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CHEMISTRY OF MATERIALS
Communication

Self-Polymerization of Dopamine as a Versatile and Robust Technique to Prepare Polymer Capsules

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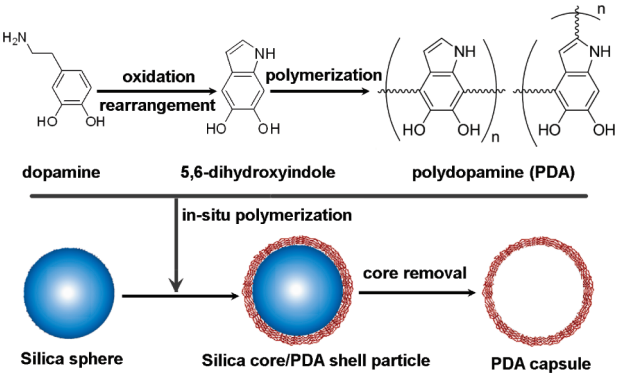
The development of versatile and robust strategies for the formation of polymer capsules is expected to underpin new advances in the generation of engineered particles for applications in therapeutic delivery, catalysis, sensing, and (bio)chemical reactions. A prominent method to form polymer capsules with tailored properties is layer-by-layer (LbL) assembly.[1,2] In this process, template particles are coated with multiple layers through the sequential adsorption of polymers from solution, followed by removal of the template cores. The polymer layers can be assembled by exploiting electrostatic interactions, hydrogen bonding, and covalent bonding strategies.[3,4] The deposition of polymer films on particles through a single-step solution-based technique would provide direct benefits in the construction of capsules, minimizing labor, cost, and assembly complexity. Furthermore, the ability to control the thickness of the films using a simple single-step adsorption technique would offer new opportunities in tailoring the physicochemical properties of polymer capsules.

A promising method to form thin polymer films through a single deposition process with control over film thickness is based on the oxidative self-polymerization of dopamine (2-(3,4-dihydroxyphenyl)ethylamine) onto surfaces (Scheme 1). This approach, originally inspired by the adhesive properties displayed by mussels, was recently introduced and shown to generate a range of polydopamine (PDA)-coated planar substrates.[5] Recent studies have shown that this technique can also be used for the formation of PDA films on electrodes for biosensing,[6] PDA-stabilized poly(L-lysine)/hyaluronic acid multilayered freestanding films,[7a] and multifunctional PDA-coated carbon nanotubes.[8]

Scheme 1. Assembly of a PDA Film onto a Particle and Subsequent Capsule Formation[a]



[a] Oxidative polymerization of dopamine showing two of the possible structures formed. The polymerization chemistry has recently been reviewed.[9]

Herein, we report the assembly of PDA thin films by the spontaneous oxidative polymerization of a dopamine solution onto silica (SiO_2) particles, followed by removal of the template particles to form robust capsules (Scheme 1). We further show that this PDA assembly process can be applied to SiO_2 particles with a range of sizes and mesoporous structures. We also demonstrate that the PDA capsules exhibit negligible toxicity toward cells, which is of importance for the application of these capsules in biomedical applications. The primary advantages of the outlined strategy reside in the single polymer film deposition step required for the synthesis of capsules and control over the PDA film thickness by varying the polymerization reaction time. Furthermore, the technique is versatile, relatively quick, and

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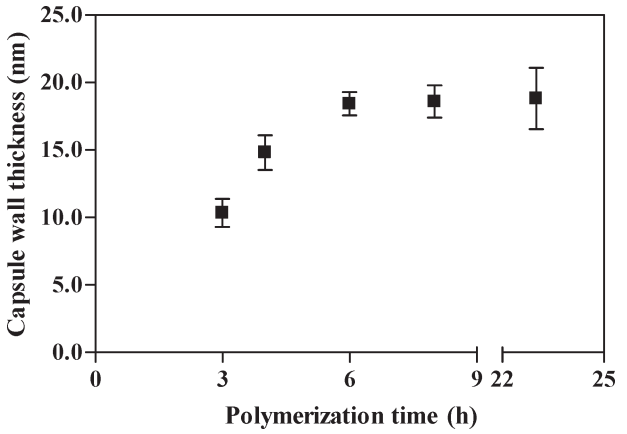

Figure 1. PDA microcapsule wall thickness as a function of polymerization time as measured by AFM. Nonporous 1 μm-diameter silica spheres were used as templates.

inexpensive, requiring a common and naturally occurring compound.

