Supplementary Information (SI)

Visible-light-triggered supramolecular valves based on β-cyclodextrin-modified mesoporous silica nanoparticles for controlled drug release

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1. Materials.

β-Cyclodextrin (β-CD, >98%), p-toluenesulfonyl chloride (TsCl, 99%), ethidene diamine (EDA) and (3-Glycidyloxypropyl)trimethoxysilane (GPS, 97%) were purchased from Sigma-Aldrich. 2,6-Dimethoxyaniline (97%), 3,5-dimethethoxyphenol (98%), 1,3-dibromopropane (>97%), dimethylaminoethyl methacrylate (DMAEMA), 1,1,4,7,10,10-hexamethyltriethylenetetramine (HMTETA), ethyl α-bromoisobutyrate (98%), copper bromide (98%), 1,1,4,7,10,10-hexamethyltriethylenetetramine (97%), 2-bromoisobutyrate (EBIB), cetyltrimethylammonium bromide (CTAB), tetraethoxysilane (TEOS), p-coumalic acid and ammonium nitrate were purchased from Aldrich. Tetrahydrofuran (THF), N, N-dimethylformamide and other reagents were purchased from Sinopharm Chemical Reagent Co.

2. Methods.

^{1}H NMR spectra were recorded with a Bruker DMX-400 spectrometer in deuterated solvent at 298 K. UV-visible absorption spectra were recorded with a Shimadzu UV-3100 UV-vis spectrophotometer. Fourier transform infrared (FT-IR) spectra were obtained on a PerkinElmer spectrophotometer with the sample/KBr pressed pellets at room temperature. The morphologies of the nanogels were characterized with a JEM-2010 EX/S transmission electron microscope (TEM). Small-angel power X-ray diffraction (SA-XRD) measurements were carried out using a Rigaku SmartLab III powder diffractometer. The radiation source was copper (Ka=1.39225 Å). Dynamic light scattering (DLS) measurement was performed on a Zetasizer Nano ZS instrument. N_2 adsorption and desorption isotherms (BET and BJH) were carried out using a Micromeritics Gemini instrument. LED irradiators (5.2 mWcm^{-2} at 365 nm; 7.5 mW cm^{-2} at 450 nm) were used for the photoisomerization of azobenzene.

3. Synthesis

Mono-6-dexoy-6-ethylenediamine-β-CD (NH_2-β-CD) and poly{6-[(2,6-dimethoxyphenylphenyl)azo-4-(2',6'-dimethoxy)phenoxy]propyl dimethylaminoethyl methyl methacrylate-random-PDMAEMA} (Azo-PDMAEMA) used in this work are homemade, the synthesis and characterization of which have been reported before.[1]

Preparation of mesoporous silica nanoparticles (MSNs) and β-CD modified MSNs (MSNs-CD). MSNs was prepared by an adopted literature procedure.[2,3] CTAB (0.5 g, 1.37 mmol) was dissolved in an aqueous solution (240 mL) of sodium hydroxide (2 M, 1.75 mL). The obtained solution was stirred for half an hour and then TEOS (2.5 mL, 11.21mmol) was added and the mixture was refluxed for 2 h at 80 ^oC. The mixture was filtered and washed with water and alcohol to remove the surfactant. The product was dried under a vacuum at 50 ^oC for 24 h. Afterward, MSNs (0.5 g) was dissolved in 150 mL of alcohol, ammonium nitrate (1.2 g) was added, and the mixture was refluxed for 3 h at 68 ^oC. The crude product was washed by water and alcohol sequentially and dried in an oven at 45 ^oC for over 24 h to get MSNs.

β-CD was grafted onto MSNs surface to synthesize MSNs-CD. MSNs (150 mg) was dissolved in 10 mL of toluene, GPS (50 μL) was added, and the mixture was refluxed for 8 h at 80 ^oC. The nanoparticles were collected via centrifugation and then dried in vacuum at 40 ^oC to get β-CD-GPS. Then the β-CD-GPS was treated with NH_2-β-CD (1.76mM in DMF) for 24 h at 60 ^oC and then washed with water and alcohol for three times to get MSNs-CD.

