Fabrication and Phase Behavior of Thermo- and/or pH-Responsive Polymer-Grafted SiO$_2$ Nanoparticles

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Abstract: Three series of thermo- and/or pH-responsive polymer-grafted SiO$_2$ nanoparticles, SiO$_2$-graft-poly(oligo(ethylene glycol) methacrylate) (SiO$_2$-g-P(OEGMA), SiO$_2$-graft-poly(acrylic acid) (SiO$_2$-g-PAA) and SiO$_2$-graft-poly(oligo(ethylene glycol) methacrylate-stat-acrylic acid (SiO$_2$-g-P(OEGMA-stat-AA)), were prepared by grafting POEGMA and/or PAA onto the surface of silica nanoparticles through the surface-initiated atom transfer radical polymerization (SI-ATRP). The lower critical solution temperature (LCST) of SiO$_2$-g-P(OEGMA ($M_{OEGMA} = 300$ g/mol) was found to be 64 $^\circ$C. For SiO$_2$-g-PAA nanoparticles, at the pH range from 8 to 12, the hydrodynamic diameter of the nanoparticles increases with increasing pH, and the zeta potential of SiO$_2$-g-PAA nanoparticles is negatively charged and decreases with increasing pH. Owing to the thermo- and pH-responsive, the hydrodynamic diameters of SiO$_2$-g-P(OEGMA-stat-AA) nanoparticles increase with the increasing pH, and the LCSTs of those nanoparticles increase with the increase of POEGMA content.

Keywords: thermo-responsive; pH-responsive; polymer-grafted nanoparticle; lower critical solution temperature

1. Introduction

Organic-inorganic nanocomposites composed of polymers and inorganic nanoparticles provide broad design possibilities for functional materials [1]. Polymer-grafted nanoparticles have attracted attention due to their various applications in many different fields, such as drug delivery [2,3], bioimages [4,5], and lubrication [6,7]. Notably, there has been an increasing interest in the preparation of grafting stimuli-responsive polymers onto inorganic nanoparticles because the stimuli-responsive polymer-grafted nanoparticles are able to exhibit unique and combined properties of the inorganic cores and the polymer shells [8–14]. Over the past two decades, polymers of different structures, including homopolymers, random copolymers, block copolymers, and bottlebrush polymers, have been successfully grafted onto silica surfaces by the surface-initiated atom transfer radical polymerization (SI-ATRP) method [15–19].

A stimuli-responsive polymer usually shows conformational and solubility changes as external environmental changes, such as pH, temperature, and ionic strength [15,20–22]. Among stimuli-responsive polymers, pH-responsive and thermo-responsive polymers have been extensively explored due to their potential applications in nanotechnology and biotechnology. pH-responsive polymers are prepared from the monomers that are either weakly acidic or basic, such as carboxylic, phosphoric acid, or amino groups, and these moieties charge and discharge reversibly as pH changes [15,20,23]. Water-soluble...
thermo-responsive polymers display a lower critical solution temperature (LCST), providing potential biomedical applications, for instance, drug delivery and biosensors [24–26]. As known, poly(ethylene glycol) (PEG) is a neutrally charged, water-soluble, non-toxic polymer, and thus, it has been widely applied in biomedical applications. Further, the nonlinear PEG analogues, for example, macromolecules prepared from oligo(ethylene glycol) methacrylate (OEGMA), are as biocompatible as their linear counterparts [27,28]. It has been found that polymers of oligo(ethylene glycol) methacrylate (POEGMA) are thermo-responsive, and the LCST of the POEGMA polymers increases with increasing the side-chain length of the oligo(ethylene glycol) unit [29]. Importantly, the copolymerization of two oligo (ethylene glycol) methacrylate (OEGMA) of different chain-lengths can form thermo-responsive copolymers that their LCST can be tuned by changing the ratio of the two OEGMA monomers [29–31]. Thus, POEGMA based thermo-responsive polymers can be considered smart biocompatible materials for various applications in biotechnology.

In this study, silica nanoparticles were firstly synthesized by the Stöber method and followed with modification by 3-aminopropyltrimethoxysilane (APTMS) and 2-bromoisoobutyryl bromide (BiBB) to synthesize spherical particle initiator (SiO$_2$-Br). The SI-ATRP method was then used to graft oligo(ethylene glycol) methacrylate (OEGMA, $M_n = 300$ g/mol) and/or tert-butyl acrylate (tBA) monomers onto the surface of silica nanoparticles. Through this synthesis procedure, we prepared SiO$_2$-g-POEGMA, SiO$_2$-g-PtBA and SiO$_2$-g-P(OEGMA-stat-tBA) nanoparticles. Next, SiO$_2$-g-PtBA and SiO$_2$-g-P(OEGMA-stat-tBA) were then hydrolyzed to obtain SiO$_2$-g-PAA and SiO$_2$-g-P(OEGMA-stat-AA), respectively. Fourier transform infrared spectra (FT-IR), thermogravimetric analysis (TGA), transmission electron microscopy (TEM), gel permeation chromatography (GPC), and proton nuclear magnetic resonance ($^1$H NMR) were used to characterize the prepared polymer-grafted nanoparticles. Further, thermo- and/or pH-responsive behavior of SiO$_2$-g-POEGMA, SiO$_2$-g-PAA, and SiO$_2$-g-P(OEGMA-stat-AA) in an aqueous solution was investigated by dynamic light scattering (DLS) under different temperature and at different pH.

