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ORIGINAL CONTRIBUTION

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Stability and thermosensitive properties of various poly(*N*-vinylcaprolactam) microgels

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Abstract Thermally responsive microgels have been synthesised by polymerising *N*-vinylcaprolactam under various conditions. Stabilisation of the latices was of special interest and, thus, electrostatically, sterically, and electrosterically stabilised particles were prepared. Electrostatic stabilisation was achieved by the use of an ionic initiator and/or an ionic detergent. Steric stabilisation was realised through a macromonomer technique, where polymerisable poly(ethylene oxide)-containing macromonomers were utilised as a detergent. Capillary electrophoresis was used to compare the electrokinetic properties of the polymer particles. All the product particles show thermal behaviour typical of poly(vinylcaprolactam), but sterically stabilised ones are superior in the stability against added electrolytes.

Keywords Poly(*N*-vinylcaprolactam) · Macromonomer technique · Microgel particles · Capillary electrophoresis · Colloidal stability

Introduction

Poly(*N*-vinylcaprolactam) (PVCL) is a polymer with amphiphilic and responsive character. It dissolves in cold water but undergoes a sudden conformational change, collapses and precipitates, upon heating. In this sense, PVCL closely resembles a well-known thermally responsive polymer, poly(*N*-isopropylacrylamide) (PNIPAM). Both polymers have a lower critical solution temperature (LCST) in water around 32 °C. Several potential applications have been suggested for both polymers; however, PVCL is expected to be more biocompatible than PNIPAM and, thus, to have a wider range of applicability [1, 2].

The syntheses of responsive polymers with different topological structures, like macroscopic, micro, or nanoscaled networks, is interesting not only for fundamental understanding of the properties of these materials but also for practical applications. Recently, microgels have attracted noticeable attention owing to the possibility of utilising them in constructing intelligent drug release systems [3, 4]. For demanding biotechnological applications or for those where polymer particles are used to bind metal ions, responsive polymer particles stable in various electrolyte solutions are needed. The stability of responsive microgels in electrolyte solutions has recently been studied using PNIPAM [5] and poly(*N*-isopropyl methacrylamide) (PNIPMAM) [6]. Methods of synthesising cross-linked PVCL particles stable against addition of electrolytes have not been studied so far.

The stability of aqueous polymer dispersions can be enhanced in several ways. In general, three methods are used: electrostatic, steric, or electrosteric stabilisation.

Of these, the first, based on the repulsion of surface charges of the particles, is most common. Electrostatic stabilisation is typically realised by using either ionic initiators or ionic surfactants in the polymer syntheses conducted in emulsions. Particles are obtained which repel each other owing to their electric charges. The strength of the repulsion force between the particles and the thickness of the electric double layer may be altered by changing the ionic strength of the aqueous medium [7]. At high electrolyte concentrations the repulsion between the particles vanishes and the coagulation out of the aqueous phase is fully diffusion controlled [8, 9]. Steric stabilisation may be achieved by grafting the particles with, for example, poly(ethylene oxide) (PEO) or with some other water-soluble polymer. The use of PEO is often considered advantageous because PEO considerably prevents the adsorption of proteins onto polymer surfaces and, thus, increases the biocompatibility of the polymer [10].

Steric stabilisation by nonionic hydrophilic polymers is independent of ionic strength, assuming that the added electrolyte does not change the thermodynamic quality of the aqueous solvent. PEO has been shown to be an effective steric stabilisor even at high electrolyte concentrations as long as the molecular mass of PEO is high [11]. Electrosteric stabilisation is a combination of electrostatic and steric stabilisation.

In this work, PVCL particles with varying surface charges and with different surface structures were synthesised. Thus, it was possible to compare the effectiveness of the stabilisation in each case and further to study the effects of electric charges and nonionic polymeric grafts on the thermal properties of the polymers. Particles stabilised electrostatically, sterically, and electrosterically, were prepared. Negatively charged particles were obtained by using potassium persulphate (KPS) ionic initiator, which upon decomposition forms sulphate anion radicals that covalently bind to the growing polymer. Ionic surfactants, like sodium dodecyl sulphate (SDS) can bind to the polymers and, in spite of a thorough purification of the product, introduce an electric charge [12]. Nonionic microgel particles were prepared in emulsions where both the initiator and the surfactant are electrically neutral. Stable microgels were obtained by the use of amphiphilic PEO-containing macromonomers.

