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A facile route to synthesize silver nanoparticles in polyelectrolyte capsules

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ABSTRACT

We are reporting a novel green approach to incorporate silver nanoparticles (NPs) selectively in the polyelectrolyte capsule shell for remote opening of polyelectrolyte capsules. This approach involves in situ reduction of silver nitrate to silver NPs using PEG as a reducing agent (polyol reduction method). These nanostructured capsules were prepared via layer by layer (LbL) assembly of poly(allylamine hydrochloride) (PAH) and dextran sulfate (DS) on silica template followed by the synthesis of silver NPs and subsequently the dissolution of the silica core. The size of silver nanoparticles synthesized was 60 ± 20 nm which increased to 100 ± 20 nm when the concentration of $AgNO_3$ increased from 25 mM to 50 mM. The incorporated silver NPs induced rupture and deformation of the capsules under laser irradiation. This method has advantages over other conventional methods involving chemical agents that are associated with cytotoxicity in biological applications such as drug delivery and catalysis.

1. Introduction

Polyelectrolyte capsules (PECs) have in recent times become the subject of extensive research because of their potential applications as carrier systems in areas such as drug delivery, artificial cells or viruses, microreactors and catalysis [1–4]. These capsules are fabricated by LbL technique which consists of stepwise adsorption of oppositely charged polyelectrolytes onto sacrificial colloidal particles followed by dissolution of the cores [5]. A variety of chemical and biological substances ranging from proteins and DNA to rather small drug molecules, have been successfully encapsulated into PECs by manipulating their wall permeability [6,7]. To release the encapsulated materials into biological tissues, the modified PECs have to undergo a enzymatic, thermal and magnetic triggering treatment [8–10]. Thermal pulses activate the thermo responsive hydrogels to release their contents [9], while in the case of magnetic triggering, the applied magnetic field disrupts the microcapsules that contain magnetically sensitive nanoparticles [10]. Laser light based optical triggering presents another mechanism for manipulation of delivery systems [11]. The presence of inorganic nanoparticles, especially silver/gold nanoparticles, significantly improves the efficiency of the radiation-stimulated release in near-infrared (NIR) region [11,12], which is particularly attractive in biomedical applications due to weak absorption of NIR radiation by most tissues.

Among the known metal NPs, silver is known for its antimicrobial properties and has been used for years in the medical field for the same reason [13]. While being relatively non-toxic to human cells, silver possesses antibacterial properties for a broad spectrum of bacterial strains and even prevents HIV binding to host cells [14]. It is believed that Ag NPs attach to the surface of cell membrane disturbing the permeability and respiration functions of the cells which leads to microbial cell death [15]. Due to these unique properties, incorporation of Ag NPs in PECs gives an added advantage of biocompatibility for laser triggering of drug molecules in biomedical applications.

Previously, NPs were incorporated into PECs by either using them as one of the shell components or were introduced into the pre-formed capsule suspension [11,12]. However, this often leads to inhomogeneous distribution of NPs in the capsules. One solution to overcome this limitation is the in situ synthesis of Ag NPs in the capsules, which involves the reduction of Ag salts within the capsule interior by UV/vis radiation [16]. The synthesis of silver NPs involves two main steps: (i) complexation of Ag^+ ions with SO_3^- groups of previously co-precipitated poly(styrene sulfonate) (PSS) in the capsule interior and (ii) reduction of complexed Ag^+ ions into Ag NPs under UV/vis irradiation. It has been reported that when melamine formaldehyde (MF) is used as the template, the oligomers formed during MF core dissolution form a complex with this co-precipitated PSS [17], which can affect the formation and stability of silver NPs and also the activity of drug/biomolecules encapsulated in it. Furthermore, NPs have been synthesized inside the capsules instead of the wall. Such capsules need high intensity laser and more exposure time for remotely opening the drug loaded capsules *in vivo*. This can affect the living tissues which are sensitive to monochromatic coherent radiation. So it is important to develop a simple, time saving green approach to synthesize Ag NPs selectively

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within the polyelectrolyte capsule shell for biomedical applications.

2. Materials and methods

2.1. Materials

Dextran sulfate (DS) (M_W = 500 kDa), poly(allylamine hydrochloride) (PAH) (M_W = 70 kDa), poly(ethylene glycol) (PEG) (M_W = 6 kDa), HF (Sigma–Aldrich) and silver nitrate (Ranbaxy, India) were used without any further purification. Mono-disperse silicon oxide particles with mean diameter of 4.27 ± 0.25 μm were obtained from Microparticles (Germany). The water used in all experiments was obtained from Milli-Q system with resistivity greater than 18 MΩ cm. All pH adjustments were done with 0.1 M HCl or 0.1 M NaOH.

2.2. Preparation of polyelectrolyte capsules

PAH and DS solutions (1 mg/ml, in 0.2 M NaCl) were used for alternate adsorption of $(PAH/DS)_3$ multilayers on silica particles at pH 5. After each adsorption step, the coated particles were collected by centrifugation and the residual non-adsorbed polyelectrolyte was removed by washing thrice with pH 5 water. After deposition, the coated particles were resuspended and 0.1 M HF was added to dissolve the silica core. After 20 min, the resultant suspension of hollow capsules was washed five times with pH 5 water and used for further experiments. Since the SiO_2 particles are negatively charged, cationic PAH was used for the deposition of the first layer.

