Effect of Reaction Parameters on the Particle Size in the Dispersion Polymerization of 2-Hydroxyethyl Methacrylate

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ABSTRACT: Poly(2-hydroxyethyl methacrylate) particles in the micron size range were obtained by the dispersion polymerization. Cellulose acetate butyrate and dibenzoyl peroxide were used as steric stabilizer and initiator, respectively. The ultimate particle size could be adjusted by the selection of a suitable polymerization medium consisting of an alcohol added to toluene and by varying their relative amounts. The particle size increased with increasing solubility parameter of the mixture, i.e., by decreasing the toluene/2-methylpropan-1-ol, toluene/butan-2-ol, and toluene/3-methylbutan-1-ol ratio. The particle size decreased with increasing concentration of the stabilizer and/or initiator. At the same time, the particle size distribution became narrower. Particles prepared from polymerization mixtures purged with nitrogen before the start of polymerization were smaller, and of narrower distribution, than those prepared from nitrogen-non-purged mixtures. Equilibrium swelling of particles in toluene decreased with the decreasing content of toluene in the polymerization mixture. © 1999 John Wiley & Sons, Inc. J Polym Sci A: Polym Chem 37: 3785–3792, 1999

Keywords: poly(2-hydroxyethyl methacrylate); dispersion polymerization; solubility parameter; micron-size range

INTRODUCTION

Recently, dispersion polymerization has been widely investigated as an alternative method for preparing monodisperse polymeric particles in the 1–10 μm size range in a single step.1 It is a process in which polymeric particles are formed in a continuous liquid medium through polymerization of monomer which is completely soluble in this medium. At the same time, a steric stabilizer is dissolved in the medium. The reaction begins as a solution polymerization. Particles are assumed to be formed by precipitation of growing polymer chains and subsequently stabilized. The critical chain length for precipitation is largely controlled by the nature of the medium. The reaction kinetics is a combination of that of solution polymerization and of polymerization inside swollen polymer particles. The particle size and its distribution are known to be affected by the monomer and its concentration, the medium, the amount and type of both the stabilizer and the initiator, and the temperature of polymerization.

The earlier studies have concentrated mainly on the dispersion polymerization of styrene and methyl methacrylate.2,3 Less effort was, however, devoted to the hydrophilic monomers, an example of which is 2-hydroxyethyl methacrylate (HEMA). The only report on dispersion polymerization of HEMA describes the effect of various stabilizers on the particle size.4 Since such particles can find use in a number of industrial and biomedical applications, e.g., carriers of biologically active compounds, chromatography, model systems, we have continued the investigation of the influence of several reaction parameters on the poly-(HEMA) particle size and distribution and swell-
ing behavior. The experiments described in this report establish mainly the effect of medium solvency controlled by the ratio of toluene to various alcohols and monomer, steric stabilizer, and initiator concentrations.

**EXPERIMENTAL**

**Materials**

2-Hydroxyethyl methacrylate (HEMA; Röhm GmbH, Germany) and ethylene dimethacrylate (EDMA; Ugilor, France) were purified by distillation under reduced pressure in nitrogen atmosphere. Cellulose acetate butyrate (CAB; acetyl/butyryl groups 35/15; $M_n = 100,000$) was a kind gift of Eastman, Kingsport, USA. All other chemicals were bought from Aldrich and used without purification.

**Polymerization Procedure**

Dispersion polymerization of HEMA in the mixture of toluene and an alcohol (2-methylpropan-1-ol, butan-2-ol, or 3-methylbutan-1-ol) of a given composition was stabilized using cellulose acetate butyrate. Dibenzoyl peroxide was an initiator of polymerization. The solubility parameter of the reaction mixture $\delta$ was calculated from the solubility parameters of components $\delta_i$ according to the equation $\delta = (\Sigma v_i \delta_i^{3/2})$, where $v_i$ is the volume fraction of the i-th component, $\delta$ (HEMA) = 23.3 MPa$^{3/2}$, $\delta$ (toluene) = 18.2 MPa$^{1/2}$ and $\delta$ (3-methylbutan-1-ol) = 20.5 MPa$^{1/2}$, $\delta$ (2-methylpropan-1-ol) = 21.5 MPa$^{1/2}$ and $\delta$ (butan-2-ol) = 22.1 MPa$^{1/2}$.

