Supporting Information

Aerosol Fabrication of Hollow Mesoporous Silica Shells and Encapsulation of L-Methionine as A Candidate Drug Cargo

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Aerosol generation of hollow spherical silica particles

4.0g cetyltrimethyl ammonium bromide (CTAB) was dissolved in a solution containing 1.12g 1N HCl. 22.8g ethanol, 56g DI water, 10.4g tetraethylorthosilicate (TEOS), and 4g $(NH_4)_2SO_4$ or 4g NH_4Cl to give the final precursor solution. An aerosol was generated from the precursor solution using a TSI 9302A atomizer and 20 psi N_2 as the carrier gas. The aerosol droplets were carried into a 2.5 cm in diameter glass tube maintained at 400°C and collected on filter paper maintained at 80°C. The residence time was ~2s in the heating zone. The particles were characterized by TEM, XRD and N_2 sorption before or after calcination at 500°C over 5hr in air (heating rate, 1°C/min) to remove CTAB, NH_4Cl or $(NH_4)_2SO_4$.

XRD, TEM characterizations of mesoporous silica particles:

The hollow spherical silica powder was characterized by small angle XRD. As shown in Figure S1, the silica has highly ordered hexagonal mesoporous structure. Figure S2 shows the TEM image for $(NH_4)_2SO_4$-CTAB templated silica particles.

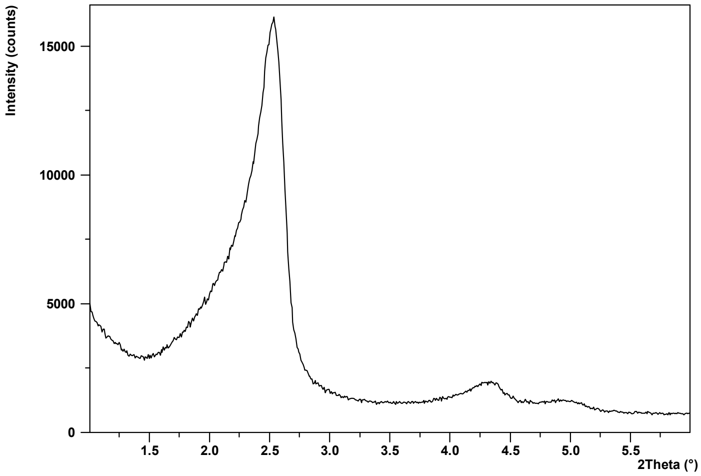

Figure S1. XRD pattern for calcined silica hollow spheres.

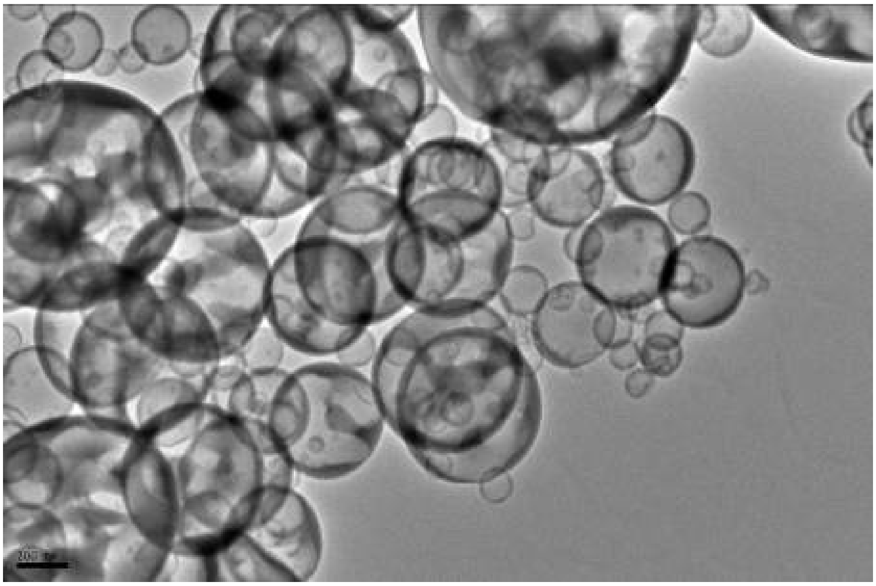

Figure S2. TEM image for calcined $(NH_4)_2SO_4$-CTAB templated silica spheres.

