Electronic Supplementary Information

Novel Fluorinated Polysilsesquioxane Hollow Spheres: Synthesis and Application in Drug Release

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Experimental Methods

Materials.

(3,3,3-trifluoropropyl)trimethoxysilane (FTMS, 99%) was purchased from Gelest. Styrene (St, 99%), Polyvinylpyrrolidone (PVP40), 5-fluorouracil (5-FU), 5-Flucytosine and captopril were obtained from Sigma-Aldrich. Potassium persulfate (KPS) was supplied by Hayashi Pure Chemicals. Ammonia aqueous solution (28 wt%) was purchased from Junsei Chemical. All chemicals were used as received without any further purification. Distilled water ($\approx$ 17 MΩ cm^{-1}) from a Milli-Q water system was used throughout the experiment.

Preparation of PVP-functionalized polystyrene template latexes

The PVP-functionalized PS spheres were synthesized by emulsion polymerization according to reference with slight modification.[1] Briefly, 10.0 g of St, 1.50 g of PVP, 0.2 g KPS and 100.0 g of H_2O were charged into a 250 mL three neck flask equipped with a mechanical stirrer in water bath. The solution was stirred and deoxygenated by bubbling N_2 at room temperature for 60 min. Then, the mixture was slowly heated to 70 °C and kept reaction for 24 h.

Preparation of FPSQ-coated PS particles and FPSQ hollow spheres

FTMS was hydrolyzed and polycondensed on PVP-functionalized polystyrene latexes in ammonia aqueous solution to yield FPSQ-coated particles in a seeded growth process. PS suspension (2g, containing 0.14 g PS solid) and 28 g distilled water were charged into a 100mL bottle in water bath at 50 °C. Different amount of ammonia (0.5, 1.5, 2.5, 3.5, 4.5 mL, respectively) was added into the mixture dropwise. Then, the FTMS (0.55, 1.09, 2.18 g) was added slowly dropwise. The reaction was carried out at 50 °C for 12 h and washed by ammonia solution and distilled water. The final FPSQ hollow spheres were obtained after filtration and drying in vacuum at room temperature.

Drug loading and in vitro drug release

We first dispersed the hollow spheres (100 mg) into 10mL aqueous drug solution (10 mg/mL). The suspension was stirred overnight and then filtered and dried to get the drug-loaded carriers. Release was carried out in 30 ml of phosphate buffered saline (PBS, 0.1M, pH=7.4) solution at 37

^{o}C. Aliquots of 2 mL were taken out from the solution periodically. After each sampling, the volume of solution in cuvette was put back into the vessel. The drug concentration was determined by measuring the absorbance at the wavelength of 265 nm (5-FU), 274 nm (flucytosine), and 206 nm (captopril) at given time intervals. The amount of the released drugs was calculated according to the absorbance of the solution.

Characterization

Scanning electron microscopy (SEM) images were recorded with a field emission XL-30 SEM with energy-dispersive X-ray spectrometer (EDX). A thin gold film was sprayed on the sample before measurements. For the particle size estimation, over 100 particles on the SEM images were averaged.

Particle size distributions were determined by dynamic light scattering (DLS) method using electrophonic light scattering spectrophotometer (ELS-8000, OTSUKA Electronics, Japan). All sample suspensions were diluted in distilled water. After ultrasonic irradiation, the solution was then transferred to a standard quartz cuvette. The hydrodynamic diameters of the particles were determined via a 632.8 nm He-Ne laser (10Mw) source with the conditions of the light scattering at an angle of 90°, the viscosity of 1.104 cp, and the refractive index of 1.332 at room temperature. Data analysis was conducted using a software package (ELS-8000 software) supplied by the manufacturer.

Transmission electron microscopy (TEM) images were taken using a JEM-2011 electron microscope operating at 200 kV. The obtained dispersions were diluted with water and ultrasonicated for 10 min, and then collected using carbon-film-covered copper grids for analysis.

Nitrogen adsorption measurements were performed on an ASAP 2010 volumetric adsorption analyzer (Micromeritics, Norcross, GA, USA) at 77K. Brunauer-Emmett-Teller (BET) method was utilized to determine the surface area.

Fourier transform infrared spectroscopy (FTIR) of KBr powder-pressed pellets was recorded on a Perkin-Elmer Spectrum GX-Spectrophotometer with spectral resolution of 1 cm^{-1}.

The ^{29}Si NMR spectrum was obtained on a Varian Inc., 400 MHz UNITY INOVA spectrometer at room temperature with the resonance frequencies of 79.5 MHz, a magic-angle spinning at 5 kHz, 90^{o} pulse length of 6.5 μs and a repetitions delay of 60 s.

X-ray diffraction (XRD) pattern of the sample was recorded using a Philips diffractometer with a Geiger counter . The X-ray tube was operated at 40 kV and 30 mA (Cu Kα radiation with Ni filter, λ = 1.5406 Å). Scans were made from 1.2 to 50^{o} (2 θ) at the speed of 1°/min. The d-spacings were calculated using the Bragg's equation. UV-vis absorption spectra were taken on a spectrophotometer (Hitachi UV-2010).

