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SHORT COMMUNICATION

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A comparison of the swelling behaviour of copolymer and interpenetrating network microgel particles

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Abstract A comparison of the swelling behaviour of two types of hydrogel particles, namely, random poly[(acrylic acid)-*co*-(acrylamide)] [P(AAc-*co*-AAm)] particles and PAAc/PAAm interpenetrating network (IPN) particles, has been made using temperature and pH as the triggers. Both types of particles were synthesised by inverse microemulsion polymerisation. The conversion yield of AAc was found to be around 60 wt% due to the partition of this monomer between the aqueous and organic phases. The AAc content was thus lower in the final particles than in the initial composition. Both types of hydrogel particle exhibit an upper critical solution temperature associated with the breakage of the polymer–polymer hydrogen bonds. The maximum swelling ratio occurred in both cases at approximately equimolar AAc and AAm content of the particles. A sharper swelling transition was observed for the PAAc/PAAm IPN particles. This is because of the co-operative nature of the interactions between the PAAc and PAAm chains, the so-called "zipper effect". A very much higher swelling ratio was obtained using pH as the trigger compared to using temperature. This difference in behaviour is related to the relative strengths of the forces involved in the particle swelling. Electrostatic repulsion forces, associated with the AAc dissociation with increasing pH, are much stronger than the hydrogen bonds.

Key words Microgel particles · Interpenetrating networks · Copolymer latex particles · Latex swelling

Introduction

Polymer gels, which are capable of expanding their structure in response to changes in some external conditions such as pH [1], osmotic strength [2], solvent composition [3] and temperature [4], have been investigated for the past 20 years or so. These materials have received growing attention for applications in various technologies, including medical applications [5]. For example, controlled drug release may be achieved using the swelling/collapse properties of such gels. The subject of aqueous-based, thermosensitive gels and their potential medical applications has been reviewed by Okano [6]. He showed that two general classes of gel could be synthesised:

1. Simple hydrogels, such as poly(*N*-isopropylacrylamide), or related copolymers, which deswell on heating above some temperature, usually closely related to the lower critical solution temperature of the corresponding homopolymer (or copolymer) in solution [7].
2. Interpenetrating polymer network (IPN) hydrogels containing two different types of polymer molecules [8].

Hydrogels may exhibit swelling, as well as deswelling, with increasing temperature. The former situation pertains when hydrogen bonds between two types of polymer segments, for example, acrylic acid (AAc) and acrylamide (AAm), dominate the interactions within the gel. Also, poly(AAm) (PAAm) and poly(AAc) (PAAc) in solution are known to be homopolymers which mutually interact, i.e. form associative complexes, by intermolecular hydrogen bonding at low temperature [9]. The strength of the hydrogen bonds decreases with increasing temperature. Thus, the PAAc/PAAm complexes dissociate at higher temperature, due to breakage of the intersegment hydrogen bonds, accompanied by simultaneous hydration of the separate polymers [10, 11].

Thermosensitive poly(AAm-*co*-butyl methacrylate)/PAAc IPN hydrogels have been synthesised by Katono et al. [8]. Their complex formation and dissociation, with increasing temperature, has been described as a "zipper" process [10] in which the polymer–polymer hydrogen bonds are disrupted sequentially and are replaced by association of the segments with water molecules instead. PAAc/PAAm IPN hydrogels similarly swell with increasing temperature. Katono et al. [8] have demonstrated the principle of controlled drug release (using ketoprofen as the drug) from PAAc/PAAm IPN hydrogels in response to a temperature increase.

Microgel particles should, in principle, be more effective as delivery systems than macroscopic gels for agrochemical or medical applications. They have a much high interfacial area per unit mass of gel, effecting much greater exchange rates. Also, they may be readily packed in columns or used internally in the body. The objective of the present work was to synthesise and characterise the swelling behaviour of thermosensitive poly(AAm-*co*-AAc) microgel particles. The preparative method used was inverse microemulsion polymerisation. More traditional methods for the preparation of latex particles, such as dispersion or emulsion polymerisation, cannot be used with polar monomers such as AAm and AAc because of their high solubility in water. The inverse microemulsion polymerisation approach was first proposed by Birrenbach and Speiser [12] for protein encapsulation, and it has been described in detail by Candau et al. [13]. This technique is now classically used for enzyme immobilisation [14, 15].

This paper describes the preparation and characterisation of both copolymer and IPN particles containing various AAc/AAm ratios and different cross-linker (methylenebisacrylamide, MBAAm) amounts. Their swelling behaviour has been investigated in response to both temperature and pH changes.