Four samples of stabilised PVCL microgels were synthesised using both ionic and nonionic initiators and surfactants. The initiators and surfactants are shown in Fig. 1. Thermal and electrokinetic properties of the polymers are compared. The stability of the particles at temperatures above and below the LCST were studied by comparing the neutral grafted particles with the charged ones in aqueous solutions with varying concentrations of barium chloride.

Experimental

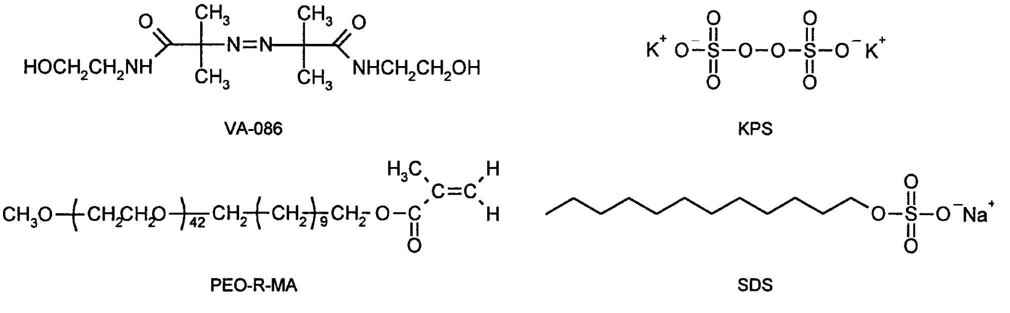
Materials

N-Vinylcaprolactam, purchased from Polysciences, was purified by distillation in vacuum. *N*,*N*′-Methylenebisacrylamide (BA, Electran), KPS (Merck, p.a.), 2,2′-azobis[2-methyl-*N*-(2-hydroxyethyl)propionamide] (VA-086, Wako) and SDS (Fluka) were used without further purification. The amphiphilic PEO macromonomer (PEO-R-MA) was synthesised as reported previously [13]. Water used as a solvent was purified with an Elgastat UHQ-PS purification system.

Preparation of the microgels

All PVCL microgels were prepared by batch emulsion polymerisation in a 500-cm^3 thermostated double-walled reactor fitted with a mechanical Teflon stirrer. Vinylcaprolactam monomer, the cross-linker, surfactant (either SDS or PEO-R-MA), and 240 cm^3 water were transferred to the reactor. The amount of the cross-linker BA was 2 mol% of the monomer feed, except in the case of E1, where 3 mol% of BA was needed to retain the stability of the emulsion. The details of the polymerisation reactions are collected in Table 1. The solution was purged with nitrogen for 60 min to remove dissolved oxygen. At the same time the mixture was emulsified by stirring at 400 rpm. The initiator, either KPS or VA-086, was added through the septum to start the reaction. The polymerisation was carried out at 70 or 75 °C for 20 h. After the reaction the resulting microgels were purified by two different methods. One part of the microgel dispersion was dialysed for 1 week and the other was purged of unreacted monomers and surfactants using successive three-cycle centrifugation (Sigma 2K15C) at 15,300 rpm and 40 °C, decantation, and redispersion in water. Two methods of

Fig. 1 Structure of the initiators and the surfactants. Water-soluble initiator 2,2′-azobis[2-methyl-*N*-(2-hydroxyethyl)propionamide] (*VA-086*) and the amphiphilic poly(ethylene oxide) macromonomer (*PEO-R-MA*) are both nonionic. Sodium dodecyl sulphate (*SDS*) and potassium persulphate (*KPS*) are ionic



VA-086

KPS

PEO-R-MA

SDS

Table 1 Summary of polymerisation recipes. *N*-Vinylcaprolactam (*VCL*), sodium dodecyl sulphate (*SDS*), poly(ethylene oxide) macromonomer (*PEO-R-MA*), potassium persulphate (*KPS*), 2,2′-azobis[2-methyl-*N*-(2-hydroxyethyl)propionamide] (*VA-086*)

Sample	VCL (g/dm^3)	Surfactant (g/dm^3)		Initiator (g/dm^3)		Reaction time (h)	*T* (°C)
		SDS	PEO-R-MA	KPS	VA-086		
E1	6.70	0.42	–	0.25	–	20	70
E2	6.70	0.42	–	–	2.69	20	75
E3	6.70	–	2.94	0.25	–	20	70
E4	6.70	–	2.94	–	2.69	20	75

purification were observed to produce polymer dispersions with identical properties.

