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ORIGINAL CONTRIBUTION

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Monosized cationic nanoparticles prepared by emulsifer-free emulsion polymerization

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Abstract Monosized poly(styrene/*N*-[3-(dimethylamino)propyl]methacrylamide/poly(ethylene glycol) ethyl ether methacrylate) [poly(St/PEG-EEM/DMAPM)] cationic nanoparticles were synthesized by emulsifier-free emulsion polymerization conducted in the presence of a cationic initiator, 2,2′-azobis (2-methylpropionamidine) dihydrochloride (APDH or V-50). Particle sizes and surface charge densities were measured with a Zeta Sizer. The structure of the terpolymers was determined by Fourier transform IR and ^{1}H NMR spectroscopies. The amounts of the main monomer (St), cationic comonomer (DMAPM), stabilizer (PEG-EEM), and initiator (APDH), and the water-to-monomer phase ratio were all effective on both the average size and the surface charge of the nanoparicles. The average particle size was in the range 75–400 nm depending on the recipe applied; it decreased on increasing the amount of DMAP or PEG-EEM or the water-to-monomer phase ratio in the feed, while it increased with increasing St or APDH content. These nanoparticles were quite monodisperse with a polydispersity index of 1.008–1.14.

Keywords Cationic nanoparticles · Emulsifier-free emulsion polymerization · Cationic comonomer · Polymerizable stabilizer · Cationic initiator

Introduction

Polymer microspheres with controlled surface morphology and/or structure have received widespread attention owing to their potential applications in biomedical and pharmaceutical areas [1]. Such microspheres are thought to be more suitable for the previously mentioned uses owing to their large specific surface areas, though they have to satisfy some essential requirements, including reasonable colloidal properties [2]. The colloidal behavior and properties of polymer microspheres usually depend on their surface morphology and properties as well as structure, for example, attached surface groups [3].

Microemulsion polymerization is one of the few methods to produce stable colloids with ultrafine latex particles within the size range of 10–100 nm and with narrow size distributions. Several groups have studied microemulsion polymerization. Styrene (St) and methyl methacrylate (MMA) are typical monomers that have been polymerized in ternary oil-in-water microemulsions [4, 5, 6]. In our previous studies, we polymerized MMA with ethyl methacrylate, butyl methacrylate, hydroxyethyl methacrylate, acrylic acid, and acrylamide in microemulsion systems, and investigated their film-forming abilities [7, 8, 9, 10]. In another study, we included a hydrophilic poly(*N*-acetylethyleneimine) macromer with a cinnamoyl polymerizable end group, as an active cosurfactant in the formulations [11]. The main disadvantage of microemulsion polymerization is the use of a large amount of surfactant, which makes these nanoparticles less valuable for a variety of biological applications.

It was reported that monodisperse particles with much cleaner surfaces can be synthesized by emulsifier-free emulsion polymerization and that purer and more monodisperse samples would be synthesized [12, 13, 14, 15]. In this approach, the particle formation occurs by the precipitation of growing macroradicals within the continuous medium. Precipitation takes place when the macroradicals reach to a certain critical chain length depending upon the solvency of the continuous phase. The average particle size values are in the range 0.5–1.5 μm, depending upon the polymerization conditions. The type and concentration of the monomer, the initiator concentration, the ionic strength of the continuous medium, and the polymerization temperature strongly affect the polymerization rate, the final particle size, and the average molecular weight of the latex particles in the emulsifier-free emulsion polymerization process [16]. In this system, the decomposed initiator fragments incorporated onto particle surfaces played a certain role in particle and colloidal properties, for example, colloidal stability. Recently, poly(ethylene glycol) (PEG)-ethyl ether methacrylate (EEM) macromonomer was used as a stabilizer in a synthesis of monodisperse cationic polystyrene particles (460–1,200 nm) [17, 18].

In this study, monosized cationic poly(St/PEG-EEM/*N*-[3-(dimethylamino)propyl]methacrylamide, DMAPM) nanoparticles with permanent charge were synthesized by emulsifier-free emulsion polymerization of the respective comonomers by also using a cationic initiator, 2,2′-azobis(2-methylpropionamidine) dihydrochloride (APDH).