2. Materials and Methods

2.1. Materials

Tetraethoxysilane (TEOS, 98%), (3-Aminopropyl)trimethoxysilane (APTMS, 97%), α-Bromoisoobutyryl bromide (BiBB, 98%), anisole (anhydrous, 99.7%), trifluoroacetic acid (TFA, 99%), CuBr (99.0%) and 2,2’-Bipyridine (bpy, $\geq 99$%) were purchased from Macklin Chemical Reagents Co., Ltd, Shanghai, China. Tetrahydrofuran (THF, $\geq 99.0$%), ammonium hydroxide solution (NH$_4$OH, 25 wt%), ethanol (C$_2$H$_5$OH, 99.5%), toluene (C$_6$H$_5$CH$_3$, AR), hydrochloric acid (HCl), sodium hydroxide (NaOH), dichloromethane (CH$_2$Cl$_2$), triethylamine (Et$_3$N), 2-Propanol (IPA, 99.5%) were purchased from Sinopharm Chemical Reagent Co., Ltd, Xi’an, China. Ethyl α-bromoisoobutyrate (EBiB, 98%), tert-Butyl acrylate (tBA, 98%), oligo (ethylene glycol) methacrylate (OEGMA, $M_n = 300$ g/mol, 99%) were purchased from Sigma-Aldrich, Shanghai, China. The inhibitors in tBA and OEGMA were removed by passing through a basic alumina column. THF and toluene were refluxed with sodium under nitrogen and distilled prior to use. Other chemicals and reagents were used as received without further purification. Milli-Q water was used for the sample preparation.

2.2. Synthesis of SiO$_2$ Nanoparticle

SiO$_2$ nanoparticles were synthesized by the Stöber method [32]. Ammonium hydroxide (25 mL, 25 wt%) was mixed with ethanol (500 mL), and the mixture was stirred at a speed of 1000 $r$/min at 50 °C for 1 h. A mixture of 12.5 mL TEOS and 14 mL ethanol was then added drop-wise, and the reaction was conducted at 50 °C in an oil bath for 24 h. The synthesized silica nanoparticles were collected by centrifugation (15,000 rpm, 20 min), followed by washing with ethanol several times. The obtained SiO$_2$ nanoparticles were then dispersed and stored in 50 mL ethanol.
2.3. Synthesis of SiO$_2$-NH$_2$

A measure of 45 mL of the prepared SiO$_2$ nanoparticles was transferred to a flask and heated at 60 °C. Ammonium hydroxide (100 µL, 25 wt%) was then added. Next, APTMS (0.8 mL, 3.4 mmol) was added drop-wise, and the reaction was conducted at 60 °C in an oil bath for 12 h. The SiO$_2$-NH$_2$ nanoparticles were separated by centrifugation (15,000 rpm, 20 min). After removing the supernatant, the sediment was washed with toluene three times to remove unreacted APTMS. The SiO$_2$-NH$_2$ nanoparticles were redispersed in 50 mL toluene.

2.4. Synthesis of SiO$_2$-Br

A measure of 45 mL of the prepared SiO$_2$-NH$_2$ nanoparticles was mixed with dry Et$_3$N (0.6 mL, 7.4 mmol) in a flask, and the mixture was cooled to 0 °C in an ice bath. Then, 2-bromoisobutyryl bromide (0.5 mL, 4.0 mmol) was added drop-wise. The reaction was conducted at 0 °C for 0.5 h, and then at room temperature for 12 h. The SiO$_2$-Br nanoparticles were separated by centrifugation (15,000 rpm, 20 min). After removing the supernatant, the sediment was washed with ethanol at least three times to remove unreacted 2-bromoisobutyryl bromide. The SiO$_2$-Br nanoparticles were then dried under vacuum overnight.