Light scattering

The hydrodynamic radii of the microgel particles at different temperatures were measured by dynamic light scattering. The measurements were performed using a Brookhaven Instruments BI-200SM goniometer and a BI-9000AT digital correlator. A laser (LEXEL 85, 1 W) operating at 514.5 nm was used as a light source. Time correlation functions were analysed with a Laplace inversion program (CONTIN) or by the cumulant method. The scattering angle was 90°. When measuring the LCSTs, the samples were heated at a rate of 5 °C/min.

Capillary electrophoresis

The capillary electrophoretic experiments were carried out with a Hewlett-Packard Chemstation ^{3D}CE system equipped with a diode-array detector, an air-cooling device for the capillary cassette, and a water cooling device for the sample and buffer vials (Agilent Technologies). Uncoated fused silica capillaries of dimensions 50-μm inner diameter, 375-μm outer diameter, with 30 cm to the detector and with a total length of 38.5 cm were used throughout the study (Composite Metal Services). The separation conditions were as follows: voltage 15 kV; temperature of the buffer/sample carousel and of the capillary cassette 25 °C; sample injection for 5 s at 50 mbar; detection at 200 nm. The running electrolyte solution was aqueous ammonium acetate with an ionic strength of 20 mM at pH 9. A Jenway pH meter and electrode were used to adjust the pH of the buffer solution.

The electrophoretic mobilities of charged analytes depend on their sizes and charges, and on the type of solvent. For large particles retardation and relaxation effects have to be considered [14] and for (rigid) spherical particles with $\zeta < 25$ mV, the electrophoretic mobility is given by

$$\mu = (2\varepsilon\zeta)/(3\eta)f(\kappa r) \ . \tag{1}$$

Here, ε is the permittivity, ζ the electrostatic potential at the shear surface (the zeta potential), η the viscosity of the medium, r the radius of the particle, and κ the Debye–Hückel parameter. The reciprocal of κ is referred to as the thickness of the electrostatic double layer (the Debye length). The Henry function $f(\kappa r)$ approaches 1 for small κr and 1.5 for large κr. Hence, for larger particles of relatively small potentials, Eq. (1) can be used to determine the zeta potential of the particle. κ is related to the ionic strength of the electrolyte solution according to

$$\kappa = [(2000F^2)/(\varepsilon_0\varepsilon_r RT)]^{1/2} I^{1/2} \ , \tag{2}$$

where F is the Faraday constant, ε_0 the permittivity of a vacuum, ε_r the relative permittivity, R the gas constant, T the temperature, and I the ionic strength of the electrolyte solution. For the particles investigated in this study $\kappa r > 1$ (using the relative permittivity of water), and the Henry function was calculated from Eq. (3):

$$f(\kappa r) = 1.5 - [9/(2\kappa r)] + [75/(2\kappa^2 r^2)] - [330/(\kappa^3 r^3)] \ . \tag{3}$$

Accordingly, the surface charges of the synthesised PVCL particles were calculated by the use of Eqs. (1), (2), and (3). A simplifying assumption was made that the particles behave as hard spheres regardless of temperature. This somewhat affects the calculated values of the zeta potentials [15] but does not prevent the comparison of the samples.

Stability of microgels

The stability of the microgels in the presence of added electrolyte was studied spectrophotometrically by following the changes in absorbance at various concentrations of barium chloride. A 2 cm^3 sample of diluted microgel suspension was transferred to a clean tube and 2 cm^3 barium chloride solution of known concentration was added. After 30 min, the suspension was gently shaken and after 60 min was centrifuged at 2,000 rpm for 15 min to remove coagulated particles. Then, the absorbance of the remaining dispersion was measured. A UV spectrophotometer (UV-2101, Shimadzu) was used for the measurements, with an incident wavelength of 450 nm. The relative turbidity was calculated by dividing the absolute reading by the absorbance obtained in a control experiment without added electrolyte. The critical coagulation concentration (ccc) was determined by extrapolating the sharply decreasing part of the turbidity curve to zero turbidity.

