



Preparation of polymer/silica/polymer tri-layer hybrid materials and the corresponding hollow polymer microspheres with movable cores

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ABSTRACT

Tri-layer poly(methacrylic acid-co-ethyleneglycol dimethacrylate)/silica/poly(ethyleneglycol dimethacrylate) (P(MAA-co-EGDMA)/SiO₂/PEGDMA) and P(MAA-co-EGDMA)/SiO₂/polydivinylbenzene hybrid microspheres were prepared by distillation precipitation polymerization of ethyleneglycol dimethacrylate (EGDMA) and divinylbenzene (DVB) in the presence of 3-(methacryloxy)propyl trimethoxysilane (MPS)-modified P(MAA-co-EGDMA)/SiO₂ microspheres as the seeds. The polymerization of EGDMA and DVB was performed in neat acetonitrile with 2,2'-azobisisobutyronitrile (AIBN) as initiator to coat the MPS-modified P(MAA-co-EGDMA)/SiO₂ seeds through the capture of EGDMA and DVB oligomer radicals with the aid of vinyl groups on the surface of modified seeds in the absence of any stabilizer or surfactant. Monodisperse P(MAA-co-EGDMA)/SiO₂ core-shell microspheres were synthesized by coating of a layer of silica onto P(MAA-co-EGDMA) microspheres via a sol-gel process, which were further grafted by MPS incorporating the reactive vinyl groups onto the surface to be used as the seeds for the construction of hybrid microspheres with tri-layer structure. Hollow poly(ethyleneglycol dimethacrylate) (PEGDMA) and poly(divinylbenzene) (PDVB) microspheres with movable P(MAA-co-EGDMA) core were subsequently developed after the selective etching of the silica mid-layer from the tri-layer hybrid microspheres in hydrofluoric acid. The morphology and structure of the tri-layer polymer hybrids and the corresponding hollow polymer microspheres with movable P(MAA-co-EGDMA) core were characterized by transmission electron microscopy (TEM), Fourier transform infrared spectra and X-ray photoelectron spectroscopy (XPS).

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1. Introduction

The development of materials with a novel structure has been a fundamental focus of chemical research, which promotes the advances in both the academic and the industrial areas. During the last decade, organic-inorganic hybrid materials, which combine the properties of inorganic and organic building blocks within a single material, have attracted rapidly expanding interest for material scientists due to the combination of the various functional groups from the organic components and the advantages from a thermally stable and robust inorganic substrate [1,2]. The organic-inorganic hybrid materials have found diverse applications as drug-delivery system, diagnostic, coating and catalyst because of their novel and excellent properties such as mechanical, chemical, electrical, rheological,

magnetic and catalytic, by varying their composition, dimension, and structure of the materials [3–8].

The silica/polymer hybrid/composite particles with various interesting morphologies, such as silica core/organic shell [9], organic core/silica shell [10], raspberry-like [11], snowman-like [12], daisy-shaped and multipod-like [13] and raisin bun-like [14], have been afforded by different techniques. The preparation of the silica/polymer hybrid/composite particles can be generally classified into two categories: the self-assembly of the resultant silica and polymer particles via physical or physicochemical interaction, and the direct polymerization of monomer on the surface of silica particles. Bourgeat-Lami et al. [15–17] synthesized silica/organic hybrid particles with silica microspheres as seeds, in which the reactive vinyl groups were introduced by 3-trimethoxysilylpropyl methacrylate (MPS). The hedgehog-like or raspberry-like hybrid particles were prepared by miniemulsion polymerization [18], in which the silica nanoparticles behaved as surfactants and fillers. Surface-initiated atom transfer radical polymerization (ATRP) has been widely used to fabricate silica/polymer hybrids with the initiator-modified silica particles as

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macro-initiators [19–21], in which the synthesis was tedious with long reaction time and low conversion of monomer to polymer.

Hollow microspheres have proven their wide applications in many fields, including catalysis, controlled drug-delivery systems, artificial cells, fillers, pigments, light weight structural materials, nano-reactors, low dielectric constant materials, acoustic insulation, and photonic crystals [22–26], which were attributed to their unique properties, such as low density, high specific area and good flow ability and surface permeability. Many efforts have been paid onto the preparation of hollow polymer microspheres with different physical and chemical methods, including the encapsulation of a hydrocarbon non-solvent [27], layer-by-layer assembly of polymer electrolyte [28,29], micelle formation of block copolymer [30], and surface-initiated ATRP [31]. Further, core-shell spherical colloids with movable gold cores were produced by three major steps, which allowed the optical sensing of chemical diffusion into the cavity [32]. Polypyrrole (PPy) hollow capsules with movable hematite cores were synthesized via soaking sandwich ellipsoids in a hydrofluoric acid (HF) aqueous solution [33,34]. Tin-encapsulated spherical hollow carbon for the anode material in lithium secondary batteries has been prepared by a sol-gel polymerization process with subsequent decomposition of tributylphenyltin (TBPT) at 700 °C under an argon atmosphere [35]. An important concern of hollow microspheres is to accommodate guest nanoparticles in their cavity, which results in an interesting structure as hollow microspheres with movable cores and novel properties different from those of the host hollow microspheres and the guest nanoparticles. In such a way, nanoparticles such as gold [32,36], silver [37], tin [35], silica [38], and iron oxide [39] have been incorporated into the interior of the hollow microspheres by various techniques. In addition, monodispersity and polarity of the hollow polymer spheres are important to improve their performance for many applications. If the size distribution of particles is narrow, physical and chemical properties are more uniform, thereby making it easier, for example, to formulate more sophisticated drug deliver system (DDS) [40]. Furthermore, the interaction with biological cells is dependent on particles' size and size distribution [41]. However, it was difficult to control the size and size distribution of the hollow spheres or hollow spheres with movable cores for both dispersion polymerization and emulsion polymerization.

