Supporting Information

Light-triggered Reversible Assemblies of an Azobenzene-Containing Amphiphilic Copolymer with β-Cyclodextrin Modified Hollow Mesoporus Silica Nanoparticles for Controlled Drug Release

Xiao Mei, Shun Yang, Dongyun Chen, Najun Li*, Hua Li, Qingfeng Xu, Jianfeng Ge and Jianmei Lu*

Laboratory of Absorbent Materials and Techniques for Environment, College of Chemistry, Chemical Engineering and Materials Science, Soochow University, Suzhou, China 215123

E-mail: lujm@suda.edu.cn; linajun@suda.edu.cn; Fax: +86 (0) 512-6588 0367; Tel: +86 (0)512-6588 0368

Materials and methods

Materials

(2-(Acryloyloxy)ethyl) trimethylammonium chloride (AETAC, 80 wt% in water), 2,2'-azobis(2-methylpropionamidine) dihydrochloride (V-50, >97.0%), hexadecyltrimethylammonium bromide (CTAB, >99.0%), poly(ethylene glycol) methyl ether methacrylate (PEGMEM, 950 g/mol) were purchased from Aldrich. 1, 6-dihydroxyhexane, methacryloyl chloride, *p*-toluenesulfonyl chloride, sodium azide (NaN_3), (3-aminopropyl) triethoxylsilane (KH550), propargyl bromide (80 wt% in toluene) were purchased from Alfa. Azobisisobutyronitrile (AIBN) was recrystallized in chloroform. Other reagents were commercially available and used as received.

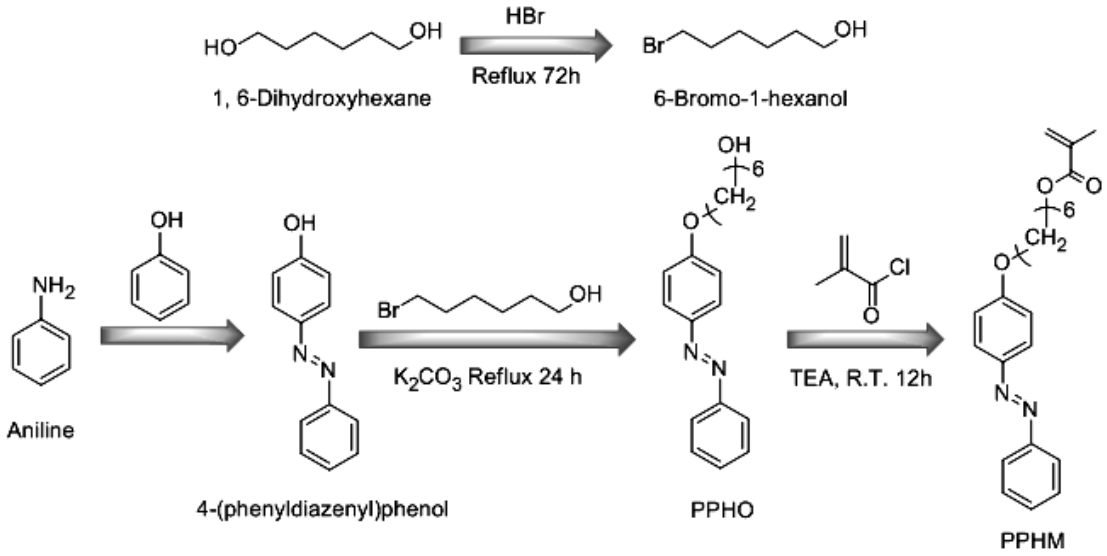
Synthesis of hollow mesoporous spherical (HMS) particles

The hollow mesoporous spherical particles were synthesized according to the literature [1] with some modifications. To prepare the polystyrene latex templates, 1.0 g of AETAC (80 wt% in H_2O) was dissolved in 390.0 g water in a 500 mL round-bottom flask. 40.0 g styrene was added slowly to the solution and kept stirring at 800 rpm by mechanical raking for 30 min. The mixture was purged with nitrogen for 20 min and then heated to 90 ^oC with an oil bath. Afterwards, 10 mL of an aqueous solution containing 1.0 g V-50 was added. The emulsion was kept at 90 ^oC for 24 h under nitrogen to complete the polymerization. The polystyrene latex was get by centrifugation at 18000 rpm for 15 min, and washed with ethanol several times. To get the HMS, 0.8 g of CTAB was dissolved in a mixture of 29.0 g of water, 12.0 g of ethanol and 1.0 ml of ammonium hydroxide solution. 930 mg of PS powders was dispersed in 10.0 g water by sonication and then added dropwise to the above CTAB solution at room temperature under vigorous stirring, followed by sonication for 10 min. The derived milky mixture was then magnetically stirred for 30 min before adding dropwise 4.0 g of TEOS. The mixture was kept stirring at room temperature for 48 h before the mesoporous silica coated latex was harvested by centrifugation at 7000 rpm for 40 min. The precipitate was washed with copious amounts of ethanol and then dried at room temperature. Finally the material was calcined in air at 600 ^oC

for 8 h using a heating rate of 3 ^{o}C/min.

Synthesis of hydrophobic monomer 6-(4-(phenyldiazenyl)phenoxy)hexyl methacrylate （PPHM）

The synthetic process of PPHM was showed in Scheme S1.



Scheme S1 The synthesis route of PPHM.

Synthesis of 6-Bromo-1-hexanol. 6-Bromo-1-hexanol was synthesized according to the literature with some modifications [2]. Briefly, 1, 6-dihydroxyhexane (5.26 g, 0.0445mmol), aqueous 40% hydrobromic acid (18 g, 0.089 mmol) and toluene (40 mL) was refluxed for 72 h. The organic layer was separated from the spent acid and the solvent removed on a rotary evaporator. The crude product was purified by column chromatography (ethyl acetate-hexane, 1:4).

