Supplementary materials

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1. Materials and methods

1.1 Materials

Triethylamine (TEA) was acquired from Alfa Aesar, China. Methoxyl PEG(2000) and PEG(2000) were purchased from Shanghai aladdin Biochemical Technology Co.,Ltd. Methyl 4-bromobutyrate (97%), benzimidazole (BM, 97%), pentamethyldiethylenetriamine (PMEDTA, 98%) and lactobionic acid (98%) were purchased from J&K Scientific LTD., China. β-Cyclodextrin (β-CD) was acquired from Tianjin Kermel Chemical Reagents Development Center (Tianjin City, China), and purified by recrystallization from water twice prior to use. NaN3, was purchased from TCI, Japan. Doxorubicin was obtained by treating hydrochloride (DOX•HCl, 99%) purchased from Sigma with TEA through dialysis, extraction, reduced pressure distillation and exsiccation. CuBr was stirred with acetic acid overnight, then washed with ethanol and dried under vacuum at 25 ^{o}C. Other common reagents were purchased from Tianjin Kermel Chemical Reagents Development Center (Tianjin City, China). They were dried with 4 Å grade molecular sieves before use without further purification.

1.2 Polymer structure characterization

The FTIR spectra were obtained on a Nicolet iS10 spectrometer (Nicolet, USA) casting samples into thin films on KBr. Transition mode was used and the wave number range was set from 4000cm^{-1} to 500cm^{-1}. Measurement of ^{1}H NMR and ^{13}C NMR spectra was conducted on a Bruker Avance 300 spectrometer (Bruker BioSpin, Switzerland) operating at 300MHz (^{1}H) in $CDCl_3$, DMSO-d_6 or D_2O. Two-dimensional nuclear o verhauser enhancement spectroscopy (2D NOSEY) and Diffusion-ordered NMR spectroscopy (DOSY) experiments were carried out with a BRUKER AVANCE 600 NMR Spectrometer.

1.3 Polymer Solution Characterization

The size and morphology of the micelles with different polymer concentrations 1.0 mg·mL^{-1} were revealed by TEM (Hitachi H-7650, Japan) at an acceleration voltage of 80 kV. Samples were prepared by dropping 10 mL of polymer solution on copper grids without staining and then let them dry in air. UV-vis spectrophotometer measurement was performed on Shimadzu UV-2550 model

spectroscopy (Shimadzu, Japan). A Zetasizer Nano-ZS DLS (Malvern Instruments, UK) was used to determine the hydrodynamic diameter of self-assemblies. Each sample was kept at a predetermined temperature for 3 min before measurement without any filter.

2. Standard curve of DOX

Moderate amount of DOX·HCl was accurately weighted and dissolved in deionized water.

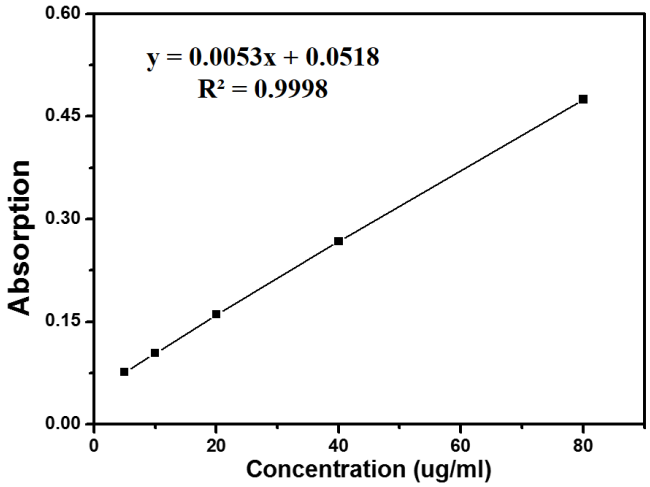


Figure S1 UV–vis absorption spectra of DOX·HCl

3 Standard UV–vis absorption spectra of DOX

Moderate amount of DOX·HCl was dissolved in deionized water. HCl and NaOH were used in controlling the pH value.