In our previous work, monodisperse silica/poly(*N,N'*-methylenebisacrylamide) ($\text{SiO}_2/\text{PMBAAm}$) [42], silica/polydivinylbenzene (SiO_2/PDVB) and silica/poly(ethylene glycol dimethacrylate) ($\text{SiO}_2/\text{PEGDMA}$) [43] core-shell hybrid microspheres, tri-layer Au/silica/PMBAAm [34], hematite/silica/PDVB [44] and poly(divinylbenzene-co-acrylic acid)/polyacrylic acid/poly(divinylbenzene-co-acrylic acid) ($\text{P}(\text{DVB-co-AA})/\text{PAA}/\text{P}(\text{DVB-co-AA})$) [45] and their corresponding hollow polymer microspheres with movable functional cores were successfully prepared by distillation precipitation polymerization. In these works, the size and size distribution of the polymer microspheres can be well controlled in absence of any stabilizer or surfactant. Here, we describe a facile method for the preparation of hollow polydivinylbenzene (PDVB) and poly(ethylene glycol dimethacrylate) (PEGDMA) microspheres with movable functional poly(methacrylic acid-co-ethylene glycol dimethacrylate) ($\text{P}(\text{MAA-co-EGDMA})$) cores with subsequently selective removal of the inorganic mid-silica layer in hydrofluoric acid from the corresponding $\text{P}(\text{P}(\text{MAA-co-EGDMA})/\text{SiO}_2/\text{PDVB}$ and $\text{P}(\text{MAA-co-EGDMA})/\text{SiO}_2/\text{PEGDMA}$ tri-layer microspheres, respectively, which were prepared by a three-stage reaction. The present method offered an alternative approach to the preparation of monodisperse hollow polymer microspheres having various polarities and functional groups with movable cores.

2. Experimental

2.1. Chemicals

Ethylene glycol dimethacrylate (EGDMA) was purchased from Alfa Aesar and used without any purification. Divinylbenzene (DVB, 80% divinylbenzene isomers) was supplied as technical grade by Shengli Technical Factory, Shandong, China, which was washed with 5% aqueous sodium hydroxide and water, then dried over anhydrous magnesium sulfate prior to use. Methacrylic acid (MAA) was purchased from Tianjin Chemical Reagent II Co. and purified by vacuum distillation. 3-(Methacryloxy)propyl trimethoxysilane (MPS) was bought from Aldrich and distilled under vacuum. Tetraethylorthosilicate ($\text{Si}(\text{OEt})_4$, TEOS) was obtained from Aldrich and used without further purification. Ammonia (25%, aqueous solution) was purchased from Tianjin Dongsheng Fine Chemical Reagent Factory, China. 2,2'-Azobisisobutyronitrile (AIBN) was provided by Chemical Factory of Nankai University and recrystallized from methanol. Hydrofluoric acid (HF, containing 40 wt% of HF) was obtained from Tianjin Chemical Reagent Institute. Acetonitrile (analytical grade, Tianjin Chemical Reagent II Co.) was dried over calcium hydride and purified by distillation before utilization. All the other reagents were of analytical grade and used without any further treatment.

2.2. Synthesis of MPS-modified $\text{P}(\text{MAA-co-EGDMA})/\text{SiO}_2$ core-shell nanoparticles

Monodisperse poly(methacrylic acid-co-ethylene glycol dimethacrylate) ($\text{P}(\text{MAA-co-EGDMA})$) microspheres were prepared by distillation precipitation polymerization of EGDMA and MAA ($\text{EGDMA}/\text{MAA} = 4/6$ as volume ratio in the comonomer feed) with AIBN as initiator in neat acetonitrile according to our previous paper [46]. A typical procedure for such synthesis of $\text{P}(\text{P}(\text{MAA-co-EGDMA}))$ was as follows: In a dried 100-mL two-necked flask, MAA (1.20 mL) and EGDMA (0.80 mL) (monomer total as 2.5 vol% of the reaction system), and AIBN (0.04 g, 2 wt% corresponding to the comonomers) were dissolved in 80 mL of acetonitrile. The two-necked flask attaching with a fractionating column, Liebig condenser and receiver was submerged in a heating mantle. The reaction mixture was heated from ambient temperature till the boiling state for further 10 min. Then the polymerization was carried out with distilling the solvent out of the reaction system and the reaction was ended after 40 mL of acetonitrile was distilled off the reaction mixture within 90 min. After the polymerization, the resultant $\text{P}(\text{MAA-co-EGDMA})$ nanoparticles were purified by repeating centrifugation, decantation and resuspension in acetonitrile for three times. The nanoparticles were then dried in a vacuum oven at 50 °C till constant weight.

Poly(methacrylic acid-co-ethylene glycol dimethacrylate)/silica ($\text{P}(\text{MAA-co-EGDMA})/\text{SiO}_2$) core-shell microspheres were synthesized by coating of an outer layer of silica onto $\text{P}(\text{MAA-co-EGDMA})$ nanoparticles via a sol-gel process. About 0.20 g of $\text{P}(\text{MAA-co-EGDMA})$ nanoparticles, 2.40 mL of ammonia and 1.0 mL of TEOS were introduced into a water/ethanol (40 mL/160 mL) mixture with vigorous stirring. The sol-gel process was allowed to proceed for 12 h, then another 2.40 mL of ammonia and 1.0 mL of TEOS were added to the reaction system under vigorous stirring to proceed the reaction for 12 h further at room temperature.

Modification of $\text{P}(\text{MAA-co-EGDMA})/\text{SiO}_2$ microspheres with MPS to incorporate the reactive vinyl groups was achieved by introducing MPS (2.0 mL) into the above ethanol suspension of core-shell particles under stirring and the mixture was stirred for 48 h at room temperature. The resultant MPS-modified $\text{P}(\text{MAA-co-EGDMA})/\text{SiO}_2$ core-shell microspheres were purified by centrifugation, decantation, and resuspension in ethanol for three cycles to

remove the excessive MPS. The final MPS-modified P(MAA-co-EGDMA)/SiO₂ core-shell microspheres were dried in a vacuum oven at 50 °C till constant weight.

2.3. Preparation of P(MAA-co-EGDMA)/SiO₂/PEGDMA and P(P(MAA-co-EGDMA))/SiO₂/PDVB tri-layer hybrid microsphere

A typical procedure for the distillation precipitation polymerization to synthesize poly(methacrylic acid-co-ethyleneglycol dimethacrylate)/silica/polyethyleneglycol dimethacrylate (P(MAA-co-EGDMA)/SiO₂/PEGDMA) tri-layer hybrid microspheres: In a dried 100-mL two-necked flask, 0.10 g of MPS-modified P(MAA-co-EGDMA)/SiO₂ particles were suspended in 40 mL of acetonitrile as white suspension. Then EGDMA (0.50 mL, total as 1.25 vol% of the reaction system) and AIBN (0.01 g, 2 wt% relative to the monomer) were dissolved in the suspension. The two-necked flask attaching with a fractionating column, Liebig condenser and receiver was submerged in a heating mantle. The reaction mixture was heated from ambient temperature till the boiling state within 12 min and the reaction system was kept under refluxing state for further 10 min. Then the polymerization was performed with distilling the solvent out of the reaction system and the reaction was ended after 20 mL of acetonitrile was distilled off the reaction mixture within 60 min. After the polymerization, the resultant P(MAA-co-EGDMA)/SiO₂/PEGDMA tri-layer hybrid microspheres were purified by repeating centrifugation, decantation, and resuspension in acetonitrile for three times. Then the tri-layer hybrids were dried in a vacuum oven at 50 °C till constant weight.

