Supporting Information

Cationic-cationic Co-surfactant Templating Route for Synthesizing Well-defined multilamellar vesicular silica with adjustable number of layers

Yan Zhang, Guowei Zhou, Bin Sun, Minnan Zhao, Jinyu Zhang, Fengjiao Chen*

Key Laboratory of Fine Chemicals in Universities of Shandong, School of Chemistry and Pharmaceutical Engineering, Qilu University of Technology, Jinan 250353, P. R. China

Tel: +86 531 89631696

*Conresponding author: guoweizhou@hotmail.com (G. W. Zhou)

1 Experimental

1.1 Chemicals

DDAB was purchased from Sigma-Aldrich. CTAB and TEOS were obtained from Shanghai Chemical Reagent Inc. of Chinese Medicine Group. Metformin hydrochloride (MH) (content > 98%) was purchased from Shandong Linuo Pharmaceutical Group. Other chemicals were all of analytical grade and were used as received without any further purification.

1.2 Synthesis of mesoporous spheroidal silica and multilamellar vesicular silica

In a typical synthesis process, CTAB and DDAB were used as the structure-directing agents. First, 0.142 g of CTAB was dissolved in 35.00 mL deionized water with continuous stirring at 30 °C to form a clear solution. Then specified amounts of DDAB (with molar ratios of CTAB:DDAB being 1:0.312, 1:0.625, 1:0.832 and 1:1.104) were added for the preparation of a set of samples. The mixture was stirred until DDAB was completely dissolved. Into the solution, 0.69 mL ammonia was added. The aqueous solution was stirred for another 2 h. Second, 2.0 g TEOS was added dropwise under vigorous stirring. The reaction solution was constantly stirred at 30 °C for 24 h, followed by transfer into a Teflon-lined autoclave and heating, and then storing at 100 °C for 24 h under static conditions. Finally, the white solid products were collected by filtration, washed with water, air-dried at room temperature, and calcined at 550 °C in a tube furnace for 6 h to remove the surfactant template. The samples were denoted as DS, DLV-1, DLV-2, DLV-3.

1.3 MH adsorption and release

MH adsorption and release were operated as follows: 0.2 g powered SiO_2 was immersed in 20 mL MH aqueous solution with a concentration of 20 mg ml^{-1} at room temperature under ultrasonic dispersion. The mixture was continuous stirred for 2

days and then centrifuged at 6000 rpm for 10 min for obtaining MH-loaded sample. The filtrate (1.0 mL) was obtained and properly diluted to 20 mL and then determine the drug concentration using a UV-vis spectrophotometer at 248 nm. The drug loading amount was then calculated as Equ. S1:

$$wt.\% = \frac{m_1 - \frac{20}{v}CV}{m_2 + \left(m_1 - \frac{20}{v}CV\right)} 100\% \qquad \text{S(1)}$$

where m_1 and m_2 correspond to the initial mass of MH and mesoporous materials added into aqueous solution, respectively. C is the concentration of filtrates diluted in 20 mL volumetric flask, v is sampled volume from filtrates, and V is the volume of aqueous solution for drug loading.

For release, typically, 100 mg sample, which was previously saturated with MH, was immersed into 50 mL simulating human intestinal fluid (phosphate buffered saline, PBS, pH = 6.8) with a magnetic stirring speed of 100 rpm at 37 ºC. 3.0 mL of the mixture was withdrawn at given time intervals and immediately replaced by another 3.0 mL of fresh PBS. The extracted mixture was passed through a 4.5 μm membrane filter and monitored using a UV-vis spectrophotometer. The actual concentration of released MH according to the following Equ. S2:

$$C_{t-cor} = C_t + \frac{v}{V}\sum_{0}^{t-1} C_t \qquad \text{S(2)}$$

where $C_{\text{t-cor}}$ is the actual concentration of released MH at time t (mg mL^{-1}), C_t is the apparent drug concentration at time t (mg mL^{-1}), v is the removed volume of release fluid (mL), and V is the total volume of release fluid (mL).

The actual amount of MH released from mesoporous SiO_2 in the release fluid was calculated based on $C_{\text{t-cor}}$ and Equation S1. The measurements were repeated three times for each sample, and the results were averaged.

1.4 Materials characterizations

Transmission electron microscopy (TEM) images were observed on a JEM-100CX II electron microscope with an acceleration voltage of 100 kV. High-resolution transmission electron microscopy (HRTEM) measurements were carried out on JEM-2100 at accelerating voltage of 200 kV. The samples were dispersed in ethanol by sonication, dropped onto carbon-coated copper grids, and dried in air. Field emission scanning electron microscopy (FESEM) micrographs of samples were obtained by a SUPRA^{TM} 55 microscope operated at an acceleration voltage of 5.0 kV. Powder samples were dispersed in ethanol by sonication, then dropped onto the surface of silicon wafer and dried in air. The specimens were sputter-coated for two cycles with gold to avoid charging by ion sputtering prior to examination. Small-angle X-ray powder diffraction (SAXRD) patterns were recorded using a Bruker D8 advance diffractometer with Cu Kα radiation (35 kV, 30 mA, λ = 0.15406 nm). The data were collected from 0.5° to 5° with a resolution step size of 0.02° s^{-1}. N_2 adsorption-desorption experiments were performed by TriStar 3020. The surface area and pore size distribution were estimated via the Brunauer-Emmett-Teller (BET) and Barrett-Joyner-Halenda (BJH) methods based on the adsorption isotherm.