Experimental

Materials

St (Sigma, USA) was used as the main monomer, and was distilled before use. The cationic comonomer, DMAPM (Sigma, USA), and the polymerizable stabilizer, PEG-EEM (Aldrich, USA, catalog no.40,954-5,) were used as purchased. APDH (or V-50) (Aldrich, USA) was used as the cationic initiator. The dispersion medium was distilled water in all the experiments.

Preparation of polymeric particles

Polymerizations were conducted in an oil-in-water system. In a typical procedure, the comonomers, St, DMAPM, and PEG-EEM, and the initiator, APDH, were added to distilled water (i.e., the dispersion medium), in a Pyrex glass reactor. Polymerizations were carried out in a constant-temperature shaking bath at 65 °C, under a nitrogen atmosphere for a polymerization period of 24 h; these conditions were determined in the preliminary experiments. We changed the initial concentrations of the monomers and initiator and also the ratio of the water phase to the monomer phase (v/v) and determined the size and charges of the nanoparticles produced (Table 1). The reaction medium was acidic with a pH around 2.5–3 in all the polymerizations.

Characterization

The average particle size, the size distribution, and the surface charge density measurements were carried out with a Zeta Sizer (Malvern 3000 HSA, France). An atomic force microscope (Digital Instruments, AFM Nanoscope, Dimension 3000, USA) was used for the imaging of the nanoparticles. The nanoparticles were mixed thoroughly with KBr (IR grade), and Fourier transform (FT) IR spectra were taken with a FTIR spectrophotometer (FTIR-8000 series, Shimadzu, Japan). ^{1}H NMR spectra were recorded with a NMR spectrometer (Bruker spectrospin Avance Ultrashield, Germany–Sweden) working at 400 MHz at room temperature by using polymer samples dissolved in $CDCl_3$.

Results and discussion

Polymer characterization

In this study cationic nanoparticles were prepared by emulsifer-free emulsion polymerization. The influence of monomers and initiator concentrations and the dispersion medium concentration on particle dimensions and surface charge density were examined. For all recipes applied (Table 1) stable latexes were obtained, and no precipitation was observed after more than 6-months storage.

The following characteristic peaks were observed in the FTIR spectra of the terpolymer synthesized (KBr, pellet), (cm^{-1}): 3,300 (w) secondary amide (NH stretching), 3,100–3,000 (m) aromatic CH, 1,950 overtone bands of C = O, 1,875 and 1,800 C = O, 1,600 aromatic benzene ring (C = C stretch), 1,490 secondary amides (NH deformation, amide II band), 1,450 CH_2 scissor vibration, 1,380 and 1,360 doublet twist bands for CH_3 deformation, 1,335 (w) CH_2 bending, 1,235 (w) *trans*-amide III band, 1,175 CN stretching in DMAPM unit, 1,160, 1,125 and 1,075 (s) C–O–C stretch bands, 1,025 CH in-plane bending, 975–840 (m-w) C–C stretching of main chain, 760 (s) CH out of plane deformation of monosubstituted benzene, 700 (s) CH rocking, 625 (w) out-of-plane CH deformation, 540 (s) C = O out-of-plane bends.

A representative ^{1}H NMR spectra and also the chemical formula of the terpolymer are presented in Fig. 1, which shows that (in $CHCl_3$-d_1 at 27 °C), δ ppm: (1) 1H, CH (backbone) 2.40–2.39, (2) 2H, CH_2 (backbone) 1.72, (3–7) 5H, CH (benzene ring) (broad peaks) 6.97–7.02 for St unit; (8) 2H, CH_2 (backbone) 2.08–2.05, (9) 3H, CH_3 1.19, (10–11) 2H, CH_2 3.76–3.28, (12) 2H, CH_2 3.43, (13) 3H, CH_3 0.85–0.74 for PEG-EEM unit; (14) 2H, CH_2 (backbone) 1.98, (15) 3H, CH_3 1.14, (16) 1H, NH (broad peak) 4.19–3.90, (17–19) 2H, CH_2 (broad peak) 3.17–3.02, (20–21) 3H, CH_3 1.35 for DMAPM unit.

