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Controlled release using mesoporous silica nanoparticles functionalized with 18-crown-6 derivative

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**Experimental sections**

**Characterization:** $^1$H and $^{13}$C NMR spectra were measured with a Bruker ARX 300 MHz spectrometer. MS spectra were obtained with a JEOL JMS-700 mass spectrometer. IR spectra were obtained for KBr pellets, in the range 400–4000 cm$^{-1}$, with a Shimadzu FTIR 8400S instrument, and the MS spectrum was obtained with a JEOL JMS-700 mass spectrometer. Time-of-flight second ion mass spectrometer (TOF-SIMS) was analyzed on Model PHI 7200 equipped with Cs and Ga ion guns for positive and negative ion mass detection. Transmission electron microscopy (TEM) images were taken with a JEOL JEM-2100 F instrument operated at 150 kV. Images were recorded on 2k CCD (Gatan Inc. USC 1000). Scanning electron microscopic (SEM) images was taken on a Hitachi S-4500 instrument. The accelerating voltage of SEM was 5–15 kV and the emission current was 10 $\mu$A. All fluorescence spectra were recorded in RF-5301PC spectrophotometer.

**Compound 4:** Nitrobenzo-18-crown-6 (1g, 0.28mmol) and 10% Pd/C (0.15g) added anhydrous ethanol (60 mL) were mixed. The reaction mixture was stirred overnight at room temperature. Then, 10% Pd/C was filtered off using celite, and filtrate was evaporated to obtain a yellow liquid. $^1$H NMR (300 MHz, CDCl$_3$, 25 ºC): $\delta$ 6.59 (s, 1H, J=8.1Hz), 6.13 (s, 2H), 6.07 (d, 2H, J=8.4 Hz), 3.95 (t, 4H, J=4.5 Hz), 3.76 (t, 4H, J=3.9Hz), 3.60(t, 12H, J=7.5Hz); MS (EI) m/z 350.33 (M+Na)$^+$. Anal. Calcd for C$_{16}$H$_{25}$NO$_6$: C, 58.70; H, 7.70; N, 4.28. Found; C, 58.90; H, 7.80; N, 4.30.

**Compound 3:** Compound 4 (1g,0.28mol) was dissolved in 7.2mL of water and 0.81mL of conc. HCl was added dropwise to the solution with cooling in an ice bath. Then, (0.24g, 0.003mol) of sodium nitrite was added and the reaction mixture was stirred for 30minutes. To the reaction mixture was added dropwise 8mL of 2.5 M NaOH solution that contained (2.4g, 0.025mol) of phenol. 0.1M HCl was added until keeping pH=2. After stirring for about 1h, the solution was extracted by chloroform. After removal of solvent, dissolved small volume of chloroform, then added excess of ether, keep refrigerated for 1day. All materials were filtered, washed with ether. The crude product was purified by column chromatography with 10% MeOH/CHCl$_3$. $^1$H NMR (300 MHz, CDCl$_3$, 25 ºC): $\delta$ 8.58 (s, 1H), 7.58 (d, 2H, J=8.7 Hz), 7.39 (d, 1H, J=2.1 Hz), 7.36 (t, 3H, J=4.2 Hz), 4.18 (t, 4 H, J=1.8 Hz), 3.90 (t, 4H, J=6.3 Hz), 3.70 (t, 12H, J=4.8 Hz); MS (EI) m/z 353.29 (M+Na)$^+$. Anal. Calcd for C$_{22}$H$_{28}$N$_2$O$_7$: C, 61.10; H, 6.53; N, 6.48. Found; C, 61.30; H, 6.63; N, 6.50.
**Compound 1:** Compound 3 (0.3g, 6.931x10^{-4}mol) and (3-bromopropyl) trimethoxysilane (0.20g, 0.0008mol), K$_2$CO$_3$ (0.11g, 0.0008mol) were dissolved in 20mL of DMF and refluxed for 24h. After removal of solvent, the crude product was purified by column chromatography with MeOH/CHCl$_3$ (7 : 93 V/V). $^1$H NMR (300 MHz, CDCl$_3$, 25 ºC): $\delta$ 7.77 (d, 2H, J=8.4 Hz), 7.45 (d, 2H, J=8.1Hz), 6.90 (d, 3H, J=8.7 Hz), 4.15 (s, 4H), 3.93 (d, 6 H, J=3.3 Hz), 3.65 (t, 12H, J=12 Hz), 3.53 (s, 9H); $^{13}$C NMR (75 MHz, CDCl$_3$, 25 ºC): $\delta$ 161.1, 161.0, 151.1, 149.1, 147.1, 124.3, 119.9, 114.6, 112.4, 104.072, 77.6, 77.1, 76.7, 70.8, 70.7, 70.5, 69.3, 68.9, 68.7, 50.5, 50.3, 36.5, 26.5, 22.6, 22.5, 9.5, 6.6, 5.2 ; IR (KBr, cm$^{-1}$): 3300, 3050, 3010, 3000, 1750, 1600, 1500, 1320, 1270 ; MS (EI) m/z 594.26 (M+Na)$^-$. Anal. Calcd for C$_{28}$H$_{42}$N$_2$O$_{10}$Si: C, 56.55; H, 7.12; N, 4.71. Found; C, 56.75; H, 7.15; N, 4.81.