2.5. Synthesis of SiO$_2$-g-POEGMA

A mixture of SiO$_2$-Br (100 mg, 0.017 mmol of initiator site), OEGMA (0.153 g, 5.1 mmol), EBiB (5 mg, 0.025 mmol), 4 mL IPA, and 1 mL Milli-Q water was prepared in a Schlenk tube and deoxygenated through three freeze-pump-thaw cycles. CuBr (3.6 mg, 0.025 mmol) and bpy (3.9 mg, 0.025 mmol) were added to the tube under a gentle N$_2$ flow. Next, the reaction mixture was degassed via three more freeze-pump-thaw cycles. The polymerization was then conducted at 50 °C in an oil bath for 6 h. After this, the reaction mixture was cooled to room temperature, exposed to air, and diluted with IPA. The SiO$_2$-g-POEGMA nanoparticles were separated by centrifugation (9000 rpm, 20 min), and then the supernatant and precipitate were dialyzed and purified in Milli-Q for more than two days; Milli-Q water was replaced three times per day. The dialysis-purified supernatant was freeze-dried to collect the free POEGMA polymer. The prepared SiO$_2$-g-POEGMA nanoparticles were separated by centrifugation (9000 rpm, 20 min) and then dried under vacuum overnight.

2.6. Synthesis of SiO$_2$-g-PtBA, SiO$_2$-g-PAA

A mixture of 100 mg SiO$_2$-Br, tBA (1.088 g, 8.5 mmol), 4 mL anisole, and EBiB (5 mg, 0.025 mmol) was prepared in a Schlenk tube and deoxygenated through three freeze-pump-thaw cycles. CuBr (3.6 mg, 0.025 mmol) and bpy (3.9 mg, 0.025 mmol) were added to the tube under a gentle N$_2$ flow. Next, the reaction mixture was degassed via three more freeze-pump-thaw cycles. The polymerization was then conducted at 50 °C in an oil bath for 6 h. After this, the reaction mixture was cooled to room temperature, exposed to air, and diluted with tetrahydrofuran. The SiO$_2$-g-PtBA nanoparticles were separated by centrifugation (9000 rpm, 20 min), and then the supernatant and precipitate were dialyzed and purified in Milli-Q water for more than two days; Milli-Q water was replaced three times per day. The dialysis-purified supernatant was freeze-dried to collect the free PtBA polymer. The SiO$_2$-g-PtBA nanoparticles were separated by centrifugation (9000 rpm, 20 min) and then dried in a vacuum oven overnight. The SiO$_2$-g-PtBA nanoparticles were hydrolyzed under acidic conditions to obtain the SiO$_2$-g-PAA. To do this, 100 mg of SiO$_2$-g-PtBA nanoparticles were dissolved in 20 mL CH$_2$Cl$_2$ and 3.00 g TFA was then added. The mixture was then stirred at room temperature for 36 h. The nanoparticles were separated by centrifugation (9000 rpm, 20 min). After removing the supernatant, the SiO$_2$-g-PAA nanoparticles were washed with CH$_2$Cl$_2$ three times and then dried under vacuum overnight.

2.7. Synthesis of SiO$_2$-g-P(OEGMA-stat-tBA), SiO$_2$-g-P(OEGMA-stat-AA)

A mixture of 200 mg SiO$_2$-Br, OEGMA, tBA, 6 mL anisole, and EBiB (10 mg, 0.05 mmol) was prepared in a Schlenk tube and deoxygenated through three freeze-pump-thaw cycles.


CuBr (7.2 mg, 0.05 mmol) and bpy (7.8 mg, 0.05 mmol) were added to the bottle under a gentle N₂ flow. Finally, the reaction mixture was degassed via three more freeze-pump-thaw cycles. The polymerization was then conducted at 60 °C in an oil bath for 24 h. After this, the reaction mixture was cooled to room temperature, exposed to air, and diluted with tetrahydrofuran. The nanoparticles were separated by centrifugation (9000 rpm, 20 min), and then the supernatant and precipitate were dialyzed and purified in Milli-Q water for more than two days; Milli-Q water was replaced three times per day. The dialysis-purified supernatant was freeze-dried to collect free P(OEGMA-stat-tBA) polymer. The SiO₂-g-P(OEGMA-stat-tBA) nanoparticles were further separated by centrifugation (9000 rpm, 20 min) and dried in a vacuum oven overnight. We have prepared a series of SiO₂-g-P(OEGMA-stat-tBA) nanoparticles by changing the ratio between OEGMA and tBA monomers (Table 1). The SiO₂-g-P(OEGMA-stat-AA) nanoparticles were obtained by hydrolysis of the SiO₂-g-P (OEGMA-stat-tBA) nanoparticles under acidic conditions. Then, a measure of 100 mg SiO₂-g-P(OEGMA-stat-tBA) was dissolved in 20 mL CH₂Cl₂, and a sixfold molar excess TFA (with respect to the tert-butanol group) was then added. The mixture was stirred at room temperature for 36 h. The SiO₂-g-P(OEGMA-stat-AA) nanoparticles were separated by centrifugation (9000 rpm, 20 min). After removing the supernatant, the sediment was washed with CH₂Cl₂ three times and then dried under vacuum overnight.

