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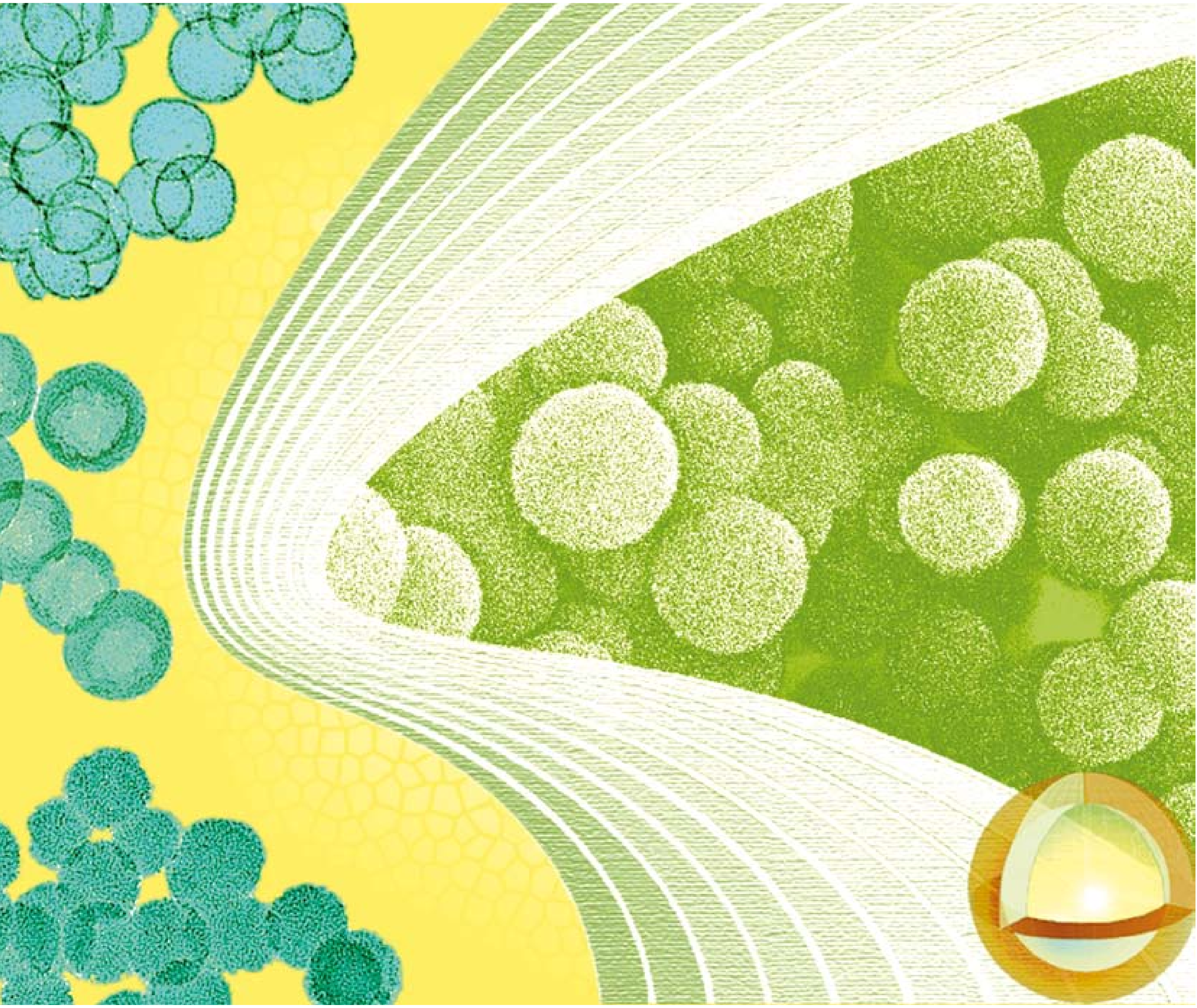

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A facile route to hollow nanospheres of mesoporous silica with tunable size

A facile route to hollow nanospheres of mesoporous silica with tunable size†

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Hollow mesoporous silica nanospheres (HMSNs) with tunable sizes of both sphere diameter (around 100 nm) and shell thickness have been successfully fabricated.