Synthesis of 4-(phenyldiazenyl)phenol. Freshly distilled aniline (5 g, 53.8 mmol) was dissolved in a mixture of concentrated hydrochloric acid (15 mL) and water (40 mL). The solution was cooled to 0 ^{o}C before subsequent dropwise addition of a solution of sodium nitrite (4.01 g, 60.4 mmol) in water (20 mL). This was stirred for 15 min and added dropwise to a phenol (5.56 g, 54.9 mmol) in an aqueous solution of sodium hydroxide (1 M, 150 mL). This was stirred for another 5 h and adjusted to acidic by adding excessive HCl. After filtering, washing with abundant of water and drying in vacuo, a dark brown solid was obtained. ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.99-7.82 (m, 4H, Ar-H), 7.56-7.41 (m, 3H, Ar-H), 6.95 (d, J = 8.4 Hz, 2H,

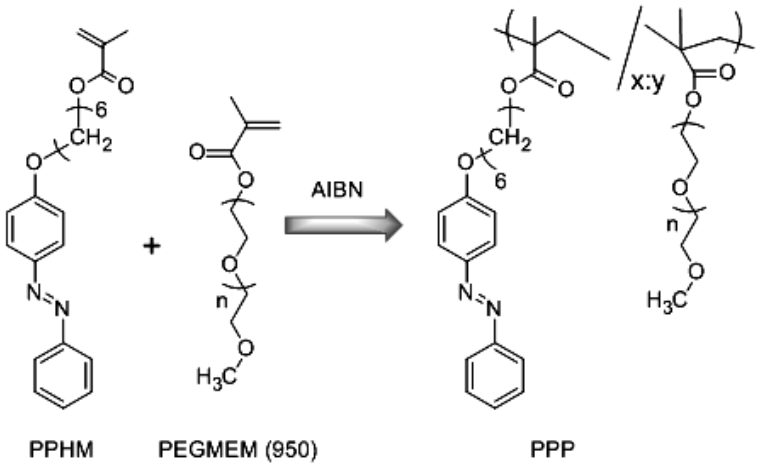
Ar-H), 5.41 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): 116.8, 123.50, 126.1, 130.2, 131.4, 147.6, 154.2, 162.3. HRMS: calcd for $C_{12}H_{10}N_2O$ $[M + H]^+$ 198.08, found 199.0873.

Synthesis of 6-(4-(phenyldiazenyl)phenoxy)hexan-1-ol (PPHO). 4-(phenyldiazenyl) phenol (1.98 g, 10 mmol) and 6-Bromo-1-hexanol (1.82g, 10 mmol) were dissolved in DMF solution (50 mL) containing anhydrous potassium carbonate (2.76 g, 17.99 mmol) and potassium iodide (16.6 mg, 0.1 mmol). After heating under reflux with stirring for 24 h, the reaction mixture was concentrated using a rotary evaporator and the residual mass was washed with a large amount of water. The product was extracted with chloroform, dried over anhydrous $MgSO_4$ and the solvent was removed by evaporation. After recrystallization from ethanol, a dark brown solid, 6-(4-(phenyldiazenyl)phenoxy)hexan-1-ol was obtained, denoted as PPHO. ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.96-7.79 (m, 4H, Ar-H), 7.55-7.38 (m, 3H, Ar-H), 7.04-6.96 (m, 2H, Ar-H), 4.05 (t, J = 6.0 Hz, 2H, OCH_2), 3.73-3.58 (m, 2H, C$\underline{H_2}$OH), 1.87-1.78 (m, 2H, $OCH_2C\underline{H_2}$), 1.70-1.34 (m, 6H, $OCH_2CH_2C\underline{H_2}C\underline{H_2}C\underline{H_2}CH_2OH$). ^{13}C NMR (75 MHz, $CDCl_3$): 162.11, 153.22, 147.32, 130.81, 129.51, 125.23, 123.01, 115.16, 68.67, 63.35, 33.13, 29.65, 26.36, 26.03. HRMS: calcd for $C_{18}H_{22}N_2O_2$ $[M + H]^+$ 298.1683, found 299.1756.

Synthesis of 6-(4-(phenyldiazenyl)phenoxy)hexyl methacrylate (PPHM). An anhydrous tetrahydrofuran (10 mL) solution containing PPHO (820 mg, 2.75 mmol) and triethylamine (1.1 g, 11 mmol) was cooled to 0 ^{o}C in a water-ice bath. Then an anhydrous tetrahydrofuran (5 mL) solution containing methacryloyl chloride (2.3 g, 22 mmol) was added dropwise for more than 15 min. After constantly stirring for another 12 h at room temperature, 20 mL water was added. The product was extracted with chloroform, dried over anhydrous $MgSO_4$ and the solvent was removed by evaporation. An orange solid, 6-(4-(phenyldiazenyl) phenoxy) hexyl methacrylate was obtained after purifying by column chromatography (ethyl acetate–petroleum ether, 1 : 5), denoted as PPHM. ^{1}H NMR(400 MHz, $CDCl_3$), δ (ppm): 7.91 (dd, J = 17.0, 8.1 Hz, 4H, Ar-H), 7.47 (dt, J = 26.2, 7.2 Hz, 3H, Ar-H), 7.00 (d, J = 8.8 Hz, 2H, Ar-H), 6.10 (s, 1H, CCH_2), 5.55 (s, 1H, CCH_2), 4.17 (t, J = 6.6 Hz, 2H, OCH_2), 4.05 (t, J =

6.3 Hz, 2H, C$\underline{H_2}$OH), 1.95 (s, 3H, CH_3), 1.89-1.79 (m, 2H, $OCH_2C\underline{H_2}$), 1.78-1.67 (m, 2H, $C\underline{H_2}CH_2OH$), 1.60-1.39 (m, 4H, $OCH_2CH_2C\underline{H_2}C\underline{H_2}CH_2CH_2OH$). ^{13}C NMR (75 MHz, $CDCl_3$): 168.02, 162.10, 153.27, 147.39, 136.99, 130.80, 129.51, 125.74, 125.24, 123.03, 115.17, 68.62, 65.12, 30.20, 29.58, 29.06, 26.30, 26.23, 18.84. HRMS: calcd for $C_{22}H_{26}N_2O_3$ $[M + H]^+$ 366.195, found 367.2023.