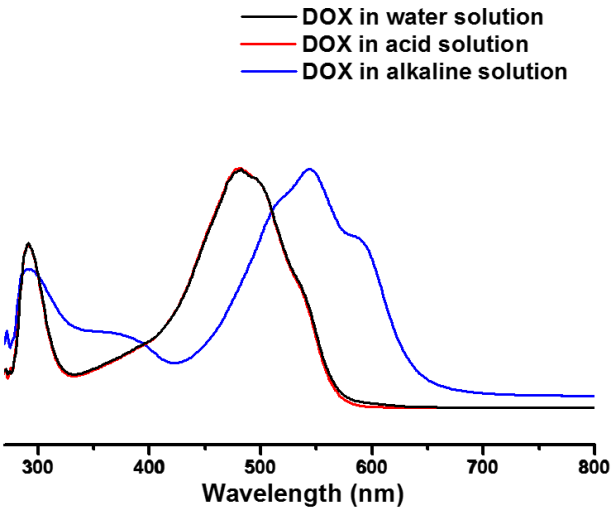
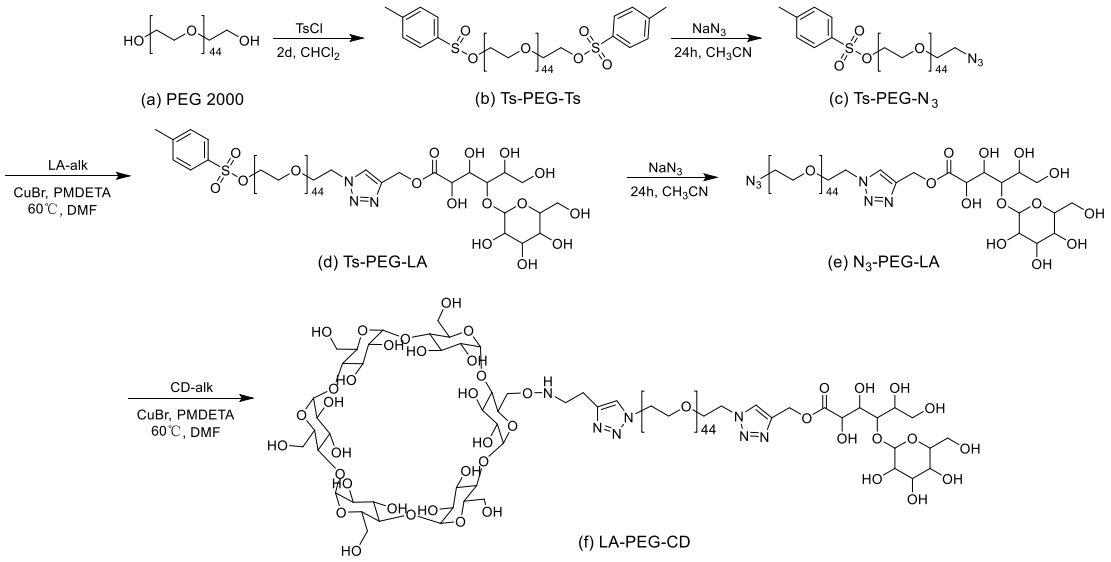


Figure S2 UV–vis absorption spectra of DOX

4. Synthesis of β-cyclodextrin modified PEGylated LA (LA-PEG-CD)

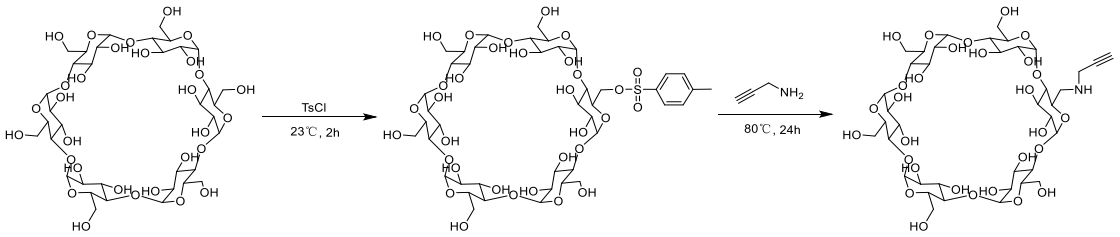


Scheme S1 Synthetic route of LA-PEG-CD

4.1 Synthesis of alkynyl cyclodextrin (CD-alk)

4.1.1 Synthesis of sulfonated β-cyclodextrin (CD-Ts)

Mixture A was prepared by dissolving β-cyclodextrin (60g, 52.9mmol)into NaOH solution (500mL, 328.5mmol/L) and cooling it to 0^{o}C. Mixture B was made by dissolving p-toluenesulfonyl chloride (TsCl) (10.08g, 52.9mmol) into 30mL acetonitrile. With immersed in an ice bath, mixture B was added into A by drops under stirring condition. The following was to let it return to room temperature and stir the mixture for 2h at 23^{o}C. The crude product was obtained through vacuum filtering, acidation and sedimentation method. CD-Ts was collected by the loop for 3 times: the solid in crude product was washed by diluted NaOH solution and water to neutral; then is was washed by acetone to remove water adhering to solid; next the solid was dried in vacuum and was dissolved in boiling water to filter the insoluble matter; finally, recrystallization was completed by acidation and sedimentation method in cool condition. Yields: 10%. ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.43 （C**H**$_3$-C-）; 3.2-3.5 (3, 5, 6-**H**); 3.5-3.7 (2, 4-**H**); 4.51 (6-O**H**); 4.84 (1-O**H**); 5.56-5.75 (2, 3-O**H**); 7.44 (-CH-C**H**-C-); 7.74 (CH$_3$-C-C**H**-CH-).



Scheme S2 Synthetic route of CD-alk

4.1.2 Synthesis of CD-alk

CD-Ts (4g, 3.1mmol) and propynylamine (1.7g, 30.1mmol) were dissolved in 20mL DMF and deoxygenization was accomplished by bubble method for 20min. Then it was immersed in an oil bath at 80°C for 24h. The crude product was obtained by precipitating in 200mL acetone and precipitating again after dissolved with a little methanol. To purification, the crude product was washed by acetone and dried in vacuum. Yields: 10%. ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.16 (-C**H**-C-CH_2-); 2.71 (-C-C**H**$_2$-NH-); 2.93 (-CH_2-N**H**-CH_2-);3.2-3.5 (3, 5, 6-**H**); 3.5-3.7 (2, 4-**H**); 4.47 (6-O**H**); 4.84 (1-O**H**); 5.65-5.75 (2, 3-O**H**).