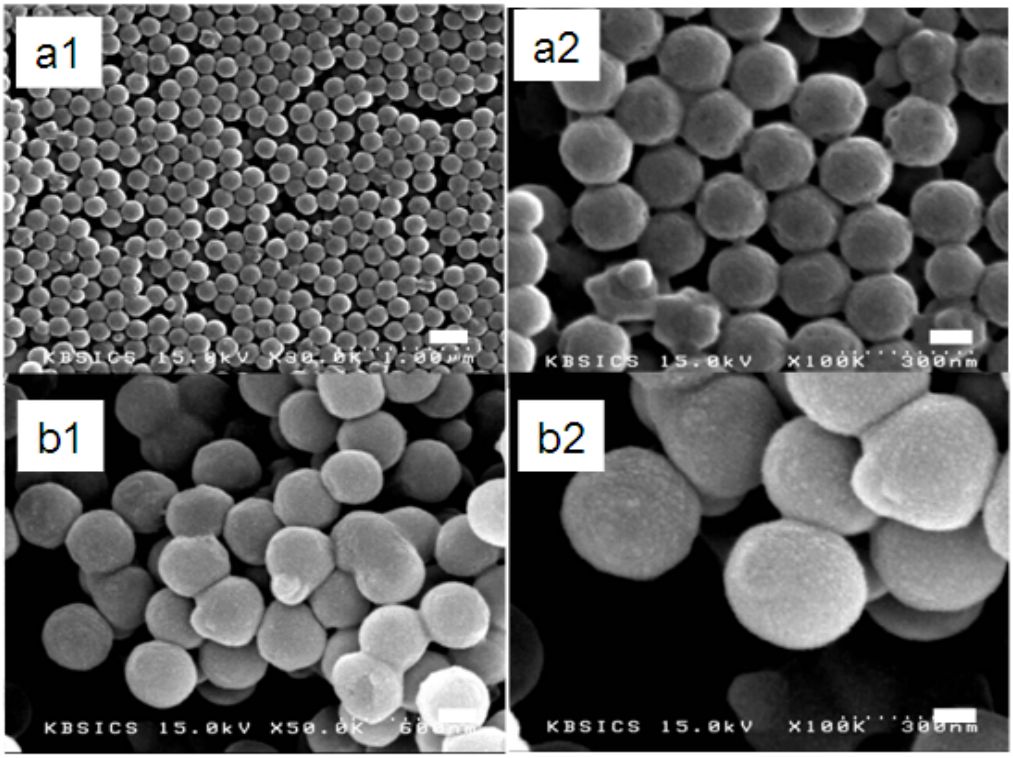

Fig. S1. SEM images of the FPSQ hollow spheres generated with various amounts of FTMS precursor. a1, a2) 0.55 g; b1, b2) 2.18 g. The volume of ammonia was 0.5 mL in all the above formulations. The scale bars are 300 nm for the images (a1, b1) and 100 nm for the images (a2, b2).

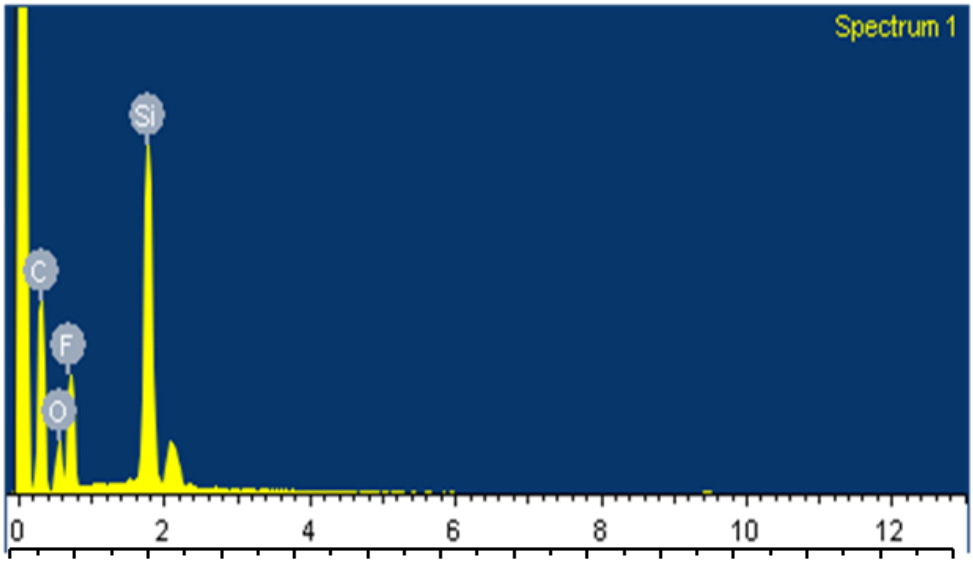

Fig. S2 EDX map of the FPSQ hollow spheres.

Table S1 Element content of FPSQ hollow spheres measured by EDX.

Element	Weight%	Atomic%
C	61.42	71.76
O	10.90	9.56
F	20.29	14.98
Si	7.39	3.69
Totals	100.00	

1. H. Zou, S. S. Wu, Q. P. Ran and J. Shen, *J. Phys. Chem. C*, 2008, **112**, 11623-11629.