Chapter 2
Synthesis of Hollow Mesoporous Silica Nanoparticles by Silica-Etching Chemistry for Biomedical Applications

2.1 Introduction

With the fast development of mesoporous materials for biomedical applications, many requirements on the morphology and structure of materials have been proposed [1–3]. Scientists need to design and fabricate mesoporous nanomaterials with unique functionalities based on the principles of chemical synthesis. Numerous studies have demonstrated that the performance of mesoporous silica-based material systems is strongly related to the composition, morphology, and structure of fabricated materials [4–7]. Therefore, mesoporous silica with diverse morphologies have been designed and synthesized, such as spherical, rod, fiber, tube, sheet, polyhedral shape, etc. [8]. The regulation of the morphologies of mesoporous silica is important in nanomedicine and nanobiotechnology because mesoporous silica nanoparticles (MSNs) with different morphologies show significantly different biological behaviors [9–11]. In addition, the particle sizes of MSNs strongly influence their in vivo bio-distributions and excretions [12, 13].

Among MSNs with abundant morphologies and nanostructures, hollow mesoporous silica nanoparticles (designated as HMSNs) have attracted tremendous attentions due to their unique hollow and mesoporous nanostructure [14–17]. The large hollow interiors of HMSNs leave more room for the loading of guest molecules compared to traditional MSNs. Thus, HMSNs show the high drug-loading capacity. The well-defined mesopores within the shell provide the diffusion path for guest molecules. In addition, the abundant surface chemistry of HMSNs make the surface engineering/modification possible such as PEGylation or targeting modification. On this ground, it is of high significance to design and fabricate HMSNs based on the principle of organic–inorganic nanosynthetic chemistry. Prof. Shi’s group is one of the earliest research teams to prepare MSNs with large hollow interior and ordered mesopores [18, 19]. Their preliminary applications in biomedicine were also conducted. It was found that the large
hollow interior of HMSNs could significantly enhance the drug-loading capability. For instance, the drug-loading amount of HMSNs toward ibuprofen (IBU) could reach as high as 744.5 mg/g, while traditional MCM-41-type MSNs without the hollow structure only encapsulated 358.6 mg IBU per gram MSNs [19].

However, there are still no simple, efficient, economic, and environment-friendly synthetic strategies to fabricate HMSNs with high dispersity, tunable particle size, and controllable mesopore size. In addition, the research on the biomedical applications of HMSNs is much less than that of MSNs. The most representative method to prepare HMSNs is so-called “templating method” [20]. Typically, such a templating method initially employs various soft/hard templates as the substrate, followed by coating a shell with desirable composition/structure onto the surface of the templates. After removing the templates, the hollow spheres can be obtained. Generally, the chemical composition between the core and shell is different, causing the different physiochemical properties. Based on these different physiochemical properties, the core template can be completely removed while the shell keeps intact by various physical or chemical approaches. In this chapter, we successfully developed a new templating method to prepare HMSNs, but the templating principle is not the traditional composition difference between the core and shell. We found that the structural differences between the core and shell could also be employed for the fabrication of HMSNs, though the chemical composition between the core and shell was the same with each other. We defined this method as “structural difference-based selective etching” (SDSE) strategy. Based on SDSE strategy, we successfully constructed HMSNs with desirable structure, composition and, physicochemical property. The formation mechanism and principle of HMSNs based on SDSE strategy were systematically investigated. We further studied the biological behaviors of HMSNs, including cytotoxicity and in vitro hemocompatibility. In addition, the specific function of HMSNs for in vitro anticancer drug delivery was revealed.

2.2 Experimental Section

2.2.1 Synthesis of HMSNs Based on SDSE Strategy

The fabrication of HMSNs includes three steps, i.e., fabrication of solid SiO₂ as the hard template, coating the SiO₂ template by mesoporous silica, and the final removal of SiO₂ template by chemical etching. Typically, ethanol (142.8 mL), H₂O (20 mL), and ammonia solution (3.14 mL) were premixed, followed by adding tetraethyl orthosilicate (TEOS, 6 mL) under magnetic stirring at 30 °C. After further 1 h reaction, the mixture of TEOS and octadecyltrimethoxysilane (C₁₈TMS) was added for another 6 h reaction. The product was collected by centrifugation and divided into six parts. Each part was etched in Na₂CO₃ solution (0.6 M, 50 mL) for 0.5 h at 80 °C. The etched sample was collected by centrifugation and washed several times by water and ethanol. After drying under vacuum
at room temperature, the sample was calcined at 550 °C for 6 h to remove the organic part.

