Cross-Linked Poly(Methyl Methacrylate) Particles with Surface Amino Groups

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Abstract—Positively charged monodisperse particles have been synthesized via emulsifier-free emulsion copolymerization of methyl methacrylate with vinylformamide and ethylene glycol dimethacrylate. The effect of the cross-linking agent on the conversion of the monomers, as well as on the shape, size distribution, and surface characteristics of the obtained particles, has been determined. Addition of the cross-linking agent (5 wt %) to the reaction system has been shown to result in the formation of particles, which, after hydrolysis, have positive ζ potentials at pH 2–10.

INTRODUCTION

Recently, monodisperse polymer particles bearing surface functional groups have found wide application in nanotechnology as systems with an internal hierarchical structure. These systems may serve as a novel elemental base in optoelectronics [1], for binding biologically active substances and realization of biospecific processes on particle surfaces in biotechnology [2], and for creation of solid-state structures manifesting the properties of photon crystals [3–5]. The development of new metamaterials based on polymer particles has required the search for methods of synthesis of monodisperse particles with desired diameters and surface layer structures (controlled degree of cross-linking, the presence of surface centers for molecular identification or reactive functional groups for specific interactions with target compounds, etc.).

Methods for the synthesis of polymer particles with aldehyde, chloromethyl, epoxy, carboxyl, and hydroxyl surface groups have been described in detail in the literature [6]. However, preparation of polymer particles with amino groups in the surface layer is a more complex problem. The synthesis of amino-containing polymer particles via polymerization of functional monomers, such as aminostyrene [7], 2-aminoethyl acrylate, 2-dimethylaminoethyl methacrylate, and allylamine [8], is rather uncommon because of the high cost of the monomers and the low stability of suspensions of polymer microspheres produced from them. Moreover, particles with a narrow size distribution are difficult to synthesize because of the high hydrophilicity of the mentioned monomers. Amino-containing polymer particles are much easier to obtain

through modification of ready-made suspensions of particles containing hydroxyl, chloromethyl, amide, and other groups. However, in the course of this modification, polymer particles may lose aggregation stability.

We have proposed to synthesize monodisperse particles with an aminated surface layer using *N*-vinylformamide (VFA) as a functional comonomer, thereby making it possible to transform amide groups into aliphatic amino groups by hydrolysis [9–11]. In our previous work [12], copolymerization of methyl methacrylate (MMA) with VFA was carried out in the presence of dextran. This process was shown to result in the formation of particles with a hydrophilic bifunctional surface, because the hydrolysis of unreacted initiator cationic groups and VFA units gave rise to the formation of carboxyl and amino groups on the particle surface, respectively. Therewith, VFA units are located inside the surface layer and not all units are accessible to chemical reactions of particle modification with target compounds. However, as was shown for copolymerization of styrene with VFA [13], the addition of ethylene glycol dimethacrylate (EGDM) as a cross-linking agent allows one to achieve a constant size and structure of the particle surface layer.

Thus, the aim of this work was to study the feasibility of forming polymer particles with aliphatic amino groups in the surface layer via emulsifier-free emulsion copolymerization of MMA with VFA in the presence of EGDM, as well as to determine the effect of the process conditions on the shape, size distribution, and surface characteristics of resulting particles.

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Table 1. Synthesis conditions, sizes, and degrees of cross-linking of copolymer particles

Sample no.	MMA : VFA : EGDM ratio, wt %	pH_{in}	pH_{fin}	D, nm			Sol/gel ratio, %
				DLS data	PI	TEM data	
1	97 : 3 : 0	5.81	3.82	400	0.18	275	100/0
2	96 : 3 : 1	5.55	3.20	525	0.13	405	42/58
3	95 : 3 : 2	5.60	3.05	630	0.16	410	39/61
4	94 : 3 : 3	5.75	3.30	515	0.07	415	32/68
5	93 : 3 : 4	5.50	3.10	655	0.23	415	13/87
6	92 : 3 : 5	5.75	3.31	450	0.03	360	9/91

EXPERIMENTAL

Materials

Methyl methacrylate (98%, Acros Organics, United States), *N*-vinylformamide, and ethylene glycol dimethacrylate (both, 98%, Sigma-Aldrich, United States) were purified from a stabilizer with 10X molecular sieves [14]. 2,2'-azobis[2-(2-imidazolin-2-yl)propane] dihydrochloride (Waco Pure Chemical Industries, Japan) was used as an initiator as received. Alkali solutions were prepared by dissolving NaOH granules (Sigma-Aldrich) in bidistilled water, after the granules were washed from sodium bicarbonate. Prepared NaOH solutions were used within no more than 2 days. HCl solutions were prepared by diluting concentrated acid standard titers (reagent grade). Sodium chloride (analytical grade) and methylene chloride (reagent grade) were purchased from OOO Vekton and used as received.

