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Facile fabrication of pH-sensitive core–shell nanoparticles based on HEC and PMAA via template polymerization

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ABSTRACT

Taking advantage of the specific hydrogen bonding interactions between the components, core–shell nanoparticles based on poly(methacrylic acid) (PMAA) and hydroxyethyl cellulose (HEC) can be efficiently prepared via facile one-step polymerization of MAA on HEC template in water. Various techniques were used to characterize in detail the sizes, morphology, and structures of the nanoparticles, as well as the interactions between the components. The core–shell structures of the nanoparticles were confirmed by TEM observation. Dynamic light scattering and fluorescence spectrometry were used to monitor the polymerization process, which indicates a size decrease and a hydrophobicity increase of the nanoparticles. A mechanism was proposed to explain the formation of core–shell nanoparticles during the template polymerization. The obtained nanoparticles are stable against urea, salt, temperature and in the storage; meanwhile, they exhibit pH-response: the volume of the nanoparticles increased more than six times as pH value of the medium increased from 2.8 to 3.7.

1. Introduction

Core–shell polymeric nanoparticles materials on the submicron or nanometer scales, have been attracting enormous attention because of their unique structures and various potential applications, such as nano-reactors, catalyst carriers, drug delivery, and water purification [1,2]. The core–shell nanoparticles are usually prepared via emulsion polymerization [3–6], self-assembly routes [7–14] and layer-by-layer technique. However, few of them are facile and efficient, which greatly limits the practical application of the nanoparticles. Recently, some new convenient and efficient approaches were reported. For example, Jiang and co-workers fabricated thermo-sensitive core–shell nanoparticles via localizing the copolymerization of *N*-isopropyl acrylamide (NIPAM) and *N*,*N*-methylenebisacrylamide (MBA) on the surface of poly(ε-caprolactone) nanoparticles [15–17]; Jiang and co-workers synthesized hollow nanospheres via polymerization of acrylic acid (AA) in the presence of chitosan [18,19]; also, various well-defined core–shell polymeric nanoparticles were prepared via facile graft copolymerization from water-soluble polymers [20,21] or biomacromolecules [22,23].

Taking advantage of the simultaneous polymerization and self-assembly between the components, we developed a facile and efficient way to prepare well-defined core–shell nanoparticles, i.e., template polymerization [24,25]. Using derived protein gelatin as the template macromolecule and acrylic acid (AA) as the monomer, core–shell PAA/gelatin nanoparticles with multi-stimuli responses and good biocompatibility were prepared. The preparation concentration could reach more than 100 mg/mL. During the polymerization, driven mainly by the electrostatic interactions between the components, PAA produced in situ self-assembles with gelatin, resulting in the nanoparticles with cores of PAA/gelatin inter-polymer complexes and shells of gelatin. Using another protein macromolecule (i.e., Bovine Serum Albumin (BSA)) as the template and AA as the monomer, we also obtained

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well-defined core–shell PAA/BSA nanoparticles. Thus, the feasibility to prepare core–shell nanoparticles via template polymerization using specific electrostatic interactions was well illustrated. Various ionic macromolecules can be expected to be used as the template to prepare core–shell nanoparticles. To extend the application of the template polymerization method to many non-ionic macromolecules, here, we explored the feasibility to prepare core–shell nanoparticles via template polymerization using another kind of common specific interactions, i.e., hydrogen bonding interaction.

Hydroxyethyl cellulose (HEC), an important commercial water-soluble non-ionic polysaccharide, bears hydroxyl and ether proton-accepting groups and can form hydrogen bonds with proton-donors such as carboxylic acid groups. Because of its excellent biocompatibility and unique physicochemical properties, HEC has wide applications in the areas of coatings, fibers, dyeing, paper making, cosmetics, medicine, pesticides and oil exploitation [26,27]. In this paper, HEC was chosen as the template macromolecule, and core–shell nanoparticles composed of HEC and poly(methacrylic acid) (PMAA) were successfully prepared via template polymerization. The morphology, structures, in situ formation mechanism and pH-response of PMAA/HEC nanoparticles were studied in detail.