2.2.2 Synthesis of HMSNs by Chemical Etching in Ammonia Solution

The fabrication of HMSNs in ammonia solution was similar to the etching procedure in Na₂CO₃ solution. When sSiO₂@mSiO₂ was ready, they were dispersed into diluted ammonia solution (70 mL, 0.12 M or 0.24 M). They were further transferred into Teflon-lined stainless steel autoclave, which was treated at 150 °C for 24 h. When the autoclave was cooled down to room temperature, the product was collected by centrifugation and dried under vacuum. The sample was finally calcined at 550 °C for 6 h.

2.2.3 Study of the Formation Mechanism of HMSNs

A: Synthesis of Stöber method-based SiO₂ nanoparticles
TEOS (6 mL) was directly added into the mixture of ethanol (142.8 mL), H₂O (20 mL), and ammonia solution (3.14 mL) at 30 °C under magnetic stirring. After further 2 h reaction, the product was collected by centrifugation, washed by ethanol three times, and finally dried under vacuum at room temperature.

B: Synthesis of MSNs templated by C₁₈TMS
Ethanol (142.8 mL), H₂O (20 mL), and ammonium solution (3.14 mL) were pre-mixed and stirred at 30 °C, followed by adding the mixture of TEOS (5 mL) and C₁₈TMS (2 mL). After further reaction at 30 °C for 1 h, the sample was collected by centrifugation, washed by ethanol three times, and dried under vacuum at room temperature.

2.2.4 Synthesis of Multifunctional Rattle-Type HMSNs Based on SDSE Strategy

A. Au@mSiO₂
Au nanoparticles were initially synthesized by heating HAuCl₄ · 3H₂O solution (18.0 mg in 30 mL water) at 100 °C under vigorous stirring, followed by adding sodium citrate solution as the reducing agent for another 30 min reaction. The surface of as-synthesized Au nanoparticles was coated by PVP10 (Polyvinylpyrrolidone, 12.8 g/L, and 0.235 mL) to facilitate the subsequent coating process. The PVP-modified Au nanoparticles were redispersed into water.
(3.0 mL) by mild ultrasound treatment. Then, Au solution (1.0 mL) was added into a mixture solution with ammonia solution (0.62 mL), ethanol (13.6 mL), and H2O (3.3 mL), followed by the addition of TEOS (0.86 mL) in ethanol (9.2 mL) under vigorous magnetic stirring. After further 1 h reaction, TEOS (0.714 mL) and C18TMS (0.286) mixture were directly added into above solution under vigorous stirring, which further lasted for another 1 h. The product was collected by centrifugation and washed by ethanol and water for several times. After drying at 100 °C, the sample was calcined at 500 °C for 6 h.

B. Fe2O3@mSiO2 and Fe3O4@mSiO2
Ellipsoidal Fe2O3 nanoparticles were initially synthesized by a hydrothermal method. Typically, Fe(ClO4)3 · 6H2O (11.6 g), urea (1.5 g), and NaH2PO4 (0.16 g) were dissolved into deionized water (250 mL) to form a homogeneous solution, which was further transferred into an oven and incubated at 100 °C for 24 h. The product was collected by centrifugation and dried for further use. For the coating process, the as-synthesized Fe3O4 (30 mg) was dispersed into the solution containing ethanol (71.4 mL), H2O (10 mL), and ammonia solution (3.14 mL), followed by adding TEOS (0.53 mL TEOS in 4.7 mL ethanol) at the speed of 4 mL/h. Then, the mixture of TEOS (0.3 mL) and C18TMS (0.2 mL) were added into the reaction system dropwise. The product was collected by centrifugation and washed by ethanol and water several times. The as-synthesized Fe2O3@SiO2@mSiO2 was treated in ammonia solution (0.12 M) at 150 °C for 24 h. After centrifugation and washing steps, the sample was dried and calcined at 550 °C for 6 h. The inner core of Fe3O4@mSiO2 was reduced into Fe3O4 nanocrystals by the thermal treatment in mixed H2 (5 % in volume) and Ar (95 % in volume) gases at 410 °C for 5 h.