Methods

Particles were synthesized via emulsifier-free emulsion copolymerization at 70°C and a monomer mixture-to-aqueous phase ratio of 1 : 10 in a reactor described previously [15]. The concentration of initiator AIP was 2 wt % relative to the monomers. Bidistilled water boiled and cooled under argon was used as a dispersion medium.

In the course of copolymerization, samples were taken to determine the conversion of monomers by gravimetric analysis. After the completion of the synthesis, residual monomers were removed by steam distillation. Water-soluble impurities were eliminated by triple successive centrifugation and redispersion of copolymer particles in bidistilled water.

The shape and size D of the resulting particles were determined using transmission electron microscopy (TEM) with a JEM 100 S instrument (Japan). In addition, the diameter and polydispersity index (PI) of the particles were estimated using dynamic light scattering (DLS) with a Zetasizer Nano ZS DLS spectrometer (Malvern, United Kingdom). The same spectrometer was used to measure the ζ potentials of polymer particles in 10^{-3} M aqueous NaCl solutions at preset pH values, which were regulated with the use of HCl and NaOH solutions.

The content of the sol fraction in the polymer particles was determined via extraction in a Soxhlet apparatus with methylene chloride [16, 17].

Surface functional groups were hydrolyzed in an HCl solution with pH 2 for 3 h at 50°C. The reagents were then removed via repeated centrifugation and redispersion of particles in bidistilled water until a neutral reaction of supernatant was reached [18].

The surface concentrations of functional groups before and after hydrolysis were determined by conductometric titration of dispersions of polymer particles with a SevenMulti conductometer (Mettler Toledo, Switzerland).

RESULTS AND DISCUSSION

Emulsifier-free emulsion copolymerization of MMA with VFA in the presence of EGDM was carried out in a weakly acidic reaction medium (Table 1). Such initial pH values (pH_{in}), on the one hand, provided protonation of imidazoline groups of the initiator and, hence, the stability of dispersions of polymer–monomer particles (PMPs) in the course of synthesis due to the electrostatic factor [19], and, on the other hand, they ensured conditions under which the MMA units were not hydrolyzed to yield carboxyl groups [20]. As a result, particles with positive ζ potentials in a 10^{-3} M aqueous NaCl solution were formed (Table 2).

According to the TEM data, in the absence of EGDM as a cross-linking agent in the reaction mixture, monodisperse particles 275 nm in diameter with a smooth surface are formed (Fig. 1a). The addition of EGDM to the monomer mixture increases the particle diameter up to 415 nm [21]. Variations in the EGDM concentration in the reaction system within a range of 1–5 wt %, significantly affect the width of particle size distribution and the structure of the particle surface layer (Figs. 1b, 1c), whereas the average size of formed particles P(MMA–VFA–EGDM) changes insignificantly (Table 1). For example, only at EGDM con-

Table 2. Concentrations of surface functional groups and ζ potentials of copolymer particles before and after hydrolysis

Sample no.	EGDM content, wt %	ζ potential in 10^{-3} M NaCl solution, mV		[COOH + NH$_2$], μmol/m^2	
		before hydrolysis	after hydrolysis	before hydrolysis	after hydrolysis
1	0	+30	+33	0.32	0.91
2	1	+16	+50	0.36	1.13
3	2	+43	+48	0.42	1.31
4	3	+21	+43	0.30	1.40
5	4	+36	+33	0.46	1.21
6	5	+42	+37	0.37	1.17

centrations above 4 wt % particles are formed with a narrow size distribution and a smooth surface layer (Fig. 1c). The addition of 1−3 wt % EGDM to the monomer mixture leads to the formation of nonspherical particles with a nonuniform structure of the surface layer (Fig. 1b). This particle morphology seems to be due to nonuniform cross-linking of polymer chains in the surface layer of growing PMPs [21, 22]. In this case, the addition of EGDM in small amounts to the reaction system results in the formation of a polymer network constituting no more than 60% of particle mass (Table 1, samples 2−4). An increase in the EGDM concentration to 4 and 5 wt % leads to more uniform cross-linking of polymer chains in growing PMPs. As a result, the content of the gel fraction in the polymer particles increases to 90 wt % (Table 1, samples 5 and 6). Note that the polymerization rate grows regularly with an increase in the concentration of the cross-linking agent in the system within a range of 1−4 wt % (Fig. 2). However, at an EGDM content in the comonomer mixture of 5 wt %, the polymerization rate somewhat decreases, which seems to be caused by increased viscosity and hindered diffusion mobility of monomer molecules in the growing PMPs [23]. Moreover, in the presence of 5% EGDM, the copolymerization is accompanied by a strongly pronounced gel effect (see Table 1, experiment 6, and Fig. 2).