Synthesis of amphiphilic copolymer poly (PPHM-co-PEGMEM) (PPP)

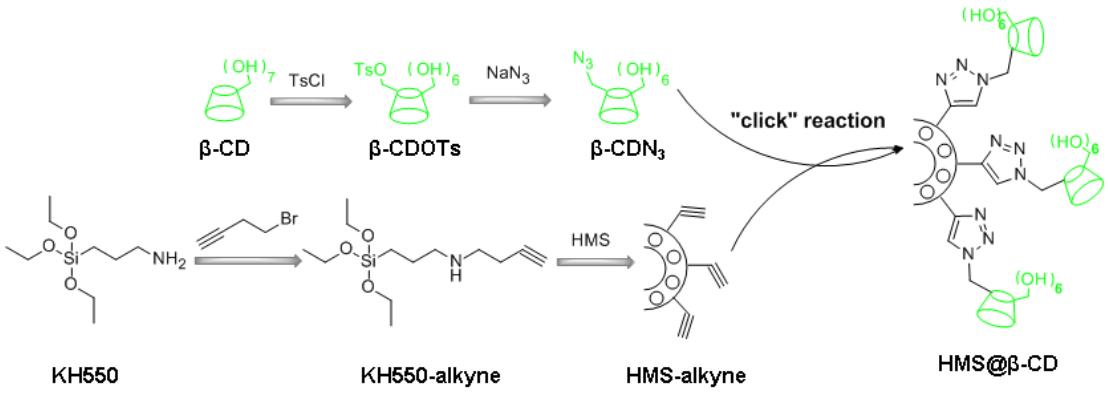


Scheme S2 The synthesis route of amphiphilic copolymer PPP.

An amphiphilic copolymer was synthesized by free radical copolymerization of PPHM and PEGMEM (average M_n=950) in cyclohexanone at 70 °C with AIBN as initiator (Scheme S2). The ratio of the hydrophilic and hydrophobic units in the copolymer was controlled by using different feed ratios of the monomers. A typical procedure for synthesizing PPP with the feed ratio of 1: 3 was described as below. PPHM (146.4 mg, 0.4 mmol), PEGMEM (570 mg, 1.2 mmol) and AIBN (2.63 mg) were dissolved in 8.0 mL of cyclohexanone, and the tube was sealed and cycled between vacuum and nitrogen for several times. After 24 h reaction in oil bath, the mixture was poured into a large amount of anhydrous ethyl ether. The crimson viscous precipitate was purified by centrifugation and washed by anhydrous ethyl ether and n-hexane several times, dried under vacuum.

Modifying the surface of hollow mesoporous silica nanoparticles with β-CD (HMS@β-CD)

The synthetic process of HMS@β-CD was showed in Scheme S3.



Scheme S3 the synthesis route of HMS@β-CD.

Synthesis of Mono-6-deoxy-6-(p-tolylsulfonyl)-β-cyclodextrin (β-CDOTs). Mono-6-deoxy-6-(p-tolylsulfonyl)-β-cyclodextrin was synthesized according to the literature [3] with some modifications. Briefly, NaOH (657 mg, 16.4 mmol) was dissolved in H_2O (2 mL) and added into 50 mL aqueous suspension of β-CD (6 g, 529 mmol). The suspension became homogeneous and slightly yellow before the addition was complete. Then *p*-toluenesulfonyl chloride was dissolved in 3 mL acetonitrile and added into the alkaline aqueous solution of β-CD above, causing immediate formation of a white precipitate. After stirring for 2 h at 23^{o}C, the precipitate was removed by suction filtration and the filtrate refrigerated overnight at 4^{o}C. The resulting white precipitate was recovered by suction filtration and dried in vacuum. The obtained white powder was denoted as β-CDOTs. ^{1}H NMR (400 MHz, DMSO-d_6), δ (ppm): 7.74 (d, 2H), 7.42 (d, 2H), 5.87-5.58 (m, 14H), 4.82 (br s, 4H), 4.76 (s, 3H), 4.55-4.13 (m, 6H), 3.74-3.43 (m, 28H), 3.42-3.18 (m, overlaps with HOD), 2.42 (s, 3H). ^{13}C NMR (75MHz, DMSO-d_6), δ (ppm): 144.9, 132.8, 129.8, 127.8, 102.1, 81.8, 73.3-71.4, 70.0, 68.7, 59.5, 21.1.

Synthesis of Mono-6-deoxy-6-azido-β-cyclodextrin (β-CDN$_3$). NaN_3 (0.15 g, 2.28 mmol) and β-CDOTs (258 mg, 2.28 mmol) were dissolved in 25 mL DMF, the solution was stirred at 80 ^{o}C for 4 h. After the reaction, the reaction solution was concentrated to 10 mL. 30 mL H_2O and 180 mL acetone were added, causing immediate formation of a white precipitate. The resulting white precipitate was recovered by suction filtration, washed by large amount of ethanol and dried in vacuum. The obtained white powder was denoted as β-CDN$_3$. ^{1}H NMR (400 MHz,

DMSO-d_6), δ (ppm): 5.84-5.60 (m, 14H), 4.87 (shoulder, 1H), 4.81 (br s, 6H), 4.57-4.42 (m, 6H), 3.80-3.45 (m, 28H), 3.43-3.22 (s, overlaps with HOD). ^{13}C NMR (75 MHz, D_2O), δ (ppm): 102.1, 101.9, 82.3, 81.3, 73.3, 73.1, 72.1, 70.8, 60.3, 51.1. MS(FAB) m/s 1182.5$(M+Na)^+$. Anal. calcd for $C_{42}H_{69}N_3O_{34}$: C, 43.49; H, 6.00; N, 3.62; O, 46.89; found: C, 43.28; H, 5.92; N, 3.49; O, 47.03.