2.2.5 Hemolytic Effect Evaluation

The red blood cells (RBCs) were kindly provided by Shanghai Blood Center, which was diluted to 1/10 of their initial volume by PBS for assessment. Typically, the RBCs suspension (0.3 mL) was co-incubated with (a) 1.2 mL PBS as the negative control, (b) 1.2 mL deionized water as the positive control, and (c) 1.2 mL HMSNs PBS suspensions at different concentrations (from 25 to 200 µg/mL). After the co-incubation for 2 h, the cells were centrifuged, and the supernatants were collected for UV-vis characterizations at λ = 541 nm to determine the hemolytic percentage.

2.2.6 In Vitro DOX-Loading into HMSNs

HMSNs (50 mg) were dispersed into DOX PBS solution (6 mL, 0.5 mg/mL) by mild ultrasound treatment. After stirring for 24 h in the dark, the DOX-loaded HMSNs were collected by centrifugation, which was dried under vacuum at
room temperature. To determine the DOX-loading amount, the supernatant was collected for UV-vis test at $\lambda = 480$ nm.

### 2.2.7 MTT Evaluation of the Cytotoxicity of HMSNs and DOX-HMSNs

In vitro cytotoxicity of HMSNs and DOX-HMSNs was evaluated by a typical MTT method. MCF-7 breast cancer cells were initially seeded into a 96-well plate at the density of 2000 cells/well, which were cultured in 5 % CO$_2$ at 37 °C for 24 h. Free DOX and DOX-loaded HMSNs dispersed into the cell-culturing medium were used to substitute the initial solution. The adopted DOX concentrations are 0.02, 0.2, 2, and 10 µM. After the co-incubation for 24 h, the cell-culturing medium was replaced by MTT solution (0.8 mg/mL, 100 µL/well), followed by another co-incubation for 4 h. Finally, the MTT solution was replaced by dimethyl sulfoxide (DMSO, 100 µL/well), and the absorbance was recorded by a microplate reader (Bio-TekELx800) at the wavelength of 490 nm. The cytotoxicities of MCF-7 cells were expressed as the percentage of cell viability compared to the cells without the treatment.

### 2.3 Results and Discussion

#### 2.3.1 Synthesis and Characterization of HMSNs

Based on mature Stöber method, silica nanoparticles (designated as SNs) with high dispersity could be easily obtained [21]. The syntheses of mesoporous silica nanoparticles (MSNs) are typically based on sol-gel chemistry, which employs surfactants or block copolymers as the structural directing agents to generate the mesopores. We anticipated that some structural differences would be present between these two silica-based nanoparticles, though they have almost the same chemical composition.

TEM image shows that the as-synthesized SNs (Fig. 2.1a) exhibit smooth surface and spherical morphology, while the prepared MSNs (Fig. 2.1b) have the rough surface and mesopores. In FTIR spectra (Fig. 2.1c), MSNs show that a red shift from 1101 to 1086 cm$^{-1}$ occurs in the transverse-optical mode of Si–O–Si asymmetric stretching vibration band compared to SNs. Such a red shift indicates that MSNs have a more open structure and higher condensation degree of silica species. In $^{29}$Si MAS NMR spectra (Fig. 2.1d), there are three distinctive signals at –92, –101 and –111 ppm, which can be indexed to Q$^2$[(SiO)$_2$Si(OH)$_2$], Q$^3$[(SiO)$_3$SiOH], and Q$^4$[(SiO)$_4$Si] species, respectively. The calculated Q$^4$/($Q^2 + Q^3$) ratio of MSNs is much higher than that of SNs, indicating that MSNs have enhanced condensation degree compared to SNs [14].
To validate this idea, we used the layer-by-layer coating procedure to coat a mesoporous silica layer onto the surface of solid silica nanoparticles (sSiO$_2$@mSiO$_2$) · N$_2$CO$_3$ and ammonia solution were chosen as two alkaline etchants to etch sSiO$_2$@mSiO$_2$ nanoparticles. The evolution of the morphology and structure of hollow nanoparticles during the etching process can be observed by TEM images. As shown in Fig. 2.2a, the as-synthesized sSiO$_2$@mSiO$_2$ nanoparticles display the high dispersity and apparent core/shell structure. After the etching of sSiO$_2$@mSiO$_2$ in Na$_2$CO$_3$ solution (0.6 M) at 80 °C for 0.5 h, the core of sSiO$_2$@mSiO$_2$ could be completely etched away while the mesoporous silica shell are kept intact (Fig. 2.2b), by which highly dispersed HMSNs could be fabricated. After the treatment of sSiO$_2$@mSiO$_2$ within ammonia solution (0.12 M) at 150 °C for 24 h, the typical rattle-type HMSNs could be synthesized (Figs. 2.2c and 2.3). Further increase of the concentration of ammonia solution (from 0.12 to 0.24 M) completely removed the inner SiO$_2$ core to produce HMSNs, as shown in Fig. 2.2d.