**Preparation of mesoporous silica nanoparticle:** The silica precursor, tetraethyl orthosilicate (TEOS), was added as a surfactant to an aqueous solution of octadecyltrimethylammonium bromide (ODTMA) under strong acidic conditions at room temperature, with the molar ratio of 100 H$_2$O (360 mL): 7 HCl (142 mL): 0.02 ODTMA (1.6g): 0.03 TEOS (1.3 mL). The mixture was then covered and moved into an isothermal oven set at 80 ºC, where it was kept without stirring for 3 days. Spontaneous growth of suspended flocculates and precipitated particles was observed. They were washed with distilled water three times and dried at 100 ºC in air. To remove cationic surfactants, dried fiber-like flocculates and particles were calcined in a box furnace in air at 500 ºC for 5 h, with a ramp rate of 1 ºC/min.

**Immobilization of 1 onto mesoporous silica.** Compound 1 (0.35 g) was dissolved in mesoporous silica nanoparticles suspension of anhydrous toluene (7 mL) and it was stirred under reflux in N$_2$ for 24 h. The collected solid was washed several times with ethanol to rinse away excess. The solid product was dried by vacuum.

**Loading of curcumin to 18-crown-6 derivative attached mesoporous silica nanoparticle (C-MS):** C-MS (10 mg) was added to curcumin solution (2.0 x 10$^{-3}$ M). The suspension of C-MS was stirred for 1 hr in the presence of Cs$^+$ (0.7 equivalent). Then, the collected solid was washed copiously with ethanol (50 mL) to rinse away any surplus curcumin and dried under vacuum.

**Controlled releasing capacities of curcumin-loaded C-MS (C-C-MS) in the presence of Cs$^+$:** The releasing capacities of C-C-MS (10 mg) were observed at 550 nm ($\lambda_{Ex}$= 425 nm)
by fluorescence spectrophotometer upon addition of KCl (0-3 equivalents) in aqueous solution.
Scheme S1. Synthetic route of ligand 1.
Fig. S1 XRD pattern of C-MS.
Fig. S2 IR spectrum of (a) mesoporous silica and (b) 18-crown-6 derivative (I) attached mesoporous nanoparticle (C-MS).
Fig. S3 TOF- SIMS spectrum of C-MS.
Fig. S4 $^{13}$C CP-MAS spectrum of C-MS.
**Fig. S5** XPS spectra of mesoporous silica nanoparticle (a) before and (b) after immobilization of 1 onto mesoporous silica nanoparticle.
Fig. S6 UV-Vis spectra of (a) 1 and (b) C-MS.
Fig. S7 (A) N$_2$ adsorption-desorption isotherms and (B) pore sizes of (a) mesoporous and (b) C-MS at 78K.
Fig. S8 TGA data of C-MS.
Fig. S9 $^1$H NMR titrations of the 18-crown-6 derivative (1, 1.0 mmol) upon addition of Cs$^+$ in DMSO-d$_6$. 
Fig. S10 $^1$H NMR titrations of the 18-crown-6 derivative (1, 1.0 mmol) upon addition of $\text{K}^+$ in DMSO-$d_6$. 

[Diagram showing NMR titration results]
Fig. S11 IR spectrum of (a) Mesoporous silica (b) C-MS and (c) Curcumin encapsulated C-MS (C-C-MS).
Fig. S12 $^{13}$C CP-MAS spectrum of (a) C-MS and (b) curcumin encapsulated C-MS (C-C-MS).
Fig. S13 TGA data of (a) C-MS and (b) curcumin encapsulated C-MS (C-C-MS).