Preparation of MSNs-CD/Azo-PDMAEMA loaded with p-Coumalic acid (MSNs-CD/Azo-PDMAEMA@CA). MSNs-CD/Azo-PDMAEMA@CA was synthesized by two steps: For the CA loading step, CA was loaded into the MSNs-CD nanoparticles via a free diffusion process. CA (1.5 mg) was dissolved in hot water (5 mL) and then MSNs-CD (50 mg)

were added to the solution, stirred for 24 h at 70 °C. The MSNs-CD@CA were washed with water for three times to remove the free cargos, then sonicated to disperse in the solution. For the Azo-PDMAEMA capping step, Azo-PDMAEMA (36 mg) was added to the solution and the mixture was kept stirring in the dark for another 24 h. The nanoparticles were collected via centrifugation and then dialyzed (MWCO: 3500 Da) against distilled water for 24 h to remove the free cargos. The product was dried in vacuum at room temperature for 24 h to get MSNs-CD/Azo-PDMAEMA@CA. The samples were lyophilized to obtain the MSNs-CD/Azo-PDMAEMA@CA, which were kept at 4 ºC for further study. All the drug loading processes were performed under dark. The CA concentration was determined by spectrophotometry (λ_{max} = 285 nm) using a CA calibration curve (Fig. S4). The loading capacity (LC) of MSNs-CD/Azo-PDMAEMA was about 1% which was calculated by the following formula:

$$LC\ (wt\%) = \frac{weight\ of\ loaded\ CA}{weight\ of\ MSNs-CD/Azo-PDMAEMA} \times 100\%$$

4. Visible-light-triggered cargos release.

MSNs-CD/Azo-PDMAEMA@CA (50 mg) was dissolved in 1 mL of deionized water and introduced into a dialysis membrane (MWCO: 3500 Da). The released CA outside of the dialysis membrane was sampled at defined time period and assayed by UV-vis absorption at 285 nm.

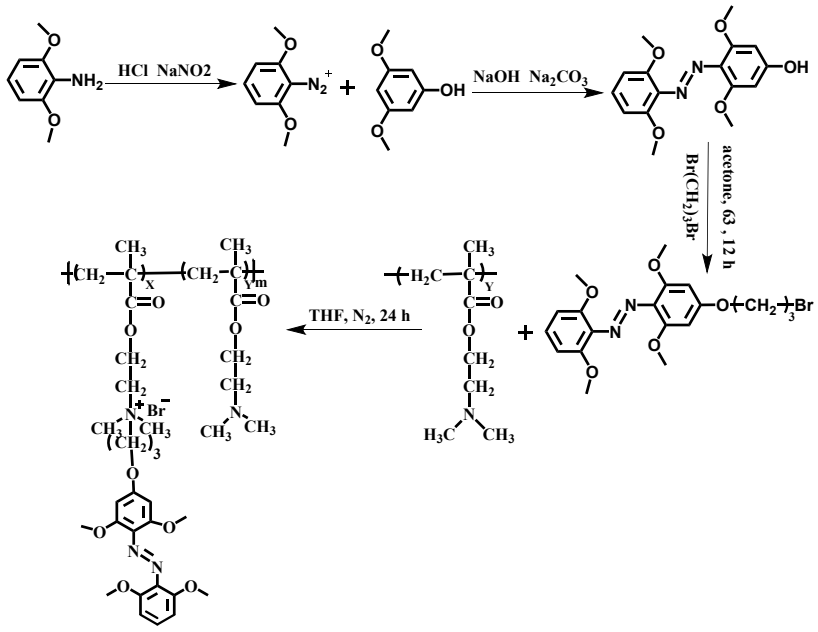

Figure S1. Synthetic route of Azo-PDMAEMA.

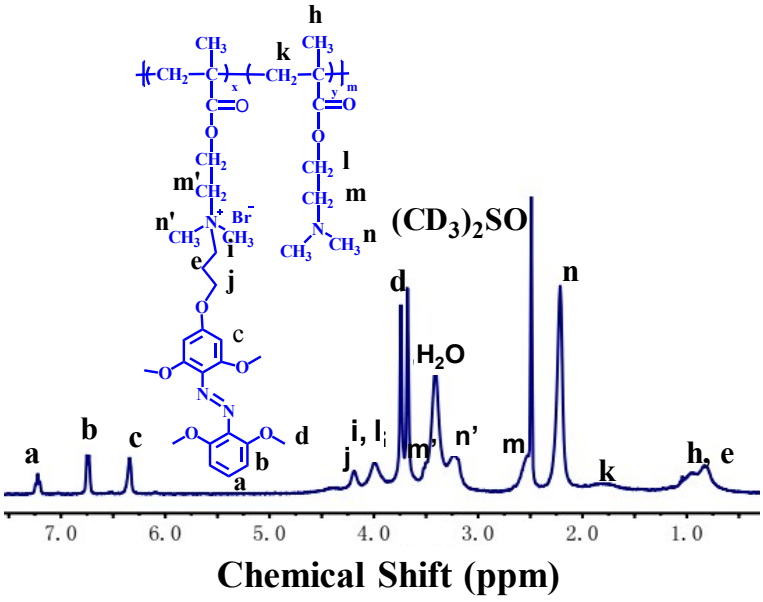

Figure S2. ^{1}H NMR spectra of Azo-PDMAEMA.