Modify the surface of HMS with alkynyl (HMS-alkynyl). Propargyl bromide (80 wt% in toluene, 337.58 mg, 2.27 mmol) and KH550 (502.51 mg, 2.27 mmol) were dissolved in 10 mL DMF, then K_2CO_3 (595 mg, 4.035 mmol) was added, the mixture was stirred at 70 ^oC for 24 h under N_2 atmosphere. After the reaction, the mixture was filtered, and 100 mg HMS was added in the filtrate. The mixture was stirred for 24 h at room temperature, and a crude product was harvested by centrifugation at 8000 rpm for 10 min. The precipitate was washed with copious amounts of DMF and ethanol and then dried at room temperature. Finally, a pale yellow powder was obtained, and denoted as HMS-alkynyl.

"Click" chemistry for the preparation of HMS@β-CD. The HMS@β-CD was synthesized according to the literature with some modification [4]. Briefly, HMS-alkyne (50 mg) was dispersed in a 1:1 water/t-butanol mixture (10 mL) containing β-CDN_3 (100 mg, 1.185 mmol), $CuSO_4$ (98.75 mg, 0.395 mmol) and sodium ascorbate (160 mg, 0.79 mmol). After reaction for 48 h, the product was obtained by centrifugation (8000 rpm, 15 min) then successively washed with water, ethanol (15 mL) and acetone (15 mL). The last three washings were repeated 5 times. The resulting material was dried under reduced pressure and denoted as HMS@β-CD.

Drug loading experiment (IBU@HMS@β-CD)

Ibuprofen (IBU) was used as model drug according to the literature with some modifications [5]. Ibuprofen (300 mg) was dissolved in hexane (5 mL), then, HMS@β-CD (100 mg) was added to this solution. After stirring for 24h at room temperature, the HMS@β-CD with adsorbed IBU was separated by centrifugation and washed with a solution of pH 1.4 several times. Finally, the product was dried at 60 ^oC in vacuum. This product is denoted as IBU@HMS@β-CD.

To evaluate the amount of drug loaded by HMS@β-CD, UV-Vis spectroscopy was used as analysis approaches. Firstly, the calibration curve of ibuprofen was determined by taking absorbance versus ibuprofen concentration between 0 and 2 mg/ml as parameters, and the calibration curve fits Lamber and Beer's law as the following equation:

$$A = 0.02584 + 0.99556 \times C$$

Where A is the absorbance and C is the concentration (mg/ml).

After adsorption, the IBU solution (0.1 mL) were extracted and diluted to 10 mL, and then analyzed by UV-Vis spectroscopy at a wavelength of 265 nm. The calculation of drug loading content was discussed below.

Coating the surface of IBU@HMS@β-CD with PPP by host-guest interactions (IBU@HMS@β-CD@PPP)

IBU@HMS@β-CD (10 mg) was dispersed in 3 mL distill water, then 2 mL aqueous solution of PPP (20 mg) was added slowly. The mixture was stirred strongly at 25 ^{o}C for 24 h, and an yellow product was obtained by centrifugation (8000 rpm, 15 min) and washed with distill water, dried in vacuum, The yellow powder denoted as IBU@HMS@β-CD@PPP.

Drug release experiment in vitro

Light-triggered of controlled drug release test. Two equal samples of IBU@HMS@β-CD@PPP (50 mg) were immersed in simulated body fluid (SBF) (20 mL) at 37 ^{o}C. One was placed under visible light and the other was treated by UV irradiation (λ = 365 nm). The drug releasing solution in specified time (0, 0.25, 0.5, 1, 2, 4, 8, 16, 32, 64 and 96 h) were obtained by dialysis against distill water (MWCO = 3500). The drug concentration was analyzed by UV-Vis spectroscopy.

The ability of reversible "gate-keeper" system for controlled drug release studies. One sample of IBU@HMS@β-CD@PPP (50 mg) was immersed in SBF (20 mL) at 37 ^{o}C, and the sample solution was treated by the conversion of UV and Vis light. The drug releasing solution in specified time (we sampled every 2 h and converted the light every 6 h) was obtained by dialysis against distill water (MWCO =

3500). The drug concentration was analyzed by UV-Vis spectroscopy.

Cytotoxicity experiments in vitro

Cell culture and preparation. Human mouth epidermal carcinoma (KB) cell lines (purchased from Shanghai Cell Institute Country Cell Bank, China) were cultured as a monolayer in RPMI-1640 medium supplemented with 10% heatinactivated fetal bovine serum at 37 ^{o}C in a humidified incubator (5% CO_2 in air, v/v).

In vitro cytotoxicity. The aminoxanthene dye, sulforhodamine B (SRB), was used as an assay for assessing the effects of drug carriers in various concentrations [6]. In brief, well-growing KB cells were placed in 96-well plates (1.3×10^4 cells per well) and four duplicate wells were set up in the sample. The culture medium was replaced with the medium containing the drug carriers with different concentrations (0, 0.390625, 0.78125, 1.5625, 3.125, 6.25, 12.5, 25, 50, 100 μg/mL) and cultured at 37 ^{o}C in a humidified incubator (5% CO_2 in air, v/v) with the cells anchored to the plates. After being cultured for 24 h, the medium was poured away and 10% (w/v) trichloroacetic acid in Hank's balanced salt solution (100 μL) was added and stored at 4 ^{o}C for 1 h. Then the stationary liquid was discarded, the cells were washed with deionized water for five times before air drying and stained with 0.4% (w/v) SRB solution (100 μL per well) for 30 min at room temperature. After removing the SRB, the cells were washed with 0.1% acetic acid solution for five times. Bound SRB dye was dissolved with 10 mmol/L tris-base solution (150 μL, pH=10.5). The optical density (OD) value of each individual well was calculated using a spectrophotometer at 531 nm.