Table 1. Ratio of OEGMA and tBA monomers for preparation of SiO₂-g-P(OEGMA-stat-tBA) nanoparticles.

| OEGMA (m) | tBA (n) | m/n   | SiO₂-g-P(OEGMA-stat-tBA) Nanoparticles            |
|-----------|---------|-------|--------------------------------------------------|
| 2.04 mmol | 4.76 mmol | 30/70 | SiO₂-g-P(OEGMA₃₀-stat-tBA₇₀)                      |
| 3.40 mmol | 3.40 mmol | 50/50 | SiO₂-g-P(OEGMA₅₀-stat-tBA₅₀)                      |
| 4.76 mmol | 2.04 mmol | 70/30 | SiO₂-g-P(OEGMA₇₀-stat-tBA₃₀)                      |

Methods for characterization of the nanoparticles are provided in the Supporting information.

3. Results and Discussions

3.1. Synthesis of Polymer-Grafted Nanoparticles

Scheme 1 shows the synthesis pathway of bare silica, amino-modified, initiator-modified silica nanoparticles, and polymer-grafted nanoparticles. Firstly, SiO₂ nanoparticles were synthesized by the Stöber method [32]. The nanoparticles were then modified by 3-aminopropyltrimethoxysilane (APTMS) and then by 2-bromoisobutyryl bromide (BiBB) to obtain silica nanoparticle initiator, SiO₂-Br. Next, SI-ATRP was employed to graft oligoethylene glycol methyl ether methacrylate (OEGMA) and/or tert-butyl acrylate (tBA) monomers onto SiO₂-Br. By this, we prepared SiO₂-g-POEGMA, SiO₂-g-PBBA, and SiO₂-g-P(OEGMA-stat-tBA) nanoparticles. SiO₂-g-P(POEGMA-stat-tBA) nanoparticles were then hydrolyzed to obtain SiO₂-g-PAA and SiO₂-g-P(OEGMA-stat-AA), respectively. For SiO₂-g-P(OEGMA-stat-AA), three nanoparticles containing different ratios of OEGMA and tBA monomers were prepared (Table 1). After hydrolysis, SiO₂-g-P(OEGMA₃₀-stat-AA₇₀), SiO₂-g-P(OEGMA₅₀-stat-AA₅₀) and SiO₂-g-P(OEGMA₇₀-stat-AA₃₀) were obtained.

The nanoparticles were characterized by TEM, and the images of the polymer-grafted nanoparticles clearly show that the nanoparticles have a silica core and a polymer shell (Figure 1). The diameter of SiO₂ is 40 nm, calculated based on the TEM images. The thickness of the polymer shell of SiO₂-g-POEGMA and SiO₂-g-PAA is approximately 5 nm and 3 nm, respectively. For SiO₂-g-P(OEGMA₃₀-stat-AA₇₀), SiO₂-g-P(OEGMA₅₀-stat-AA₅₀), and SiO₂-g-P(OEGMA₇₀-stat-AA₃₀) particles, the thickness of the polymer shells are similar, approximately 2.5 nm. These results indicate that the polymers were successfully grafted onto the silica nanoparticle.
Scheme 1. Synthesis of SiO$_2$-g-POEGMA, SiO$_2$-g-PAA and SiO$_2$-g-P(OEGMA-stat-AA) nanoparticles by SI-ATRP.

The nanoparticles were characterized by TEM, and the images of the polymer-grafted nanoparticles clearly show that the nanoparticles have a silica core and a polymer shell (Figure 1). The diameter of SiO$_2$ is 40 nm, calculated based on the TEM images. The thickness of the polymer shell of SiO$_2$-g-POEGMA and SiO$_2$-g-PAA is approximately 5 nm and 3 nm, respectively. For SiO$_2$-g-P(OEGMA$_{30}$-stat-AA$_{70}$), SiO$_2$-g-P(OEGMA$_{50}$-stat-AA$_{50}$), and SiO$_2$-g-P(OEGMA$_{70}$-stat-AA$_{30}$) particles, the thickness of the polymer shells are similar, approximately 2.5 nm. These results indicate that the polymers were successfully grafted onto the silica nanoparticle.

Figure 1. TEM images of bare SiO$_2$ (a), SiO$_2$-g-POEGMA (b), SiO$_2$-g-PAA (c), SiO$_2$-g-P(OEGMA$_{30}$-stat-AA$_{70}$) (d), SiO$_2$-g-P(OEGMA$_{50}$-stat-AA$_{50}$) (e), and SiO$_2$-g-P(OEGMA$_{70}$-stat-AA$_{30}$) (f).

