsion polymerization. The microgel with lower SDS concentration (G-1) has larger size than the microgel with higher SDS concentration (G-2). Surfactants play a major role during the particle nucleation and growth, with direct impact on latex particle size, size distribution, polymerization rate, molecular weight and particle morphology. Emulsion polymerization is propagated in micelles which make more stable structure by surrounding the monomer, usually in continuous phase (water) [35]. When surfactant concentration is high, more micelles are formed with smaller size. Due to this small size, micelles can accommodate small amount of monomers which react to produce polymer particles with smaller size. The smaller size of the hydrodynamic radius of G-2 could be ascribed to the higher SDS concentration in G-2 than G-1.

7. Effect of Medium pH
The pH dependence of the particle size of the poly(NIPAm-co-AAc) microgel is shown in Figure 8. Small size is observed at lower pH values, but size increases with the rising pH. This is due to deprotonation of the acrylic acid and the resultant electrostatic repulsion between the negatively charged carboxylate residues. The ionized structure provide increased electrostatic repulsion between chains and hence the hydrophilicity of network. Under these conditions, microgels are capable of uptaking large amounts of solvent and forming very loose structure consequently the hydrodynamic radius of microgel
increases. It is evident from Figures 8 and 9 that the size of gel particle and swelling critically depend on the pH of medium. In Figure 9 hydrodynamic radius is higher at 15°C and 25°C because both temperatures are below VPTT and microgel is in swollen state. As 35°C is just near the collapsing temperature that’s why the size of G-1 starts decreasing as compared to 15 and 25°C at lower and higher pH values. But G-2 shows larger size at lower pH at 35°C because of greater concentration of surfactant, the aggregates formation takes place earlier as shown in Figure 10. Similar behavior is observed at 45°C for both the microgel samples at low and high pH values. It is observed that at lower pH values (2, 3) the size is surprisingly large. This is due to the formation of aggregates at higher temperature and lower pH. Because at lower pH the carboxylic acid groups are largely protonated and have little effects on phase transition. There is a small change in size at pH 9 at different temperatures (15-45°C). This is because at higher pH the microgel is less temperature responsive and the pH effect is dominant to increase its size.

8. Influence of salt concentration on the swelling behavior of the microgels

The hydrodynamic radius in the presence and absence of salt (NaCl) is given in figure 11. It is observed that the presence of salt decreases the size of microgel particles and VPTT also shifts to lower value. In the absence of salt at pH 9 the VPTT is 42°C but when 0.05M NaCl is added into the microgel the VPTT decreases to 34°C which is a large shift. In general, an increase in ionic strength decreases the Debye screening length, and hence will diminish the repulsive electrostatic forces between the dissociated acrylic acid groups at pH 9. Therefore, it is expected that addition of salt will have a strong effect on the swelling behavior. Effect of salt on the microgel size is investigated by changing the NaCl concentrations up to 0.5M. It is noted that the size of the swollen particles at low temperature decreases with increasing salt concentration. This effect could be attributed to reduced osmotic swelling pressure, because at higher salt concentration the concentration gradient between the NaCl concentrations inside and outside the microgel particles decreases. At low pH, the effect of salt on the microgel size is shown in Figure 12. At lower temperature the size was decreased but after VPTT, due to formation of aggregates size was increased further by the addition of salt. Figure 13 shows the salt effect on the microgels comparing both samples (G-1 and G-2). There is more reduction in size of G-2 on adding salt because of higher surfactant concentration. We have observed that multi-responsive microgels show transition in their size when their external environment is changed. Therefore, the VPTT can be shifted by changing the stimuli. The summary of VPPT of P(NIPAM-co-AAc) microgels is given in the tables 3 and 4 under different external conditions.

| pH  | VPTT of G-1 (°C) | VPTT of G-2 (°C) |
|-----|-----------------|-----------------|
| 3   | 34              | 32              |
| 5   | 36              | 36              |
| 7   | 38              | 38              |
| 9   | 42              | 40              |
Table 4. Summary of VPTT of microgels in different NaCl conc. at pH 3 and pH 9

| NaCl (M) | VPTT at pH 3 (oC) | VPTT at pH 9 (oC) |
|----------|-------------------|-------------------|
|          | G-1 | G-2 | G-1 | G-2 |
| 0.00     | 34  | 32  | 42  | 40  |
| 0.05     | 30  | 30  | 34  | 34  |
| 0.1      | 28  | 28  | 30  | 30  |
| 0.5      | 26  | 26  | 28  | 28  |

Figure 4. \( R_h \) of G-1 as a function of temperature at pH 7

Figure 5. \( R_h \) of G-1 and G-2 as a function of temperature at pH 7

Figure 6. \( R_h \) of G-1 vs Temperature at different pH

Figure 7. \( R_h \) of G-2 vs Temperature at different pH
Figure 8. Hydrodynamic radius vs pH at 25°C

Figure 9. Rh of G-1 vs pH at different temperatures

Figure 10. Rb of G-2 vs pH at different temperatures

Figure 11. Rh vs T of G-1 in the presence of 0.0M and 0.05M NaCl at pH 9.

Figure 12. Rb of G-1 vs T at 0.0M and 0.05M NaCl at pH 3

Figure 13. Rb vs NaCl concentration at 25°C and pH 9
9. Static Laser Light Scattering (SLLS)
The Static Laser Light Scattering experiment was carried out at 25°C to find the Molar mass (Mw) and radius of gyration (Rg) of both samples as shown in the table 4.4. As clear from the table, both the samples of P(NIPAm-co-AAc) microgel have the same molar mass but different values of radii of gyration. We used different amount of surfactant during polymerization keeping the monomers and crosslinker concentrations the same in both samples. After synthesis the surfactant was removed by dialysis. There is a small difference in the values of radii of gyration of both the microgels because static light scattering measurements were performed at 25°C which is below VPTT and microgel is in swollen state.

Table 5. Static laser light scattering results of micogels

| Microgel sample | Mw (g mol⁻¹) | Rg (nm) |
|-----------------|--------------|---------|
| G-1             | 5 x10⁵       | 137.4   |
| G-2             | 5 x10⁵       | 134.8   |

10. Conclusion
Our results indicate that P(NIPAm-co-AAc) microgel is multi-responsive. It is in hydrated state at low temperature and show response upon exposure to various environmental stimuli such as change in pH, temperature and ionic strength. Emulsifier concentration has an important role during emulsion polymerization. The size of microgel decreases with increasing the concentration of surfactants and vice versa. Presence of salt also suppresses its electrolyte behavior by decreasing the VPTT. Increasing the pH up to basic value, VPTT increases and increasing the salt concentration VPTT decreases. At pH 7 and very low salt concentration, VPTT is near human body temperature, so it can be used for drug delivery. The responsive properties of these microgels make them ideal candidates for biological and optical applications as smart materials.

11. References
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