A PDA film was deposited onto SiO_2 particles by the oxidative self-polymerization of dopamine. Nonporous SiO_2 particles were exposed to a 2 mg mL^{-1} dopamine solution in air at pH 8.5 in 10 mM tris(hydroxymethyl)-aminomethane (TRIS) buffer for the allotted time and under constant agitation (see Supporting Information). The PDA-coated SiO_2 particles were then washed several times in 10 mM TRIS (pH 8.5) buffer until the supernatant remained colorless. During the colloidal surface polymerization step, some particulate PDA was observed to form in solution. This was selectively removed by centrifugation during the washing steps. PDA capsules were then obtained by etching the SiO_2 from the PDA-coated SiO_2 particles with a 2 M hydrofluoric acid/8 M ammonium fluoride solution (pH 5).[10] The growth of the PDA film was monitored by atomic force microscopy (AFM) (see Supporting Information) by taking a cross-sectional profile of the capsules where the film folded only once and then halving the thickness measurement.[3d] AFM data revealed that PDA film growth on the particles was almost linear over the first 6 h, followed by a slower growth, plateauing at a thickness of ~19 nm after 24 h (Figure 1). This trend in the PDA growth profile is in agreement with that reported for planar substrates.[5] The appearance of a plateau in film growth can be attributed either to depletion of dissolved oxygen within the system, which impedes the oxidative formation of intermediates prior to polymerization, or to the depletion of reactive dopamine in solution.[7] The kinetics of PDA film growth is currently under investigation. We found that capsules produced from incubation times of less than 3 h were fragile and significantly distorted upon drying; hence, data for these capsules were not included in the AFM measurements. The single-step PDA deposition procedure produces polymer capsules with a wall thickness

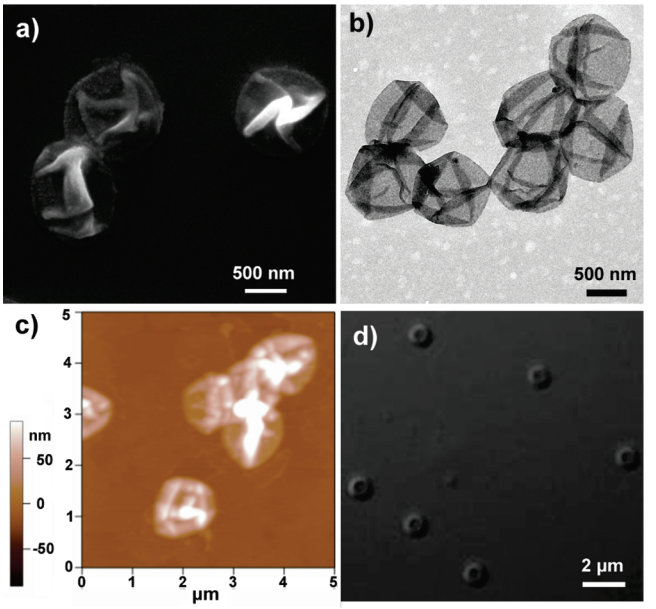

Figure 2. (a) SEM, (b) TEM, (c) AFM, and (d) optical (Nomarsky filter) microscopy images of PDA microcapsules prepared from nonporous 1 μm-diameter silica particles. The polymerization times used for the PDA coatings were between 4 and 21 h.

comparable to those formed by the conventional LbL (multistep) technique.[3]

Both electron microscopy (Figure 2a,b) and AFM (Figure 2c) analysis of the PDA capsules confirmed the formation of intact capsules with characteristic folding of the capsule walls upon drying.[3] Additionally, optical microscopy (Figure 2d) confirmed that the capsules were hydrated and stable under aqueous conditions.

Different sized nonporous SiO_2 cores (0.5, 1, 3, 5 μm diameters) were also investigated as templates (Figure S2, Supporting Information). All of these templates were found to produce PDA capsules with retained structural integrity.

The recent emergence of colloidal particles with nanosized pores has initiated new investigations with a number of notable advancements, such as engineered colloidal catalysts, drug delivery vehicles, and particle templates.[10,11] Here, monodisperse silica particles with a solid core and mesoporous shell (SC/MS) and commercial SGX mesoporous silica microspheres were also used as examples to demonstrate the PDA assembly in the confined nanopores of particles. First, the SC/MS particles with a diameter of ca. 420±10 nm and a shell thickness of ~60 nm were used as templates. Following PDA assembly and removal of the SC/MS template particles, PDA nanocapsules were obtained (Figure 3a,b). SEM and TEM analysis revealed that the individual nanocapsules are ~400±10 nm in diameter, around 5% smaller than the template particles. The capsules preserve their structural integrity and show significantly less folds and creases when air-dried than the PDA capsules prepared by using nonporous silica templates (see Figure 2). This is likely to be caused by the relatively small size of