As nanocarriers, hollow mesoporous spherical materials with a large inner core and penetrating mesopores have attracted much attention due to their properties of low density, high specific surface area and well-defined mesoporous wall structure.[1] Up to now, hollow mesoporous spheres of various materials (such as titania, carbon, silica and so on) have been synthesized as high-performance catalysts, biomolecule separators and drug storage and delivery carriers, *etc.*[2] Among them, silica was demonstrated to be a nontoxic, highly biocompatible, and mechanically stable material, so it has many more practical applications in the areas mentioned above.[3] As shown in previous studies, the most widely used approaches such as hard templating[4] (inorganic, metal, and polymer beads) and soft templating[5] (emulsion, vesicles, *etc.*) methods have been demonstrated to be successful in fabricating hollow mesoporous spheres. However, the removal of the hard beads, which are sometimes expensive, is uneconomic and time consuming, and on the other hand, the synthesis of the soft sacrificial templates (usually surfactants) is commonly not simple.[5a] Moreover, hollow mesoporous spheres in the nanometric range ($\sim$100 nm) have rarely been reported,[5b] although they are desired in many potential applications, especially in drug delivery systems.

Herein, we report a facile synthesis of hollow mesoporous silica nanospheres (denoted as HMSNs) with uniform size ($\sim$100 nm) through a simple micellar aggregate templating route. In this work, (−)-*N*-dodecyl-*N*-methylephedrinium bromide (DMEB), which can easily form small micellar aggregates in water at low critical aggregation concentration, was employed as a 'dual' template to direct the formation of the hollow core and the mesostructure of HMSNs.[6a,b] Carboxyethylsilanetriol sodium salt (CSS) was used to assist the formation of HMSNs. Importantly, the sphere diameter and the shell thickness of HMSNs could be tuned by simply altering the composition of the synthetic precursor. To the best of our knowledge, this is the first report on the fabrication of nano-sized hollow mesoporous silica spheres ($\sim$100 nm).

Fig. 1 presents the TEM images of three HMSN samples prepared with different ratios of CSS/NaOH. In Fig. 1A, B and C, it is observed that HMSN-1, synthesized at a CSS/NaOH ratio of 0.2/1.5, is composed of uniform hollow spheres with very thin shells. The mean diameter and shell thickness are estimated to be around 150 nm and 8 nm, respectively, and the shell has a disordered worm-like mesoporous structure (Fig. 1B and C), which is in accordance with the XRD results where only one broad Bragg diffraction was present at $2\theta = 2$–3° (see ESI†). When the ratio of CSS/NaOH was changed to 0.2/1.0, TEM images (Fig. 1D, E and F) illustrate that the size of HMSN-2 becomes smaller, while the shell gets thicker. The diameter and shell thickness are in the ranges 90–120 nm and 15–20 nm, respectively. A SEM image (see ESI†) shows that HMSN-2 is made up of uniform nanospheres with a mean diameter of 130 nm, which is a little larger than that estimated from TEM images probably due to the presence of a thin layer of carbon (10–15 nm) coated for SEM analysis. As the ratio of CSS/NaOH was increased to 0.2/0.5, it is worth noting that there are no hollow cores in HMSN-3 and monodispersed solid spherical particles are obtained (Fig. 1G, H and I). Furthermore, the diameters of the mesoporous spheres decrease to about 75 nm, much smaller than the other two samples.

The N_2 adsorption–desorption isotherms of the surfactant extracted HMSN samples (Fig. 2) exhibit typical type-IV hysteresis, indicative of the presence of mesopores. It can be seen that the adsorption isotherm of each sample shows an apparent capillary condensation step at relative pressure (P/P_0) of 0.12–0.22, corresponding to the pore size of 2.2 nm, as calculated with the Barett–Joyner–Halenda (BJH) method. H4-type hysteresis loops at relative pressure (P/P_0) above 0.5 are present for each sample, suggesting the adsorption of N_2 molecules in the interparticle voids. The BET surface areas are measured to be 360 m^2 g^{-1}, 453 m^2 g^{-1} and 490 m^2 g^{-1} for HMSN-1, HMSN-2 and HMSN-3, respectively. It is noticeable that HMSN-1 shows the lowest surface area, which can probably be attributed to the rather dense structure of the thin shell and some small particles around each sphere. The presence of such small particles will be explained in the following discussion on the formation mechanism of HMSNs. Therefore, it is clear that hollow