Scheme 1. Synthesis of SiO$_2$-g-POEGMA, SiO$_2$-g-PAA and SiO$_2$-g-P(OEGMA-stat-AA) nanoparticles by SI-ATRP.
The bare silica and the polymer-grafted nanoparticles were also characterized by FT-IR (Figure 2). For the bare silica nanoparticles (Figure 2a), the absorption peaks at 1100 cm\(^{-1}\) and 465 cm\(^{-1}\) belong to the stretching and bending vibration of the Si-O groups, respectively. In addition, the absorption peaks at 945 cm\(^{-1}\) and 800 cm\(^{-1}\) belong to the bending vibration of the Si-OH and Si-O-Si groups, respectively. Figure 2b shows a new absorption band at 1536 cm\(^{-1}\) corresponding to the bending vibration of N-H in the amide group that appears in the spectrum of the SiO\(_2\)-Br nanoparticles, indicating the silica nanoparticles were successfully functionalized with the initiator. For SiO\(_2\)-g-PtBA nanoparticles, the absorption peak at 1730 cm\(^{-1}\) was observed (Figure 2c), belonging to the stretching vibration of the \(-\text{O-C=O}\) group, indicating the successful grafting of the POEGMA polymer chains onto the silica surface by SI-ATRP. In the spectrum of SiO\(_2\)-g-PtBA, the absorption peak at 1730 cm\(^{-1}\) belongs to the stretching vibration of the \(-\text{O-C=O}\) group (Figure 2d), and the absorption peak at 3410 cm\(^{-1}\) in the spectrum of SiO\(_2\)-g-PAA belongs to the \(-\text{OH}\) group formed after the hydrolysis of TBA (Figure 2e). In the spectrum of SiO\(_2\)-g-P(OEGMA\(_{50}\)-stat-tBA\(_{50}\)), the absorption peak at 1730 cm\(^{-1}\) belongs to the stretching vibration of the \(-\text{O-C=O}\) group (Figure 2f), and the absorption peak at 3410 cm\(^{-1}\) in the spectrum of SiO\(_2\)-g-P(OEGMA\(_{50}\)-stat-AA\(_{50}\)) belongs to the \(-\text{OH}\) group formed after the hydrolysis of TBA (Figure 2g). The results of the FT-IR spectrum indicate that the polymers were successfully grafted onto silica particles.

In addition, the chemical compositions of the prepared free polymers, including POEGMA, PtBA, P(OEGMA\(_{30}\)-stat-tBA\(_{70}\)), P(OEGMA\(_{50}\)-stat-tBA\(_{50}\)), and P(OEGMA\(_{70}\)-stat-tBA\(_{30}\)) were characterized by NMR. The \(^1\text{H}\) NMR spectrum of POEGMA (Figure 3a) shows all the characteristic peaks of polymer, the signals at 1.89 ppm and 1.65 ppm are attributed to \(-\text{CH}_2\) and \(-\text{CH}_3\) of the main polymer chain, respectively. The signals between 3.41-4.25 ppm and at 3.31 ppm are attributed to \(-\text{CH}_2\) and \(-\text{CH}_3\) of OEGMA, respectively. For PtBA (Figure 3b), the signals at 2.25 ppm and 1.75 ppm are attributed to \(-\text{CH}_2\) and \(-\text{CH}_3\) of the main polymer chain, respectively. The signal at 1.41 ppm is attributed to \(-\text{CH}_3\) in the side chain. The \(^1\text{H}\) NMR spectrum of P(OEGMA\(_{30}\)-stat-tBA\(_{70}\)), P(OEGMA\(_{50}\)-stat-tBA\(_{50}\)) and P(OEGMA\(_{70}\)-stat-tBA\(_{30}\)) are shown in Figure 3c. The signals at 1.41 ppm are attributed...
to -CH$_3$ of tBA, the area of the peaks increases with tBA content in the polymers. The signals between 3.49–4.25 ppm and at 3.41 ppm are attributed to -CH$_2$- protons and -CH$_3$ of OEGMA. These results indicate that the polymerization of the monomers was successful.