Table 1 Polymerization recipes for emulsifier-free emulsion polymerizations

Nanoparticle sample	Water (ml)	Styrene (ml)	*N*-[3-(Dimethylamino) propyl] methacrylamide (ml)	Poly (ethylene glycol) ethyl ether methacrylate (ml)	2,2′-Azobis (2-methylpropionamidine) dihydrochloride (g)
SDP 1	50	1.25	0.1	0.1	0.03
SDP 2	50	2.5	0.1	0.1	0.03
SDP 3	50	5.0	0.1	0.1	0.03
SDP 4	50	1.25	0	0.1	0.03
SDP 5	50	1.25	0.3	0.1	0.03
SDP 6	50	1.25	0.6	0.1	0.03
SDP 7	50	1.25	0.1	0.1	0.03
SDP 8	50	1.25	0.1	0.2	0.03
SDP 9	50	1.25	0.1	0.4	0.03
SDP 10	50	1.25	0.1	0.6	0.03
SDP 11	50	1.25	0.1	0.1	0.03
SDP 12	50	1.25	0.1	0.1	0.06
SDP 13	50	1.25	0.1	0.1	0.12
SDP 14	50	1.25	0.1	0.1	0.03
SDP 15	75	1.25	0.1	0.1	0.03
SDP 16	100	1.25	0.1	0.1	0.03
SDP 17	120	1.25	0.1	0.1	0.03
SDP 18	140	1.25	0.1	0.1	0.03
SDP 19	160	1.25	0.1	0.1	0.03
SDP 20	200	1.25	0.1	0.1	0.03

