

Polyelectrolyte Self-assembly Approach to Smart Nanocontainers

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Summary

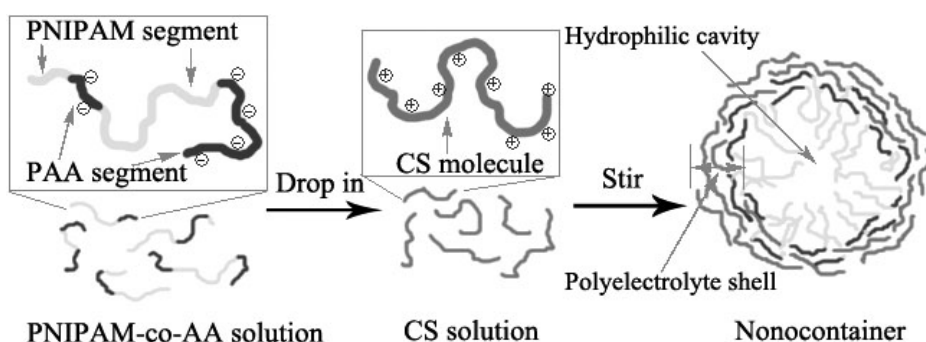
Smart polymer nanocontainers were formed by self-assembly of polyelectrolytes, which consist of chitosan and poly (N-isopropylacrylamide-*co*-acrylic acid). This is a novel easy method to synthesize smart nanocontainers. It was found that diameter and stability of the nanocontainers were changed by a variety of the environmental conditions.

Introduction

In recent years macromolecular assemblies on nanometer or sub-micrometer scales, with hollow core morphology or cavity-containing structure, have been attracting increasing interest due to their broad potential applications [1-5], which range from targeted drug delivery to advanced functional materials. Because the hollow macromolecular assemblies can encapsulate large quantities of guest molecules or large-size guest within the “empty” core domain, they are also termed as “nanocontainer”. Core-shell micelles [6,7] or vesicles [8,9] of block copolymers are the most commonly used precursors for producing nanocontainer. The other methods such as layer-by-layer (LBL) deposition of polyelectrolytes onto a template core[10,11], polymerizing monomers in lipid vesicles[12], emulsion polymerization[13], pH-induced micellization of a grafted copolymer[14], and core-template-free strategy[15] have been developed for this purpose. In addition, in order to enable the load and release guest molecules not only controlled by diffusion, “intelligent” hollow spheres have also been reported, such as sensitive to temperature [16,17], pH [2,18], ionic strength [19], or specific substance [20].

In our research, a smart polymer nanocontainer was synthesized by polyelectrolytes self-assemble method in aqueous solution without organic solvents, template cores,

emulsion phases or surfactants. We chose CS as the cation biopolymer with amino groups and poly (N-isopropylacrylamide-co-acrylic acid) (PNIPAM-co-AA) as the anion temperature-sensitive polymer with carboxylic groups. PNIPAM exhibits a lower critical solution temperature (LCST) at about 32°C [21,22]. Chitosan (CS) is a weak cationic polysaccharide obtained by extensive deacetylation of chitin, which is a biocompatible, biodegradable, and nontoxic natural polymer [23,24]. The formation of complexes by the interaction of oppositely-charged polyelectrolytes is schematically illustrated in Scheme 1.



Scheme.1. A proposed scheme of the formation of the nanocontainer

Experimental Part

Materials

N-isopropylacrylamide (NIPAM) which was purchased from Acros was recrystallized from mixture of hexane (Guangzhou Guanghua Chemical Factory Co. Ltd., Guangzhou, China) and toluene (Guangzhou Guanghua Chemical Factory Co. Ltd). Chitosan which was obtained from Golden-shell Biochemical Co., Ltd. was refined twice by dissolving it in dilute acetic acid solution, centrifugating, then precipitating with aqueous NaOH, and finally drying in vacuum at room temperature. The degree of deacetylation was about 90%, and the weight average molecular weights of chitosan were 30 kDa determined by viscometric methods. Potassium peroxydisulfate (KPS) was used without further purification.

Synthesis

The PNIPAM-co-AA was obtained by free radical polymerization of NIPAM and acrylic acid monomer using KPS as a free radical initiator. NIPAM (0.50g) and acrylic acid (0.1ml) were dissolved in 50ml of distilled water, followed by the addition of KPS (0.0120g). Nitrogen was bubbled through the solution for 15min prior to polymerization. After polymerization at 80°C for 4h under nitrogen atmosphere, the solution was diluted to 100ml for use.