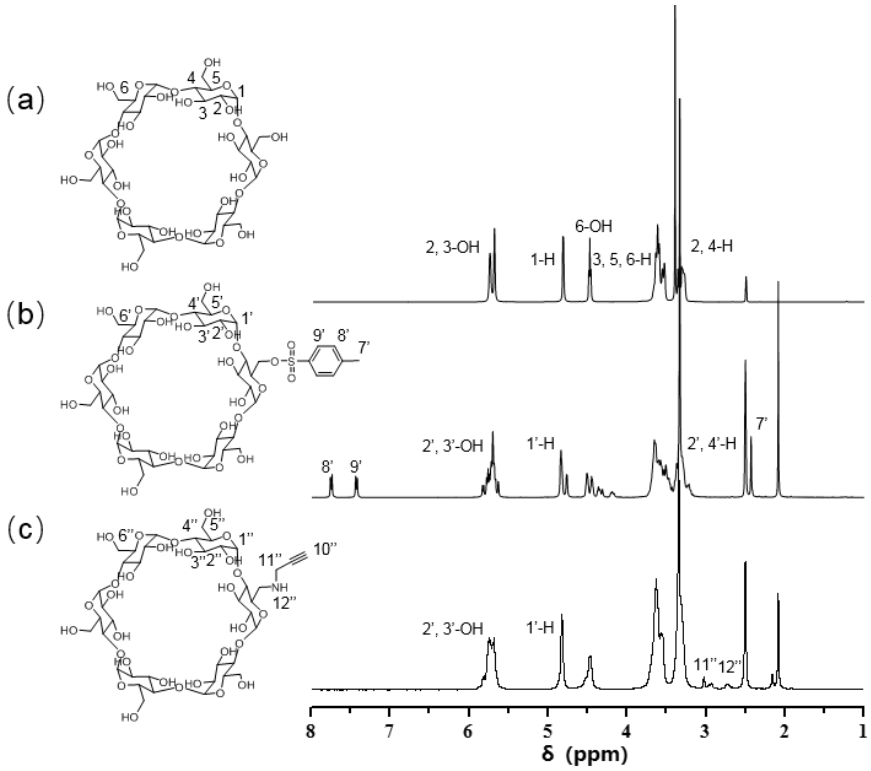
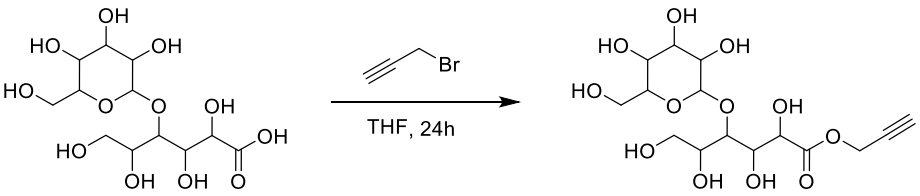


Figure S3 ^{1}H-NMR spectra of CD (a), CD-Ts (b) and CD-alk (c)

4.2 Synthesis of alkynyl lactobionic acid (LA-alk)

LA (2g, 5.58mmol) and propargyl bromide (3.32g, 29.92mmol) was dissolved in 22.2mL THF under stirring condition for 2d. Then organic solvent was removed from the mixture via decompression distillation, and the crude product was collected by precipitating in 300mL isopropanol and vacuum fitering. The final step was dialysis (molecular weight cut off: 1000 D) and lyophilization after washed by isopropanol for twice. Yields: 84%.



Scheme S3 Synthetic route of LA-alk

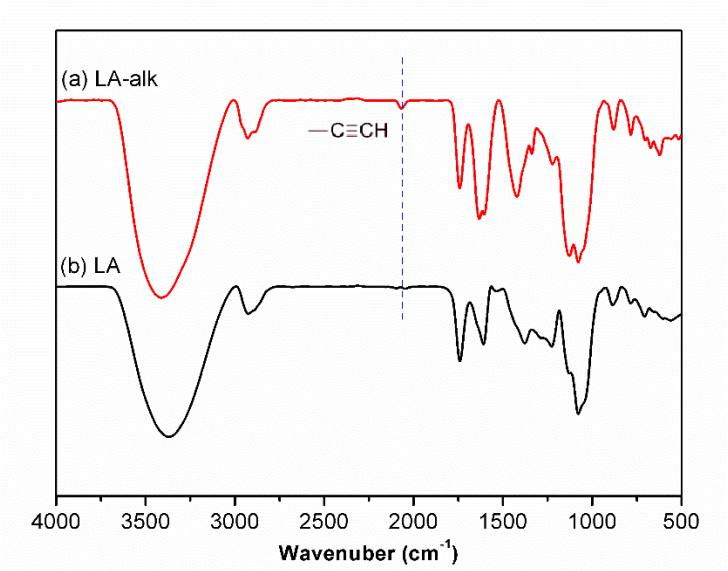


Figure S4 FTIR spectra of LA-alk (a) and LA (b).