Preparation of poly(methacrylic acid-co-ethyleneglycol dimethacrylate)/silica/polydivinylbenzene P(MAA-co-EGDMA)/SiO₂/PDVB tri-layer hybrid microspheres was much similar to the procedure for the synthesis of P(MAA-co-EGDMA)/SiO₂/PEGDMA tri-layer microspheres, while the monomer was altered from EGDMA to DVB.

2.4. Preparation of hollow PEGDMA and PDVB microspheres with movable P(MAA-co-EGDMA) cores

The resultant P(MAA-co-EGDMA)/SiO₂/PEGDMA or P(MAA-co-EGDMA)/SiO₂/PDVB tri-layer particles were immersed in 5 wt% hydrofluoric acid aqueous solution for 4 h with stirring. (Caution: Hydrofluoric acid is very corrosive and should be handled carefully!) Then the excessive HF and the formed SiF₄ were expelled from the reaction system. The hollow poly(ethyleneglycol dimethacrylate) (PEGDMA) or poly(divinylbenzene) (PDVB) with movable P(MAA-co-EGDMA) cores were purified by centrifugation/washing cycles in water until reaching a pH of 7. The resultant hollow PEGDMA or PDVB microspheres with movable P(MAA-co-EGDMA) cores were dried in a vacuum oven at 50 °C till constant weight.

2.5. Characterization

The size and morphology of the polymer microspheres and hollow polymer microspheres with movable cores were characterized by transmission electron microscopy (TEM, Tecnai G2 20-S-TWIN). All the size and size distribution reflect the averages of about 100 particles, which are calculated according to the following formula:

$$U = D_w/D_n \quad D_n = \frac{\sum_{i=1}^k n_i D_i}{\sum_{i=1}^k n_i} \quad D_w = \frac{\sum_{i=1}^k n_i D_i^4}{\sum_{i=1}^k n_i D_i^3}$$

where U is the polydispersity index, D_n is the number-average diameter, D_w is the weight-average diameter, D_i is the particle

diameter of the determined microparticles. The thickness of the outer shell layer for the core-shell particles was calculated as half of the difference between the diameter of the core and that of core-shell particles.

Fourier transform infrared spectra were determined on a Bio-Rad FTS 135 FT-IR spectrometer over potassium bromide pellet and the diffuse reflectance spectra were scanned over the range of 4000–400 cm⁻¹.

X-ray photoelectron spectroscopic (XPS) analysis was carried out with a PHI 5300 XPS surface analysis system (Physical Electronics, Eden Prairie, MN, US) using a Mg K α X-ray source operating at 250 W and 13 kV ($h\nu = 1253.6$ eV). The electron binding energy of C1s (284.6 eV) was used as the internal standard.

3. Results and discussion

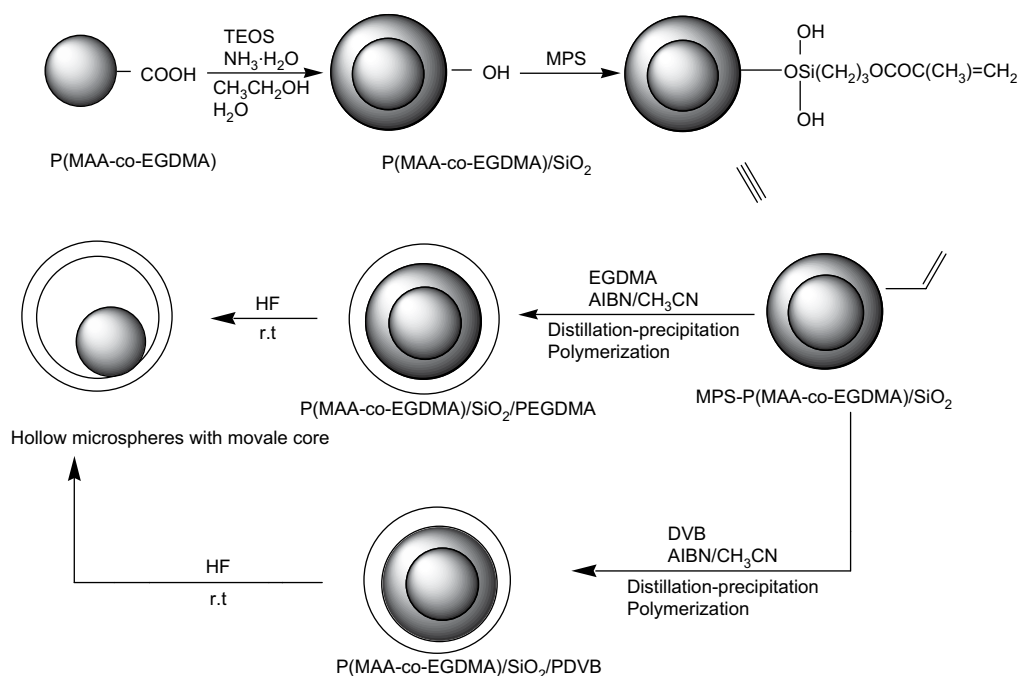
Scheme 1 illustrates the synthesis of P(MAA-co-EGDMA)/SiO₂/PEGDMA and P(MAA-co-EGDMA)/SiO₂/PDVB tri-layer hybrid microspheres via a three-stage reaction and the further development of the corresponding hollow PEGDMA and PDVB microspheres with movable P(MAA-co-EGDMA) cores after the selective removal of the silica mid-layer in hydrofluoric acid.

Distillation precipitation polymerization has been proven to be a useful and facile technique for the synthesis of monodisperse polymer microspheres with different functional groups [46,47] and various core-shell structure microspheres [42–45]. The TEM micrograph of P(MAA-co-EGDMA) microspheres by distillation precipitation polymerization is shown in Fig. 1A, which indicated that the polymer microspheres had spherical shape with average size of 69 nm with a monodispersity index (U) of 1.014 as summarized in Table 1. The loading capacity of the accessible carboxylic acid was 3.5 mmol/g as determined by acid-base titration [46].