0.1g CS was dissolved in 10ml acetic acid aqueous solution (1wt.-%), and then diluted to 100ml for use.

CS-PNIPAM-co-AA nanocontainers were prepared by adding dropwise a negatively charged PNIPAM-co-AA solution to a positively charged CS solution with strong stirring, when the two solutions were both equivalent concentration and ratio by volume of CS to PNIPAM-co-AA was 5:1. Finally, the polyelectrolytes were self-assembled in solution for 48 hours.

Measurement and Characterization

The mean size, size distribution and zeta-potential measurements of the CS-PNIPAM-co-AA nanocontainers were determined with a Zetasizer 3000 (Malvern, UK). All measurements were performed at a wavelength of 532.0 nm, an detection angle of 90°.

The FT-IR spectra of the nanocontainer samples were also recorded (Nicolet 200SXV, USA) to determine the interaction between CS and PNIPAM-co-AA. For detection samples, an aqueous solution of the nanocontainers was centrifugated at 15000 rpm and 4°C for 20min, and then the deposit was freeze dried at -50°C for 24h.

The morphology of the nanocontainers was observed by transmission electron microscopy (TEM) (JEM-100CX). Drops of nanocontainer solution were placed on a carbon film coated on a copper grid, and then dried at room temperature. Before the observation, the sample was stained by phosphotungstic acid. The TEM bright field imaging was performed with 80kV accelerating voltage.

The optical transmittance of the colloidal solutions was measured at 500nm with a UV-vis spectrophotometer (VARIAN CARY100 Cone, USA).

Results and Discussion

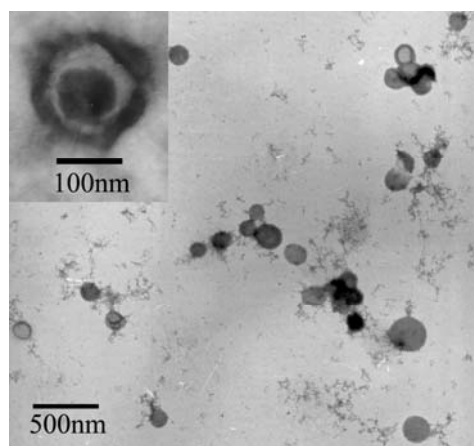


Figure.1. TEM micrograph of nanocontainers with polyelectrolyte concentration of 0.2 wt.-%. The insert is a higher magnification micrograph

Polyelectrolyte self-assembly approach was used to prepare smart nanocontainer in this study. When the aqueous solution of PNIPAM-co-AA was dropped to the CS solution with strong stirring, the PAA segments tended to conjunction with CS, and

the PNIPAM segments were pushed aside. In the solution, the PNIPAM segments, which have strong interaction with water molecules below 32°C, gathered with plentiful water in the midst of shell composed of CS and PAA segments. Thus a cavity-containing structure with water and PNIPAM segments can be formed. Figure 1 illustrated the configuration of the nanocontainers.

FT-IR Spectroscopic Analysis

The FT-IR spectroscopic data are illustrated in Fig. 2. The IR spectrum of CS [Figure 2 (a)] indicated that the peaks appeared at 1635.4 cm⁻¹, and 1073.4 cm⁻¹ could be assigned to N-H bending vibration, and C-O symmetrical stretching vibration, respectively. Figure 2 (b), obtained from PNIPAM-co-AA, shows significant peaks at 1720.0 cm⁻¹, 1649.5 cm⁻¹, 1546.8 cm⁻¹, 1459.4 cm⁻¹, 1388.5 cm⁻¹ and 1368.3 cm⁻¹, which can be attributed to the characteristic peaks of stretching vibration of PAA's carbonyl group, amide I, amide III, continuous methene of polymer fundamental chain, and methyl group in -CH(CH₃)₂, respectively.