In a typical experiment, a 100-mL reaction vessel equipped with an anchor-type stirrer was employed. 3.2 g of cellulose acetate butyrate was dissolved in 68 g of a toluene/alcohol mixture (toluene/alcohol weight ratio varied typically from 0.2 to 1.2) and 0.24 g of dibenzoyl peroxide dissolved in 12 g of HEMA was added. The reaction mixture was stirred for 5 min and bubbled with nitrogen for 10 min in most experiments. Then the reaction mixture was heated (70 °C) under stirring at 500 rpm. The overall polymerization time was 8 h. The resulting particles were centrifuged, washed 6 times with toluene, and after drying obtained as a powder.

**Determination of Particle Size Distribution**

The particle size was determined by measuring at least 300 particles for each sample on photographs taken on a scanning electron microscope (JFM 6400, Joel). Two types of the mean particle size were calculated: number-average ($d_n$) and weight-average ($d_w$), $d_n = \Sigma d_i/N$, $d_w = \Sigma d_i^n/N$, $N$ is the number of particles). Particle size distribution was characterized by polydispersity index (PDI) calculated as a ratio of weight-to-number-average particle diameter.

**Determination of Molecular Weight**

The polymers were dissolved in methanol overnight at room temperature and heated at 40 °C until a clear solution was obtained. The viscosity molecular weight was calculated from intrinsic viscosity according to the equation$^5$ $\eta = 3.61 \times 10^{-4} M^{0.58}$.

**Swelling Measurements**

Two kinds of swelling measurements were carried out in toluene at room temperature. To reach the equilibrium degree of swelling, the polymers were immersed in toluene for minimum one week. Each measurement was reproduced at least twice. The equilibrium volume swelling ratio, $q_v = V_s/V_d$, was determined by placing dry polymer particles in a calibrated cylinder and reading their constant volume, $V_d$, after thorough settling. An excess of toluene was added, the polymer stirred and the volume, $V_s$, was read at the equilibrium after thorough settling of the particles. The equilibrium weight swelling ratio, $q_w$, was calculated using the equation $q_w = w_s/w_d$, where $w_d$ and $w_s$ are the weights of the dry and swollen polymer, respectively, in a column equipped with a sintered glass after centrifugation (10 min at 850 g).

**RESULTS AND DISCUSSION**

Preparation of microspheres entailed dispersion polymerization of HEMA in a mixture of butan-2-ol, or 2-methylpropan-1-ol, or 3-methylbutan-1-ol and toluene as the solvent medium in the presence of cellulose acetate butyrate (CAB) as the steric stabilizer and dibenzoyl peroxide (BPO) as a free radical initiator. While alcoholic part of the mixture was a thermodynamically good solvent for poly(HEMA), toluene was a poor solvent. The polymerization started in a clear homogeneous system. After an induction period of about 10 min, a faint opalescence was observed. This
became stronger after a while and the mixture turned into a white, stable dispersion. At the end of the reaction, the polymeric product was isolated, washed with toluene, centrifuged and dried (Figure 1).

Effect of Solvent System

According to the theories of particle formation, the solvency of the reaction medium towards the growing polymer chains controls the critical molecular weight above which the polymer precipitates during the nucleation stage in the dispersion polymerization. This in turn regulates the size of the particles. In the dispersion polymerization of HEMA, the solvency of the polymerization mixture could be finely tuned by the selection of butan-2-ol, 2-methylpropan-1-ol, or 3-methylbutan-1-ol added to toluene and by adjustment of their concentration. Solvency is represented in terms of liquid polarity as defined by the solubility parameter. Figure 2(a) shows that poly(HEMA) particle size was proportional to the solubility parameter of the medium. On the contrary, an inverse correlation between the polystyrene or poly(methyl methacrylate) particle size and the polarity of the dispersion medium was found. This distinction results from poor solubility of non-polar polystyrene or poly(methyl methacrylate) in polar solvents, in contrast to polar polymers, such as poly(HEMA). Because toluene is thermodynamically poorer solvent for poly(HEMA) than alcohols, the critical chain length of precipitated oligomers decreased with increasing toluene content in the polymerization mixture, i.e., with a decreasing solubility parameter. This resulted in an increase in the number of nuclei and, correspondingly, in a smaller size of particles. However, as shown in Table I, these