4.3 Synthesis of disubstituted sulfonated polyethylene glycol (Ts-PEG-Ts)

P-toluenesulfonyl chloride (TsCl) (4.1g, 21.5mmol), polyethylene glycol 2000 (PEG2000) (7.2g, 3.6mmol) and 12mL TEA were dissolved in 300mL dichloromethane under stirring condition at room temperature for 2d. Then organic solvent was removed from the mixture via decompression distillation, and the crude product was collected by extraction with dichloromethane after

being dissolved in deionized water. Anhydrous sodium sulfate was applied in removing the residual water in crude product and separated by vacuum filtering. At last, Ts-PEG-Ts was obtained through precipitation method in supercooled ether and exsiccation. Yields: 60%. ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.45 (C**H**$_3$-C-); 3.5-3.8 (protons in PEG); 7.36 (-CH-C**H**-C-); 7.79 (CH_3-C-C**H**-CH-).

4.4 Synthesis ofnitrine modified sulfonated polyethylene glycol(N3-PEG-Ts)

2g Ts-PEG-Ts and 58.9mg NaN_3(molar ratio was 2:1) were dissolved in 25mL acetonitrile, and bubble method was used to remove the oxygen in solution. The mixture was heated to reflux for 24h at 80°C. Organic solvent was removed from the mixture via decompression distillation, and the crude product was collected by extraction with dichloromethane after being dissolved in deionized water. The final purification was realized by column chromatography of which eluent was dichloromethane: methanol= 15: 1.

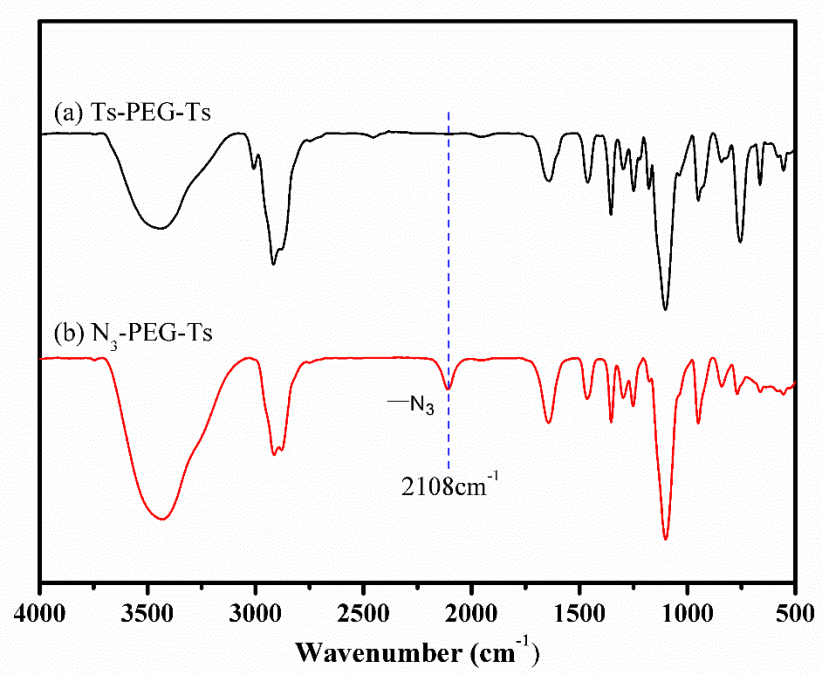


Figure S5 FTIR spectra of Ts-PEG-Ts (a) and Ts-PEG-N_3 (b).

4.5 Synthesis of LA modified sulfonated polyethylene glycol (LA-PEG-TS)

1g N_3-PEG-Ts, 0.36g LA-alk, 79.4mg PMDETA and 66mg CuBr (molar ratio was 1: 2: 1: 1) were mixed with 30 mL of DMF. The mixture was then stirred for 1 min and subjected to three freeze-vacuum-thaw cycles, and then the tube

was immersed into an oil bath at 60°C for 48 h under N_2. Then the mixture was first dialyzed in DMF/H_2O (V/V=1:1) for 12h (molecular weight cut off: 300 D), then dialyzed in H_2O for 2 d. Yields: 76%. ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.21 (C**H**$_3$-C-); 4.23, 4.30, 4.51 (protons in LA); 7.48 (-CH-C**H**-C-); 7.83 (CH3-C-C**H**-CH-); 8.31 (-C-CH-N-).

4.6 Synthesis of nitrine modified lactosepolyethylene glycol (LA-PEG-N_3)

50mg LA-PEG-Ts and 6.31mg NaN_3 (molar ratio was 1:5) were dissolved in 9mL acetonitrile, and bubble method was used to remove the oxygen in solution. The mixture was heated to reflux for 24h at 80°C. Organic solvent was removed from the mixture via decompression distillation, and the crude product was collected by extraction with dichloromethane after being dissolved in deionized water. The final purification was realized by dialyzed in H_2O for 2d and lyophilisation. Yields: 51%. ^{1}H-NMR (DMSO-d_6, δ, ppm): 3.3-3.6 (protons in backbone of PEG and LA); 3.8-4.3 (protons related with LA); 8.24 (-C-C**H**-N-).