To investigate the formation mechanism of HMSNs, TEM observation was used to show the evolution of the hollow interior. For Na$_2$CO$_3$ etching, a lot of mesopores were present within the solid hollow interior when the Na$_2$CO$_3$
concentration was decreased (Fig. 2.4). For ammonia etching, the low-etchant concentration induced the formation of hollow interior between the solid core and mesoporous shell (Fig. 2.2c). Therefore, the evolution of the hollow interior in different etchants and etching processes varied significantly.

Based on the above results, we proposed a “structural difference-based selective etching” (SDSA) strategy to synthesize HMSNs (Fig. 2.5). After coating a mesoporous silica layer onto the surface of SiO$_2$ nanoparticles, the condensation degree of solid SiO$_2$ core is significantly lower than that of mesoporous
silica layer using C$_{18}$TMS as the pore-making agent. Thus, the stability of SiO$_2$ core is lower than that of mesoporous silica shell, by which the SiO$_2$ core can be selectively etched away while the mesoporous silica shell keeps intact. The

**Fig. 2.4** Hollow mesoporous silica spheres obtained by treating sSiO$_2$@mSiO$_2$ in 0.2 M Na$_2$CO$_3$ solution at 80 °C for 0.5 h

**Fig. 2.5** The formation schematics of hollow/rattle-type mesoporous silica spheres (left) and the microscopic structure illustration (right). Reproduced with permission from Ref. [28]. © 2010, American Chemical Society
hydrophobic part of C18TMS self-assembles with hydrolyzed/condensed silica precursors to form worm-like mesopores. When the low Na2CO3 concentration was (0.2 M) used, the SiO2 core could form a lot of mesopores, and further etching could completely remove the core. Under the ammonia etching at high temperature, the less condensed solid SiO2 core condenses further to make the solid silica core difficult to be etched away. Thus, the etching process was from the outside part to the inner part. The rattle-type hollow nanostructure can be formed by this process. Further increase of ammonia concentration can generate the entire hollow nanostructure.

The well-defined mesoporous structure of HMSNs was characterized by typical N2 adsorption–desorption technique. The isotherms of sSiO2@mSiO2, rattle-type HMSNs, and HMSNs exhibit the typical Langmuir IV hysteresis (Fig. 2.6a). Compared to initial sSiO2@mSiO2 and HMSNs, the rattle-type HMSNs show a large hysteresis loop, which indicates that the ink bottle-type mesopores are present within the shell. According to the calculation of the desorption branch of N2 isotherm by BJH method, the average mesopore sizes of rattle-type and hollow mesoporous silica were 3.2 nm and 3.4 nm, respectively (Fig. 2.6b). The enlarged mesopore size was due to the slight etching of the framework of the shell during the chemical etching process. Such an etching process could cause the significant increase of pore volume from 0.33 cm3/g (sSiO2@mSiO2) to 0.66 cm3/g (rattle-type HMSNs) due to the formation of large hollow cavity within HMSNs.

The particle size of HMSNs was controlled by choosing the initial SiO2 templates with different particulate sizes. The mature Stöber method facilitates the fabrication of SiO2 templates. As shown in Fig. 2.7, the particle sizes of HMSNs were adjusted to be about 60 nm (Fig. 2.7a), 180 nm (Fig. 2.7b), and 360 nm (Fig. 2.7c). More precise controlling of the particle size can be achieved by choosing different sized SiO2 cores, which is also one of the specific features of hard-templating method to easily control the particle size of hollow nanoparticles.
Various inorganic functional nanocrystals could be coated with SiO$_2$ layer by either Stöber method (for hydrophilic nanoparticles) or reversed-phase microemulsion method (for hydrophobic nanoparticles), which can change the surface status of nanocrystals and facilitate their further applications [22–26]. This research subarea has become relatively mature. It was considered that the formation of solid SiO$_2$ layer and mesoporous SiO$_2$ layer was both based on the traditional sol-gel chemical procedure. Therefore, it is easy to coat a mesoporous silica layer onto the surface of solid SiO$_2$ layer to form M@SiO$_2$@mSiO$_2$ multilayer composite structure (M: inorganic nanocrystals). Based on the above-mentioned SDSE method, the middle solid SiO$_2$ layer of M@SiO$_2$@mSiO$_2$ could be selectively etched away to form M@mSiO$_2$ with large hollow cavity between the core and shell (Fig. 2.8a).