Results and discussion

Thermosensitivity of the microgels

The sizes of the electrically charged and electroneutral particles were measured as a function of increasing temperature and are shown in Fig. 2. The thermal collapse of the various PVCL particles turned out to be a more or less continuous process regardless of the particle charge and the presence or absence of amphiphilic grafts. The PEO derivatives bound to the particle surfaces had only a minor effect on the transition temperature. Even though the sizes of the particles at lower temperatures varied, in every case the hydrodynamic radius decreased to approximately half its original value upon heating above the LCST. Owing to the complexity of emulsion polymerisation systems there are several reasons for the differences in the particle sizes. The surfactants used in the present study probably differ

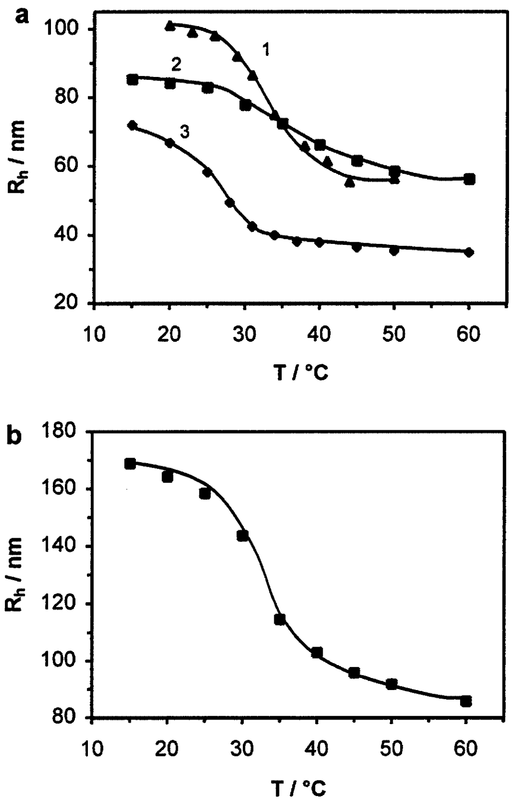


Fig. 2 **a** Temperature dependence of the hydrodynamic radius of charged poly(*N*-vinylcaprolactam) (*PVCL*) microgels E1 (*1*), E2 (*3*), and the grafted one E3 (*2*). **b** Temperature dependence of the hydrodynamic radius of the electroneutral grafted PVCL microgel E4

in their effectiveness in stabilising the growing polymer particles. An ionic initiator produces oligomeric radical anions which may act as surfactants. Different dissociation rates of the initiators influence the number of polymer particles produced and, thus, also the rate of polymerisation. These factors consequently lead to differences in the particle sizes.

Capillary electrophoretic studies

Electrophoretic mobilities of the PVCL particles were measured at two temperatures, 25 and 45 °C, to determine the surface charge introduced by the ionic initiator, KPS, and the surfactant, SDS. The measurements were conducted using uncoated fused silica capillaries and an ammonium acetate buffer (pH 9). For the determination of the electrophoretic mobilities the PVCL particles were dispersed in the electrolyte solution, in order to avoid any possible changes in the properties of the particles during injection and electrophoresis.

Because the size of the microgel particles is expected to depend on the ionic strength and the pH of the aqueous medium, the hydrodynamic radii of two particles, E2 and E4, were measured as functions of temperature in the ammonium acetate buffer (Fig. 3). The anionic particle E2 started to aggregate at temperatures below the LCST, whereas the sterically stabilised nonionic particle E4 behaved as in pure water. The observed decrease in the colloidal stability of some of the particles in a buffer solution needed to be taken into account in interpreting the results from the capillary electrophoretic measurements.

As can be seen in Table 2, the zeta potentials of the particles differed noticeably. When either an ionic initiator or surfactant was used in the synthesis, a particle with a slightly negative zeta potential at 25 °C was obtained (E2, E3). A particle with the highest negative potential was obtained by the use of an ionic initiator together with an ionic surfactant (E1). As expected, the particles synthesised using a nonionic initiator and surfactant (E4) had zero charges; however, the E4 particles were observed to slightly adsorb onto the uncoated fused silica capillary. This was probably due to the absence of repulsive electrostatic interactions between the silica wall and the E4 particles. The electrophoretic mobility of the negatively charged particles increased with increasing temperature, both as a result of the collapse of the particles and of a decrease in the viscosity of the electrolyte solution (Eq. 1). The increase in the electrophoretic