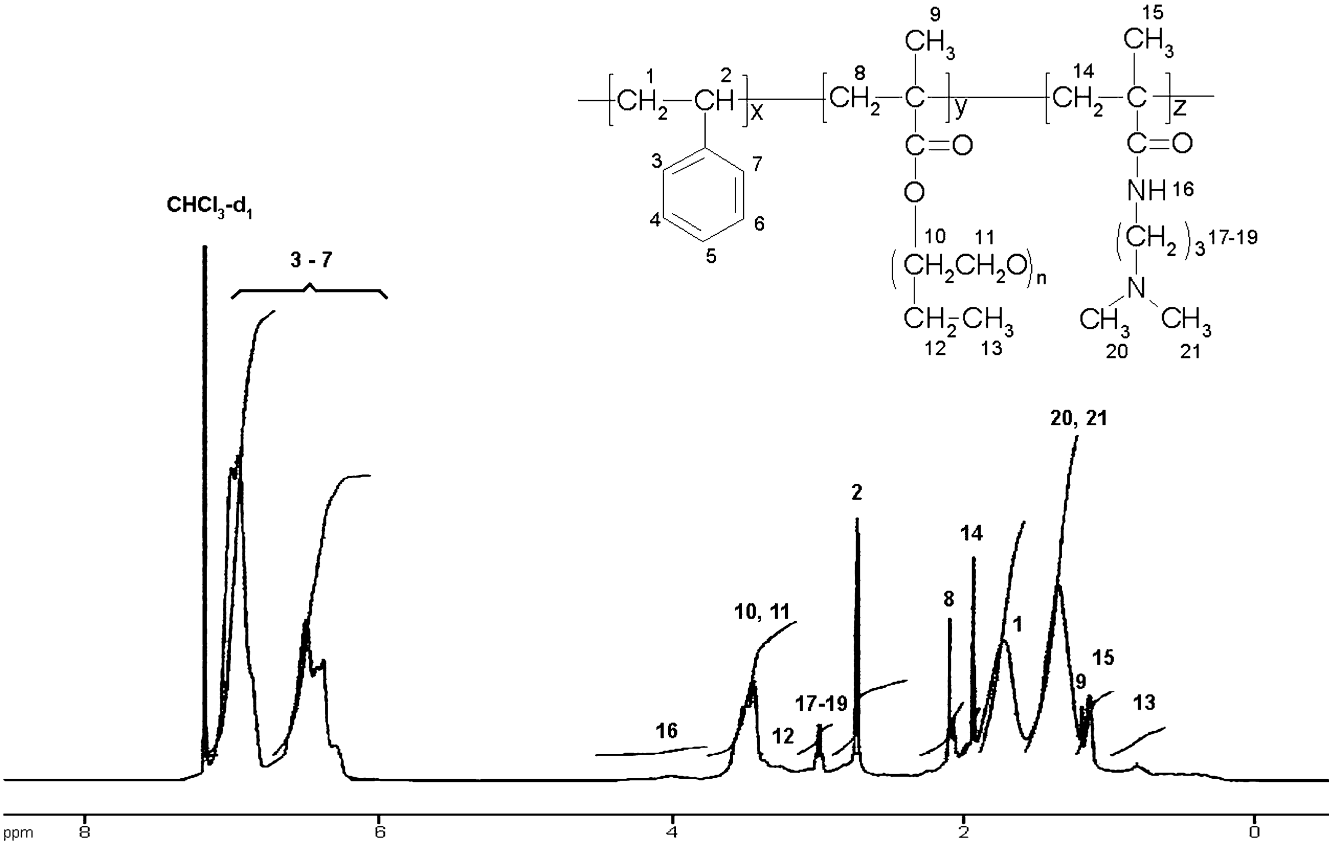


Fig. 1 ^{1}H NMR spectra of the terpolymer SDP 17

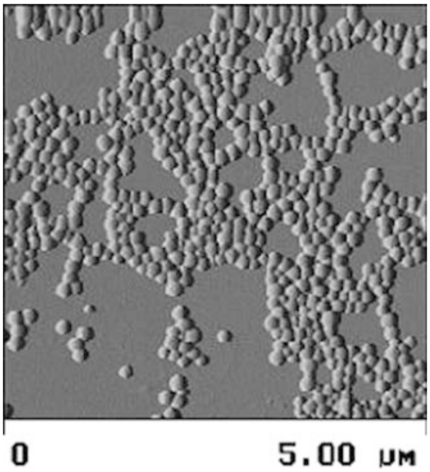


Fig. 2 Atomic force microscope micrograph of sample SDP 7

The composition of the terpolymer (SDP 17) was determined by comparing the integrals of the phenyl and methyne group regions in the ^{1}H NMR spectra of St, DMAPM, and PEG-EEM units, respectively [19]. The characteristic peaks observed at 6.97 ppm for the phenyl group in the St unit, 2.7 ppm $(CH_2)_3$ in the DMAPM unit, and 3.5 ppm $(CH_2CH_2)_{n=2.2}$ in the PEG-EEM unit were used as analytical signals for quantitative analysis of terpolymer composition. For sample SDP 74 the composition was found to be St 76.33 mol%, DMAPM 10.01 mol%, and PEG-EEM 13.16 mol%.

A typical micrograph of sample SDP 7 is shown in Fig. 2. The average particle size measured from this image was 112 nm, which is quite close to the value obtained with the Zeta Sizer (117.3 nm).

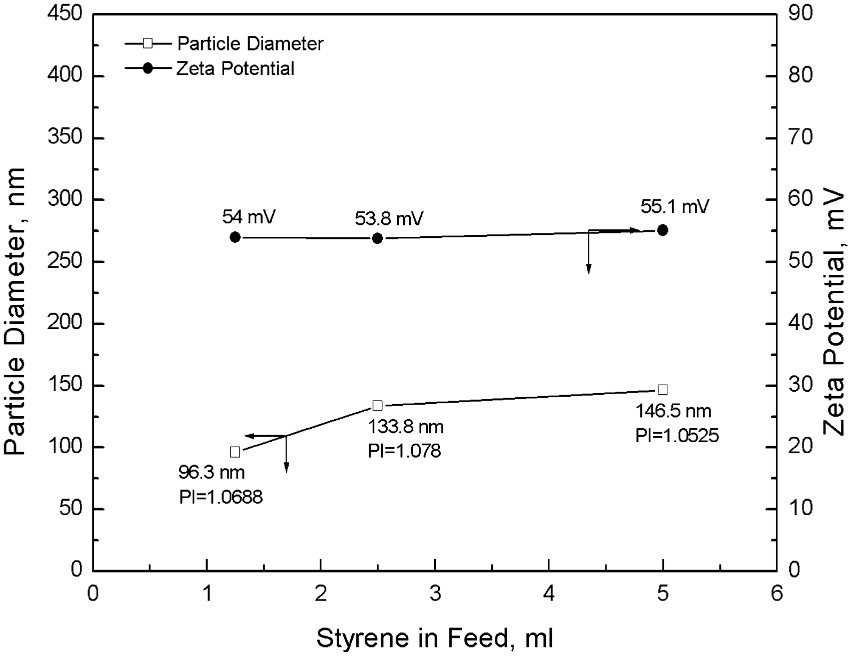
Effects of several parameters on the size and charge of the nanoparticles