4.7 Synthesis of β-cyclodextrin modified PEGylated LA (LA-PEG-CD)

100mg LA-PEG-N_3, 96.54mg CD-alk, 7.02mg PMDETA and 5.84mg CuBr (molar ratio was 1: 2: 1: 1) were mixed with 30 mL of DMF. The mixture was then stirred for 1min and subjected to three freeze-vacuum-thaw cycles, and then the tube was immersed into an oil bath at 60°C for 48 h under N_2. Then the mixture was first dialyzed in DMF/H_2O (V/V=1:1) for 12h (molecular weight cut off: 500 D), then dialyzed in H_2O for 2 d. Yields: 35%. ^{1}H-NMR (DMSO-d_6, δ, ppm): 4.47 (6-O**H**); 4.57, 4.62 (protons in LA); 4.83 (1-**H**); 5.68-5.76 (2, 3-O**H**); 7.91 (-C-C**H**-N-).

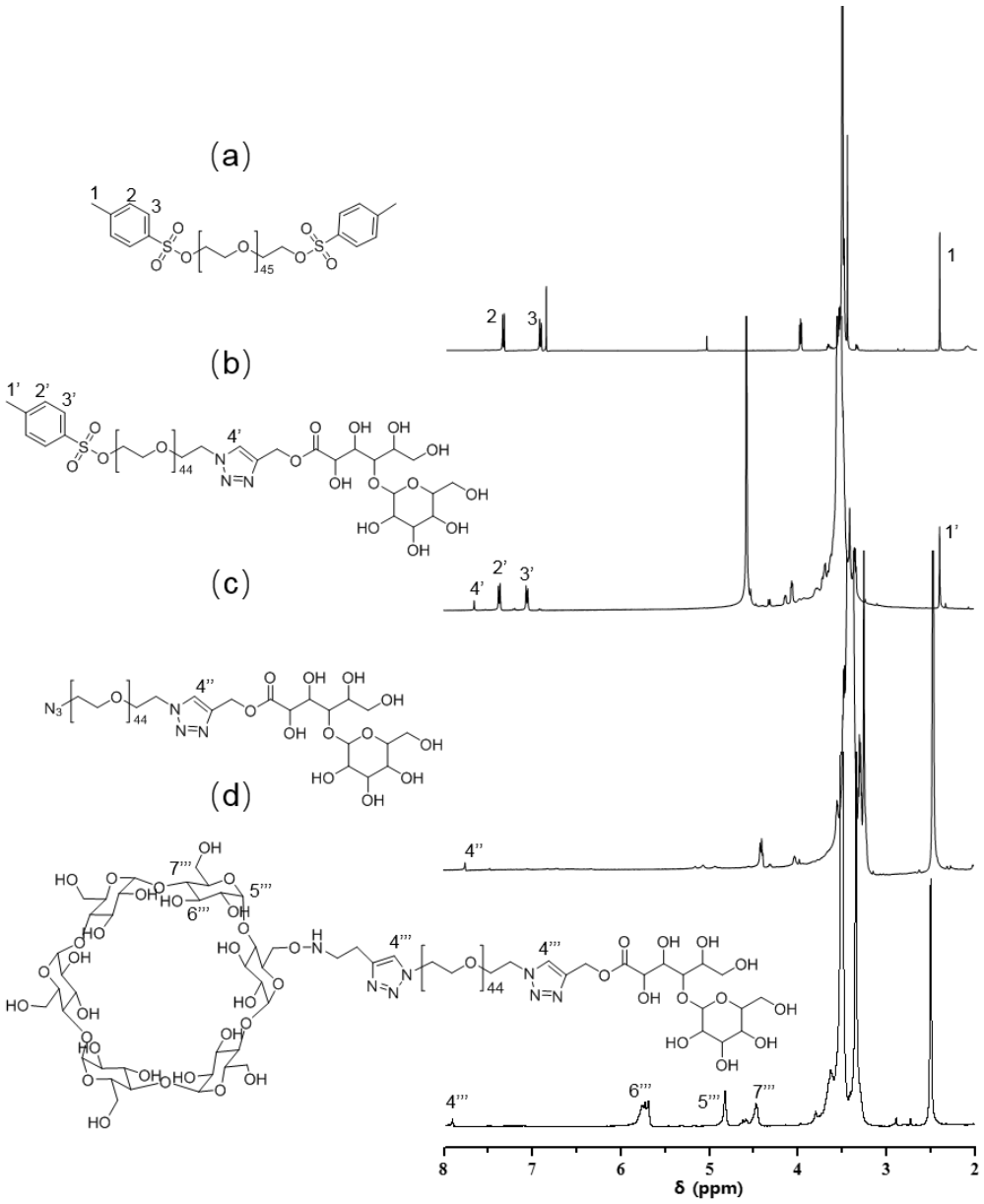
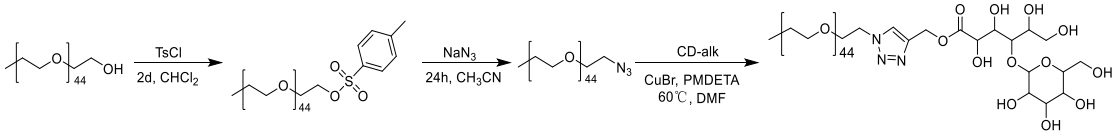


Figure S6 ^{1}H-NMR spectra of Ts-PEG-Ts (a), Ts-PEG-LA (b), N_3-PEG-LA (c) and LA-PEG-CD (d).