At the same time, the DLS data show that the dependence of P(MMA−VFA−EGDM) particle size

on the concentration of the cross-linking agent exhibits a distinct maximum at an EGDM content of 2 wt % (Fig. 3). Therewith, the hydrodynamic particle diameter varies from 400 to 650 nm, whereas the diameter measured by TEM is equal to 360−415 nm (see Table 1, Fig. 3). Noticeably larger (by 100−200 nm) hydrodynamic diameter of P(MMA−VFA−EGDM) particles cannot be explained by "protrusion" of hydrophilic polymer chains into the dispersion medium alone and seems to be due to the formation of rather thick hydration shells on the particles.

The ζ potential of the synthesized polymer particles (and its dependence on dispersion medium pH) in a 10^{-3} M NaCl aqueous solution, as well as the surface concentration of functional groups, were determined both before (Table 2, Fig. 4) and after their hydrolysis (Table 2, Fig. 5). Hydrolysis of VFA amide units localized in the surface layer of P(MMA−VFA−EGDM) and P(MMA−VFA) particles yields aliphatic amino groups [9−11]. However, the positive charge of the particles in acidic or neutral media is caused by not only aliphatic amino groups, but also the protonated terminal imidazoline groups of unreacted initiator molecules. In this case, the AIP terminal groups are partially hydrolyzed to yield carboxyl groups, which are responsible for the negative charge of the particles in a strongly alkaline pH region (Fig. 6). Moreover, carboxyl groups may also be formed in the course of acid hydrolysis of MMA units.

(a) (b) (c)
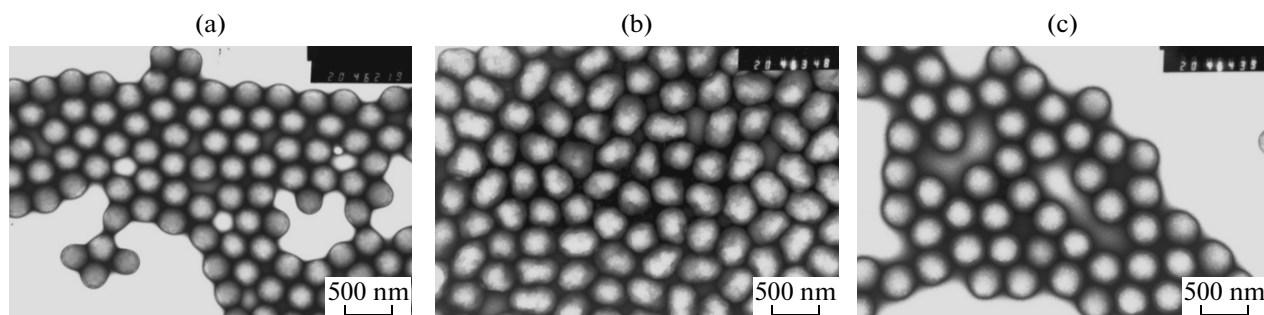
Fig. 1. Electron images of P(MMA−VFA) and P(MMA−VFA−EGDM) particles: (a) sample 1, (b) sample 4, and (c) sample 6 from Table 1.
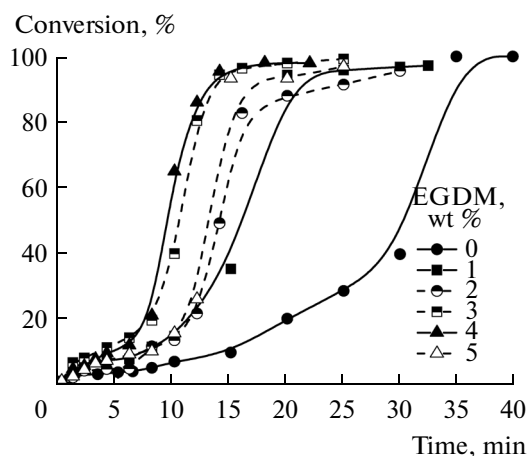
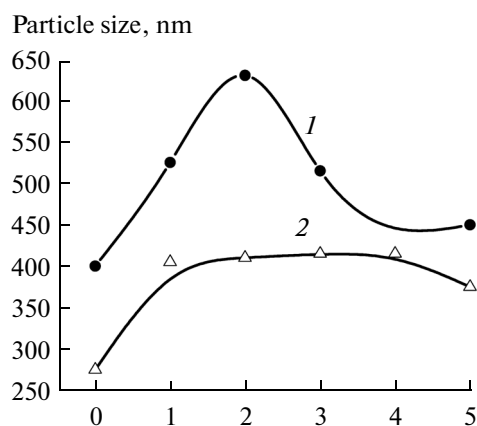**Fig. 2.** Kinetics of MMA conversion during the synthesis of P(MMA–VFA) and P(MMA–VFA–EGDM) particles.