Characterization

FT-IR measurement was performed as KBr pellets on a Nicolet 4700 spectrometer (Thermo Fisher Scientific) in the range of 400-4000 cm^{-1}. Gel permeation chromatography (GPC) analysis was carried out on a Waters 1515 pump and a differential refractometer, THF was used as a mobile phase at a flow rate of 1.0 mL/min. ^{1}H NMR and ^{13}C HNMR spectra were measured by an INOVA 400MHz NMR instrument with $CDCl_3$ or DMSO-d_6 as deuterated solvent. Transmission

electron microscopy (TEM) was obtained by a TecnaiG220 electron microscope at an acceleration voltage of 200 kV. Brunauer, Emmett, and Teller (BET) and Barrett, Joyner, and Halenda (BJH) analysis that used to determine the surface area, pore size and pore volume were obtained with a Quantachrome Autosorb 1C apparatus at -196 ^{o}C under continuous adsorption conditions. The UV-Vis absorption spectra were measured on a TU-1901 spectrophotometer.

Table S1 Properties of poly (PPHM(x)-co-PEGMEM(y)) with different feed ratios

Feed ratio (x:y)	Conversion (%)	Mn (g/mol)	PDI	Polymer Composition (x:y)
3:1	94	25300	2.0	2.7:1
1:1	95	29100	1.9	0.8:1
1:3	98	30900	2.1	1:3.1
1:6	95	42300	2.7	1:5.6
1:8	97	53200	2.5	1.7.5

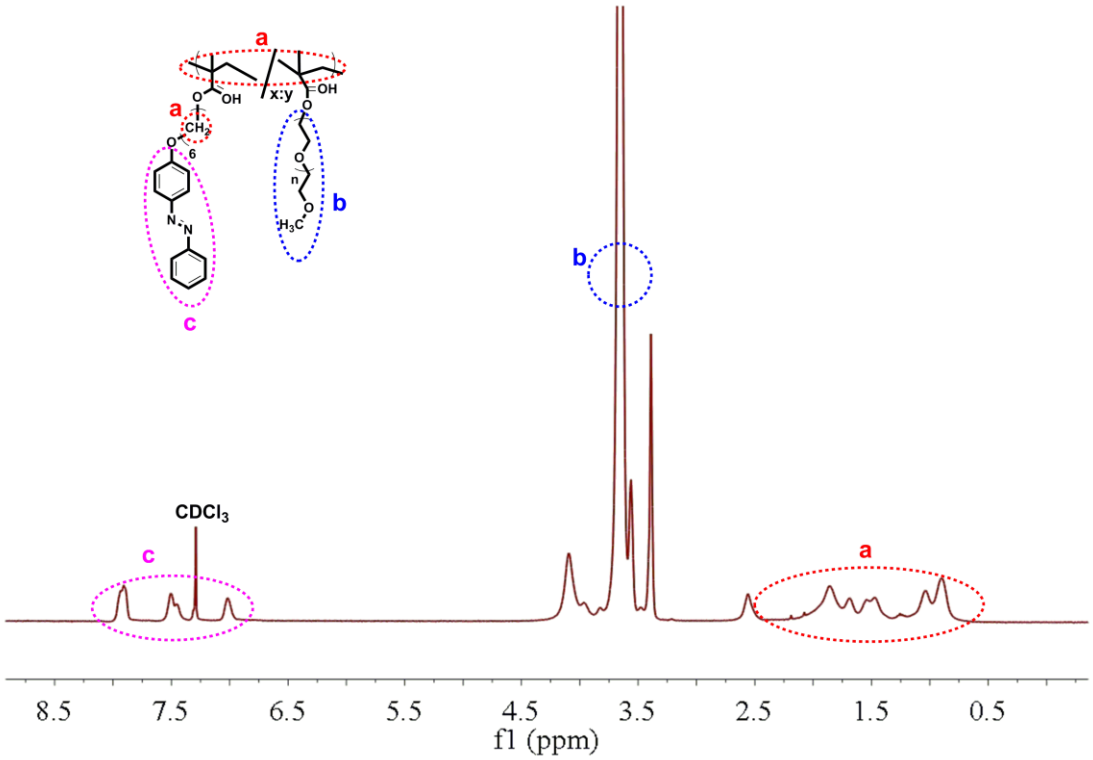


Fig. S1 ^{1}H NMR spectrum ($CDCl_3$, 400MHz) of poly (PPHM-co-PEGMEM)

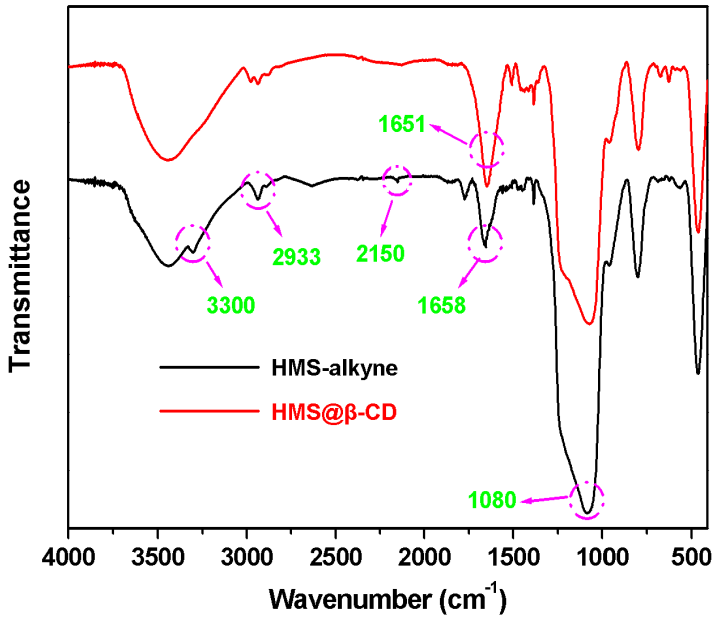


Fig. S2 FT-IR spectrum of HMS-alkyne and HMS@β-CD

The bands owing to Si-O-Si (1080 cm^{-1}) and C≡C (2150 cm^{-1}) were observed in the spectrum of HMS-alkyne, indicating that HMS was successfully functionalized with alkynyl-terminated silanes. After the "click" reaction, the characteristic peak of C≡C at 2150 cm^{-1} disappeared, accompanied by the increased peaks of triazole around 1651cm^{-1}. These results confirm the successful binding of β-CD to the surface of HMS [7].