![Figure 1. Scanning electron micrograph of poly(HEMA) particles. Polymerization conditions: 22.2 g toluene, 45.8 g 2-methylpropan-1-ol, 12 g HEMA, 3.2 g CAB (acetyl/butyryl groups = 35/15; $M_n = 100,000$), 0.36 g BPO in the mixture; temperature 70 °C; purging with nitrogen.](image)

![Figure 2. Dependence of poly(HEMA) particle size $d_n$ (a) and polydispersity index PDI (b) on the solubility parameter $\delta$. Effect of the solvent system. Polymerization conditions: 68 g toluene/alcohol; 12 g HEMA, 0.24 g BPO, 3.2 g CAB (acetyl/butyryl groups = 35/15; $M_n = 100,000$); no purging of monomer mixture with nitrogen.](image)
small-sized particles formed from the mixtures with high proportions of toluene contained relatively high-molecular-weight poly(HEMA) compared with the larger particles. As a result, the poly(HEMA) particle size decreased with increasing molecular weight. An inverse correlation between the particle size and molecular weight is typical of any dispersion polymerization product and can be accounted for by changes in the locus of polymerization. A larger total surface area and density of smaller particles ensures that they efficiently capture growing oligomeric radicals initiated in solution, leading to solid-phase polymerization which gives higher molecular weight polymer because of the gel effect. On the other hand, larger particles capture dead polymer, which terminated in the continuous phase, with a lower molecular weight typical of solution polymerization. In accordance with these assumptions and if the toluene/alcohol ratio was kept constant, smallest poly(HEMA) particles were formed under otherwise identical conditions from a mixture toluene/3-methylbutan-1-ol, since 3-methylbutan-1-ol has the lowest value of the solubility parameter (20.5 MPa$^{1/2}$) of all the used alcohols. On the other hand, since butan-2-ol has the highest solubility parameter (22.1 MPa$^{1/2}$), the particles formed from its mixture with toluene were the largest.

In some ranges of toluene/alcohol dilution and depending on the removal of oxygen from the system by nitrogen purging before the start of polymerization, regular spherical particles were not formed, but only agglomerates. Generally speaking, spherical particles resulted in a broad range of toluene/alcohol ratios from nitrogen-non-purged mixtures. The particles were formed from nitrogen-purged toluene/2-methylpropan-1-ol mixtures containing 2 wt % BPO (relative to HEMA) and 4 wt % CAB, if $\delta$ was set within the limits 20.55 MPa$^{1/2}$ (20.42 MPa$^{1/2}$ in non-purged polymerization mixtures) and 21.1 MPa$^{1/2}$. The size distribution was, however, rather broad in nitrogen-non-purged experiments [Fig. 2(b)], probably due to the lengthened particle formation stage. From nitrogen-purged toluene/2-methylpropan-1-ol mixtures, relatively narrow particle size distribution was obtained for $\delta$ 20.7–20.97 MPa$^{1/2}$ [Fig. 2(b)]. Spherical particles of relatively narrow particle size distribution (PDI about 1.03–1.06) were also obtained in nitrogen-purged toluene/butan-2-ol mixtures, if $\delta$ was fixed at 20.7–20.8 MPa$^{1/2}$ (Table II). Outside these $\delta$ limits, an agglomerate resulted. The same mixtures, but non-purged with nitrogen, then generated spherical particles within a much broader range of $\delta$ 20.6–21.15 MPa$^{1/2}$ [Fig. 2(a)]; the particle size distributions were, however, broader [Fig. 2(b)]. It was difficult to obtain beads from nitrogen-purged toluene/3-methylbutan-1-ol mixtures. No beads were formed if $\delta$ was lower than 20.5 MPa$^{1/2}$ and, moreover, the monodispersity of resulting particles was poor even if $\delta$ was above this value (Table II). Again, identical systems, but non-purged with nitrogen, gave spherical particles within a much broader range of solubility parameter values — $\delta$ 19.98 MPa$^{1/2}$ and higher [Fig. 2(a)]. However, at $\delta$ higher than 20.2 MPa$^{1/2}$, the particle size distribution became very broad, since oxygen was not removed before the start of polymerization [Fig. 2(b)]. The decrease in the particle size and narrowing of the particle size distribution associated with the removal of oxygen from the polymerization mixture can be attributed to the fact that oxygen mostly behaves as a radical scavenger and inhibitor causing an in-