5. Synthesis of PEGylated β-cyclodextrin (mPEG-CD)



Scheme S4 Synthetic route of mPEG-CD

5.1 Synthesis of sulfonatedmethoxypolyethylene glycol(mPEG-Ts)

P-toluenesulfonyl chloride (TsCl) (2.7g, 14.3mmol), methoxyl polyethylene glycol 2000 (mPEG2000) (7.2g, 3.6mmol) and 8mL TEA were dissolved in 300mL dichloromethane under stirring condition at room temperature for 2d. The subsequent processing steps were completed referring to S2.3.Yields: 70%. ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.45 (C**H**$_3$-C-); 3.37 (C**H**$_3$-CH_2-CH_2-); 3.5-3.7 (protons in PEG); 7.35 (-CH-C**H**-C-); 7.79 (CH_3-C-C**H**-CH).

5.2 Synthesis of methoxypolyethylene glycolazide (mPEG-N3)

500mg mPEG-Ts and 55.4mg NaN_3 (molar ratio was 1:2) were dissolved in 25mL acetonitrile, and bubble method was used to remove the oxygen in solution. The mixture was heated to reflux for 24h at 80°C. The subsequent processing steps were completed referring to S2.4.Yields: 83%.

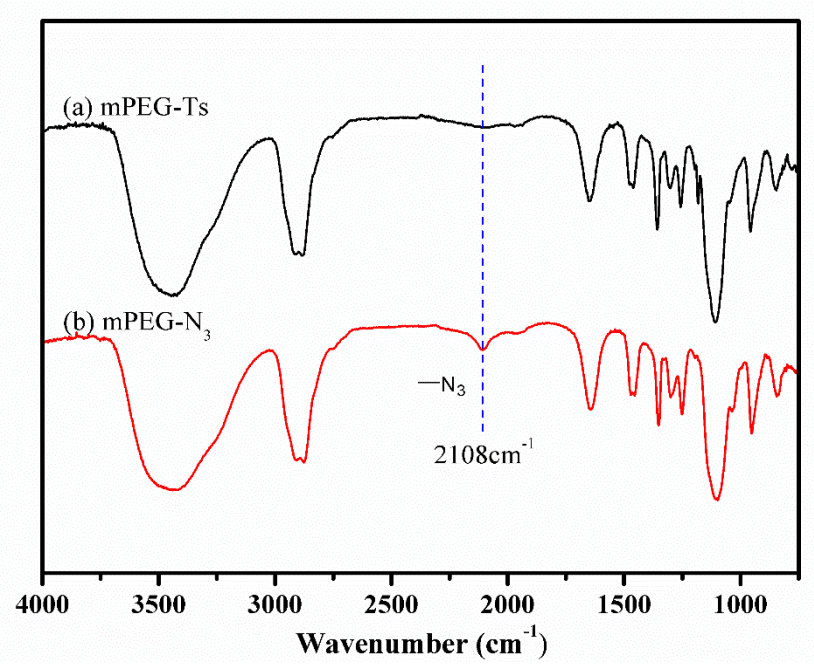


Figure S7 FTIR spectra of mPEG-Ts (a) and mPEG-N_3 (b).

5.3 Synthesis of mPEG-CD

85mg mPEG-N_3, 96.54mg CD-alk, 7.02mg PMDETA and 5.84mg CuBr (molar ratio was 1: 2: 1: 1) were mixed with 30 mL of DMF. The mixture was then stirred for 1min and subjected to three freeze-vacuum-thaw cycles, and then the tube was immersed into an oil bath at 60°C for 48 h under N_2. The subsequent

processing steps were completed referring to S2.7.Yields: 40%. ^{1}H-NMR (DMSO-d_6, δ, ppm): 4.41 (6-O**H**); 4.78 (1-**H**); 5.63-5.70 (2, 3-O**H**); 7.86 (-C-C**H**-N-).

