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Fluorescent mesoporous silica nanotubes incorporating CdS quantum dots for controlled release of ibuprofen

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Abstract

Mesoporous silica nanotubes (MSNTs) and amine-functionalized MSNTs (NH_2-MSNTs) have been successfully synthesized via a sol–gel route using needle-like $CaCO_3$ nanoparticles as inorganic templates and post-modification with 3-aminopropyltriethoxysilane. Subsequently, the preformed nanotubes were functionalized with blue fluorescent CdS quantum dots, as demonstrated by transmission electron microscopy and confocal laser scanning microscopy. The morphology and microstructure of the produced materials were characterized by scanning electron microscopy and N_2 adsorption–desorption measurements. A comparative study of the capacity of several kinds of nanotube materials to store ibuprofen indicated that the drug-loading amount in CdS-NH_2-MSNTs (CdS-incorporated NH_2-MSNTs) could reach up to 740 mg/g silica, similar to that in as-prepared MSNTs (762 mg/g silica) and NH_2-MSNTs (775 mg/g silica). Drug release studies in simulated body fluid revealed that the loaded ibuprofen released from amine-functionalized systems at a significantly lower release rate as compared to that from amine-free systems, and the incorporation of CdS quantum dots had nearly no effect on the ibuprofen release process. Further study on the ibuprofen release from CdS-NH_2-MSNTs in other media, i.e. borate buffer saline, pure water and normal saline, indicated that CdS-NH_2-MSNTs are pH- and ion-sensitive drug carriers, which should facilitate controlled drug delivery and disease therapy.

Keywords: Mesoporous silica nanotubes; CdS quantum dots; Controlled release; Ibuprofen

1. Introduction

Since the invention of M41S (a family of silicate mesoporous molecular sieve materials) by Mobil researchers in 1992 [1], mesoporous silica materials have been a focus of research due to their mesoporous structure, adjustable pore size and high surface area with abundant Si–OH bonds. Their potential applications in catalysis, adsorption/separation, sensing and optically active materials have made them very attractive [2,3]. Recently, much attention has been paid to mesoporous silica materials as drug supports for controlled drug delivery [4–6] due to their non-toxic and biocompatible nature [7–9]. Controlled drug delivery offers numerous advantages over conventional forms of dosage, including the ability to maintain the patient's blood level, enhanced effectiveness, fewer deleterious side effects, improved patient compliance, etc. [10,11]. Several research groups have reported the design of controlled drug-delivery systems based on mesoporous silica materials such as MCM-41 [12], SBA-15 [13], MCM-48 [14] and hollow silica spheres [15]. However, the drug storage capacity of conventional mesoporous materials is relatively low. To overcome this disadvantage, two main strategies are currently available. One strategy is to synthesize hollow mesoporous silica materials with pore channels penetrating from outside to the inner hollow cores [16,17]. The other strategy

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is to modify the surface of mesoporous silica materials with organosilanes [16,18], and thus strengthen the interaction force between the surface of silica materials and drug molecules. Organic groups grafted onto the surface of mesoporous silica materials can also regulate drug-delivery rate [19]. Recently, our group has successfully synthesized mesoporous silica nanotubes (MSNTs) with large hollow cores [20]. It has been proved that MSNTs are ideal carriers for immobilization of penicillin G acylase [21] and glucose oxidase [22] as biocatalysts, and for the immobilization of silver nanoparticles [23] and lysozyme [24] as antimicrobials.

Quantum dots as fluorescence biolabels have been extensively explored in many domains due to their bright fluorescence, narrow emission, broad UV excitation and high photostability [25]. The first milestone application of quantum dots as fluorescence biolabels was reported by Alivisatos' group [26], which demonstrated the multicolor labeling of fixed mouse 3T3 fibroblasts. In addition, water-soluble quantum dots have also been labeled with the protein transferrin in cultured HeLa cells [27]. Further applications of quantum dots as biolabels have been achieved in live animals [25,28–31]. Very recently, quantum dots as biolabels have been anchored in various materials such as lipid nanotubes [32] and mesoporous silica materials [17] for drug delivery.