3.1. Preparation of P(MAA-co-EGDMA)/SiO₂ core-shell nanoparticles

The P(MAA-co-EGDMA)/SiO₂ core-shell nanoparticles were prepared by direct encapsulation of P(MAA-co-EGDMA) core microspheres via condensation hydrolysis of TEOS with ammonia as catalyst in absence of any additive during the modified Stöber sol-gel process, as shown in Scheme 1. The TEM image of the resultant P(MAA-co-EGDMA)/SiO₂ core-shell microspheres is shown in Fig. 1B, in which a typical core-shell structure was clearly observed with a light contrast of P(MAA-co-EGDMA) core and a deep contrast of silica shell layer. The results in Fig. 1B demonstrated that the P(MAA-co-EGDMA)/SiO₂ core-shell microspheres had spherical shape with uniform shape in absence of any secondary silica particles from self-nucleation during the sol-gel hydrolysis. The driving force for the formation of the silica shell layer was probably due to the efficient hydrogen-bonding interaction between the carboxylic acid groups on the surface of P(MAA-co-EGDMA) core microspheres and the hydroxyl groups of silica component during the condensation hydrolysis of TEOS via the modified Stöber method, which was much similar to the construction of silica/polymethacrylic acid/silica tri-layer composite particles in our previous work [48]. The mechanism of the hydrogen-bonding interaction as a driving force for the growth of non-crosslinked polymethacrylic acid (PMAA) microspheres [49] and the formation of silica/PMBAAm core-shell composite microspheres [43] were reported in detail in our previous papers.

The particle size of the P(MAA-co-EGDMA)/SiO₂ core-shell microsphere was significantly from 69 nm of P(MAA-co-EGDMA) core to 121 nm with a monodispersity index (U) of 1.007 as summarized in Table 1 and the encapsulation yield of silica shell



Scheme 1. Preparation of P(MAA-co-EGDMA)/silica/polymer tri-layer hybrid particles and the corresponding hollow polymer microspheres with movable P(MAA-co-EGDMA) cores.

layer was 24%. Here, the thickness of the silica shell layer was calculated as half of the difference between the diameter of P(MAA-co-EGDMA) (light contrast color) core and that of P(MAA-co-EGDMA)/SiO₂ core-shell particles as shown in Fig. 1B. In such case, the diameter (76 nm) of P(MAA-co-EGDMA) core from ethanol in Fig. 1B was a little larger than that of P(MAA-co-EGDMA) seed (69 nm) in Fig. 1A because the P(MAA-co-EGDMA) particles were in a higher swollen state in ethanol during the coating of silica shell layer than those in acetonitrile after the first-stage polymerization. In short, the thickness of the silica shell layer was 22 nm via coating of the P(MAA-co-EGDMA) cores during the second-stage sol-gel hydrolysis of TEOS with the aid of hydrogen-bonding interaction.

The successful encapsulation of silica layer onto P(MAA-co-EGDMA) core microspheres was confirmed further by the XPS spectra as shown in Fig. 2, in which the electronic binding energy of C_{1s} (284.6 eV) was used as the internal standard. The XPS spectrum of P(MAA-co-EGDMA) core microspheres had the strong peaks at 531.4 and 288.0 eV (Fig. 2A) ascribing to the binding energy of O_{1s} and C_{1s}, respectively. While for the XPS spectrum of P(MAA-co-EGDMA)/SiO₂ core-shell microspheres, the peaks at 531.4, 288.0, 150.0 and 102.1 eV were clearly observed corresponding to the binding energy of O_{1s}, C_{1s}, Si_{2s}, and Si_{2p}, respectively. The atom concentration on the surface of the P(MAA-co-EGDMA)/SiO₂ core-shell microspheres in Fig. 2B indicated that the Si concentration was calculated as high as 33.7%. This result implied that the silica shell layer with thickness of 22 nm was successfully encapsulated onto the P(MAA-co-EGDMA) core microspheres through the modified Stöber sol-gel hydrolysis.

3.2. Preparation of P(MAA-co-EGDMA)/SiO₂/PEGDMA and P(MAA-co-EGDMA)/SiO₂/PDVB tri-layer hybrid microspheres

The formation of monodisperse polydivinylbenzene (PDVB) [47] and poly(ethyleneglycol dimethacrylate) (PEGDMA) [50] demonstrated that acetonitrile met the solvency condition required for such distillation precipitation polymerization, during which acetonitrile dissolved the monomer but precipitated the resultant polymer network. The residual reactive vinyl groups on the surface

of PDVB cores were essential for the further growth of polymer microspheres [47] and the construction of the core-shell functional polymer microspheres by two-stage distillation precipitation polymerization [51], in which the newly formed oligomers and monomers were captured by these reactive vinyl groups without formation of any secondary-initiated particles during the further polymerization.

It is difficult to directly perform the polymerization of EGDMA and DVB coating the P(MAA-co-EGDMA)/SiO₂ seeds for the construction of the tri-layer hybrid microspheres due to lacking of an appropriate interaction between the core particles and monomers. In nature, the surface of P(MAA-co-EGDMA)/SiO₂ seeds with active hydroxyl groups is hydrophilic, while EGDMA and DVB components are hydrophobic. To overcome such a problem, the modification of the P(MAA-co-EGDMA)/SiO₂ nanoparticles is necessary with suitable reactivity for the further polymerization. Monodisperse MPS-modified silica microspheres were synthesized via the condensation of the hydroxyl groups during the hydrolysis of MPS in ethanol with the silica seeds to incorporate the reactive vinyl groups on the surface [15,43]. In the present work, the TEM micrograph of MPS-modified P(MAA-co-EGDMA)/SiO₂ microspheres (figure shown in Supporting information) indicated that these particles had spherical shape and smooth surface with an average diameter of 121 nm and monodispersity index (*U*) of 1.007. Comparing to the size of P(MAA-co-EGDMA)/SiO₂ particles, much the same diameter after the modification implied that only a very thin MPS layer was formed on the outer layer of P(MAA-co-EGDMA)/SiO₂ during such modification.