2. Experimental

2.1. Materials

Hydroxyethyl cellulose (HEC, $M_\eta = 90{,}000$, Aldrich, Scheme 1) with an average number of substituted hydroxyl groups (DS) and a molar substitution degree (MS) of 1.5 and 2.5, respectively, was used after desiccation to remove absorbed moisture. Acrylic acid (AA) and methacrylic acid (MAA) (Shanghai Reagent Co.) were distilled under reduced pressure to remove inhibitors prior to use. Initiator potassium persulfate (KPS) (Shanghai Reagent Co.) was purified by re-crystallization in water. Accelerator *N,N,N′,N′*-tetraethylmethylene diamine (TEMED, Acros) and pyrene (Aldrich) were used as received. Cellulose dialysis membranes with a cut-off molecular weight of 14,000 were used.

2.2. Preparation of PMAA/HEC nanoparticles via template polymerization

A typical process was as follows: 0.42 g HEC powder was first dissolved in 60 mL of deionized water, followed by pH adjustment to about 0.7 with HCl aqueous solution. Then, 0.4 mL of MAA was added under gentle stirring and nitrogen bubbling. Polymerization was initiated at 33 °C by adding KPS and TEMED successively. The reaction continued for 3 h, followed by dialyzing against HCl aqueous solution (pH 0.7) for 3 days to remove small molecule impurities such as un-reacted MAA. The dialyzed solution was diluted by 20 times for various measurements. Keeping the total concentration of 13.3 mg/mL, three nanoparticles with a feeding weight ratio of HEC/MAA of 2/1, 1/1, and 1/2 were prepared. The nanoparticles with a feeding ratio of 1/1 were characterized in the following part except when otherwise stated.

2.3. Infrared spectra

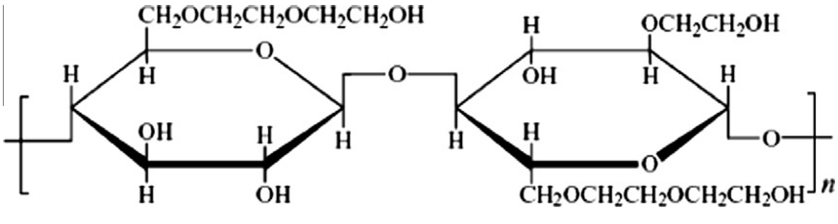
FT-IR spectra of various samples, obtained via freeze-drying of dialyzed nanoparticle solutions, were recorded from 400 to 4000 cm^{-1} on a Nicolet Magna-550 spectrometer as KBr pellets.

2.4. Thermo-gravimetric analysis

Various dialyzed nanoparticle solutions were freeze-dried to obtain powders for TGA analysis. TGA measurements were conducted on a TG209F1 (Netzsch) thermo-gravimetric analyzer at a heat rate of 20 °C/min under nitrogen protection.

2.5. Dynamic light scattering and electrophoretic light scattering measurements

Hydrodynamic diameter and ζ-potential of the nanoparticles were determined by dynamic light scattering (DLS) and electrophoretic light scattering using a Malvern Zetasizer (DTS1060, Malvern, UK). In DLS, the line-width distribution ($G(\Gamma)$) can be calculated from the Laplace inversion of the intensity–intensity time correlation function ($G^{(2)}(q,t)$) [28]. Using $\Gamma = Dq^2$ and the Stokes–Einstein equation $D_h = k_BT/(3\pi\eta D)$, $G(\Gamma)$ can be converted into a hydrodynamic diameter distribution ($f(D_h)$). The average hydrodynamic diameter ($\langle D_h \rangle$) and polydispersity index (PDI, i.e., $\langle \mu_2 \rangle / \Gamma^2$) were obtained by the CONTIN analysis. The measurements were carried out at 25 °C except for the study of the nanoparticle size dependence on the temperature, where the equilibrium time for each temperature was more than 30 min. The results were the average of three repeated measurements.



Scheme 1. Chemical structure of HEC.