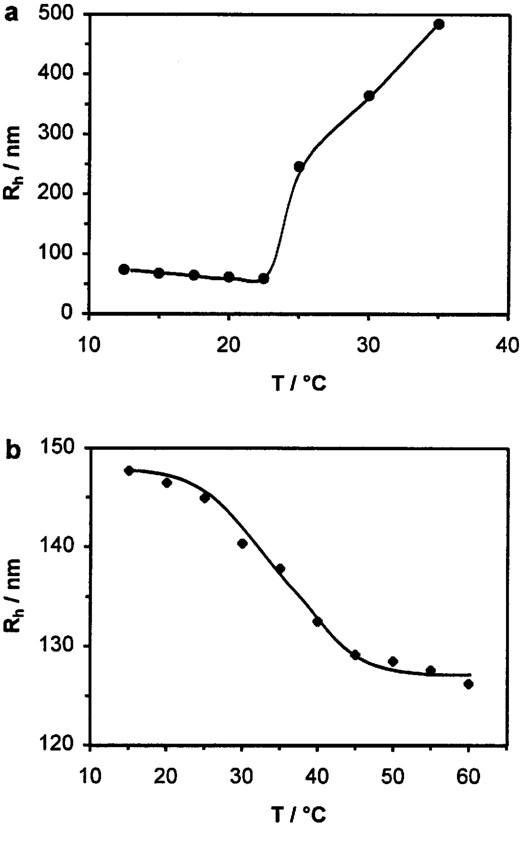


Fig. 3 R_h of microgel particles **a** E2 and **b** E4 against temperature in 20 mM ammonium acetate buffer (pH 9)

Table 2 Summary of the capillary electrophoretic study

Sample	T = 25 °C			T = 45 °C		
	R_h (nm)	μ_e (10^{-8}m^2/V/s)[a]	ζ (mV)[b]	R_h (nm)	μ_e (10^{-8}m^2/V/s)	ζ (mV)
E1	98	−1.27	−16.1	57	−2.10	−17.4
E2	58	−0.44	−5.6	36	−1.97	−16.3
E3	83	−0.24	−3.0	62	−6.46	−5.4
E4	159	–	–	96	–	–

[a] Electrophoretic mobility
[b] Zeta potential

mobility due to the collapse may be caused not only by the reduction in the particle size but also by an increased surface fraction of the charged groups, when the water content inside the particle decreases. The same phenomenon has been observed with other responsive particles [5, 6]. The zeta potentials of samples E1 and E2 differed noticeably at 25 °C but reached almost similar values at 45 °C. This somewhat surprising finding is probably attributable to the observed instability of sample E2 at elevated temperatures, as shown in Fig. 3.

Colloidal stability

The stability of the responsive microgel particles was studied as a function of increasing concentration of an added electrolyte. The turbidities of samples E2 and E4 are shown against barium chloride concentration in Fig. 4. As can be seen in Fig. 4a, at 21 °C both polymer particles can stand high electrolyte concentrations without coagulation, especially sample E4, which seems to be very effectively sterically stabilised. Also, sample E2 turned out to be surprisingly stable. The ccc at 21 °C was around 0.4 mol/dm^3; this obviously resulted from a certain degree of steric stabilisation.

At 45 °C the situation is somewhat different. Electrostatically stabilised particles (E2) start to coagulate and form large aggregates at very moderate electrolyte concentration and during the centrifugation these aggregates finally precipitate. The first stage of aggregation can be seen as the very abrupt increase in the relative turbidity at low electrolyte concentration (Fig. 4b). The ccc for E2 at 45 °C was in the range 5×10^{-5}–1×10^{-3} mol/dm^3. However, sterically stabilised particles (E4) do not form such large aggregates that might precipitate when centrifuged and the increase in turbidity in the early stage of aggregation is only moderate at very high electrolyte concentrations, i.e., above 0.05 M.

According to the Derjaguin–Landau–Verwey–Overbeek (DLVO) theory, the repulsion of the particles due to the electric double layer decreases with increasing ionic strength of the medium. The effect of different electrolytes depends on the charge of the cation; the higher the charge, the higher the reduction in the repulsive potential between the particles. On the other hand, added electrolytes are known to strongly affect the solubility of PEO and, thus, to decrease its ability for steric stabilisation [16, 17]. The effect of electrolytes on the solubility of PEO is also dependent on the charge of the cation; by decreasing the valency the solubility of PEO decreases [16]. When comparing electrostatically stabilised particles with those sterically stabilised with PEO derivatives, one should take into account these two contradictory effects. In the present case, barium chloride was chosen as the electrolyte and clearly affects the electric double layer but has only a minor effect on the solubility of PEO at low temperatures and concentrations [11, 16]. A concentrated electrolyte solution may, however, be a poor solvent for PEO. In such a solution the thickness of the stabilising PEO shell decreases, and