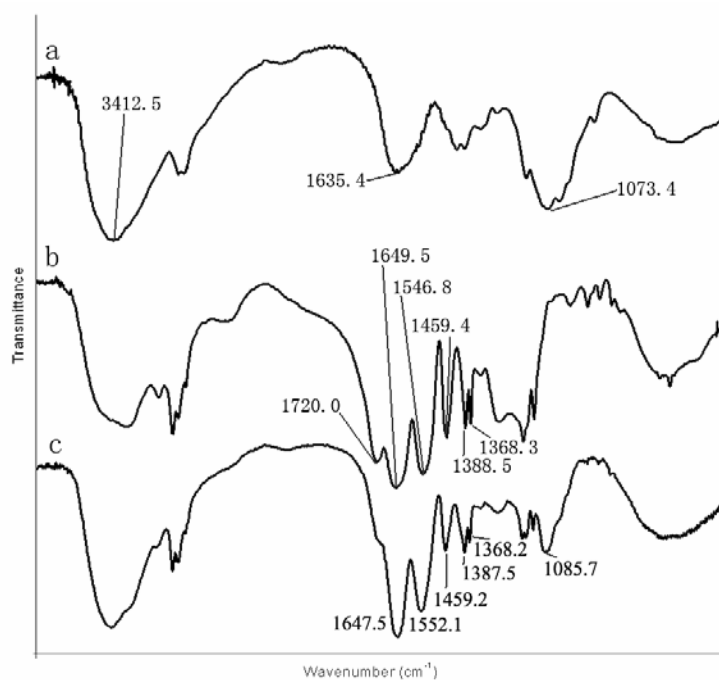


Figure.2. FT-IR of CS, PNIPAM-co-AA and the nanocontainer

For the nanocontainer sample [Figure 2 (c)], the peak at 1720.0 cm⁻¹ is red shifted and concealed by amide I and amide III. It implied that ionic bond is formed between carbonyl group of PAA and amino group of CS.

Effect of polyelectrolyte concentrations

The particle size and stability of nanocontainer, prepared by dropwise addition of PNIPAM-co-PAA into a CS solution at various concentrations, were determined. The results are displayed in Table 1. The data showed that the particle size of the sample increased from about 70 nm to 370nm with an increase in the PNIPAM-co-PAA and CS concentration. The result may be due to the increased number of mutually attracted polyelectrolytes in the same region at higher polymer concentration. Nevertheless excessive polyelectrolytes lead to aggregation of a mass of macromolecules, which result in forming macroscopic gel. Accordingly the whole polyelectrolyte system was instable and nanocontainers were destroyed. The zeta-potential measurements can testify the change of stability. According to currently accepted theory, the lower of zeta-potential show higher of system instability [25].

Table.1. Effect of the concentration of polyelectrolyte on the size and zeta potential of nanocontainer

Concentration ^{a)}	Mean size (\pm S.D.) (nm)	pH ^{b)}	Zeta potential (\pm S.D.) (mV)
0.05	78.26 \pm 6.44	3.76	25.80 \pm 1.971
0.1	70.64 \pm 9.72	3.60	25.71 \pm 2.236
0.2	187.5 \pm 37.65	3.69	23.72 \pm 1.891
0.3	194.7 \pm 50.15	3.34	23.31 \pm 1.606
0.4	199.8 \pm 21.47	3.38	19.67 \pm 1.718
0.5	257.4 \pm 68.55	3.29	17.54 \pm 1.670
0.6	318.7 \pm 33.05	3.31	19.07 \pm 1.689
0.7	369.1 \pm 48.20	3.21	18.09 \pm 1.769
0.8	* ^{c)}	3.45	19.05 \pm 1.839

^{a)}The unit of concentration is wt.-%, and the concentration of anion polyelectrolyte means the percentum of PAA segment; ^{b)}pH of the initial preparation of the nanocontainers; ^{c)}At the concentration, there were a lot of macroscopic gels

Effect of pH value and salt concentration

In order to investigate the effect of pH on the CS/PNIPAM-co-AA nanocontainers, a series of experiments were carried out. Nanocontainers were prepared at pH 3.69, then the pH value of the system was adjusted by adding either dilute acetic acid or ammonium solution.

The variation of transmittance illustrated that there were not polyelectrolyte complexes when pH value was under 3.0 or above 7.0 [Figure 3 (a)]. The attraction of static electricity was nonexistence, because polyelectrolytes were deionized under such condition. The change of nanocontainer diameter [Figure 3 (c)] shows nanocontainers can steadily exist at the range of pH 3.0 to 5.0, and the distribution of diameter was broadening when pH value was close to 3.0 or 5.0. Large quality polyelectrolytes was aggregated here about pH 5.5, hence zeta potential of nanocontainers was about 0 [Figure 3 (b)].