To demonstrate the versatility of SDSE strategy, we employed Au nanoparticles as the functional core to fabricate rattle-type Au@mSiO$_2$ nanorattles. Au nanoparticles were initially synthesized by a sodium citrate reduction method, followed by coating a dense SiO$_2$ layer onto the surface of Au nanoparticles (Au@SiO$_2$). Furthermore, a mesoporous silica layer was deposited onto the surface of Au@SiO$_2$ to form Au@SiO$_2$@mSiO$_2$ composites. The middle solid SiO$_2$ layer was selectively etched away with the treatment in Na$_2$CO$_3$ solution (0.05 M, 80 °C) for 10 min. The triple-layer structured Au@SiO$_2$@mSiO$_2$ nanoparticles were revealed by the contrast difference in TEM image (Fig. 2.8b). The middle SiO$_2$ layer could be completely removed to form the rattle-type hollow structure (Fig. 2.8c). The as-prepared Au@mSiO$_2$ exhibited the similar ink bottle-type mesoporous structure with the surface area of 297 m$^2$/g, pore volume of 0.48 cm$^3$/g, and average pore size of 4.6 nm (Fig. 2.9a and b). The presence of Au nanocrystals was further demonstrated by X-ray diffraction pattern (Fig. 2.9d, JCPDS No. 04-0784). The maximum adsorption peak of Au@SiO$_2$@mSiO$_2$ at 536 nm showed a 10 nm red shift compared to initial Au nanoparticles (526 nm), and Au@mSiO$_2$ (532 nm) showed a 4 nm blue shift compared to that of Au@SiO$_2$@mSiO$_2$ (Fig. 2.9c). Such a change in the maximum adsorption peak is due to the variations of the local refractive index of the surrounding medium [27].

Fig. 2.7 TEM images of HMSNs with different particle sizes: a 60, b 180 and c 360 nm

2.3.2 Synthesis of Multifunctional M@mSiO$_2$ Nanorattles
Fig. 2.8 a: Schematic illustration of the synthetic procedures of heterogeneous rattle-type mesoporous nanostructures with inorganic nanocrystals (e.g., spherical Au and ellipsoidal Fe₂O₃ nanoparticles) as the core and mesoporous silica as the shell; TEM images of Au@SiO₂@mSiO₂ (b), rattle-type Au@mSiO₂ (c), ellipsoidal Fe₂O₃@SiO₂@mSiO₂ (d and inset picture), rattle-type Fe₂O₃@mSiO₂ (e, inset SEM image of selected broken ellipsoids). Reproduced with permission from Ref. [28]. © 2010, American Chemical Society
In order to further reveal that the composition, nanostructure and morphology of M@mSiO$_2$ could be easily controlled, we chose ellipsoidal Fe$_2$O$_3$ as another example to synthesize rattle-type Fe$_2$O$_3$@mSiO$_2$. Monodispersed ellipsoidal Fe$_2$O$_3$ was synthesized by a typical hydrothermal synthesis. After sequentially coating a dense SiO$_2$ layer and a mesoporous SiO$_2$ layer onto the surface, the
as-synthesized Fe$_2$O$_3$@SiO$_2$@mSiO$_2$ was treated in ammonia solution to remove the middle solid SiO$_2$ layer. As shown in Fig. 2.8d and e, the triple-layer structured Fe$_2$O$_3$@SiO$_2$@mSiO$_2$ could be clearly distinguished by the contrast differences. The middle SiO$_2$ layer could be completely etched away by ammonia solution, further demonstrating the versatility of SDSE strategy. Importantly, the Fe$_2$O$_3$ core could be converted to magnetic Fe$_3$O$_4$ nanocrystal, forming Fe$_3$O$_4$@mSiO$_2$ nanorattles. Similar to Au@mSiO$_2$, the obtained Fe$_2$O$_3$@mSiO$_2$ also showed the ink bottle-type mesoporous structure with the surface area of 427 m$^2$/g, pore volume of 0.49 cm$^3$/g, and pore size of 3.8 nm (Fig. 2.9a and b). The phase change of Fe$_2$O$_3$ to Fe$_3$O$_4$ was demonstrated by X-ray diffraction patterns (Fig. 2.9e). The magnetic Fe$_3$O$_4$@SiO$_2$@mSiO$_2$ nanorattles possess the saturation magnetization of 4.36 emu/g, which show the high-potential applications in T$_2$-weighted magnetic resonance imaging, magnetic-targeted drug delivery, and magnetic hyperthermia.