For the preparation of silver NPs incorporated capsules, the $(PAH/DS)_3$ coated particles were dispersed in 2.5% PEG solution consisting of 25 mM $AgNO_3$ and heated to 50 °C for 30 min in a rotatary incubator. After 30 min, the coated particles were washed with pH 5 water and deposited with another bilayer (PAH/DS). Finally, the silver NPs incorporated hollow capsules were obtained by dissolving the silica core in 0.1 M HF for 20 min and subsequent washing in water.

2.3. Laser irradiation study

Laser irradiation study of polyelectrolyte capsules with and without the presence of silver NPs in their shell was performed using CW Nd:YAG laser (Excelsior, Spectra-Physics, USA) with an average incident power of 150 mW. The irradiation of capsule suspension was carried out in a 1 ml quartz cuvette by exposing collimated laser beam of 532 nm for 2 min. The laser intensity was measured by a newport-1830C power meter.

2.4. Characterization techniques

For atomic force microsocopy (AFM) analysis, a drop of capsule suspension was applied to a silicon wafer and air-dried overnight. Then the samples were characterized using a Nanosurf Easy Scan2 AFM (Nanoscience Instruments Inc, USA) in air at room temperature by contact mode. FE-TEM/EDAX measurements were performed on a Tecnai F30 (FEI, Eindhoven, Netherlands) microscope operating at 200 kV. Samples were prepared by applying a drop of the capsule suspension to carbon coated copper grid. In order to calculate the average size of silver NPs, 500 NPs were selected stochastically from TEM images and their average size and standard deviation were calculated by ImageJ software. For TGA analysis (SDT Q600, TA Instruments, UK), samples were dried overnight at 40 °C under air to remove residual water. Then these samples were heated to 600 °C at the rate of 10 °C min^{-1}. UV/vis spectra of capsule suspensions were recorded using T60 UV–vis spectrometer (PG Instruments Ltd., UK).

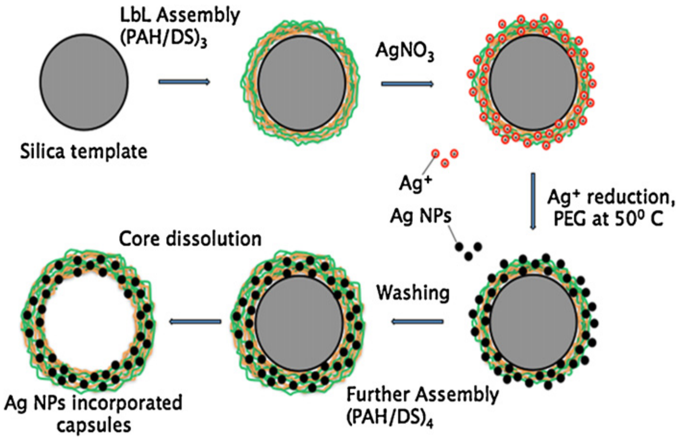

Fig. 1. Schematic illustration of deposition of silver nanoparticles within polyelectrolyte capsule shell.

3. Results and discussion

Here we report facile green approach to synthesize Ag NPs within the walls of (PAH/DS) PECs using PEG as a reducing agent. Since PEG is widely used as a prodrug in pharmaceutical and biomedical industries [18], the usage of PEG as reductant in our study offers biocompatibility for practical applications. The preparation technique is simple and even a time period of 30 min is sufficient to obtain the signature of Ag NPs in the capsule shell. In this method, the silver NPs were synthesized directly in the capsule wall by the reduction of silver nitrate in the presence of PEG which can act as a electron donor for the reduction process. It has been reported in the literature that PEG and diols can be used as reducing agents to prepare Ag NPs through the so-called polyol process at high temperatures [19,20]. Fig. 1 shows the schematic procedure of silver NPs incorporation within the capsule shell. According to our method $(PAH/DS)_3$ coated silica particles were mixed with 2.5% PEG solution consisting of 25 mM $AgNO_3$ and kept for 30 min in a shaker at 50 °C for homogeneous distribution and reduction of Ag^+ ions into silver NPs. The color of the particle suspension turned to dark brown with time indicating the formation of Ag NPs on the surface of coated particles. The sulfonate groups of DS present in the polyelectrolyte film acts as binding sites for the adsorption of silver ions that are formed by reduction of the silver salt [21]. Then the suspension was washed twice to remove any traces of silver NPs that would have formed in the surrounding solution. Further, addition of another bilayer (PAH/DS) followed by core removal in 0.1 M HF yielded hollow capsules incorporated with silver NPs within the capsule wall. Fig. 2 shows the AFM images of dried capsules with and without silver NPs. After formation of silver NPs, the PECs showed a thicker wall with a mesh kind of morphology due to the presence of silver NPs. The spherical silver NPs were homogeneously distributed within the shell throughout the capsule without any aggregation as shown in Fig. 2b (inset). TEM measurements were performed to investigate the inner structure of the NP incorporated capsules. TEM analysis after synthesis of silver NPs showed dark and rough capsule shells as compared to the original polyelectrolyte ones (Fig. 3a and b). The higher magnification image (Fig. 3b inset) reveals clearly the presence of silver NPs in the capsule shell. On the basis of TEM analysis, the size of silver NPs was estimated to be 60 ± 20 nm. The size of silver NPs formed is sensitive to the concentration of the silver nitrate precursor solution. When $AgNO_3$ concentration was increased to 50 mM from 25 mM, the amount of particles formed increased drastically which can be seen clearly in the TEM image shown in Fig. 3c. It can also be noted that large number of silver NPs are distributed