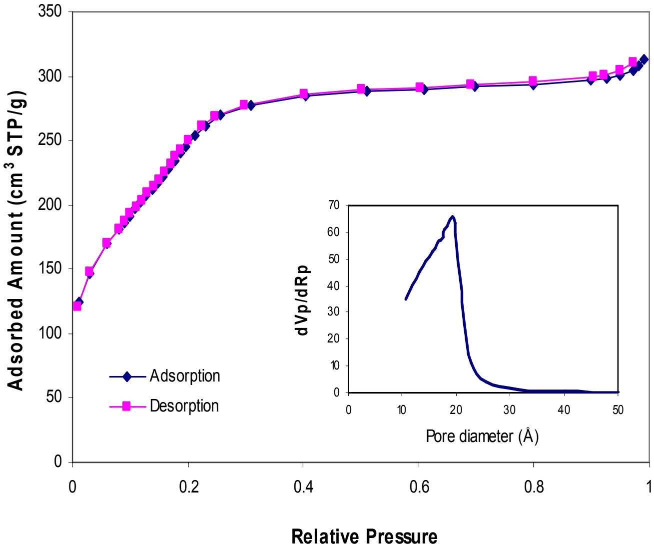

Figure S3. Nitrogen sorption isotherms for calcined silica aerosol EISA particles templated by CTAB only. Inset is BJH pore size distribution calculated from adsorption isotherm.

Encapsulation of L-methionine in hollow silica spheres:

0.0987g L-methionine from Sigma and 0.0680g hollow spherical silica particles were added into 17.4g absolute ethanol in a glass vial. The mixture was stirred at 1000rpm at 50°C for 5 hrs and kept at -20 °C overnight. After crystallization there was white L-methionine precipitate on the glass wall and the surface of the particles. To make L-methionine crystallize predominately inside the voids of silica particles, the mixture was then stirred at 1000 rpm over 10~20 min at room temperature to dissolve the precipitated crystals on glass beaker and particle surface before storage in -20 °C refrigerator. The process was repeated ~10 times. The particles were separated by centrifugation of -20 °C particle dispersion at 4000 rpm over 20 min and dried at 90°C over 2 hrs before TGA/DTA analysis. The XRD patterns for pure L-methionine and dried L-methionine loaded silica are shown in Fig. S4.

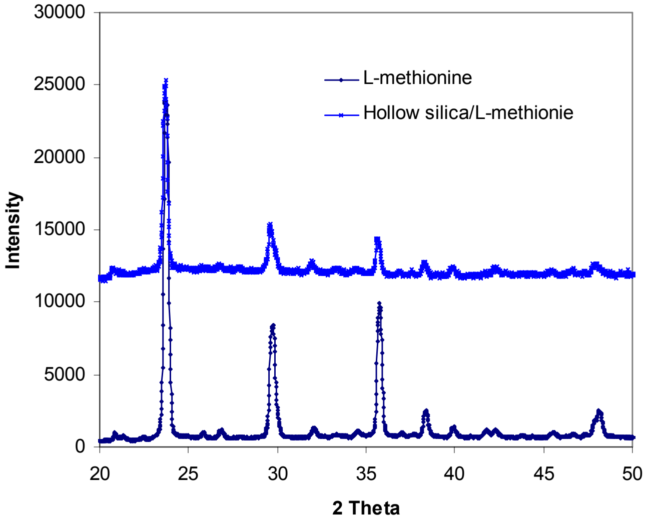

Figure S4. XRD patterns for L-methionine and L-methionine loaded silica samples.