The modification of the P(MAA-co-EGDMA)/SiO₂ core-shell microspheres by further hydrolysis of MPS with the aid of surface hydroxyl groups on the surface of the nanoparticle is investigated further by FT-IR spectrum in Fig. 3 and XPS characterization in Fig. 2, respectively. The FT-IR spectrum in Fig. 3b displayed the bands at 1651 cm⁻¹ assigning to the stretching vibration of the vinyl groups from MPS component. Furthermore, the XPS spectrum in Fig. 2C for MPS-modified P(MAA-co-EGDMA)/SiO₂ core-shell microspheres had an enhancing C_{1s} signal with simultaneous decrease of surface Si concentration from 33.4% before modification

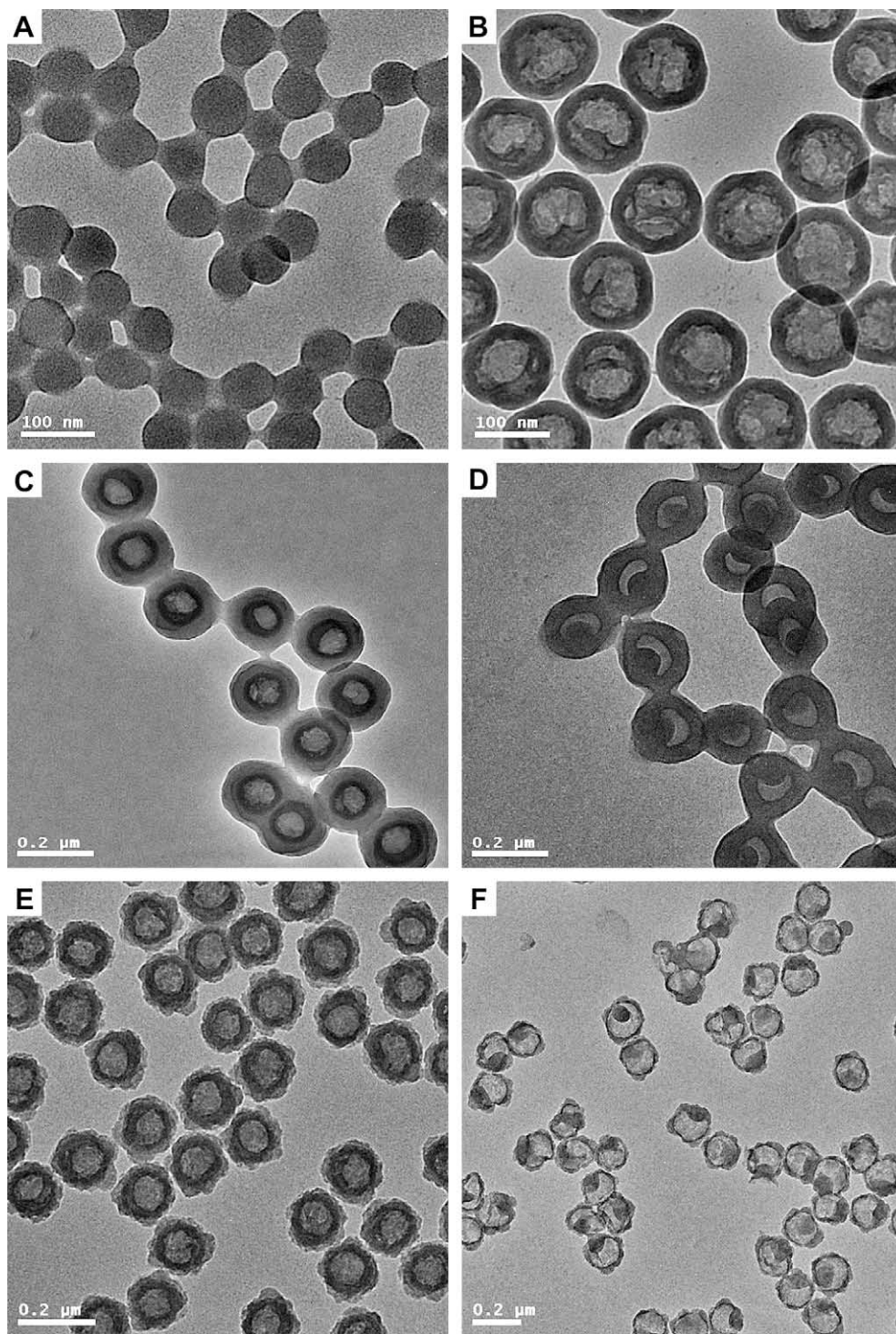


Fig. 1. TEM micrographs of P(MAA-co-EGDMA)/silica/polymer tri-layer hybrid particles and the corresponding hollow polymer microspheres with movable P(MAA-co-EGDMA) cores: A) P(MAA-co-EGDMA) nanoparticles; B) MPS-modified P(MAA-co-EGDMA)/silica core-shell microspheres; C) P(MAA-co-EGDMA)/silica/PEGDMA tri-layer hybrid microspheres (EGDMA 0.5 mL); D) hollow PEGDMA microspheres with movable P(MAA-co-EGDMA) cores; E) P(MAA-co-EGDMA)/silica/PDVB tri-layer hybrid microspheres (DVB 0.5 mL); F) hollow PDVB microspheres with movable P(MAA-co-EGDMA) cores.

to 23.3%. All these results proved the successful modification of the P(MAA-co-EGDMA)/SiO₂ nanoparticles with MPS via further sol-gel hydrolysis to introduce the reactive vinyl groups on the surface, which would permit the growth of the hybrid particles by radical capture of the newly formed oligomers and monomers during the third-stage distillation precipitation polymerization as illustrated in Scheme 1 to build the tri-layer polymer/silica/polymer hybrid microspheres.

The typical TEM images of P(MAA-co-EGDMA)/SiO₂/PEGDMA and P(MAA-co-EGDMA)/SiO₂/PDVB tri-layer hybrid microspheres are shown in Fig. 1C and E, respectively. The successful formation of a uniform polymeric outer shell layer on the surface of P(MAA-co-EGDMA)/SiO₂ was clearly observed from TEM characterization due to the strong difference in contrast between the inorganic silica mid-layer (deep color), the polymeric P(MAA-co-EGDMA) core (light color), the PEGDMA (light color in Fig. 1C) and PDVB (light

Table 1
Reaction conditions, sizes, polymer shell thickness, and yields of the P(MAA-co-EGDMA)/silica/polymer tri-layer hybrid particles.

Entry	D_n (nm)	D_w (nm)	U	Shell thickness (nm)	Yield (%)
P(MAA-co-EGDMA)	69	70	1.014	–	–
P(MAA-co-EGDMA)/SiO ₂	121	122	1.007	22	24 ^a
P(MAA-co-EGDMA)/SiO ₂ / PEGDMA	192	193	1.006	36	13 ^b
P(MAA-co-EGDMA)/SiO ₂ /PDVB	161	163	1.008	20	8 ^c

^a Yield = $(M_{P(MAA-co-EGDMA)/SiO_2} - M_{P(MAA-co-EGDMA)}) / M_{TEOS} \times 100\%$.