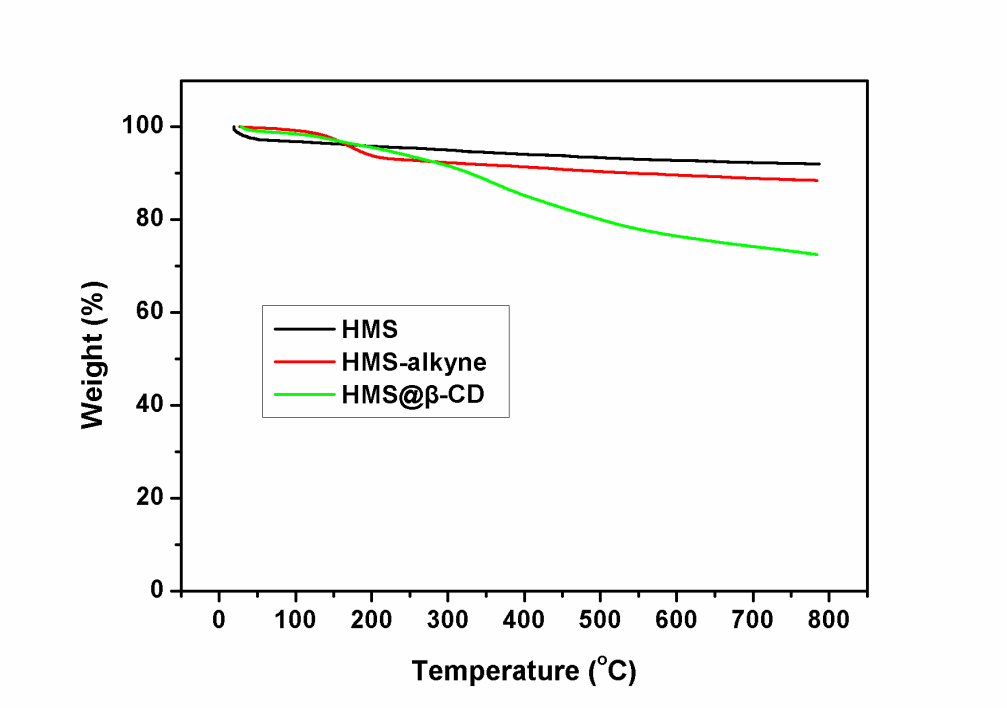


Fig. S3 TG analysis of HMS, HMS-alkyne and HMS@β-CD

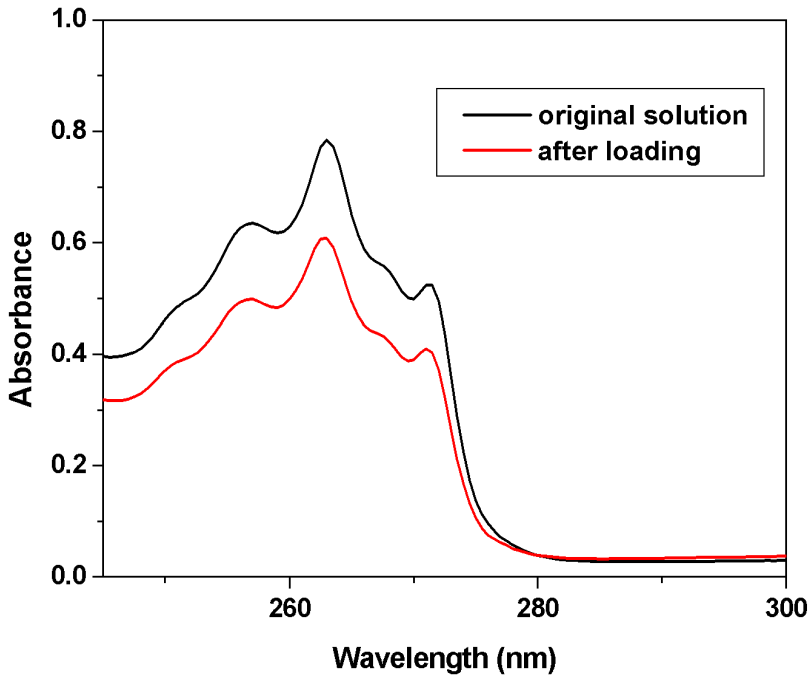


Fig. S4 UV-Vis absorption of ibuprofen solution before and after being loaded by HMS@β-CD.

Before and after loading drugs, the absorbance in UV-Vis spectroscopy of the IBU solution at 265 nm was 0.663 and 0.4815, respectively. According to the standard curve formula: A = 0.02584 + 0.99556 × C, we can calculate that the drug concentration is reduced to 0.1564 mg/mL. As the sample of IBU solution were diluted from 0.1 mL to 10 mL before testing, the concentration of the drugs loaded in HMS@β-CD is acturally reduced to 15.64 mg/mL. Since 5mL of IBU solution was taken out for testing, the quality of the drug loaded by HMS@β-CD (100 mg) can be caculated out as 78.2 mg, which was absorbed by 100 mg carriers. According to the formula: drug loaded content = weight of loaded drug/weight of the carrier, the drug loaded content was obtained as 782 mg/g (IBU/carrier).