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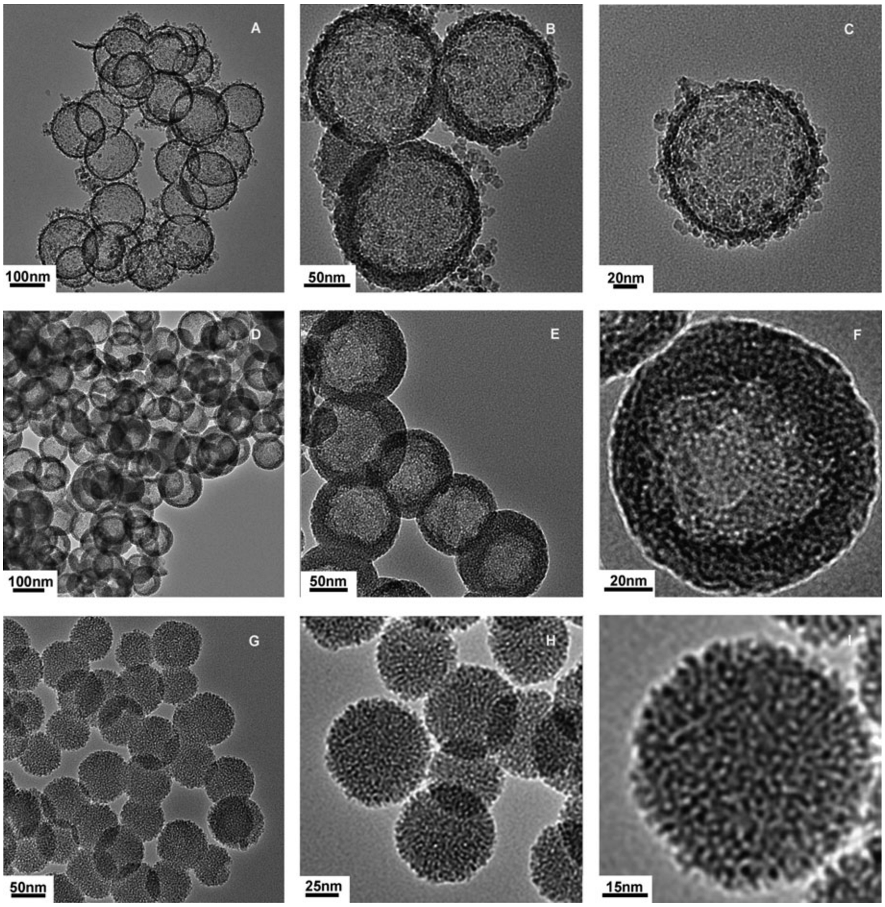


Fig. 1 TEM images of mesoporous silica nanospheres prepared with different molar ratios of CSS/NaOH. A, B, C: CSS/NaOH = 0.2/1.5; D, E, F: CSS/NaOH = 0.2/1.0; G, H, I: CSS/NaOH = 0.2/0.5.

nanospheres of mesoporous silica have been successfully fabricated, and both the morphology and the sizes, including the sphere diameter and the shell thickness of HMSNs, could be controlled by simply adjusting the molar ratio of CSS to NaOH.

Accompanying the molar ratio increase of CSS to NaOH, the pH value of the precursor solution was measured to decrease sequentially. Therefore, it is reasonable to believe that the pH value plays the key role in the morphology of HMSNs. In order to further understand the formation mechanism of HMSNs, different compositions of the precursor solution were attempted. Without using CSS, it was shown (see ESI†) that solid or partially hollowed mesoporous spheres were prepared by employing NaOH to adjust the pH value of the precursor solution. As the concentration of DMEB was increased to 10 mM or 15 mM, only solid mesoporous nanospheres were obtained (see ESI†). Besides, solid mesoporous particles with various mesostructures have been successfully fabricated by using cetyltrimethylammonium bromide (CTAB) or gemini surfactant $[C_{18}H_{37}N(CH_3)_2(CH_2)_3N(CH_3)_3]Br_2$ as template, and CSS as co-structure directing agent in our previous studies.[6c] Based on these results, it is proposed that DMEB, pH value together with CSS determine the unique features of HMSNs. The formation mechanism is proposed in Scheme 1.