^b Yield = $(M_{P(MAA-co-EGDMA)/SiO_2/PEGDMA} - M_{P(MAA-co-EGDMA)/SiO_2}) / M_{EGDMA} \times 100\%$.

^c Yield = $(M_{P(MAA-co-EGDMA)/SiO_2/PDVB} - M_{P(MAA-co-EGDMA)/SiO_2}) / M_{DVB} \times 100\%$.

color in Fig. 1E) outer shell layer. In other words, inorganic silica mid-layer was sandwiched between the polymer core and polymer outer shell layer via a three-stage reaction in absence of any secondary particles, which indicated that the reactive vinyl group from MPS modification captured all the newly formed oligomers during the third-stage distillation precipitation polymerization. The P(MAA-co-EGDMA)/SiO₂/PEGDMA tri-layer hybrid microspheres had spherical shape with smooth surface in Fig. 1C, while P(MAA-co-EGDMA)/SiO₂/PDVB tri-layer hybrids had spherical shape with lightly rough surface in Fig. 1E. The difference in surface morphology here may be attributed to a difference in solubility between the PEGDMA and PDVB in the acetonitrile.

The average diameter of P(MAA-co-EGDMA)/SiO₂/PEGDMA hybrid microsphere was significantly increased from 121 nm of P(MAA-co-EGDMA)/SiO₂ seeds to 192 nm, while the particle size of P(MAA-co-EGDMA)/SiO₂/PDVB hybrid was considerably enhanced to 161 nm as summarized in Table 1. These results indicated that PEGDMA outer shell layer with thickness of 35 nm and PDVB with

thickness of 20 nm were encapsulated onto the P(MAA-co-EGDMA)/SiO₂ seeds through the third-stage polymerization. The tri-layer hybrid microspheres remained monodisperse for P(MAA-co-EGDMA)/SiO₂/PEGDMA with U of 1.006 and P(MAA-co-EGDMA)/SiO₂/PDVB with U of 1.008, which demonstrated that the polymer outer shell layers were uniformly coated onto the surface of the P(MAA-co-EGDMA)/SiO₂ seed during the third-stage polymerization. The encapsulation efficiency of P(MAA-co-EGDMA)/SiO₂/PEGDMA was as high as 13% and the yield of P(MAA-co-EGDMA)/SiO₂/PDVB was 8% as listed in Table 1. These may be due to the higher reactivity of EGDMA than DVB monomer, which resulted in a smaller size of P(MAA-co-EGDMA)/SiO₂/PDVB tri-layer hybrids. These results were consistent with those for the homo-polymerization of DVB [47] and EGDMA [50] reported in our previous work.

To further prove the tri-layer structure of P(MAA-co-EGDMA)/SiO₂/PEGDMA, the surface components of MPS-modified P(MAA-co-EGDMA)/SiO₂ seed and tri-layer hybrids were determined by XPS spectra as shown in Fig. 2C and D, respectively. The XPS spectrum in Fig. 2D of P(MAA-co-EGDMA)/SiO₂/PEGDMA tri-layer hybrids had strong peaks at 531.4 and 288.0 eV assigning to the electronic binding energy of O_{1s} and C_{1s} from PEGDMA outer shell layer. On the other hand, the peaks for the electronic binding energy for Si_{2s} and Si_{2p} were almost disappeared with simultaneous decrease of surface Si concentration from 23.3% for MPS-modified P(MAA-co-EGDMA)/SiO₂ seeds to only 1.54% for P(MAA-co-EGDMA)/SiO₂/PEGDMA tri-layer hybrids. The peak at 1733 cm⁻¹ of FT-IR spectrum in Fig. 3c corresponding to the carbonyl group of the ester group from PEGDMA component increased significantly after the third-stage polymerization, which also implied that PEGDMA outer shell layer was successfully encapsulated as the tri-layer structure. The seed polymerization of DVB leading to P(MAA-co-EGDMA)/SiO₂/PDVB tri-layer hybrid

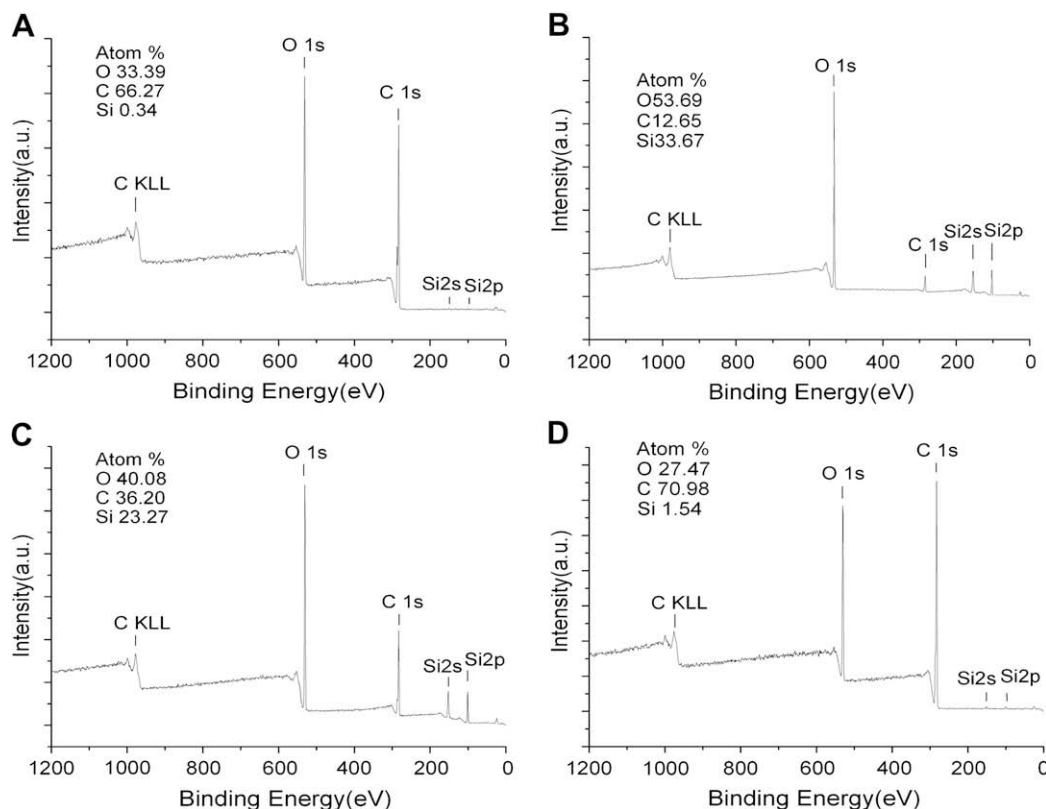


Fig. 2. XPS spectra: A) P(MAA-co-EGDMA) nanoparticles; B) P(MAA-co-EGDMA)/silica core-shell microspheres; C) MPS-modified P(MAA-co-EGDMA)/silica core-shell microspheres; D) P(MAA-co-EGDMA)/silica/PEGDMA tri-layer hybrid microspheres.