### Table I. Molecular Weight of Poly(HEMA) Particles

<table>
<thead>
<tr>
<th>Toluene/2-methylpropan-1-ol</th>
<th>$\delta$ (MPa$^{1/2}$)</th>
<th>$M_h \times 10^{-6}$</th>
<th>$d_n$ ($\mu$m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.80</td>
<td>20.58</td>
<td>0.59</td>
<td>0.91</td>
</tr>
<tr>
<td>0.63</td>
<td>20.72</td>
<td>0.51</td>
<td>1.19</td>
</tr>
<tr>
<td>0.55</td>
<td>20.81</td>
<td>0.45</td>
<td>1.31</td>
</tr>
<tr>
<td>0.48</td>
<td>20.89</td>
<td>0.40</td>
<td>1.55</td>
</tr>
<tr>
<td>0.37</td>
<td>21.03</td>
<td>0.25</td>
<td>2.86</td>
</tr>
</tbody>
</table>

$\delta$—solubility parameter; $M_h$—viscosity-average molecular weight; $d_n$—number-average particle size. Purging of polymerization mixture with nitrogen, other conditions the same as in Figure 2.

### Table II. Poly(HEMA) Particles Prepared from the Mixture Toluene and Butan-2-ol or 3-Methylbutan-1-ol

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>$\delta$ (MPa$^{1/2}$)</th>
<th>$d_n$ ($\mu$m)</th>
<th>PDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>butan-2-ol</td>
<td>20.70</td>
<td>0.80</td>
<td>1.06</td>
</tr>
<tr>
<td>butan-2-ol</td>
<td>20.81</td>
<td>0.94</td>
<td>1.03</td>
</tr>
<tr>
<td>3-methylbutan-1-ol</td>
<td>20.52</td>
<td>0.80</td>
<td>1.14</td>
</tr>
<tr>
<td>3-methylbutan-1-ol</td>
<td>20.62</td>
<td>0.87</td>
<td>1.10</td>
</tr>
<tr>
<td>3-methylbutan-1-ol</td>
<td>20.72</td>
<td>0.99</td>
<td>1.20</td>
</tr>
</tbody>
</table>

$\delta$—solubility parameter; $d_n$—number-average particle size; PDI—polydispersity index. Purging of polymerization mixture with nitrogen; other conditions are the same as in Figure 2.
The presence of oxygen may thus increase the critical chain length of oligomers precipitated from the solution, which results in a smaller number of nuclei, but of larger size. As a consequence of a prolonged nucleation period, broader particle size distribution was obtained. It is well known that monodispersity is obtained if nucleation occurs in a short time period, and after this, neither new nucleation nor coagulation takes place.10

**Effect of Monomer Concentration**

The overall polarity of the polymerization mixture depends on the fractions of individual components. Therefore it is also influenced by the concentration of the monomer dissolved in the medium. Since the solubility parameter of HEMA is higher than those of the solvent system, its contribution increases the average solubility parameter of the polymerization mixture. As a consequence, the particle size slightly increased with the concentration of the monomer in the polymerization mixture increasing from 10 to 17 wt % (Table III). The same trend was also reported for dispersion polymerization of styrene.11 If the HEMA monomer concentration in the reaction mixture was 20 wt % and more, irregular particles already resulted, probably due to large changes in the medium polarity as monomers were consumed during polymerization.