Herein, a novel kind of drug-delivery carrier, fluorescent amine-functionalized MSNTs, was synthesized and characterized. Using ibuprofen as model drug, we found that the materials have a considerable drug-loading amount and a controllable release rate controllability. Furthermore, it was also possible to trace their localization in biological systems. Ibuprofen is an extensively employed analgesic and anti-inflammatory drug. The functional carboxylic acid group in the ibuprofen molecule can form strong bonds with many functional groups via acid–base reaction. The size of the ibuprofen molecule, about 1.0 nm × 0.6 nm, is well suited to easy diffusion into or out of the mesoporous channels [16]. The loading of ibuprofen into the nanotube materials, as well as its release, were investigated in detail.

2. Materials and methods

2.1. Materials

Needle-like $CaCO_3$ templates were prepared by a unique high-gravity reactive precipitation technology [33]. All chemicals used in the experiment were obtained from commercial sources as analytical reagents without further purification. Milli-pore water with a resistivity of 18.2 $M\Omega\,cm^{-1}$ was used throughout the study.

2.2. Preparation of MSNTs

MSNTs were fabricated according to the following steps: (1) 8 g needle-like $CaCO_3$ nanoparticles were first dispersed in 380 ml of ethanol solution ($V_{ethanol}/V_{water}$ = 1:3.75) by sonication. Cetyltrimethylammonium bromide (CTAB) (4 g) and 20 ml aqueous ammonia (25 wt.%) were then added in sequence. After the suspension had been stirred for 2 h, a mixture containing ethanol, water and 6.4 ml tetraethylorthosilicate (TEOS) was slowly added dropwise into the suspension. The suspension was stirred for an additional 2 h and then aged for 24 h. The white particles were collected by filtering and washed with a large amount of water. (2) The particles were dried overnight at 373 K, heated to 973 K at a rate of 1 K min^{-1}, and calcined continuously at 973 K for 5 h. (3) The composite particles were placed in a 0.25 M hydrochloric acid solution for 24 h to remove the templates. The resulting gel was filtered, rinsed with water and ethanol, and then dried at 373 K for 12 h to obtain MSNTs.

2.3. Amine-functionalization of MSNTs

The dried MSNTs powder was dispersed in toluene by sonication for 5 min before 3-aminopropyltriethoxysilane (APTS) was added to the suspension. The molar ratio of MSNTs particles (calculated as SiO_2:APTS:toluene) was fixed at 5:1:500, and the suspension was heated under reflux (398 K) for 24 h in nitrogen. The amine-functionalized MSNTs particles were filtered from the solution, and washed in toluene and ethanol twice, respectively. Finally, the particles were dried at 353 K for 12 h and denoted as NH_2-MSNTs.

2.4. Incorporation of CdS quantum dots

To avoid the cytotoxicity of Cd^{2+} released from CdS through oxidative attack on live cells [34] and to detect the fluorescence from CdS quantum dots in excited silica materials, 0.1% mole ratio of Cd:Si was used for the incorporation of CdS quantum dots. A typical incorporation procedure was as follows: 0.6 g NH_2-MSNTs were dispersed in 96 ml water and then 125 μl $CdCl_2$ (0.1 M) were added with magnetic stirring for 4 h. The solution was then centrifuged and the residue was washed three times with water to remove Cd^{2+} from the external surface. After the redispersion of Cd^{2+}-NH_2-MSNTs in 96 ml water, 125 μl thioacetamide (TAA, 0.1 M) as a source solution of S^{2-} was added and then the mixture was continuously stirred for 24 h at 303 K. The obtained product was filtered and washed with water three times and denoted as CdS-NH_2-MSNTs. MSNTs were also incorporated with CdS quantum dots by the above-mentioned procedure for comparison and denoted as CdS-MSNTs. The experimental process for the preparation and amine-functionalization of MSNTs and subsequent incorporation of CdS quantum dots is shown in Scheme 1.

2.5. Drug storage

A typical procedure for loading ibuprofen was as follows: 1.0 g CdS-NH_2-MSNTs was added into 50 ml

ID	Title	Pages
1876	Fluorescent mesoporous silica nanotubes incorporating CdS quantum dots for controlled release of ibuprofen	9