Effects of amount of St in the feed

In this group of experiments we changed the amount of the main monomer, St, in the feed between 1.25 and 5.0 ml. The amounts of the other ingredients, water, DMAPM, PEG-EEM, and APDH, were 50 ml, 0.1 ml, 0.1 ml, and 0.03 g, respectively. Polymerizations were conducted at pH 2.5–3 (adjusted with 0.1 N HCl), at 65 °C, under a nitrogen atmosphere for a polymerization period of 24 h. The data obtained with the Zeta Sizer are given in Fig. 3. The numerical values of the zeta potentials and the average particle sizes and particle size distributions of each particle are also indicated on the graph.

As seen here, the particles size distributions are quite narrow, and the average particle size increase with the increase in the amount of St in the feed. This is expected, because St is the main monomer and is used in excess in the recipe (compared to the other comonomers), and therefore forms as a separate phase, "the monomer storage droplets" in the reaction medium. After the nucleation step, monomer molecules diffuse from these droplets into the growing polymer phase stabilized with both PEG-EEM oligomers, cationic comonomer DMAPM at the upmost layer of the particles, and also

Fig. 3 Effects of amount of styrene in the feed on the particle size/size distribution (*PI*) and the zeta potentials of the nanoparticles



with the cationic initiator attached to the ends of the growing terpolymer chains. This process continues until all the monomer is consumed [13, 16]. Therefore, if there is more monomer in the storage, the particles are be larger, as was also observed in our case.

The zeta potentials of the particles with different size were about the same. This means that there is enough cationic comonomer and initiator in the medium in all cases to cover the particles evenly.

Effects of amount of DMAPM in the feed

Here, we changed the amount of the cationic comonomer, DMAPM, in the feed between 0.0 and 0.6 ml. The amounts of the other ingredients, water, St, PEG-EEM, and APDH, were 50 ml, 1.25 ml, 0.1 ml, and 0.03 g, respectively. Polymerizations were conducted at pH 2.5–3 (adjusted with 0.1 N HCl), at 65 °C, under a nitrogen atmosphere for a polymerization period of 24 h. The data obtained in this group of experiments are given in Fig. 4.

As seen in Fig. 4, there is a very considerable decrease in the average diameter of the particles produced using an increasing amount of cationic comonomer in the polymerization recipe, while in each case the size distribution is quite narrow. As expected, there is also a pronounced increase in the zeta potential (or positive charge) of the particles when the amount of DMAPM used increased. This is a general trend that has been observed in emulsifier-free emulsion polymerization in the presence of an ionic comonomer [20]. Note that the essential role of the ionic comonomer in the emulsifier-free emulsion polymerization is that it can be chemically bonded onto the particle surfaces to provide better stability. However, different comonomers will provide different reactivities and hydrophilic properties, leading to different polymerization behaviors in the aqueous phase, and therefore in the final surface composition of the particles. Ionic comonomers can also react with the initiator molecules and form oligomer radicals, and these radicals trigger the "primary particle formation", which in turn results in smaller particles [20].

Effects of amount of PEG-EEM in the feed

In this group, we changed the amount of comonomer, PEG-EEM, in the feed between 0.2 and 0.6 ml. The amounts of the other ingredients, water, St, DMAPM, and APDH were 50 ml, 1.25 ml, 0.1 ml, and 0.03 g, respectively. Polymerizations were conducted at pH 2.5–3. (adjusted with 0.1 N HCl), at 65 °C, under a nitrogen atmosphere for a polymerization period of 24 °h. The average diameters of the particles, their polydispersity indexes, and also their zeta potentials are given in Fig. 5.