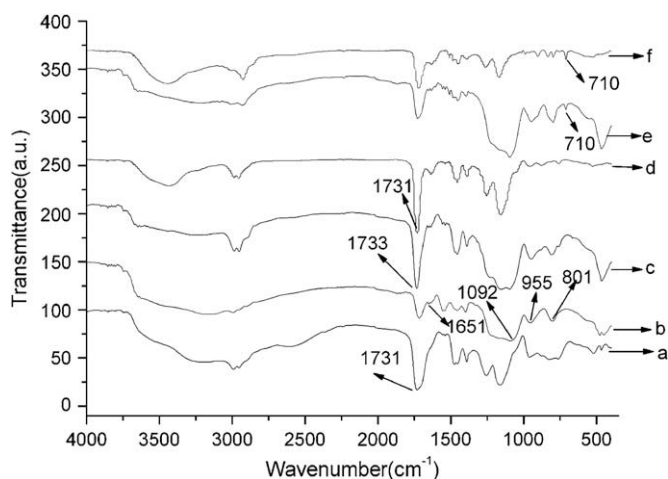


Fig. 3. FT-IR spectra: a) P(MAA-co-EGDMA) nanoparticles; b) MPS-modified P(MAA-co-EGDMA)/silica core-shell microspheres; c) P(MAA-co-EGDMA)/silica/PEGDMA tri-layer hybrid microspheres; d) hollow PEGDMA microspheres with movable P(MAA-co-EGDMA) core; e) P(MAA-co-EGDMA)/silica/PDVB tri-layer hybrid microspheres; f) hollow PDVB microspheres with movable P(MAA-co-EGDMA) cores.

microspheres was studied by FT-IR spectrum as shown in Fig. 3e, in which a new peak at 710 cm^{-1} was clearly observed assigning to the typical stretching vibration of the phenyl group of PDVB component.

3.3. Hollow polymer microspheres with movable P(MAA-co-EGDMA) core

The silica mid-layers of the resultant P(MAA-co-EGDMA)/SiO₂/PEGDMA and P(MAA-co-EGDMA)/SiO₂/PDVB tri-layer hybrid microspheres were selectively removed by etching in hydrofluoric acid to afford hollow PEGDMA and PDVB microspheres with movable P(MAA-co-EGDMA) cores as illustrated in Scheme 1. The driving force for such removal was due to the formation of SiF₄ gas, which was given off from the hybrids during the etching process. The typical TEM micrographs of hollow PEGDMA microspheres with thickness of 35 nm and PDVB hollow microspheres with thickness of 20 nm containing movable P(MAA-co-EGDMA) cores are displayed in Fig. 1D and F, respectively. The unique morphology of hollow PEGDMA with movable P(MAA-co-EGDMA) cores is clearly observed in Fig. 1D, in which the convincing hollow sphere structures were formed with the presence of circular rings of non-aggregated spheres, a cavity in the mid-layer, and an inner movable P(MAA-co-EGDMA) core. The spherical shape was well maintained after the selective removal of the silica mid-layer consistent with the robust and rigid nature of the highly crosslinked PEGDMA outer shell layer, which implied that hollow PEGDMA microspheres with thickness of 35 nm was enough to support the cavity during the etching process. Further, the disappearance of the peaks at 1092 cm^{-1} assigning to the typical stretching vibration of Si–O component in the FT-IR spectra of Fig. 3d for hollow PEGDMA microsphere and Fig. 3f for hollow PDVB microsphere with movable P(MAA-co-EGDMA) core confirmed that the silica mid-layer was successfully removed from the tri-layer hybrid microspheres to afford the unique hollow structure.

It was believed that the functional P(MAA-co-EGDMA) cores in the hollow spheres were free to move as filled with solvent, as the P(MAA-co-EGDMA) cores were not located in the center of the hollow PEGDMA microspheres for Fig. 1D and hollow PDVB microspheres for Fig. 1F. It was interesting to find that P(MAA-co-EGDMA) cores could be partially released out of the hollow PDVB microspheres by slightly destroying the outer PDVB shell layer of the resultant hollow structure as shown by the TEM micrograph in

Fig. 1F. One of the most desirable characteristics of oral delivery of peptides and proteins is the ability to protect the gastrointestinal (GI) tract. The release process in the present work may provide some effective guidance in drug protection and delivery and to mimic biological process. Therefore, the study on the organic/inorganic/organic tri-layer materials and the corresponding hollow polymer microspheres having different polarities and functional groups with movable cores may be significant for the development as functional materials for drug protection and delivery and to mimic biological process.

4. Conclusion

Hollow PEGDMA and PDVB microspheres with movable P(MAA-co-EGDMA) cores were prepared by a facile route with a three-stage reaction and subsequent removal of the silica mid-layer from P(MAA-co-EGDMA)/SiO₂/PEGDMA and P(MAA-co-EGDMA)/SiO₂/PDVB tri-layer hybrid microspheres in hydrofluoric acid. The hydrogen-bonding interaction between the carboxylic acid groups on the surface of P(MAA-co-EGDMA) cores and the hydroxyl groups of silica component acted as a driving force for the formation of P(MAA-co-EGDMA)/SiO₂ core-shell nanoparticles. P(MAA-co-EGDMA)/SiO₂/PEGDMA and P(MAA-co-EGDMA)/SiO₂/PDVB tri-layer hybrid microspheres were synthesized by the third-stage distillation precipitation polymerization in acetonitrile in the presence of MPS-modified as the seeds via the capture of the newly formed oligomers with the aid of the reactive vinyl groups, which were incorporated onto the surface of the seeds by the modification of MPS to P(MAA-co-EGDMA)/SiO₂ nanoparticles. The hollow PEGDMA microspheres with shell thickness of 35 nm and hollow PDVB microspheres with shell thickness of 20 nm were developed by the selective etching of the middle silica layer from the tri-layer hybrid microspheres to leave movable P(MAA-co-EGDMA) cores inside the hollow microspheres. P(MAA-co-EGDMA) cores could be partially moved out as the hollow PDVB structure was slightly destroyed.

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Appendix. Supporting information

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.polymer.2008.10.043.