Fig. 3. Polymer particle sizes as functions of EGDM concentration (before hydrolysis): (*1*) DLS data and (*2*) TEM data.
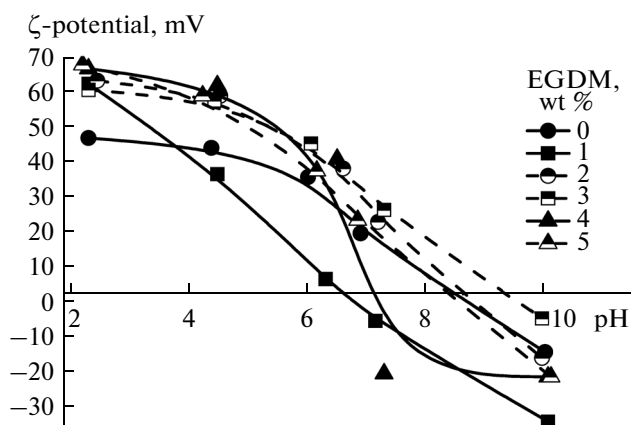

Fig. 4. pH dependences of the ζ–potentials of synthesized P(MMA–VFA) and P(MMA–VFA–EGDM) particles before hydrolysis.

Fig. 5. pH dependences of the ζ–potentials of synthesized P(MMA–VFA) and P(MMA–VFA–EGDM) after hydrolysis.

It turned out that, after hydrolysis, the ζ potential of weakly cross-linked particles (Table 2, samples 2–4) increases by, on average, 20–30 mV. However, for particles with higher degrees of cross-linking (Table 2, samples 5, 6), the ζ potential remains unchanged or somewhat decreases. The weakly cross-linked surface layer of particles makes polymer chains enriched with VFA units more accessible to hydrolysis. For particles obtained at an EGDM concentration of 1 wt % the carboxyl and amino groups are, before hydrolysis, present in the surface layer in comparable concentrations (Fig. 4). As a result, the isoelectric point of such particles falls into the neutral pH region. As the concentration of EGDM increases, particles, the surface layers of which are enriched with positively charged groups, are formed and charge sign reversal occurs in a weakly alkaline pH region (Fig. 4, Table 2).
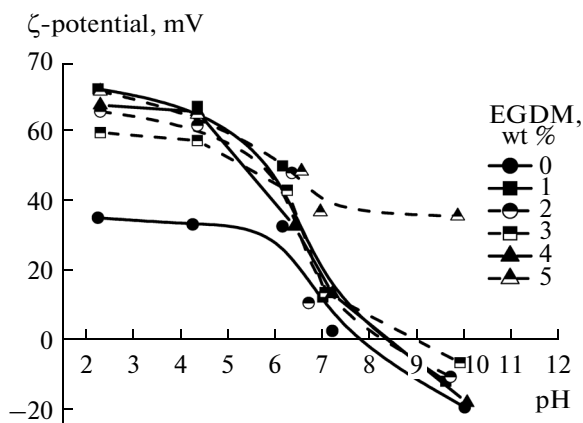
After hydrolysis, the concentration of surface functional groups increases by, on average, 0.8–0.9 μmol/m^2; however, charge sign reversal occurs in a weakly alkaline region as well. This suggests that the contents of amino and carboxyl groups remain comparable. However, after hydrolysis of P(MMA–VFA–EGDM) particles obtained in the presence of 5 wt % EGDM in the reaction system (Table 1, sample 6), the reversal of the ζ potential sign does not occur throughout the entire studied pH range (Fig. 5), thereby indicating an essential predominance of amino groups over carboxyl ones in the surface layer of these particles.

Thus, monodisperse particles of copolymers of methyl methacrylate, *N*-vinylforamide, and ethylene glycol dimethacrylate 360–415 nm in diameter have been obtained. The effect of the concentration of EGDM used as a cross-linking agent on the size, poly-
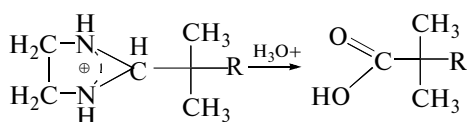
Fig. 6. Scheme of hydrolysis of terminal imidazoline groups of AIP used as an initiator.

dispersity, morphology, and surface electric properties of the particles has been studied. Particles synthesized in the presence of 5 wt % EGDM have appeared to carry a positive charge in a dispersion medium pH range of 2−10.

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