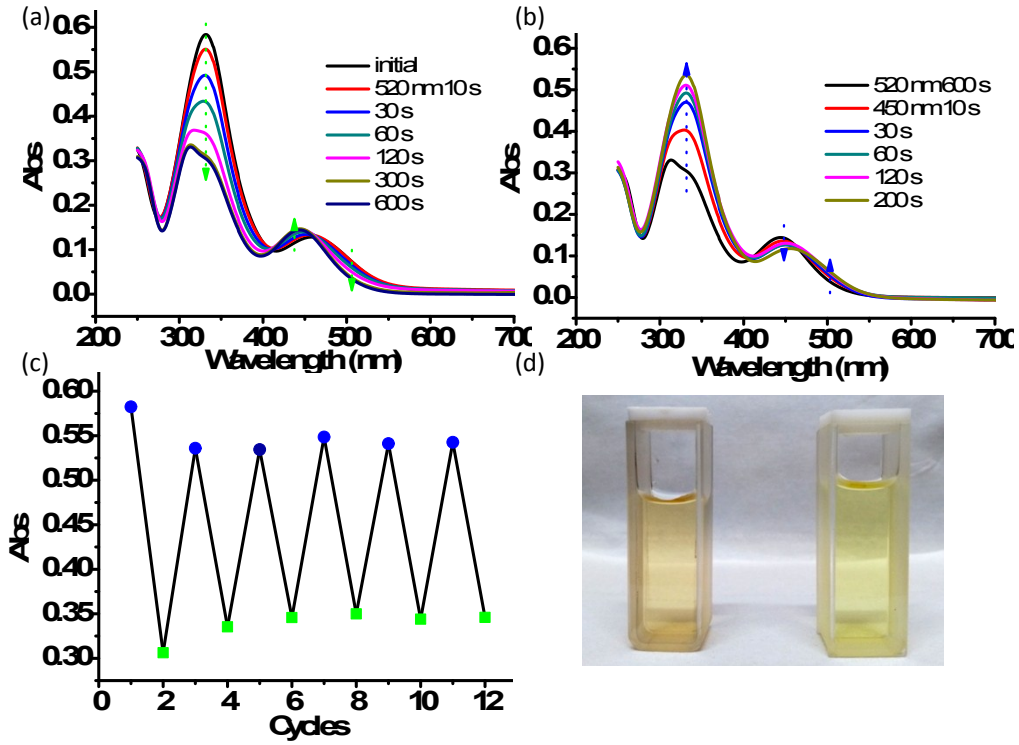

Figure S3. UV-Vis spectra of the Azo-PDMAEMA in aqueous solution under irradiation of (a) green light (520 nm, 8.5 mW cm^{-2}) and (b) blue light (450 nm, 7.3 mW cm^{-2}), respectively. (c) Reversible absorbance changes at 331 nm under the alternative green light irradiation for 10 min and blue light irradiation for 200 s. (d) Color changes of the Azo-PDMAEMA in aqueous solution under irradiation of green and blue light, respectively.

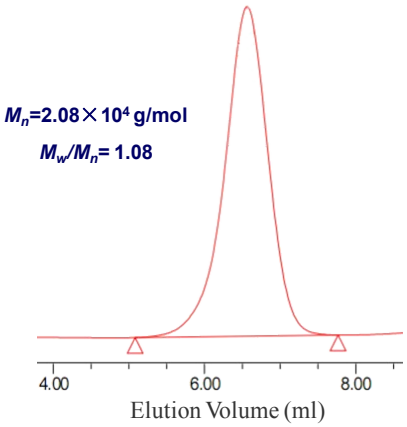

Figure S4. GPC curve of poly(2-(*N, N*-dimethylaminoethyl) methacrylate) (PDMAEMA).