References

- [1] Zhang YD, Lee SH, Yoonessi M, Liang KW, Pittman CU. *Polymer* 2006;47: 2988–96.
- [2] Strachotova B, Strachota A, Uchman M, Slouf M, Brus J, Plestil J, et al. *Polymer* 2007;48:1471–82.
- [3] Caruso F, Spasova M, Susha A, Giersig M, Caruso RA. *Chem Mater* 2001; 13:109–16.
- [4] Fleming MS, Mandal TK, Walt DR. *Chem Mater* 2001;13:2210–6.
- [5] Zhu J, Morgan AB, Lamelas FJ, Wilkie CA. *Chem Mater* 2001;13:3774–80.
- [6] Zhou J, Zhang SW, Qiao XG, Li XQ, Wu LM. *J Polym Sci Part A Polym Chem* 2006;44:3202–9.
- [7] Qi L, Chapel JP, Castaing JC, Fresnais J, Berret JF. *Langmuir* 2007;23:11996–8.
- [8] Hu YQ, Wu HP, Gonsalves KE, Merhari L. *Microelectron Eng* 2001;56:289–94.
- [9] Zhang K, Chen HT, Chen X, Chen ZM, Cui ZC, Yang B. *Macromol Mater Eng* 2003;288:380–5.
- [10] Tissot I, Novat C, Lefebvre F, Bourgeat-Lami E. *Macromolecules* 2001;34: 5737–9.
- [11] Reculusa S, Poncet-Legrand C, Ravaine S, Minogotaud C, Duguet E, Bourgeat-Lami E. *Chem Mater* 2002;14:2354–9.
- [12] Derro A, Reculusa S, Bourgeat-Lami E, Duguet E, Ravaine S. *Colloids Surf A* 2006;284–285:78–84.

- [13] Barthlet S, Mingotaud C, Bourgeat-Lami E, Duguet E, Ravaine R. *Nano Lett* 2004;4:1677–82.
- [14] Barthlet C, Hickey AJ, Carins DB, Armes SP. *Adv Mater* 1999;11:408–10.
- [15] Bourgeat-Lami E, Lang J. *J Colloid Interface Sci* 1998;197:293–308.
- [16] Bourgeat-Lami E, Lang J. *J Colloid Interface Sci* 1999;210:281–9.
- [17] Corcos F, Bourgeat-Lami E, Novat C, Lang J. *Colloid Polym Sci* 1999;277:1142–51.
- [18] Tiarks F, Landfester K, Antonietti M. *Langmuir* 2001;17:5775–80.
- [19] von Werne T, Patten TE. *J Am Chem Soc* 2001;123:7497–505.
- [20] Perruchot C, Khan MA, Kamitsim A, Armes SP. *Langmuir* 2001;17:4479–81.
- [21] Harrak AE, Carrot G, Oberdisse J, Jestin J, Boue F. *Polymer* 2005;46:1095–104.
- [22] Jiang P, Bertone JF, Colvin VL. *Science* 2001;291:453–7.
- [23] Ding JF, Liu GJ. *J Phys Chem B* 1998;102:6107–13.
- [24] Shchukin DG, Shutava T, Shchukina E, Sukhorukov GB, Lvov YM. *Chem Mater* 2004;16:3446–51.
- [25] Kim SW, Kim M, Lee WY, Hyeon T. *J Am Chem Soc* 2002;124:7642–3.
- [26] Xu XL, Asher SA. *J Am Chem Soc* 2004;126:7940–5.
- [27] McDonald CJ, Bouck KJ, Chaput AB, Stevens CJ. *Macromolecules* 2000;33:1593–605.
- [28] Park MK, Onishi K, Lockin J, Caruso F, Advincula RC. *Langmuir* 2003;19:8550–4.
- [29] Donath E, Sukhorukov GB, Caruso F, Davids SA, Möhwald H. *Angew Chem Int Ed* 1998;37:2201–5.
- [30] Stewart S, Liu GJ. *Chem Mater* 1999;11:1048–54.
- [31] Fu GD, Shang ZH, Hong L, Kang ET, Neoh KG. *Macromolecules* 2005;38:7867–71.
- [32] Kamata K, Lu Y, Xia YN. *J Am Chem Soc* 2003;125:2384–5.
- [33] Hao LY, Zhu CL, Jiang WQ, Chen CN, Hu Y, Chen ZY. *J Mater Chem* 2004;14:2929–34.
- [34] Liu GY, Yang XL, Wang YM. *Langmuir* 2008;24:5485–91.
- [35] Lee KT, Jung YS, Oh SM. *J Am Chem Soc* 2003;125:5652–3.
- [36] Kim M, Sohn K, Na HB, Hyeon T. *Nano Lett* 2002;2:1383–7.
- [37] Cheng DM, Zhou XD, Xia HB, Chan HSO. *Chem Mater* 2005;17:3578–81.
- [38] Zhang K, Zhang XH, Chen HJ, Chen X, Zhang L, Zhang JH, et al. *Langmuir* 2004;20:11312–4.
- [39] Zhang TH, Pang JB, Tan G, He JB, McPherson GL, Lu YF, et al. *Langmuir* 2007;23:5143–7.
- [40] Chattopadhyay P, Shekunov BY, Yim D, Cipolla D, Boyd B, Farr S. *Adv Drug Delivery Rev* 2007;59:444–53.
- [41] Shiga K, Muramatsu N, Kondo T. *J Pharm Pharmacol* 1996;48:891–5.
- [42] Liu GY, Yang XL, Wang YM. *Polymer* 2007;48:4385–92.
- [43] Liu GY, Zhang H, Yang XL, Wang YM. *Polymer* 2007;48:5896–904.
- [44] Liu GY, Ji HF, Yang XL, Wang YM. *Langmuir* 2008;24:1019–25.
- [45] Li GL, Yang XL. *J Phys Chem B* 2007;111:12781–6.
- [46] Bai F, Yang XL, Li R, Huang B, Huang WQ. *Polymer* 2006;47:5775–84.
- [47] Bai F, Yang XL, Huang WQ. *Macromolecules* 2004;37:9746–52.
- [48] Li GL, Liu G, Kang ET, Neoh KG, Yang XL. *Langmuir* 2008;24:9050–5.
- [49] Bai F, Huang B, Yang XL, Huang WQ. *Eur Polym J* 2007;43:3923–32.
- [50] Bai F, Yang XL, Huang WQ. *Eur Polym J* 2006;42:2088–97.
- [51] Qi DL, Yang XL, Huang WQ. *Polym Int* 2007;56:208–13.