![1H NMR spectrum of POEGMA (a), PtBA (b), P(OEGMA$_{30}$-stat-tBA$_{70}$), P(OEGMA$_{50}$-stat-tBA$_{50}$) and P(OEGMA$_{70}$-stat-tBA$_{30}$) (c), from top to bottom).](image)

The TGA thermograms obtained from the bare silica, amino-modified silica, initiator-functionalized silica, and polymer-grafted nanoparticles are shown in Figure 4. A weight loss of 13.1%, 16.1%, and 19.1% was observed from the TGA curve of SiO$_2$, SiO$_2$-NH$_2$, and SiO$_2$-Br, respectively. The weight loss of bare silica nanoparticles was likely due to the continued condensation reaction and associated water loss [33]. The TGA result shows that 3.0 wt% difference in the weight retentions of the amino-modified and initiator-modified silica nanoparticles. The grafting density of the initiators on the silica nanoparticles’ surface was calculated to be 2.43 initiator/nm$^2$, if assuming the density of the silica nanoparticles is identical to that of the bulk silica (2.07 g/cm$^3$) [34] and using the residual mass of the amino-modified silica nanoparticles as the reference. Moreover, a weight loss of 27.6%, 29.5%, 32.1%, 28.2%, and 39.5% were observed from the TGA curve of SiO$_2$-g-PtBA, SiO$_2$-g-POEGMA, SiO$_2$-g-P(OEGMA$_{30}$-stat-tBA$_{70}$), SiO$_2$-g-P(OEGMA$_{50}$-stat-tBA$_{50}$), and SiO$_2$-g-P(OEGMA$_{70}$-stat-tBA$_{30}$), respectively. The weight loss of the polymer-grafted nanoparticles is due to the grafted polymer decompsoing into small molecules at sufficiently high temperatures. These results indicate that the polymers were successfully grafted onto the silica nanoparticle by SI-ATRP.

The molecular weight and molecular weight distribution of the free polymers, including POEGMA, PtBA, P(OEGMA$_{30}$-stat-tBA$_{70}$), P(OEGMA$_{50}$-stat-tBA$_{50}$), and P(OEGMA$_{70}$-stat-tBA$_{30}$), were determined by GPC. The results are summarized in Table 2. Generally, the polydispersity index (PDI = $M_w/M_n$) of the polymer formed by atomic radical polymerization is in the range of 1.05–1.5. The PDIs of the synthesized free polymers are in the range of 1.02–1.21, indicating the polymerization was “living”/controlled. The grafting densities of the free polymers ($\sigma$) were calculated from TGA, which were found to be in the range of 0.18–0.24 chains/nm$^2$. 

![Figure 3. 1H NMR spectrum of POEGMA (a), PtBA (b), P(OEGMA$_{30}$-stat-tBA$_{70}$), P(OEGMA$_{50}$-stat-tBA$_{50}$) and P(OEGMA$_{70}$-stat-tBA$_{30}$) (c), from top to bottom).](image)
The molecular weight and molecular weight distribution of the free polymers, including POEGMA, PtBA, P(OEGMA\textsubscript{30-stat}-tBA\textsubscript{70}), P(OEGMA\textsubscript{50-stat}-tBA\textsubscript{50}), and P(OEGMA\textsubscript{70-stat}-tBA\textsubscript{30}), were determined by GPC. The results are summarized in Table 2.

Generally, the polydispersity index (PDI = $M_w/M_n$) of the polymer formed by atomic radical polymerization is in the range of 1.05–1.5. The PDIs of the synthesized free polymers are in the range of 1.02–1.21, indicating the polymerization was "living"/controlled. The grafting densities of the free polymers ($\sigma$) were calculated from TGA, which were found to be in the range of 0.18–0.24 chains/nm\textsuperscript{2}.

Table 2. Molecular weight and the polydispersity index of POEGMA, PtBA, P(OEGMA\textsubscript{30-stat}-tBA\textsubscript{70}), P(OEGMA\textsubscript{50-stat}-tBA\textsubscript{50}) and P(OEGMA\textsubscript{70-stat}-tBA\textsubscript{30}) polymers.

| Polymer                  | $M_n$ (Da) | $M_w$ (Da) | PDI | $\sigma$ (Chains/nm\textsuperscript{2}) |
|--------------------------|------------|------------|-----|----------------------------------------|
| POEGMA                   | 12,900     | 14,300     | 1.11| 0.21                                   |
| PtBA                     | 16,500     | 20,000     | 1.21| 0.18                                   |
| P(OEGMA\textsubscript{30-stat}-tBA\textsubscript{70}) | 20,600     | 21,000     | 1.02| 0.22                                   |
| P(OEGMA\textsubscript{50-stat}-tBA\textsubscript{50}) | 39,900     | 23,300     | 1.17| 0.20                                   |
| P(OEGMA\textsubscript{70-stat}-tBA\textsubscript{30}) | 24,000     | 28,600     | 1.19| 0.24                                   |