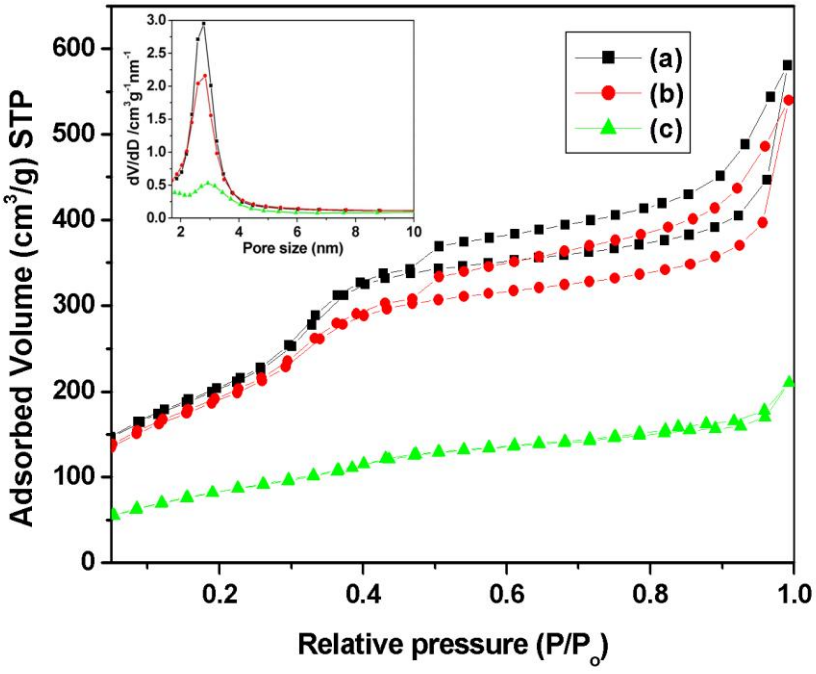


Fig. S5 N_2 adsorption–desorption isotherm and the corresponding pore size distribution inset of (a) HMS, (b) HMS@β-CD and (c) IBU@HMS@β-CD.

The N_2 adsorption-desorption isotherm of HMS@β-CD before and after loading IBU are shown in Fig. S5. The adsorption volume reduced significantly after loading drugs, indicating that the drugs have been successfully loaded into the hollow cores of HMSs [8].

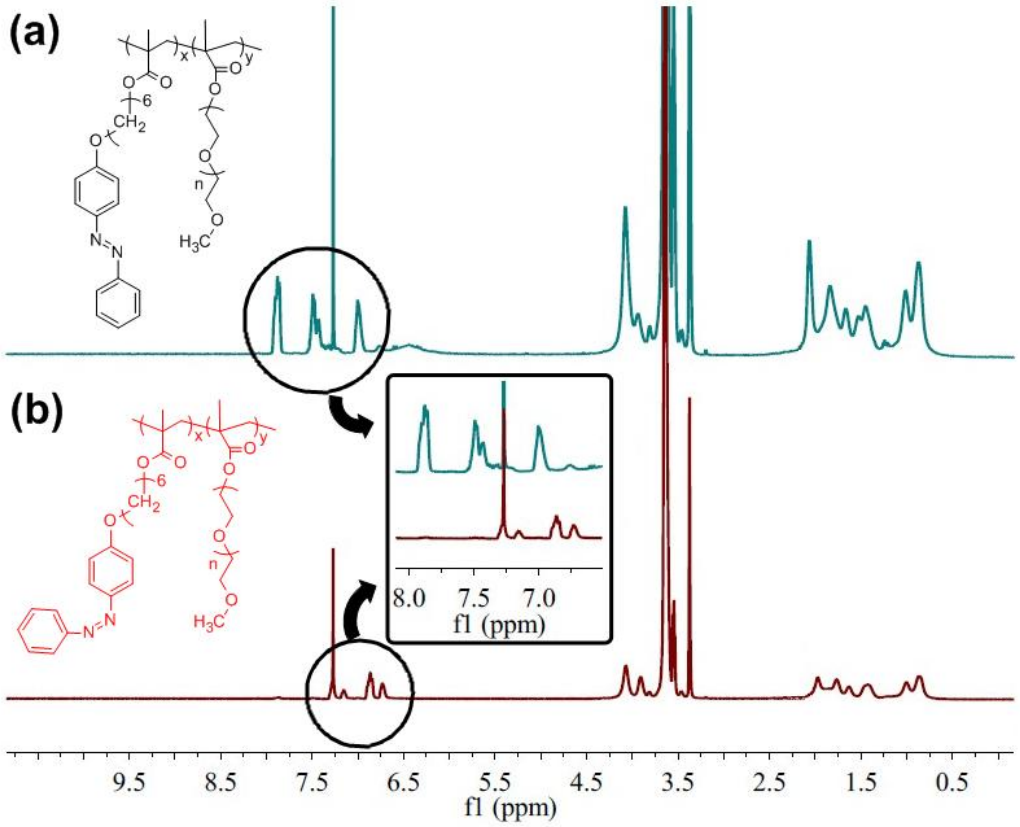


Fig. S6 ^{1}H NMR of PPP in $CDCl_3$ before (a) and after (b) irradiation with UV light.