**Effect of Steric Stabilizer and its Concentration**

The stabilizer plays a crucial role in the formation of stable particles by dispersion polymerization. Stabilization of particles is determined by the rate and extent of adsorption of the stabilizer on the particle surface and its stabilizing efficiency which itself is a function of the solvency of the medium and the nature of the polymer onto which it is adsorbing.1Grafting of homopolymer stabilizer is often reported as either an additional or essential mechanism for providing stability of the particles.12

Preliminary experiments involving the use of several conventional stabilizers, such as poly(N-vinylpyrrolidone), poly(vinyl acetate), poly(methyl methacrylate-co-butyl methacrylate), ethyl cellulose, cellulose acetate butyrate, showed that only the last-mentioned compound is promising in the dispersion polymerization of HEMA. Among several cellulose acetate butyrates differing with both the molecular weight and the contents of acetyl and butyryl groups, only the stabilizer with number-average molecular weight ca. 100,000 and containing 35% acetyl and 15% butyryl groups produced regular spherical particles without agglomerates. The concentration of CAB stabilizer in the polymerization mixture was varied from 0.5 to 7 wt %. Inside the studied range, the poly(HEMA) particle size increased with decreasing concentration of stabilizer, as illustrated in Figure 3. Similar results were also reported in the dispersion polymerization of styrene.13 Inverse proportionality between the stabilizer concentration and the particle size was given by an important role of the stabilizer in the particle formation step; if its concentration was increased, the viscosity of the medium, the rate of adsorption of

<table>
<thead>
<tr>
<th>c (wt %)</th>
<th>$d_n$ (μm)</th>
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<tbody>
<tr>
<td>10</td>
<td>1.18</td>
</tr>
<tr>
<td>15</td>
<td>1.19</td>
</tr>
<tr>
<td>17</td>
<td>1.20</td>
</tr>
<tr>
<td>20</td>
<td>no beads</td>
</tr>
</tbody>
</table>

* Purging of polymerization mixture with nitrogen; other conditions are the same as in Figure 2.
stabilizer molecules, and the number of nuclei increased, which reduced the extent of aggregation and thus smaller particles resulted. The preferable concentration of CAB in the polymerization mixture affording nearly monodisperse poly(HEMA) particles (PDI ~ 1.03) equalled 4–5 wt %. Particles of irregular shapes were formed if the concentration of the stabilizer was less than 0.5 wt %; concentrations 10 wt % and higher already induced too high viscosity of the reaction mixture to be stirred properly. This kind of behavior is typical of the dispersion polymerization of any monomer. In the presence of too large amounts of a stabilizer, the resulting smaller particles were observed to aggregate. If the amount of the stabilizer was too small, absorption of propagating and dead polymers by existing particles was incomplete, resulting in unstable polymer aggregates.

**Initiator Concentration**

The selection of a suitable initiator is very important if fine and stable poly(HEMA) dispersion particles are to be obtained. The concentration and decomposition rate of the initiator and temperature are expected to affect the rate of production of free radicals in the medium, determining thus nucleation in dispersion polymerization. The effect of temperature on the dispersion polymerization of HEMA was studied in our earlier report, where it was found that the particle size increased with increasing polymerization temperature. In this study, regular spherical poly(HEMA) particles were obtained only using the BPO initiator. If 2,2'-azobisisobutyronitrile (AIBN) or 4,4'-azobis(4-cyanopentanoic acid) initiated the polymerization instead of BPO, an agglomerated product resulted. This fact can be explained by two reasons. The decomposition rate of both last-mentioned compounds was probably too high (the half-lives being 289 or 293 min, respectively, at 70 °C) compared with BPO (half-life 1,049 min at 70 °C). Only a moderate rate of radical generation, achieved with BPO, could ensure a relatively short nucleation stage and proper adsorption of stabilizer so that spherical particles were formed. In addition, the superiority of BPO in the dispersion polymerization of HEMA to AIBN can consist in that peroxy radicals are known to be more effective than cyanoalkyl radicals in the hydrogen abstraction processes which lead to grafting of the steric stabilizer to the polymer nuclei. In a further group of experiments, the effect of the BPO initiator concentration on the dispersion polymerization of HEMA was investigated. Narrow particle size distributions were obtained for BPO concentrations ranging at about 3–4 wt % (Fig. 4). As the initiator concentration was increased over the range 1–4 wt %, the average poly(HEMA) diameter slightly decreased from 1.6 to 1.5 μm (Fig. 4). This tendency, which was observed also for the dispersion polymerization of butyl acrylate or methacrylate, is, however, opposite than in the dispersion polymerization of styrene or methyl methacrylate. The explanation of this effect in the dispersion polymerization of HEMA appears to be in the formation of lower molecular weight polymer chains during the nucleation period with the increasing initiator concentration. Thus, higher initiator concentrations produce more numerous, but smaller, particles. On the other hand, and contrary to the emulsion polymerization, in dispersion polymerization of styrene or methyl methacrylate, an increase in the initiator concentration typically leads to fewer particles. The most popular explanation for this seemingly paradoxical phenomenon is that by increasing the radical production rate, the average critical molecular weight of the polymer formed in the medium is decreased by termination or chain transfer reactions. This subsequently reduces the number of chains which either aggregate or grow long enough to form nuclei. As a consequence, the number of particles is reduced. On the
other hand, Paine, Luymes, and McNulty argued that a greater initiator concentration leads to stabilizer grafts of shorter chain lengths which would have greater solubility in the reaction medium. The adsorption of the grafted stabilizer on the particles would therefore be retarded. As a result of both suggestions, polystyrene or poly-(methyl methacrylate) particle size, contrary to poly(HEMA), increased with the concentration of initiator. Still, to explain the reason for different dependences of the particle size on the concentration of initiator, many more dispersion polymerization processes must be investigated.