Thermogravimetric / Differential Thermal Analysis (TGA/DTA) of L-methionine loaded capsules

The TGA/DTA analysis was performed on a TA Instruments STD 2960 simultaneous TGA/DTA. The temperature was increased from room temperature to 700°C with a temperature increase rate of 10 °C /min. The carrier gas is air at a flow rate of 100cc/min. A blank CTAB templated mesoporous silica sample was run to check the weight loss for dehydration of hydroxyl groups on silica pore surface during the analysis. The weight loss was ~1.9% (Figure S6). The weight loss due to L-methionine thermal oxidation is calculated as 56.3% (Figure S5), comparable to 56.6%, theoretical value assuming complete filling of the voids and mesopores for the hollow spherical silica (pore volume: 0.98cc/g). The drug loading for L-methionine is as high as 1.29g per gram hollow silica based on the TGA/DTA analysis.

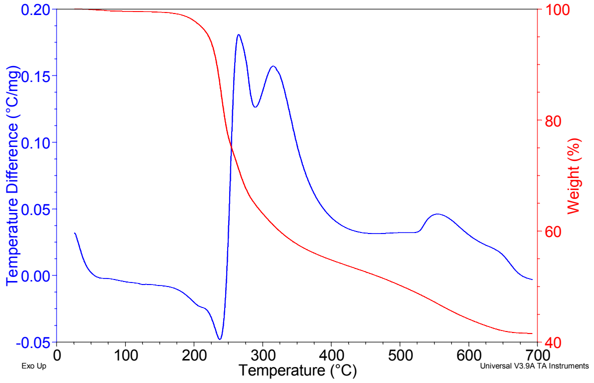

Figure S5. TGA/DTA curves for drug loaded hollow sphere silica particle sample.

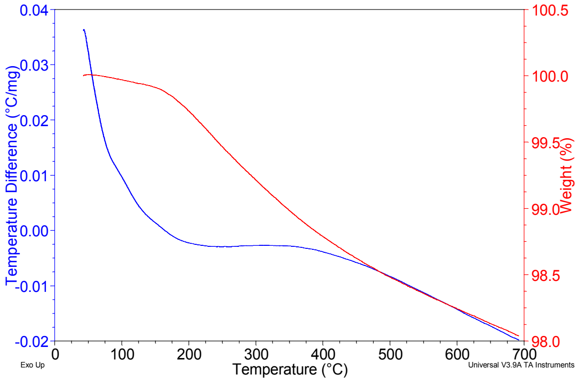

Figure S6. TGA/DTA curves for blank mesoporous silica particle sample.

Release of L-methionine from drug capsules in 1-butanol

Drug loaded silica capsules were centrifuged at 3000 rpm for 10min from ethanol mixture and dried at 90°C over 1 hr. 0.60mg of the drug capsules were washed using 10 ml hexane for three times. After evaporation of hexane, the capsules were dispersed in 18.31g 1-butanol under 1000 rpm. ~0.4 ml solution was sampled and centrifuged with acceleration 2000 times that of gravity using a Fisher Centrifuge, Model 59 (Fisher Scientific Company; Fairlawn, New Jersey). The supernatant was analyzed by UV-visible absorption spectroscopy. The UV-visible spectra were obtained using a HP 8452A diode array spectrophotometer (Colorado Springs, CO) and a 0.25-cm path length quartz cell. The peak at 208 nm in UV-vis absorption spectra of L-methionine was used to determine the change in its concentration. The release profile was shown in Fig. S7. L-methionine was released after ~50 min. After the release the particles were centrifuged and dried at 90°C before TGA/DTA characterization. The weight loss is ~ 2% for the L-methionine adsorbed in the dried released hollow silica particles (Fig. S8).