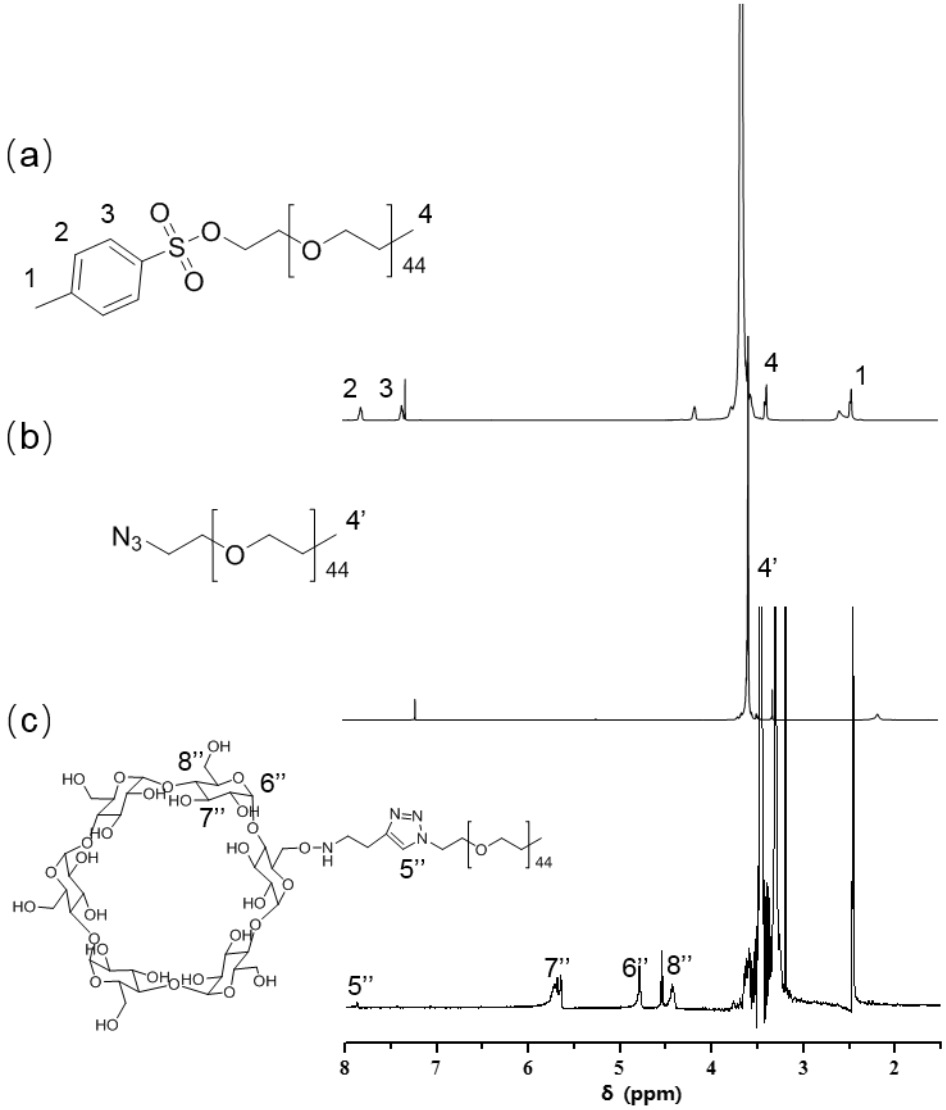
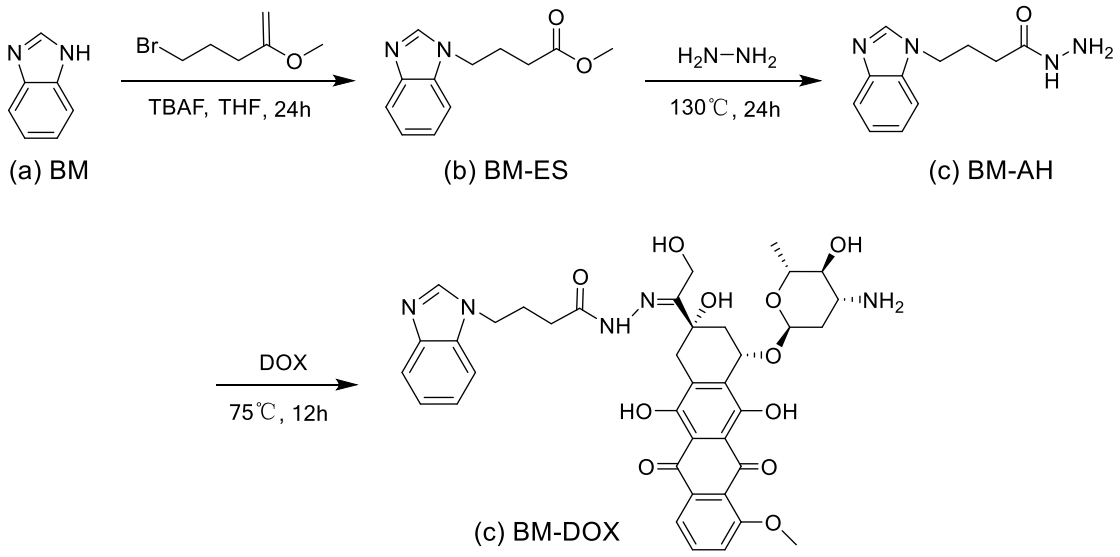


Figure S8 ^{1}H-NMR spectra of mPEG-Ts (a), mPEG-N_3 (b) and mPEG-CD (c) .