2.3.3 HMSNs for Anticancer Drug Delivery

Based on the successful fabrication of HMSNs, we further evaluated their performance in drug delivery. The hemolytic effect of HMSNs was first assessed. As shown in Fig. 2.10a, HMSNs caused the negligible hemolytic effect against red blood cells (RBCs) at the concentration of 0–200 µg/mL. According to the UV-vis test of the quantitative hemolytic percentage at the wavelength of 541 nm, the hemolytic percentage of HMSNs at the high concentration of 200 µg/mL was only 7.37%. Such a low hemolysis of HMSNs guarantees the safe intravenous administration of HMSNs for drug delivery.

The drug-loading capacity of HMSNs was evaluated by using doxorubicin (DOX) as the model drug. It was found that the DOX-loading efficiency could reach 98% when relatively large amount of HMSNs was used (50 mg, Fig. 2.10b). To investigate the maximum drug-loading capability of HMSNs, the adopted amount of HMSNs was reduced. The drug-loading amount could reach as high as 1222 mg/g. Such a high drug-loading capacity was attributed to the contribution of large hollow interior, which leaves more room for drug molecules. The therapeutic efficiency of DOX-loaded HMSNs was assessed against MCF-7 breast cancer cells. As shown in Fig. 2.10c and d, HMSNs themselves exhibited low cytotoxicities, indicating their high biocompatibility. DOX-loaded HMSNs showed enhanced cytotoxicity compared to free DOX. Such an enhanced therapeutic efficiency was due to the DOX delivery mediated by HMSNs, which could enter the cancer cells via endocytosis and release the loaded DOX within the cancer cells. Based on the above results, it can be concluded that HMSNs possess high biocompatibility and drug-loading capacity. When HMSNs are used as the DOX carrier, they show substantially improved therapeutic efficiency compared to free DOX drug.
This chapter developed a novel SDSE strategy to prepare highly dispersed HMSNs with controlled crucial structural parameters. Furthermore, this method was extended to synthesize multifunctional M@SiO₂ (M = Au, Fe₂O₃ and Fe₃O₄) hollow nanorattles. The hemolytic effect, cytotoxicity, drug-loading capacity, and therapeutic efficiency of HMSNs were also systematically evaluated. The specific conclusions are listed as follows:

1. Based on FTIR and ²⁹Si MAS NMR results, it can be concluded that traditional Stöber-based solid SiO₂ nanoparticles have low condensation degree of silicate framework compared to mesoporous silica nanoparticles templated by surfactants. Based on this chemical mechanism, SDSE method can be developed for the fabrication of HMSNs.
The evolutions of hollow interior of HMSNs by different methods are also substantially different. Chemical etching by Na$_2$CO$_3$ initially generates a lot of mesopores within the solid SiO$_2$ core and further forms the entire hollow interior. Comparatively, etching in ammonia solution initially generates the rattle-type structure and further etches the solid SiO$_2$ core from the outside part to the inner part.

Such a SDSE strategy can be extended to fabricate various functional M@mSiO$_2$ nanorattles with inorganic nanocrystals as the core, mesoporous silica as the shell, and large hollow cavity in between. In this chapter, three representative nanorattles (Au@mSiO$_2$, Fe$_2$O$_3@mSiO$_2$, and Fe$_3$O$_4@mSiO$_2$) were successfully synthesized by SDSE method.

The particulate sizes of HMSNs could be precisely controlled by choosing the solid SiO$_2$ core with different sizes. In this chapter, we successfully synthesize HMSNs with the particle sizes of about 60, 180, and 360 nm.

The obtained HMSNs possess high blood compatibility and low cytotoxicity. In addition, HMSNs show high drug (DOX)-loading capacity of as high as 1222 mg/g. Importantly, the therapeutic efficiency of DOX-loaded HMSNs is much higher than free drug.

References

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