PEG-EEM comonomer has two components, the PEG part, which is quite hydrophilic, and the polymerizable EEM part (with a double bond), which forms hydrophobic domains during polymerization. It reacts with the initiator and forms oligomer radicals which have surfactant-like character and therefore provide stability to the system. The average particle size obtained

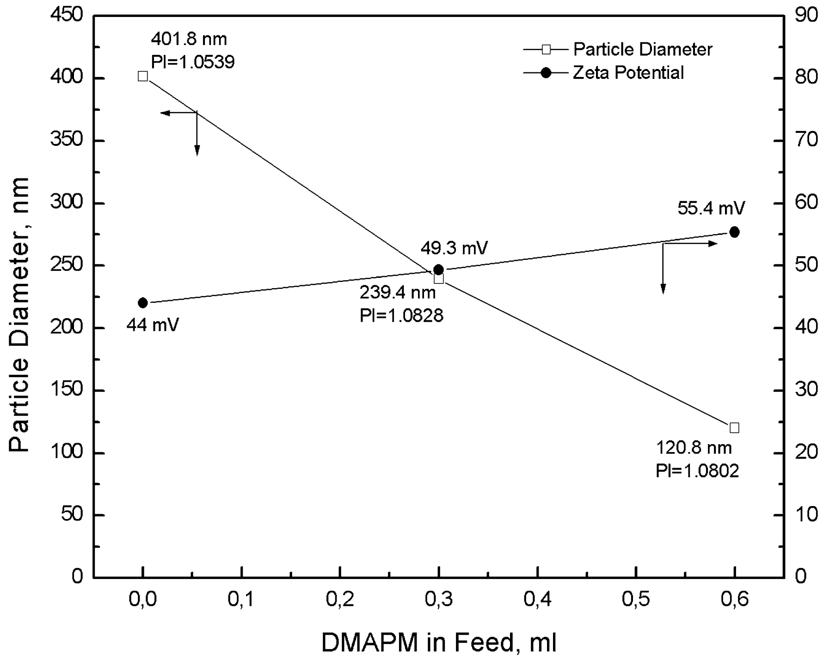


Fig. 4 Effects of the amount of *N*-[3-(dimethylamino)propyl]methacrylamide (*DMAPM*) in the feed on the particle size/size distribution and the zeta potentials of the nanoparticles

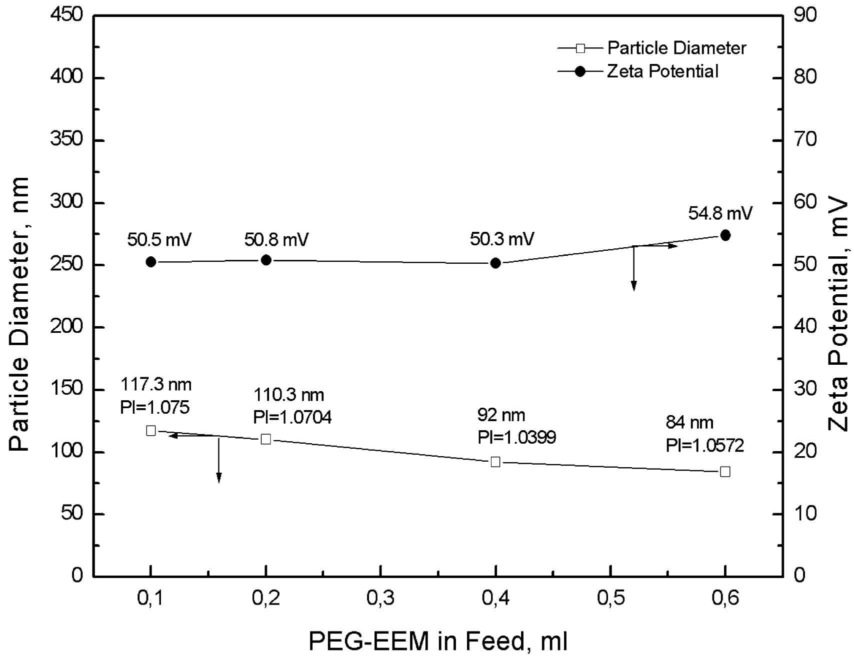


Fig. 5 Effects of the amount of poly(ethylene glycol) ethyl ether methacrylate (*PEG-EEM*) in the feed on the particle size/size distribution and the zeta potentials of the nanoparticles