Experimental

Materials

AAm (Aldrich) was recrystallized from ethanol. AAc (Aldrich) was distilled under reduced pressure. MBAAm (Aldrich), ammonium persulfate (Aldrich) and *N*, *N*, *N′*, *N′*-tetramethylethylenediamine (TEMED) (Aldrich) were used without further purification. Sodium bis(2-ethylhexyl)sulfosuccinate (Aerosol OT, AOT) and polyethylene glycol laurylether (Brij 30) (Aldrich) were used as emulsifiers.

Synthesis of random PAAc-*co*-AAm particles

These particles were synthesised by an inverse microemulsion polymerisation route [14]. All the polymerisation reactions were performed at the same composition: 13.3% surfactant, 81% oil (hexane), 5.7% aqueous solution. In a typical microemulsion polymerisation, AOT and Brij 30 were combined in a 33/17 weight ratio and were dissolved in hexane. The aqueous phase consisted of ammonium persulfate, AAm, AAc and MBAAm, this was dispersed in the oil phase using magnetic stirring to form an inverse microemulsion. Before polymerisation, the system was purged with nitrogen. The microemulsion was cooled to 0 °C for 5 min. Then the polymerisation was initiated by the addition of TEMED (200 μl) and the reaction was allowed to proceed at 25 °C for 2 h. Thereafter, the hexane was distilled under reduced pressure, and the particles were precipitated by addition of methanol or ethanol. Finally, the particles were dispersed in 10 ml distilled water and dialysed overnight to remove the surfactant and the free polymer chains.

Synthesis of PAAc/PAAm IPN particles

The particles were synthesised in two steps. Firstly, pure PAAm particles were synthesised by inverse microemulsion polymerisation following the same procedure described in the previous section. When the reaction was complete the system was cooled to 0 °C. The reaction was terminated by admitting air to the reaction vessel. The second monomer, AAc, was added, together with the cross-linker and the initiator (dissolved in the minimum amount of water required, about 0.5 g). The second polymer was then synthesised at 25 °C, in the presence of the first polymer. The resulting PAAc/PAAm IPN particles were purified using the same cleaning procedure described earlier.

Particle characterisation

Monomer composition

The particle dispersions were dialysed for several days against 'Milli-Q' water to remove the residual surfactant in order to perform an elemental analysis. The samples was first freeze-dried, then heated at 50 °C under partial vacuum (about 10^{-1} bar) in the presence of phosphorous pentoxide. The elemental analysis was carried out using a CHN EA 1108 elemental analyser (Carlo Erba Instruments).

Particle size

Hydrodynamic particle diameters were determined by photon-correlation spectroscopy (PCS) using a Brookhaven Instruments Zeta Plus apparatus: this incorporates a 635 nm He-Ne laser and operates at a fixed scattering angle of 90°. The effect of the temperature on the particle swelling was studied at pH 3 over the temperature range 10–55 °C. The influence of pH on the particle swelling was investigated, in 0.05 M citrate buffer solution, over the pH range 3–6.2.

Results and discussion

Particle characterisation

A series of PAAc-*co*-PAAm copolymer latex particles were synthesised by inverse emulsion polymerisation. In the reaction medium the cross-linker content was varied from 4 to 16 wt% and the ratio of AAc:AAm was varied from 0.65 to 1.8 (molar ratio). Pure PAAc and PAAm particles were also synthesised and used as the references for this study. According to Daubresse et al. [14], conversion of AAm monomer is virtually 100% during PAAm particle synthesis by inverse microemulsion polymerisation, but only around 60% conversion was found for AAc monomer. These different conversions are probably due to the differences in the partition of the two different monomers between the aqueous and the organic phases. The AAc/AAm molar ratio for the synthesised particles, the initial monomer composition and the conversion yield are all listed in Table 1 for the various particles synthesised in this work. The results obtained confirm the difference in conversion for the two monomers. That is, pure PAAm particles were synthesised with 96 wt% conversion, while only 58 wt% conversion was found for pure PAAc particles. Correspondingly, the AAc content in the final copolymer particles is also lower than the initial composition in the reaction mixture.

The hydrodynamic diameter of the various particles at 25 °C was determined using PCS. The scattering intensity–size distribution for the pure PAAm particles is shown in Fig. 1 (it should be remembered that larger particles scatter with a much higher intensity than smaller particles). A bimodal distribution is observed. Similar distributions were found for the other particles synthesised in this work. For the pure PAAm particles, it may be concluded that most of the particles have a hydrodynamic diameter around 50 nm, but there are a few bigger particles around 150 nm. This second particle population tends to decrease in number with increasing time of ultrasound irradiation, suggesting that they correspond to aggregated particles; however, complete deaggregation of the latex particles could not be achieved in this way. The main population centred at 50 nm exhibits a narrow size distribution; the inverse microemulsion droplets from which they are formed were reported by Curt [16] to be also fairly monodisperse.