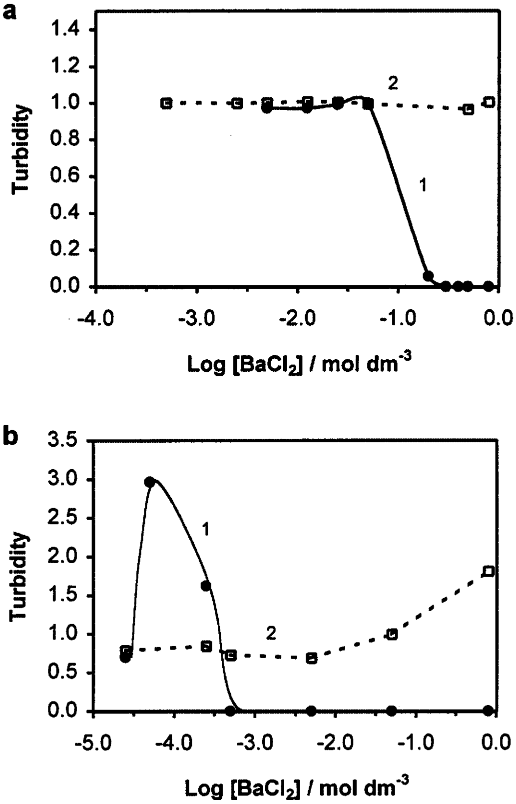


Fig. 4 Effect of $BaCl_2$ on the turbidity of the microgel dispersions: E2 (*1*) and E4 (*2*) **a** at 21 °C and **b** at 45 °C

even bridging flocculation is possible [7]. For example, an aqueous 0.39 M $MgSO_4$ solution has been observed to turn into a θ solvent for PEO when the temperature is increased above 40 °C [16, 17]. This phenomenon might be the reason for the slight instability of the PEO-grafted microgels at very high electrolyte concentrations.

PEO-grafted latex particles synthesised using the macromonomer technique have been shown to be stable even in highly concentrated electrolyte solutions [18, 19]; however, the stability of thermally responsive PEO-grafted microgels has not been studied in detail before. The cccs of PNIPAM and PNIPMAM microgels stabilised by carboxylic or sulphate groups have been measured in the presence of sodium chloride [5, 6]. Usually the values of the ccc are very high at low temperatures where the particles are fully swollen. This has been suggested to arise from the partial steric stabilisation of the particles. Owing to the different reactivity ratios of the monomer and the cross-linker, the network structure is heterogeneous and the particles carry dangling chains on their surfaces [20]. However, upon the thermal collapse of the particles, the dangling chains compress parallel to the particle surface and, thus, steric stabilisation is no longer effective. Indeed, it has been shown that loose, porous PNIPAM particles turn into hard spheres upon heating above the LCST [21]. The findings in the present study, especially for the electrosterically stabilised particle, are in accordance with the observed decrease in the ccc of PNIPAM microgels at $T >$ LCST [5].

Conclusions

Thermally responsive microgel particles were prepared by emulsion polymerisation of *N*-vinylcaprolactam. By varying the chemical nature of initiators and surfactants, particles with different types and degrees of stabilisation were obtained. The use of an ionic initiator or an ionic surfactant led to electrostatically stabilised particles, as confirmed by capillary electrophoretic measurements of the zeta potentials of the PVCL particles. Sterically stabilised particles, grafted with amphiphilic PEO derivatives, were successfully prepared utilising amphiphilic macromonomers.

Repulsive forces between the negatively charged nongrafted particles decreased with the addition of an electrolyte, as expected by the DLVO theory. This was clearly observed at temperatures above the LCST of PVCL; however, at $T <$ LCST, partial steric stabilisation due to dangling chain ends on the particle surfaces was also evident.

Grafting the responsive particles with PEO derivatives increased their stability towards added electrolytes considerably, the effect being especially pronounced at high temperatures where the PVCL particles were shrunken. However, although the grafted particles were insensitive to the addition of electrolytes at $T <$ LCST, a slight instability was observed at very high electrolyte concentrations at $T >$ LCST.

Polymerisable amphiphilic macromonomers containing PEO segments were used as reactive surfactants in emulsion polymerisation. It may be concluded that the macromonomer technique is a method of choice for the synthesis of thermally responsive PVCL microgels which do not coagulate or precipitate in solutions of high ionic strength.

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