in this group was in the range 84–117 nm. When the amount of PEG-EEM used in the recipe is increased, a decrease in the particle size is observed, accompanying a decrease in the polydispersity index (not very significant but notable). Note that PEG-EEM is more hydrophilic than the main monomer, St, and, therefore, the chance of reaction between PEG-EEM molecules and the initiator molecules is higher. The growing chains contain more PEG-EEM before nucleation, and in turn form more and smaller particles.

There was no effect of the amount of PEG-EEM on the particle surface charge at lower values; however, an observable increase was noted when the amount of PEG-EEM was 0.6 ml. It is not easy to explain this result, but, most probably, the cationic comonomer and maybe also the cationic initiator molecules were pushed out from the forming particles and were located at the outermost part, in this recipe.

Effects of amount of APDH in the feed

In this group, we changed the amount of the initiator, APDH, in the feed between 0.3 and 0.12 ml. The amounts of the other ingredients, water, St, PEG-EEM, and DMAPM, were 50, 1.25, 0.1, and 0.1 ml, respectively. Polymerizations were conducted at pH 2.5–3 (adjusted with 0.1 N HCl), at 65 °C, under a nitrogen atmosphere for a polymerization period of 24 h. The data obtained with the Zeta Sizer are given in Fig. 6.

Figure 6 shows that there is an increase in the particle size with the initiator concentration within the medium, and the polydispersities were close and quite narrow. As the number of free radicals increases (owing to higher initiator concentration), more oligomer radicals are formed, which in turn results in a decrease in the nucleation rate, which results in larger particles [17].

There is no significant change in the surface charge of the particles. One expects that when the concentration of the cationic initiator in the medium increases there should be an increase in the surface charge. But, most probably, owing to the contrary effect of the size increase which compansates the effect of the initiator concentration, no significant change in the charge of the particles occurred.

Effects of water-to-total monomer ratio

In this group, we changed the amount of the water phase used in the polymerization recipe; the ratios of the water phase to the total monomer phase were between 51.72 and 137.93 (water amount 75–200 ml). The amounts of other ingredients, St, PEG-EEM, DMAPM, and APDH, were 1.25 ml, 0.1 ml, 0.1 ml, and 0.03 g, respectively. Polymerizations were conducted at pH 2.5–3 (adjusted with 0.1 N HCl), at 65 °C, under a nitrogen atmosphere for a polymerization period of 24 h. The data obtained with the Zeta Sizer are given in Fig. 7.

Figure 7 shows that two district regions appeared when the water phase-to-monomer phase ratio is changed. First there was a significant decrease in the average diameter of the particles when the ratio was increased. The smallest particles (about 75 nm) were obtained with the recipe in which the ratio was 82.76 (120 ml water/1.45 ml total monomer), under the polymerization conditions that we applied in this study. The average