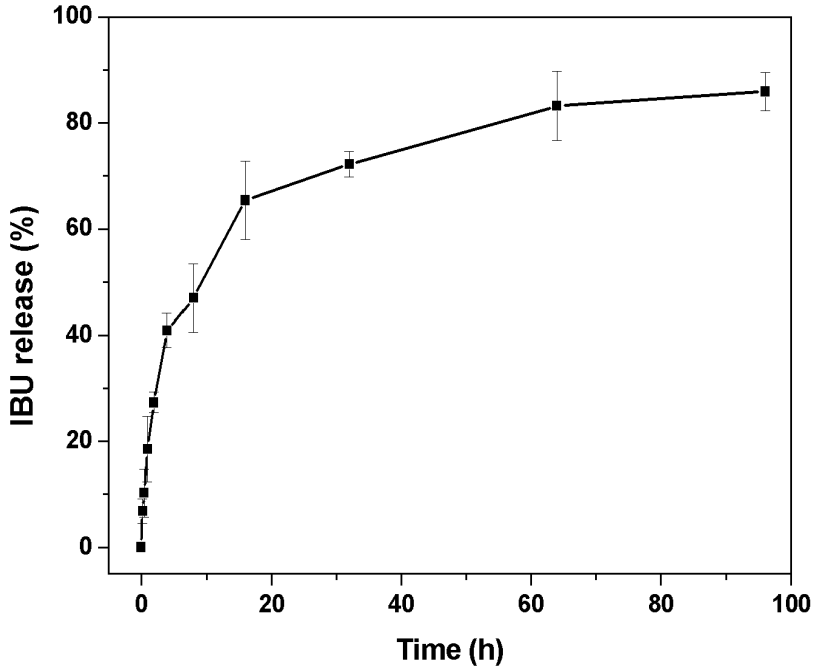


Fig. S7 Release of IBU in *vitro* from IBU@HMS@β-CD

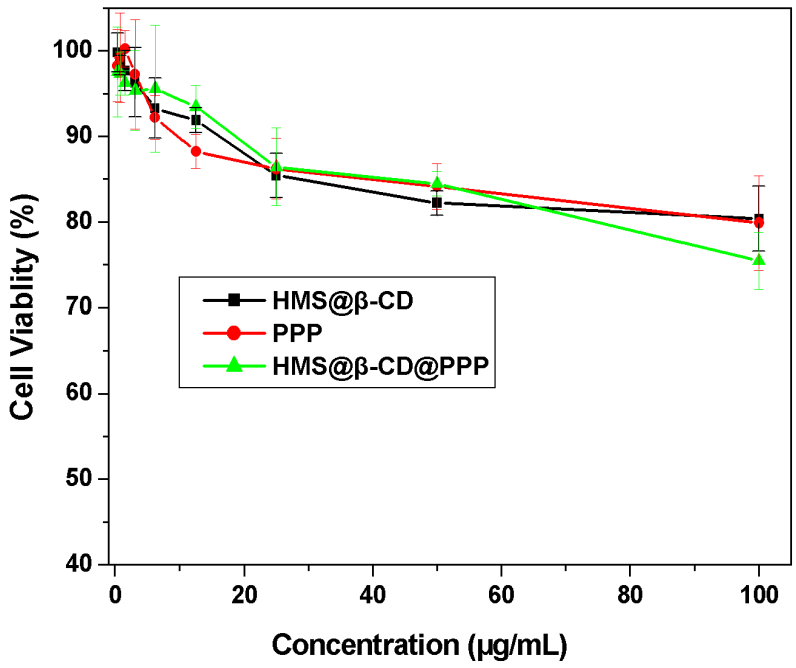


Fig. S8 In *vitro* cell viabilities, measured by the SRB assay, after culture of human mouth epidermal carcinoma (KB) cells with HMS@β-CD, PPP and HMS@β-CD@PPP as functions of different concentrations

The cytotoxicity of HMS@β-CD, PPP and HMS@β-CD@PPP were assessed in different concentrations by the SRB assay and human mouth epidermal carcinoma (KB) cells were used as model cells. As shown in Fig. S8, no cytotoxicity was evident in the preliminary observations of the cells that were treated by HMS@β-CD, PPP and HMS@β-CD@PPP for 24 h, and even the concentration of the prepared materials was as high as 100 μg/mL, the cell viability still maintains about 80%.

Reference

1 G. G. Qi, Y. B. Wang, L. Estevez, A. K. Switzer, X. N. Duan, X. F. Yang and E. P. Giannelis, *Chem. Mater.* 2010, **22**, 2693.

2 M. Novak, A. Ebel, T. Meyer-Friedrichsen, A. Jedaa, B. F. Vieweg, G. Yang, K. Voitchovsky, F. Stellacci, E. Spiecker, A. Hirsch and M. Halik, *Nano Lett.*, 2011, **11**, 156.

3 R. C. Petter, J. S. Salek, C. T. Sikorski, G. Kumaravel and F. T. Lin, *J. Am. Chem.*

Soc. 1990, **112**, 3860.

4 (a) M. O.-Mun□oz, J. L.-Jaramillo, F. H.-Mateo, and F. S.-Gonzalez, *Adv. Synth. Catal*. 2006, **348**, 2410; (b) N. Moitra, P. Trens, L. Raehm, J. -O. Durand, X. Cattoën and M. W. C. Man, *J. Mater. Chem.*, 2011, **21**, 13476.

5 (a) W. R. Zhao, M. D. Lang, Y. S. Li, L. Lia and J. L. Shi, *J. Mater. Chem.*, 2009, **19**, 2778; (b) Y. F. Zhu, J. L. Shi, W. H. Shen, X. P. Dong, J. W. Feng, M. L. Ruan and Y. S. Li, *Angew. Chem. Int. Ed.* 2005, **44**, 5083.

6 C. Yan, J. K. Kepa, D. Siegel, I. J. Stratford and D. Ross, *Mol. Pharmacol.*, 2008, **74**, 1657.

7 (a) N. Moitra, P. Trens, L. Raehm, J. O. Durand, X. Cattoën and M. W. C. Man, *J. Mater. Chem.*, 2011, 21, 13476; (b) Y. L. Li, J. Zhou, C. L. Liu and H. B. Li, *J. Mater. Chem.*, 2012, 22, 2507.

8 Y. F. Zhu, J. L. Shi, W. H. Shen, X. P. Dong, J. W. Feng, M. L. Ruan and Y. S. Li, *Angew. Chem. Int. Ed.* 2005, **44**, 5083.