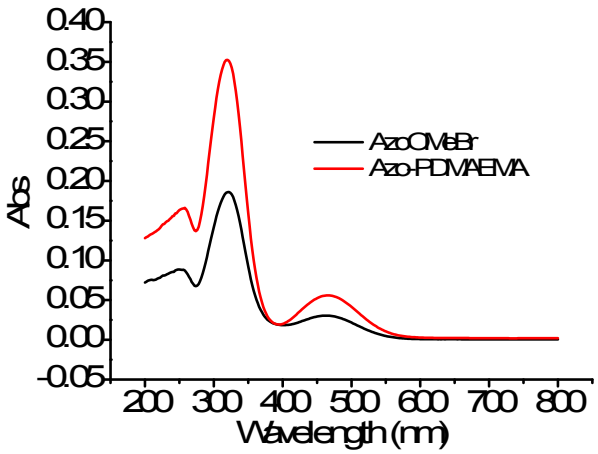

Figure S5. UV-Vis spectra of AzoOMeBr at 0.00125 mg/mL and Azo-PDMAEMA at 0.011 mg/mL in DMF.

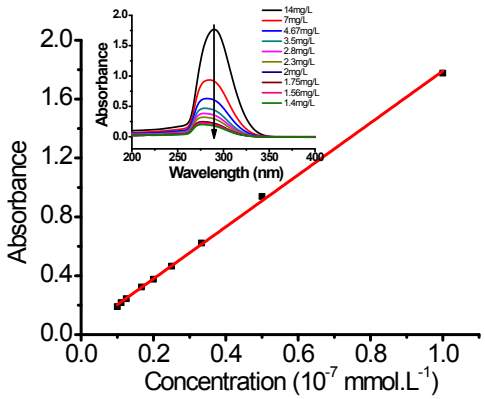

Figure S6. The calibrated curve of CA concentration. Inset: UV-vis absorption spectra of CA solution with different concentrations.

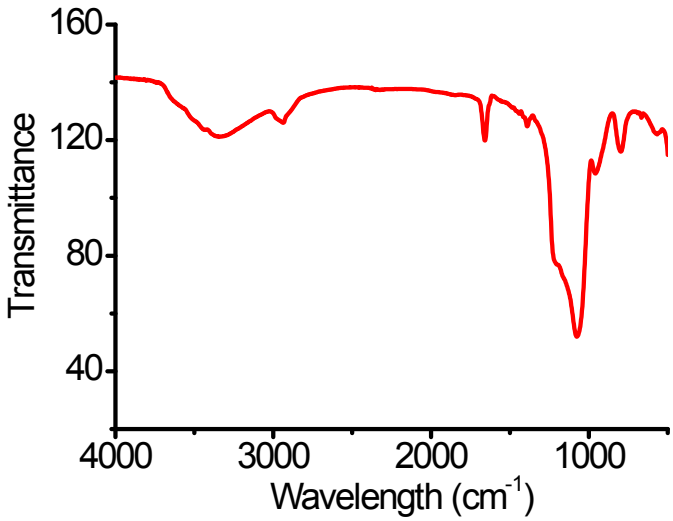

Figure S7. FT-IR of MSNs-CD/Azo-PDMAEMA@CA after green light irradiation.

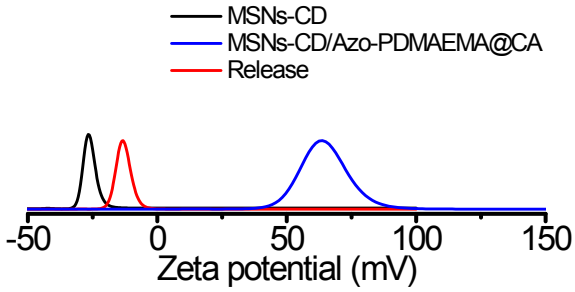

Figure S8. Zeta potentials of MSNs-CD, MSNs-CD/Azo-PDMAEMA@CA, and MSNs-CD/Azo-PDMAEMA@CA after green light irradiation.

References:

1**.** Q. Bian, M. Jin, S. Chen, L. Xu, S. Wang, G. Wang, *Polym. Chem.*, **2017**, *8*, 5525.

2. D. Wang, S. Wu, *Langmuir*, **2016**, *32*, 632.

3. G. Wang, J. Dong, T. Yuan, J. Zhang, L. Wang, H. Wang, *Macromol. Biosci*., **2016**, *16*, 990.