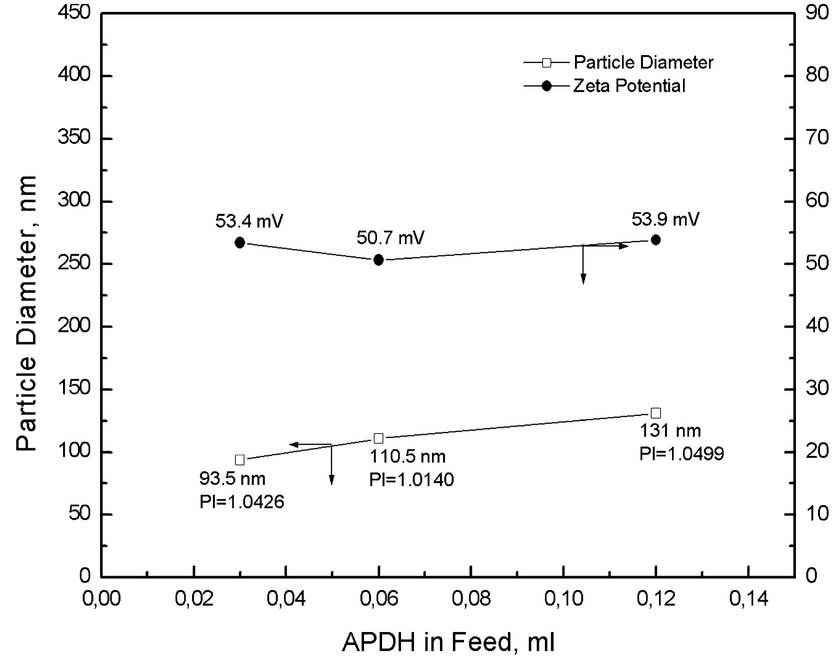


Fig. 6 Effects of the amount of 2,2′-azobis(2-methylpropionamidine) dihydrochloride (*APDH*) in the feed on the particle size/size distribution and the zeta potentials of the nanoparticles

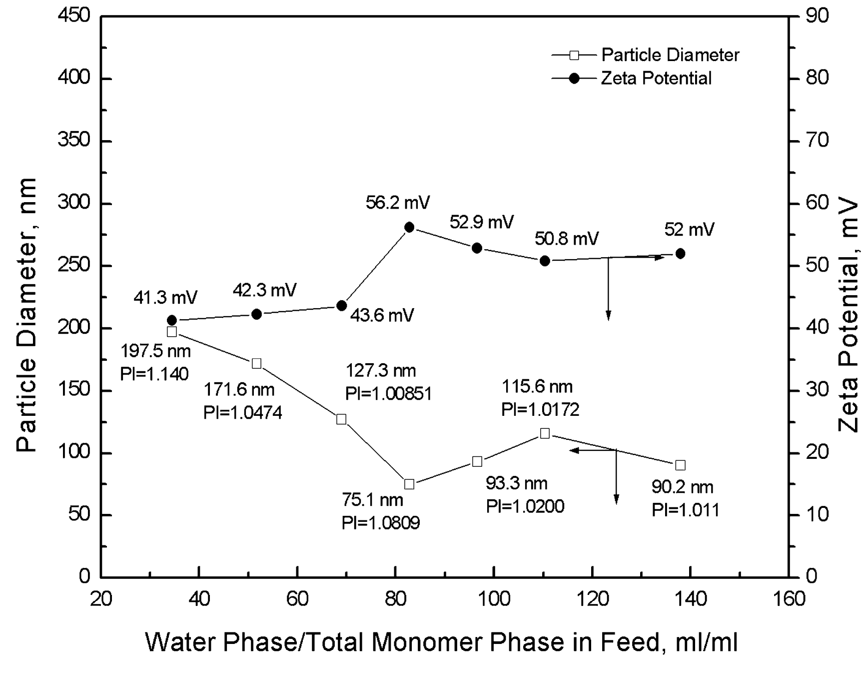


Fig. 7 Effects of the ratio of the amount of the water phase (dispersion medium) to the total amount of the monomer phase on the particle size/size distribution and the zeta potentials of the nanoparticles

diameters of the particles prepared at higher ratios did not change, and were in the range 90–115 nm. In other words, the particle size reached a plateau value with increasing amount of water. Indeed, the particle diameter behaved as expected. Because the increase in the water content of the polymerization medium involves a decrease in the monomer-to-continuous medium ratio, as also observed in the emulsifier-free emulsion polymerization of St the final particle size usually decreases with increasing water-to-monomer ratio. Of course, the decrease in the particle size should reach a limiting value corresponding roughly to the smallest size that can be obtained in the emulsion polymerization system studied. Depending upon the decrease in the average size, the specific surface area of the particles increases, which involves a decrease in the surface charge density coming from the cationic initiator. The increase in the zeta potential is probably related to the decrease in the surface charge density.

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