3.2. Thermo- and pH-Responsive Behavior in Aqueous Solution

3.2.1. Thermo-Responsive Behavior of SiO\textsubscript{2-}g-POEGMA

The hydrodynamic diameter of the SiO\textsubscript{2-}g-POEGMA nanoparticle was determined by DLS over the temperature range of 55–68 °C. The lower critical solution temperature (LCST) of SiO\textsubscript{2-}g-POEGMA was found to be 64 °C (Figure 5). In this study, the LCST is defined as the temperature at which an abrupt decrease in hydrodynamic diameter is observed. There is no significate change in the hydrodynamic diameter at temperatures below 63 °C, while the hydrodynamic diameter of SiO\textsubscript{2-}g-POEGMA nanoparticles decreases with increasing temperature above the LCST. This is attributed to POEGMA polymers becoming less water-soluble owing to the fact that the hydrophobic interactions between the polymers are thermodynamically favored as compared to polymer-water interactions [29]. Our result indicates that SiO\textsubscript{2-}g-POEGMA is thermo-responsive, which is in line with the earlier observations [35]. On the other hand, we observed a broad transition in hydrodynamic size of SiO\textsubscript{2-}g-POEGMA nanoparticles, which has been suggested to be attributed to the interactions between neighboring POEGMA polymers [36].
3.2.2. pH-Responsive Behavior of SiO$_2$-g-PAA

The hydrodynamic diameter and zeta potential of the SiO$_2$-g-PAA nanoparticles were investigated at the pH range from 8 to 12 (Figure 6). The result shows that the hydrodynamic diameter of the SiO$_2$-g-PAA nanoparticle increases with pH, and its zeta potential decreases with increasing pH, indicating that the SiO$_2$-g-PAA nanoparticles are pH-responsive. PAA polymer chains possess -COOH groups and the pKa of the PAA is 4.5 [37], meaning that at pH above 4.5, the -COOH groups in the polymer chains are dissociated, and PAA becomes more negatively charged with increasing pH. Further, in our previous study, the isoelectric point of the silica surface was found around pH = 2, above which the silica surface is negatively charged [38]. As expected, at the investigated pH range, the zeta potential of SiO$_2$-g-PAA nanoparticle is negatively charged and decreases with increasing pH (Figure 6b). The hydrodynamic diameter of the SiO$_2$-g-PAA nanoparticles increases with increasing pH (Figure 6a), attributing to the PAA polymer shell becoming more swollen due to the electrostatic repulsive force between PAA polymers increases at a higher pH.

![Figure 5](image-url)

Figure 5. Hydrodynamic diameter of SiO$_2$-g-POEGMA nanoparticle as a function of temperature. The error bars correspond to standard deviations from three measurements.

![Figure 6](image-url)

Figure 6. Hydrodynamic diameter (a) and zeta potential (b) of SiO$_2$-g-PAA nanoparticle as a function of pH, at 25 °C. The error bars correspond to standard deviations from three measurements.
3.2.3. Thermo- and pH-Responsive Behavior of SiO$_2$-g-P(OEGMA-stat-AA)

The hydrodynamic diameter and the zeta potential of the prepared SiO$_2$-g-P(OEGMA-stat-AA) nanoparticles were determined over the pH range from 8 to 12 (Figure 7a,b). For all of the three nanoparticles, the hydrodynamic diameter increases and the zeta potential decreases with increasing pH, which can be attributed to an increase of electrostatic repulsive force between polymer chains at higher pH. The zeta potential of the three nanoparticles decreases with increasing pH, owing to the -COOH groups in the polymer chains are mostly dissociated at a higher pH. The hydrodynamic diameter of SiO$_2$-g-P(OEGMA$_{30}$-stat-tBA$_{70}$) and SiO$_2$-g-P(OEGMA$_{50}$-stat-AA$_{50}$) is similar at the investigated pH (Figure 7a). The hydrodynamic diameter of SiO$_2$-g-P(OEGMA$_{70}$-stat-AA$_{30}$) is smaller than that of SiO$_2$-g-P(OEGMA$_{30}$-stat-tBA$_{70}$) and SiO$_2$-g-P(OEGMA$_{50}$-stat-AA$_{50}$) over the pH range of 8–10 while it is larger at pH 11 and 12. We suggest that this is due to AA becoming more negatively charged as pH increases, resulting in a higher swelling ratio of the polymers. At the investigated pH, the zeta potential of SiO$_2$-g-P(OEGMA$_{50}$-stat-AA$_{50}$) and SiO$_2$-g-P(OEGMA$_{70}$-stat-tAA$_{30}$) nanoparticles is similar (Figure 7b). The zeta potential of SiO$_2$-g-P(OEGMA$_{30}$-stat-AA$_{70}$) nanoparticle is slightly more negative than that of SiO$_2$-g-P(OEGMA$_{50}$-stat-AA$_{50}$) and SiO$_2$-g-P(OEGMA$_{70}$-stat-tBA$_{30}$), which can be attributed to a higher AA content in SiO$_2$-g-P(OEGMA$_{30}$-stat-AA$_{70}$).