Swelling Measurements

In these studies, the effects of the solubility parameter of the reaction medium, controlled by the toluene/2-methylpropan-1-ol ratio, concentration of initiator and temperature, on equilibrium volume and weight swelling ratio of both non-crosslinked poly(HEMA) and crosslinked poly-(HEMA-co-EDMA) particles in toluene were investigated. However, the last two named effects turned out to be insignificant. Crosslinked poly-(HEMA-co-EDMA) particles were described in our previous report. Toluene was chosen as a swelling agent since the poly(HEMA) particles do not agglomerate in it. Figure 5 shows that with increasing solubility parameter, i.e., with greater proportion of 2-methylpropan-1-ol in the medium, both equilibrium volume and weight swelling ratio decrease. In other words, the higher the toluene content in the polymerization mixture at the beginning of the process, the higher the swelling of the resulting particles in toluene. This can be probably caused by increased polydispersity of particles with increasing solubility parameter since polydisperse particles are able to fill in more space compared with particles of narrow size distribution. Another, less probable explanation of the observed swelling behavior of poly(HEMA) particles can consist in the possibility of increased toluene and CAB grafting to poly(HEMA), or formation of porosity at high toluene proportions in the polymerization mixture. It is also evident from Figure 5 that both the volume and weight swelling ratios of poly(HEMA-co-EDMA) were lower than those of non-crosslinked poly(HEMA) due to the restriction of chain motions by the crosslinking reaction. With the exception of the region of low solubility parameter values (high toluene proportion in the polymerization medium), the equilibrium weight swelling ratio was higher than the equilibrium volume swelling ratio. This can be again explained under the assumption that the particles are porous or that soft poly(HEMA) spheres deformed in a cylinder by settling.

CONCLUSION

In the dispersion polymerization of HEMA, the particle size was primarily dependent both on the solubility parameter value of the reaction medium and on the stabilizer concentration. The particle size increased with increasing polarity of toluene/alcohol (2-methylpropan-1-ol, butan-2-ol, and 3-methylbutan-1-ol) mixture. As the concentration of cellulose acetate butyrate stabilizer increased, the size of the poly(HEMA) particles decreased and the total surface area increased. An insufficient stabilizer concentration resulted in the coagulation of the dispersion. The increase in dibenzoyl peroxide initiator concentration produced slightly smaller and therefore probably more numerous particles. The systems containing oxygen before the start of polymerization yielded particles of broad size distribution. Particles of narrow size distribution were obtained from nitrogen-purged reaction systems containing tolu-
ene/2-methylpropan-1-ol or toluene/butan-2-ol if the solubility parameter of the mixture lay within the limits 20.7–20.97 or 20.7–20.8 MPa$^{1/2}$, respectively.

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