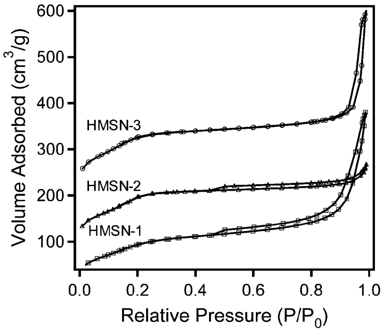
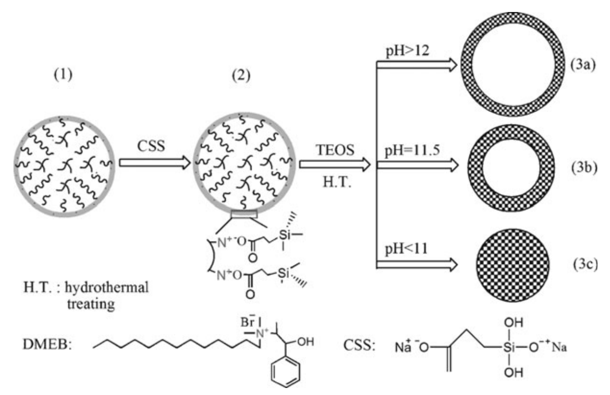


Fig. 2 Nitrogen adsorption–desorption isotherms for the samples. The isotherms for HMSN-2 and HMSN-3 are offset vertically by 80 cm^3 g^{-1} and 160 cm^3 g^{-1}, respectively.

It has been suggested[7] that DMEB could form micellar aggregates in water at low temperature (<28 °C) and spontaneously form giant vesicles above 28 °C at very low critical aggregation concentration (cac), 4 mM. Therefore, micellar aggregates should be present in the solution after DMEB was dissolved in the basic solution at room temperature at the DMEB concentration of 7.8 mM, as shown in step (1) in Scheme 1. Then, the structures of micellar aggregates could be further stabilized with the addition of CSS, owing to the electrostatic interaction between CSS and DMEB (step (2)). TEOS hydrolyzes very quickly under basic conditions, and the



Scheme 1 Schematic illustration of the formation process of HMSNs.

condensation rate of TEOS increases at increased pH value. Therefore, at very high pH value (pH >12), the assembly between condensed TEOS and DMEB around micellar aggregates took place very quickly, which led to the rapid formation of mesostructured shells which impeded the diffusion of DMEB/TEOS molecules out of/into the micellar aggregates and the further assembly between them in the micellar aggregates. As a result, the mesostructured shell is very thin (step (3a)). In the following hydrothermal treatment process, the further condensation of silica shell and the release of the trapped DMEB out of the core led to some small particles of mesostructured silica being formed and adhering to the outer surface of the hollow spheres (as shown in Fig. 1C) due to the assembly between the released DMEB and condensed TEOS. When the pH value decreased to 11.5, the condensation rate of TEOS slowed down, leading to the retarded formation of the mesostructured shells, therefore more TEOS molecules were allowed to diffuse into the micellar aggregate core to assemble with DMEB, resulting in a much thicker shell and a decreased sphere diameter (step (3b)). On decreasing the pH value to <11, the condensation rate of hydrolyzed TEOS decreased further. Enough TEOS molecules could diffuse into the micellar aggregates cores and assemble with DMEB, therefore solid mesoporous silica spheres were obtained (step (3c)), which have the smallest diameter due to the complete assembly within the micellar aggregates.

The drug loading capacity and release properties of HMSNs were measured by choosing ibuprofen (IBU), a typical anti-inflammatory drug, as a probing molecule.[8] The loading amount of ibuprofen was measured to be 346 mg, 523 mg and 425 mg per g SiO_2 for HMSN-1, HMSN-2 and HMSN-3, respectively. HMSN-2 has the highest drug loading capacity among the three samples, which is attributed to the hollow cores and mesostructured shells, but the amount is lower than those of other reported hollow mesoporous silicas.[3a,8] This is probably due to the effects of carboxylic groups,[6c] which were grafted on HMSN-2 during the synthetic process (see FT-IR spectrum in ESI†). The IBU amounts released from HMSN-1, HMSN-2 and HMSN-3 reach about 80% in 20 h, 32 h and 24 h, respectively. It is reasonable to deduce that the shell thickness as well as the size determines the releasing performance of HMSNs.

In conclusion, a facile micellar aggregate templating route has been demonstrated to fabricate nano-sized hollow mesoporous silica spheres. The diameter as well as the shell thickness of mesoporous silica nanospheres could be tuned by simply altering the pH value of the precursor solution. The ibuprofen storage capacity was measured to be as high as 523 mg IBU/g SiO_2. This provides a very promising candidate applicable in drug delivery systems, especially in targeted drug delivery systems after being modified by special molecules.

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