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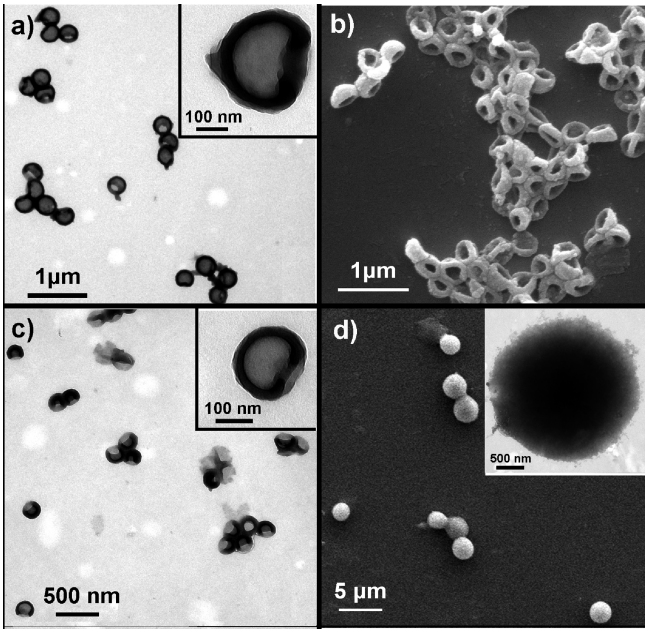

Figure 3. (a) TEM and (b) SEM images of the PDA capsules prepared using template SC/MS silica particles with a diameter of 420 nm and shell thickness of 60 nm. (c) TEM image of the PDA nanocapsules prepared using SC/MS silica particles with a diameter of 220 nm and shell thickness of 45 nm. In (a) and (c) the insets show higher magnification images. (d) SEM and TEM (inset) images of the PDA microparticles replicated from the SGX 1000 mesoporous (5 μm, pore size 20 nm) silica particles.

the capsules and the thick capsule shells.[12] At higher magnification, a uniform shell is clearly seen (Figure 3a, inset), confirming the structural integrity of the capsule shells. The PDA capsule shell, assembled by a single polymer adsorption step, has a thickness of 45 ± 5 nm, which is approximately 2 times thicker than the shell thickness of PDA ($\sim$19 nm) deposited on nonporous silica particles. Smaller capsules ($\sim$210 nm) were obtained when the SC/MS particles with a diameter of $\sim 220 \pm 10$ nm were used as the template (Figure 3c). When nanoporous silica particles (SGX 1000, 5 μm diameter; 20 nm pore size) were used as templates, intact PDA replicated microspheres with a diameter of approximately $2.6 \pm 0.4\,\mu$m were obtained. The nonhollow features of the PDA replicas can be clearly observed from TEM (Figure 3d, inset).

Polymer capsules are drawing interest because of their potential in biomedical applications. Therefore, we conducted MTT assays to examine the cytotoxicity of the PDA capsules prepared. Experiments where the capsule dose ranged from 100 capsules μL^{-1} to 100000 capsules μL^{-1}, corresponding to a capsule/cell ratio of 1:1 to

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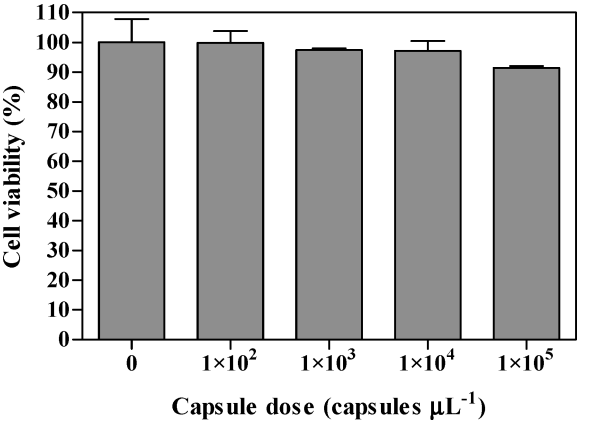

Figure 4. MTT assay of PDA capsules (prepared from 1 μm-diameter nonporous SiO_2 template particles) on LIM1215 cells incubated with increasing capsule numbers for 24 h at 37 °C with 5% CO_2. The values were normalized to the untreated cells (control) as 100%. The polymerization time used for the PDA coating was 16 h.

1000:1, did not cause significant changes in cell proliferation (Figure 4), indicating that the PDA capsules exhibit negligible toxicity. Coupled with drug loading techniques relying on preformed intact carriers,[13] this makes PDA capsules convenient and inexpensive candidates for therapeutic delivery and other biomedical applications.

In summary, we have presented a single-step thin film assembly process on various SiO_2 particles via the oxidative self-polymerization of dopamine to form a range of single component PDA capsule systems. This process was found to be highly efficient and applicable to particles of different sizes and with different porosities. PDA films were deposited on silica particles with a range of particle sizes and on a variety of mesoporous structures, affording structurally robust capsules and replicated particles. Biocompatibility tests demonstrated negligible toxicity of the PDA capsules to cells, making them promising for drug/gene delivery applications. Given its simplicity, efficiency, and generalizability, the PDA approach is expected to find widespread application in the generation of new particulate delivery systems.

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Supporting Information Available: Experimental details and instrument specifications (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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