Nanocontainers were extraordinarily sensitive by ionic strength, because nanocontainers were bound through electrostatic force between oppositely charged macromolecules. The force was easily abated by small ion with concentrated charge. Nanocontainers can be easily destroyed by a little small ion (approximately $0.01\text{mol}\cdot\text{L}^{-1}$).

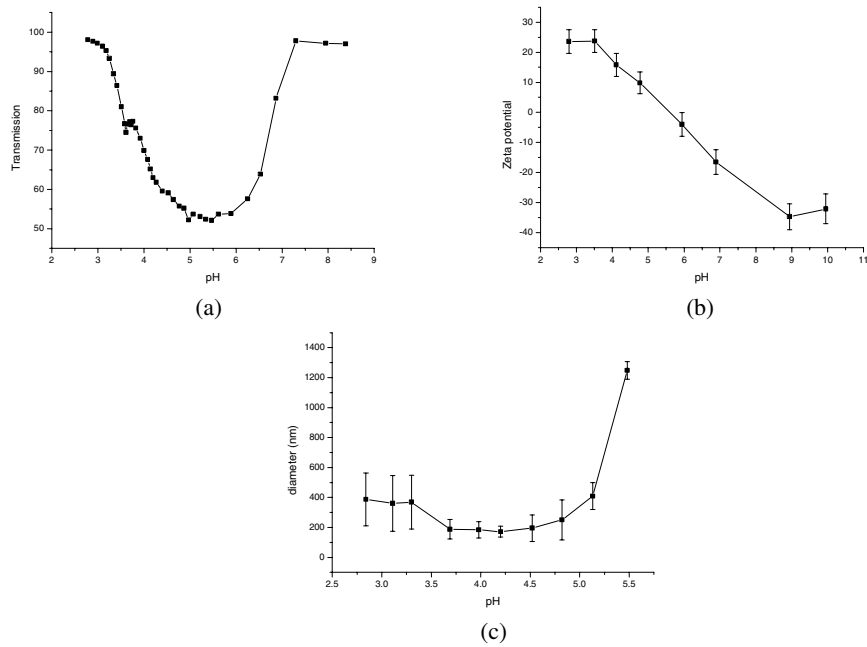


Figure.3. Effect of pH on nanocontainers, variation of (a) transmission (b) zeta potential and (c) diameter of nanocontainers with change of pH. The all hollow spheres were formed with the concentration of 0.2 wt.-%

Effect of temperature

The thermosensitive nature of the nanocontainer is based on a coil-globule transition of the PNIPAM segment. Above the LCST of PNIPAM, hollow spheres shrunk, because the PNIPAM chains changed from an extended and hydrophilic state to curly and hydrophobic one. Liquid was extruded from cavities of hollow spheres owing to hydrophobic interaction.

The structural changes of the hollow sphere in a rising and dropping in temperature cycle are reproducible and repeatable, which is illustrated by Figure 4.

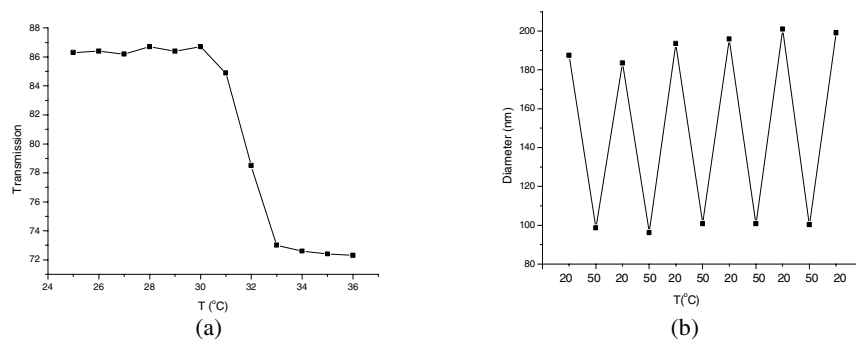


Figure.4. Effect of temperature on hollow spheres: (a) relationship between the transmission of the nanocontainers and temperature; (b) the diameter changes of nanocontainers with respect to temperature fluctuation. The all nanocontainers were formed with the concentration of 0.2 wt.-%

Conclusion

A novel route to prepare smart nanocontainers with polyelectrolyte self-assembly that was driven by electrostatic interactions has been developed. This method is simple and convenient, which is performed in aqueous solution without any organic solvent and template cores, compared with complicated and reduplicative other methods. In addition, the outer surface of nanocontainer is made from chitosan which is biocompatible and nontoxic, it will be applicable for some potential applications.

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