2 Characterization data

2.1 TEM images

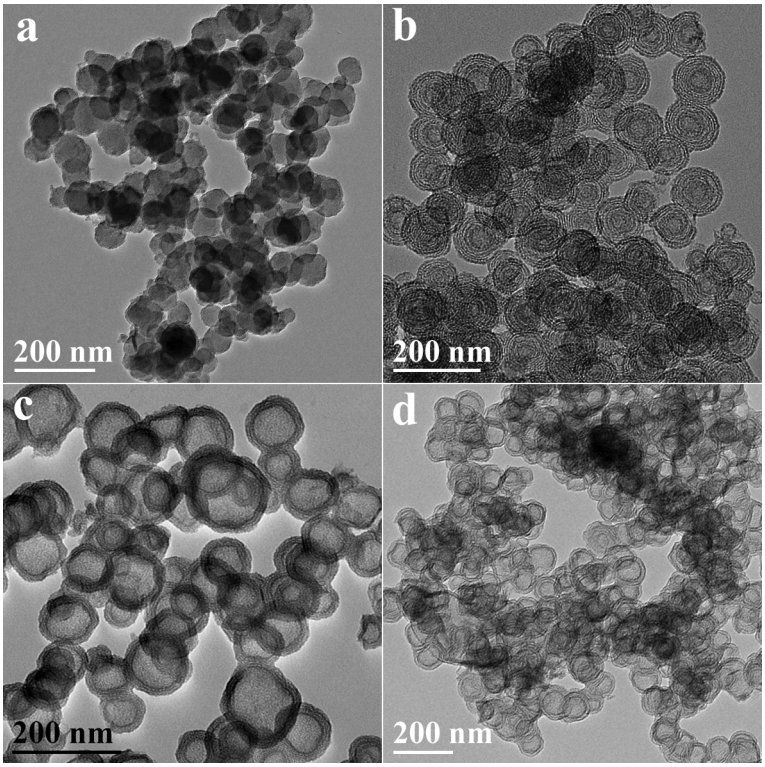

Fig. S1 Low magnification HRTEM images of DS (a), DLV-1 (b), DLV-3 (d), and TEM image of DLV-2 (c).

Low-magnification TEM images (Fig. S1) also showed surprisingly high yield (≈ 100%) morphologies, i.e., spheroid and vesicles without any other morphology.

2.2 XRD patterns

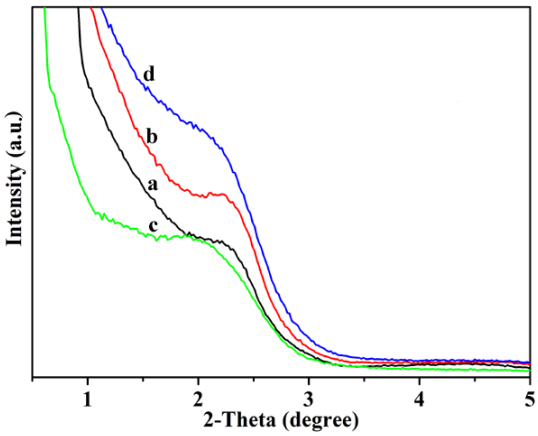

Fig. S2 XRD patterns of DS (a), DLV-1 (b), DLV-2 (c), and DLV-3 (d)

2.3 N_2 adsorption-desorption isotherms

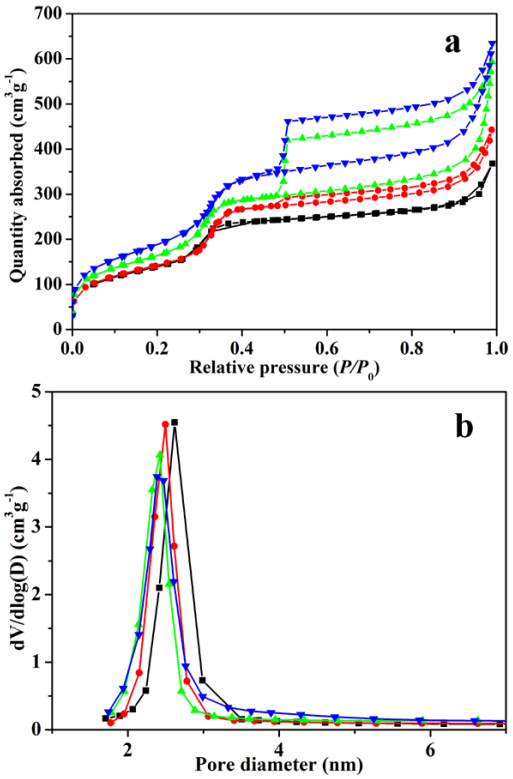

Fig. S3 N_2 adsorption-desorption isotherms (a) and corresponding BJH pore size distribution curves (b) from adsorption data of DS(■), DLV-1(●), DLV-2(▲) and DLV-3(▼).