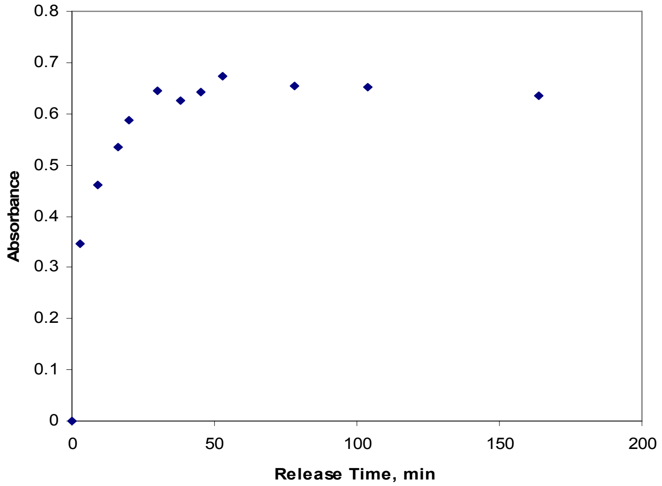

Figure S7. Release of L-methionine in 1-butanol.

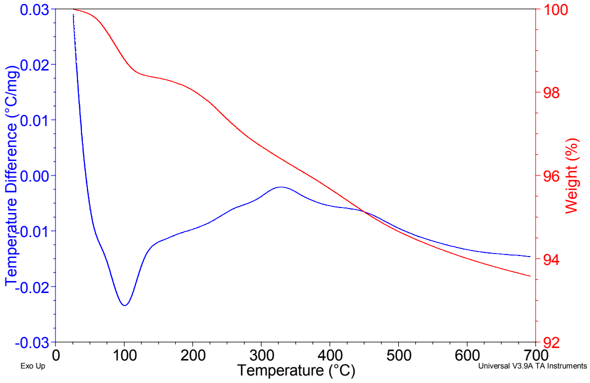

Figure S8. TGA/DTA curves for released silica particle sample.

Release of L-methionine from drug capsules in phosphate buffered saline

2.75 mg of the drug capsules were dispersed in 20.0g Dulbecco's phosphate buffered saline (1X) from Invitrogen Corporation. ~0.4 ml solution was sampled and centrifuged for 1 min with acceleration 8000 times that of gravity. The supernatant was analyzed by UV-visible absorption spectroscopy. The release profile is shown in Fig. S9. L-methionine was released within 3 minutes because of high solubility of L-methionine in water and fast diffusion of the small molecules of L-methionine through mesoporous silica shell.

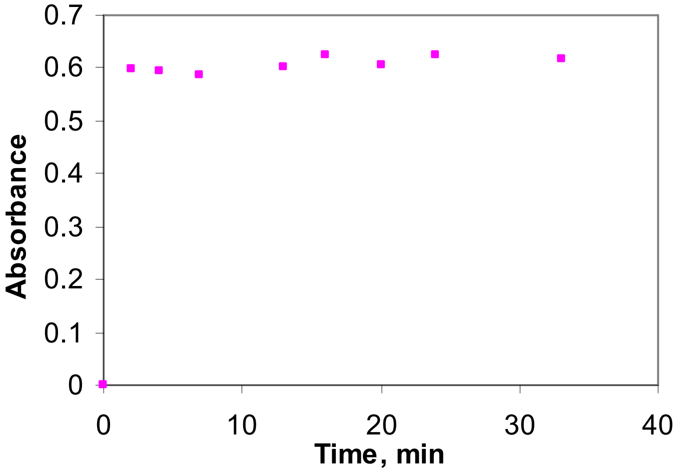

Figure S9. Release of L-methionine in Dulbecco's phosphate buffered saline.

Cavity size control by precursor composition

We assume an expansion coefficient, E for the ratio of the void volume to original salt volume. E is a function of aerosol generation conditions such as temperature, droplet size, aerosol number density, aerosol space velocity, and precursor compositions.

The void size, d_v can be related with the final particle size, d_p by the equation

$$d_v = \frac{d_p}{\sqrt[3]{1+\frac{w_{meso}\rho_s}{Ew_s\rho_{meso}}}}$$

where, w_s and w_{meso} are the weight percentages in the precursor for the salt and the surfactant/silica mesophase, and ρ_s and ρ_{meso} are the densities for the salt and the surfactant/silica mesophase separately.