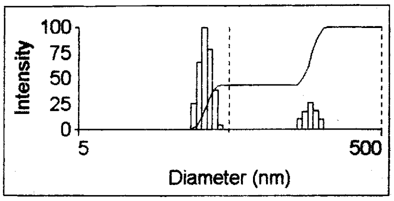

Fig. 1 Size distribution of poly(acrylamide) (*PAAm*) particles before sonication (the diameter is plotted on a logarithmic scale)

Temperature-induced swelling of copolymer particles

The hydrodynamic diameters of the pure PAAc and PAAm particles, and also of the random PAAc-*co*-AAm particles, are shown in Fig. 2 as a function of temperature at pH 3, where the AAc moieties are largely uncharged. The pure PAAm particles exhibit no temperature dependence of the particle diameter between 10 and 55 °C, i.e. they do not swell over this temperature range. This suggests that the hydrogen bonding between AAm units is relatively strong, and stable, at least over this range of temperature. On the other hand, the

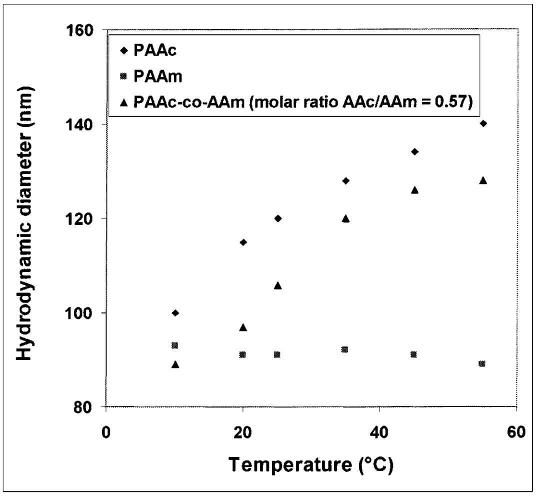

Fig. 2 Swelling behaviour of pure poly(acrylic acid) (*PAAc*) and PAAm particles and PAAc-*co*-PAAm copolymer particles (AAc/AAm molar ratio = 0.57) as a function of temperature at pH 3

Table 1 Yield of conversion, initial monomer composition and acrylic acid (*AAc*)/acrylamide (*AAm*) ratio for the synthesised particles

Nature of the particles	Conversion yield (wt %)	Theoritical ratio AAc/AAm (mol:mol)	Calculated ratio of AAc/AAm (mol:mol)
PAAc particles	58	–	–
PAAm particles	96	–	–
Random PAAc-*co*-AAm particles	79	0.67	0.34
Random PAAc-*co*-AAm particles	77	1.01	0.57
Random PAAc-*co*-AAm particles	75	1.52	0.96
Random PAAc-*co*-AAm particles	69	1.86	1.21
PAAc/PAAm interpenetrating network particles	76	1.52	0.9

hydrodynamic diameter of the pure PAAc particles does increase with increasing temperature, as described elsewhere [6, 17]. This must be due to the breakage of the (presumably weaker) hydrogen bonds between the AAc units on heating. Note, however, that homopolymer PAAc in solution does not exhibit an upper critical solution temperature.

For all the random PAAc-*co*-AAm particles synthesised here, the particle diameter increased with increasing temperature, as shown in Figs. 2 and 3. A relatively small swelling ratio (about 1.7) was observed over the temperature range 10–35 °C for the particles having a comparatively low AAc/AAm ratio of 0.34. The swelling ratio increased to 1.7 and above 3.2, on increasing the AAc/AAm ratio to 0.34 and 0.96, respectively, but note that the swelling also occurred over an increasing range of temperature. At the highest AAc content (1.21), the swelling ratio decreased again somewhat. Maximum swelling was, therefore, obtained for the particles prepared at an AAc/AAm ratio of 0.96, i.e. close to equimolar AAc and AAm content in the particle network.

Similar results were observed for IPN macrogels composed of poly(ethylene oxide) (PEO) and poly(*N*-acryloylpyrrodine) (PAPy) by Bae et al. [18]. They investigated the relationship between the swelling ratio and the (EO)/(PAPy) ratio within the IPNs. The IPNs with an equimolar ratio of (EO)/(PAPy) exhibited the largest swelling change with increasing temperature.