2.4 Structure parameters of DS and DLV

Table S1 Structure parameters of DS, DLVs before and after MH adsorption

Sample	S_{BET} (m^2 g^{-1})	V (cm^3 g^{-1})	D (nm)
DS	362	0.57	2.6
DLV-1	440	0.62	2.5
DLV-2	625	0.84	2.4
DLV-3	645	0.88	2.4
DS-MH	209	0.30	2.0
DLV-1-MH	397	0.58	2.1
DLV-2-MH	335	0.49	2.2
DLV-3-MH	498	0.74	2.3

D, S_{BET}, and V stand for average BET pore diameter for DS or interlamellar voids for DLV, surface area, and pore volume, respectively.

2.5 N_2 adsorption-desorption isotherms after loading MH

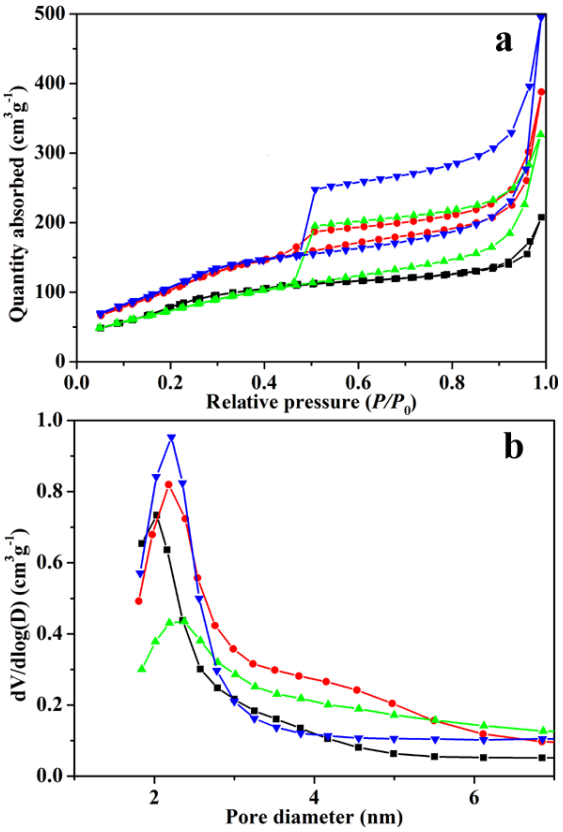

Fig. S4 N_2 adsorption-desorption isotherms (a) and corresponding BJH pore size distribution (b) of DS-MH(■), DLV-1-MH(●), DLV-2-MH(▲) and DLV-3-MH(▼).

2.6 MH release profiles

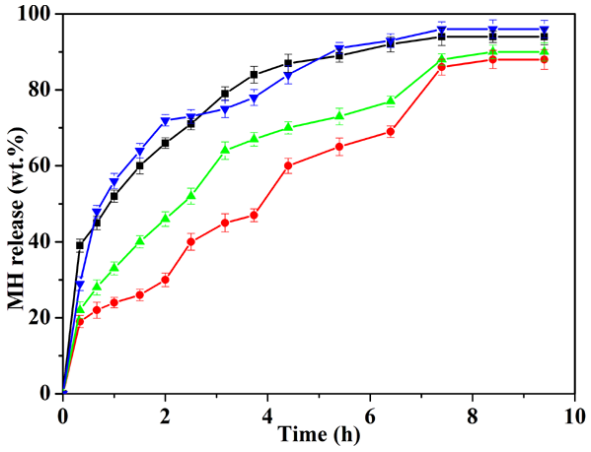

Fig. S5 The mean cumulative release rates of Metformin hydrochloride in DS-MH(■), DLV-1-MH(●), DLV-2-MH(▲) and DLV-3-MH(▼).

DS and DLV samples have wormlike or curved channels and abundant micropores (less than 2 nm) in the silica shells of the mesoporous structure.[1, 2] These

micropores are very important for facilitating the adsorption and release of guest molecules, such as drugs.[3] The MH molecules can enter DS wormlike channels from their opened ends and micropores in the silica framework, while it can enter DLV curved channels from micropores in the shell and the breaches formed during calcination. Possible physical adsorption forces of MH on mesoporous silica involved here include weak van der Waals interaction and hydrogen bonding interaction between the amidogen and imino group of MH and silanol groups on the surface of the mesoporous materials.

References

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2 G. W Zhou, Y. J. Chen, S. H. Yang, *Microporous Mesoporous Mater.*, 2009, **119**, 223.

3 Z. G. Teng, X. D. Su, Y. Y. Zheng, J. Sun, G. T. Chen, C. C. Tian, J. D. Wang, H. Li, Y. Zhao, G. M. Lu, *Chem. Mater.*, 2013, **25**, 98.