![Figure 7](image-url)

Figure 7. Hydrodynamic diameter (a) and zeta potential (b) of SiO$_2$-g-P(OEGMA$_{30}$-stat-AA$_{70}$) (black symbols), SiO$_2$-g-P(OEGMA$_{50}$-stat-AA$_{50}$) (red symbols) and SiO$_2$-g-P(OEGMA$_{70}$-stat-AA$_{30}$) (blue symbols) as a function of pH, the measurements were performed at 25 °C. The error bars correspond to standard deviations from three measurements.

Considering the stability of the polymer-grafted SiO$_2$ nanoparticles, we determined the hydrodynamic diameter of SiO$_2$-g-P(OEGMA$_{30}$-stat-AA$_{70}$), SiO$_2$-g-P(OEGMA$_{50}$-stat-AA$_{50}$), and SiO$_2$-g-P(OEGMA$_{70}$-stat-tBA$_{30}$) nanoparticles by DLS under different temperatures at a pH value of 11 (Figure 8). The LCST of SiO$_2$-g-P(OEGMA$_{30}$-stat-AA$_{70}$), SiO$_2$-g-P(OEGMA$_{50}$-stat-AA$_{50}$), SiO$_2$-g-P(OEGMA$_{70}$-stat-tAA$_{30}$) was found to be 57 °C, 66 °C, 70 °C, respectively. This result indicates that the LCST of the nanoparticles can be tunable by changing the ratio of the monomers and that the LCST of the SiO$_2$-g-P(OEGMA-stat-AA) nanoparticles increased with increasing OEGMA content. Our result shows that compared to SiO$_2$-g-POEGMA, the LCST of SiO$_2$-g-P(OEGMA$_{30}$-stat-AA$_{70}$) is lower than that of SiO$_2$-g-POEGMA, while the LCST of SiO$_2$-g-P(OEGMA$_{50}$-stat-AA$_{50}$) and SiO$_2$-g-P(OEGMA$_{70}$-stat-AA$_{30}$) is slightly higher than that of SiO$_2$-g-POEGMA. It has been reported that the LCST of P(MAA-co-OEGMA) polymers is lower than that of OEGMA and the LCST increases with increasing OEGMA content at pH below 7, owing to the intramolecular hydrogen bonding interactions between the acid groups and the ethyleneglycol chains that can expel the water from the hydration shell [39,40]. However, it should be mentioned that in the present study, the LCST was determined at a pH value of 11; it thus can be expected that the copolymer will expand due to the electrostatic repulsive force that can
increase the LCST [41]. We, therefore, think that the LCST of SiO$_2$-g-P(OEGMA-stat-AA) nanoparticles can be influenced both by the intramolecular hydrogen bonding between the ethyleneglycol chains and the -COOH groups and the intermolecular electrostatic repulsive force between the P(OEGMA-stat-AA) polymers. Taken together, our results indicate that SiO$_2$-g-P(OEGMA-stat-AA) nanoparticles are both pH- and thermo-responsive and that the LCST of the nanoparticles can be altered by changing the ratio between the monomers.

Figure 8. Hydrodynamic diameter of SiO$_2$-g-P(OEGMA$_{30}$-stat-AA$_{70}$) (a), SiO$_2$-g-P(OEGMA$_{50}$-stat-AA$_{50}$) (b), SiO$_2$-g-P(OEGMA$_{70}$-stat-AA$_{30}$) (c) nanoparticles as a function of temperature, these measurements were performed at pH = 11. The error bars correspond to standard deviations from three measurements.

4. Conclusions

Thermo-responsive SiO$_2$-g-POEGMA, pH-responsive SiO$_2$-g-PAA and thermo- and pH-responsive SiO$_2$-g-P(OEGMA-stat-AA) polymer-grafted nanoparticles were successfully prepared by SI-ATRP. The LCST of SiO$_2$-g-POEGMA nanoparticles was found to be 64 °C. The hydrodynamic diameter of the SiO$_2$-g-PAA nanoparticles increases with increasing pH, owing to an increased electrostatic repulsive force between the polymer chains. At pH 11, the LCST of SiO$_2$-g-P(OEGMA-stat-AA) nanoparticles increases with the increase of POEGMA content, which can be influenced by the intramolecular hydrogen bonding and the intermolecular electrostatic repulsive force. These results imply that the LCST of SiO$_2$-g-P(OEGMA-stat-AA) nanoparticles can be altered by changing the ratio between the monomers. Our study provides a new approach to designing dual-responsive nanoparticles and expands the range of responsive temperatures for the nanoparticles. The dual-responsive nanoparticles have potential applications in biology and chemistry fields, such as controlled drug delivery [9,42], ultra-stable Pickering emulsion [43] and bio- and chemosensors.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/app12083799/s1, Methods for characterization of the nanoparticles.

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