In order to study the effect of cross-linker content on the degree of swelling, five latex particles were prepared with varying cross-linker content, but at equimolar AAc and AAm contents (in order to maximise the swelling ratio, as described previously). The cross-linker content in the feed medium varied from 3.2 to 15 wt%. The swelling ratio of the particles is shown as a function of temperature for the five latices in Fig. 4. It is clear that the swelling ratio, at a given temperature, decreases as the amount of cross-linker increases.

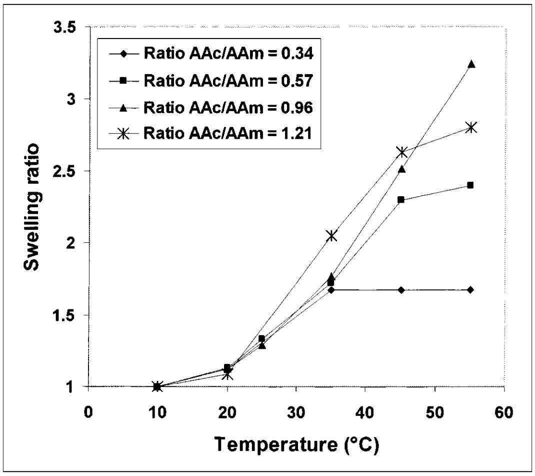

Fig. 3 Influence of the copolymer composition on the particle swelling as a function of temperature at pH 3

Comparison of the temperature-induced swelling of IPN and copolymer particles

The swelling behaviour of PAAc/PAAm IPN and PAAc-*co*-AAm random copolymer particles (both containing near equimolar amounts of AAc and AAm) as a function of temperature is compared in Fig. 5. The PAAc/PAAm IPN particles exhibit swelling behaviour

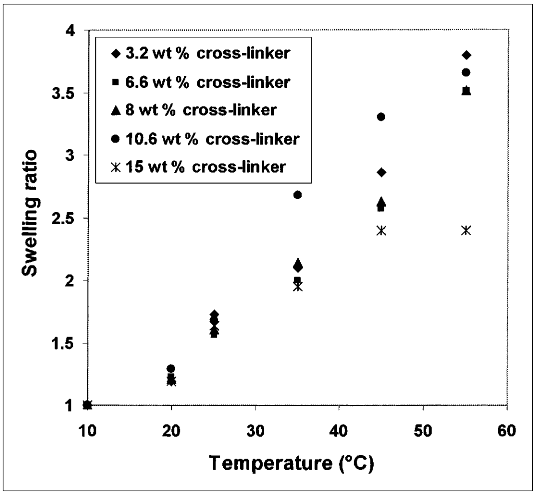

Fig. 4 Effect of the cross-linker content on the copolymer particle swelling as a function of temperature at pH 3

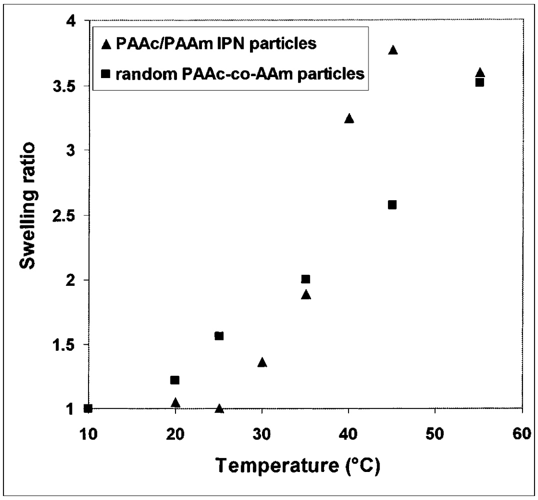

Fig. 5 Influence of the network nature on the particle swelling as a function of temperature for an AAc/AAm molar ratio of 0.96. *IPN* means interpenetrating network

over a much narrower range of temperatures (25–45 °C) compared to the PAAc-*co*-PAAm copolymer particles. These show continuous swelling behaviour from 10 °C to well beyond 55 °C (the highest temperature at which measurements were made). The sharper swelling transition for the IPN particles is due to the cooperative polymer–polymer hydrogen bonding interactions between PAAc and PAAm, i.e. the so-called "zipper effect" referred to earlier [6, 10, 11], in which dissociation of segment–segment hydrogen bonds progresses sequentially along the chains in a kind of "domino effect". Such cooperation is clearly less efficient for copolymers; consequently, the swelling in that case occurs over a broader range of temperatures.

pH-induced swelling of copolymer particles

Figure 6 shows how the hydrodynamic diameter of the PAAc-*co*-AAm particles varies with pH for the five copolymer latices having different cross-linker contents. The diameter of the particles increases with increasing pH, the magnitude of the swelling increasing with decreasing cross-linker content, as expected. At higher pH values the particles are in an extended swollen state due to the electrostatic repulsion between segments within the particles, arising from dissociation of the AAc groups. The swelling occurs over the pH range 2.8–5.8; this is consistent with the AAc pK_a value of 4.25. The swelling ratio obtained using pH as the trigger was observed to be very much higher (above 300) compared to that obtained with temperature as the trigger. This remarkable difference in behaviour is related to the strength of the forces involved in the particle swelling. When pH is used as the trigger, strong electrostatic repulsion causes the gel swelling, whereas polymer–polymer hydrogen bond dissociation is responsible for the swelling behaviour when temperature is used as the trigger.

Influence of a combination of pH and temperature on copolymer particle swelling

The variation of the hydrodynamic diameters of PAAc-*co*-AAm particles, synthesised with 6.6 wt% MBAAm in the feed medium, is presented as a function of temperature at pH values of 3.9, 4.2 and 4.8 in Fig. 7. In all three cases no significant change in hydrodynamic diameter was observed on increasing the temperature over the range 20–55 °C. The swelling ratio obtained by increasing the pH to 3.9 is already higher than that obtained by breaking the hydrogen bonds at higher temperatures. That is to say, pH is the dominating trigger; this because electrostatic repulsion forces overwhelm hydrogen-bonding effects. Consequently, a combination of pH and temperature cannot be used to control particle swelling.

Conclusion

Random PAAc-*co*-PAAm particles exhibit a positive swelling response to an increase in temperature due to the breakage of segment–segment hydrogen bonds. The swelling ratio was found to be maximum for an equimolar AAc/AAm ratio in the particle network and to decrease with increasing cross-linker content. Compared to PAAc-*co*-AAm copolymer particles, PAAc/PAAm IPN particles exhibit swelling transitions over a much narrower range of temperature. This sharper

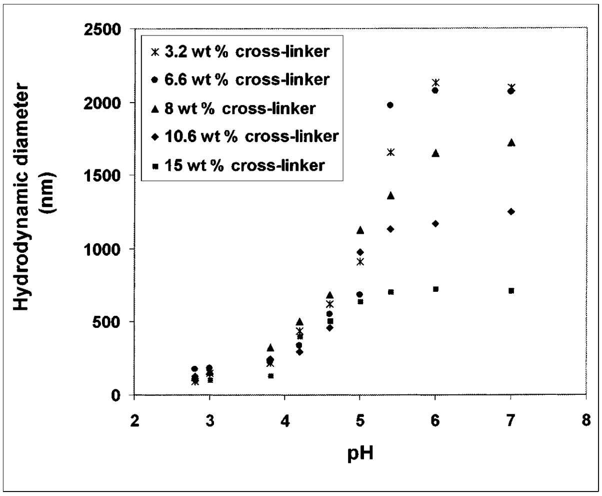

Fig. 6 Effect of the cross-linker content on the copolymer particle swelling in response to pH variation at 25 °C

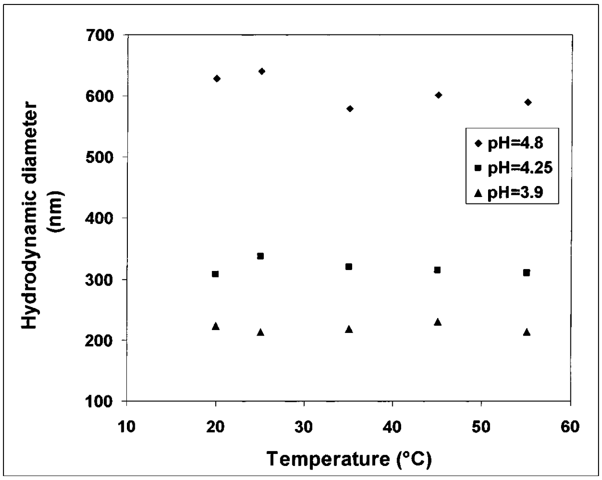

Fig. 7 Swelling behaviour of the copolymer particles in response to a combination of pH and temperature as the triggers

transition is due to the cooperative nature of the segment–segment interactions of the distinct PAAc and PAAm chains (the “zipper effect”).

Much stronger swelling of the copolymer latices was obtained using pH as the trigger compared to using temperature. This is because of strong intersegmental electrostatic repulsion effects, as a consequence of AAc deprotonation within the particles, at higher pH values.

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