6 Synthesis of BM-CD



Scheme S5 Synthetic route of BM-DOX

6.1 Synthesis of esterified benzimidazole (BM-ES)

Benzimidazole (1g, 8.5mmol) and methyl 4-bromobutyrate (1.85g, 10.2mmol) were dissolved in mixed solvent including 10mL THF and 20 mL tetrabutylammonium fluoride (TBAF) under stirring condition for 48h at room temperature. Organic solvent was removed from the mixture via decompression distillation. And purification of product was column chromatography of which eluent was ethyl acetate. Yields: 57%. ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.18 (-CH_2-C**H**$_2$-CH_2-); 2.32 (-C-C**H**$_2$-CH_2-); 3.66 (C**H**$_3$-O-C-); 4.25 (-N-C**H**$_2$-CH_2-); 7.30 (-C-CH-C**H**-C**H**-CH-C-); 7.41 (-CH-N-C-C**H**-); 7.81 (-CH=N-C-C**H**-); 7.89 (-N=C**H**-N-).^{13}C-NMR (DMSO-d_6, δ, ppm)：25.56 (-CH_2-**C**H_2-CH_2-); 30.71 (-CH_2-**C**H_2-C(O)-); 43.33 (-N-**C**H_2-CH_2); 51.91 (**C**H_3-O-C(O)-); 110.77 (-N-C-**C**H-CH-); 119.93 (-C=N-C-**C**H-); 122.74 (-CH-**C**H-**C**H-CH-); 134.21 (-C-N-**C**-CH-); 143.94 (-N-**C**H=N-); 144.46 (-CH=N-**C**-); 173.09 (CH_3-O-**C**(O)-CH_2-)

6.2 Synthesis of acylhydrazine benbinmizole(BM-AH)

500mg BM-ES was resolved in 10mL hydrazine hydrate and was heated to reflux for 24h at 130^{o}C with immersed in an oil bath. Therewith, hydrazine hydrate was removed by decompression distillation, and product was purified

by column chromatography of which eluent (including a bit TEA) was ethyl acetate: methanol=4:1. Yields: 45%. ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.03 (-CH_2-C**H**$_2$-C**H**$_2$-C-); 4.19-4.30 (-N-C**H**$_2$-CH_2-, -NH-N**H**$_2$); 7.18-7.29 (-CH-C**H**-C**H**-CH-); 7.60-7.67 (-C-C**H**-CH-CH-C**H**-C-); 8.21 (-N-C**H**=N-); 9.01 (-N-C-N**H**-NH_2). ^{13}C-NMR (DMSO-d_6, δ, ppm)：25.98 (-CH_2-**C**H_2-CH_2-); 29.09 (-CH_2-**C**H2-C-); 48.82 (-CH_2-**C**H_2-N-); 110.91 (-N-C-**C**H-CH-); 119.07 (-C=N-C-**C**H-CH-); 122.74 (-CH-**C**H-**C**H-CH-); 134.20 (-C-N-**C**-CH-); 143.87 (-N-**C**H=N-C-); 171.23 (-NH-**C**(O)-CH_2-).

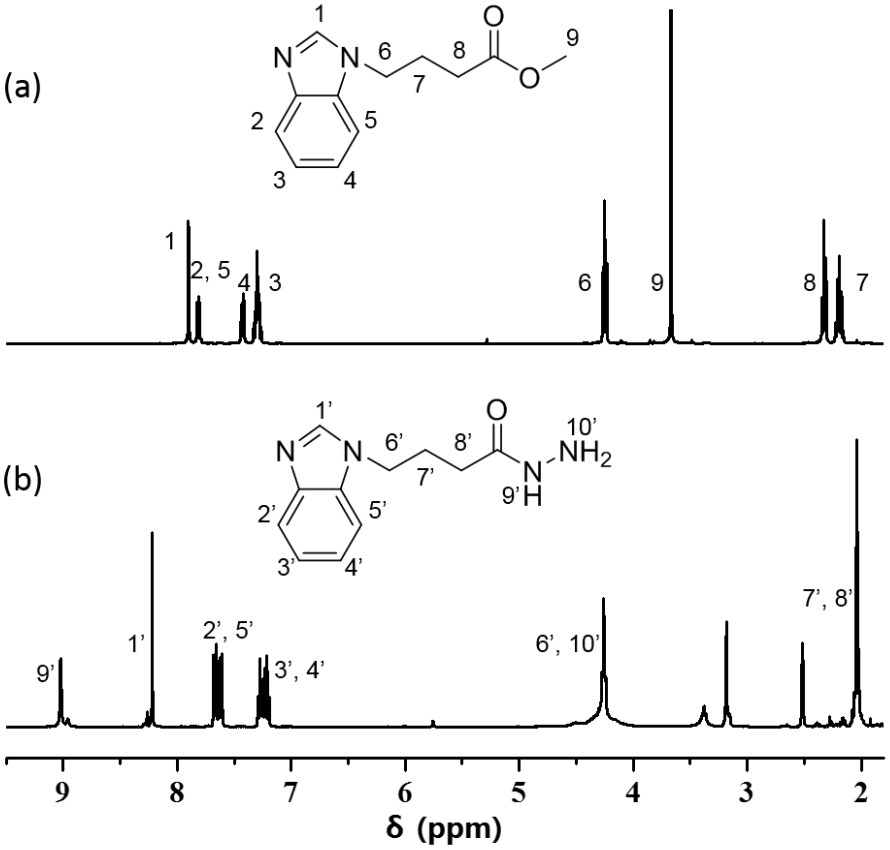


Figure S9 ^{1}H-NMR spectra of BM-ES (a) and BM-AH (b).

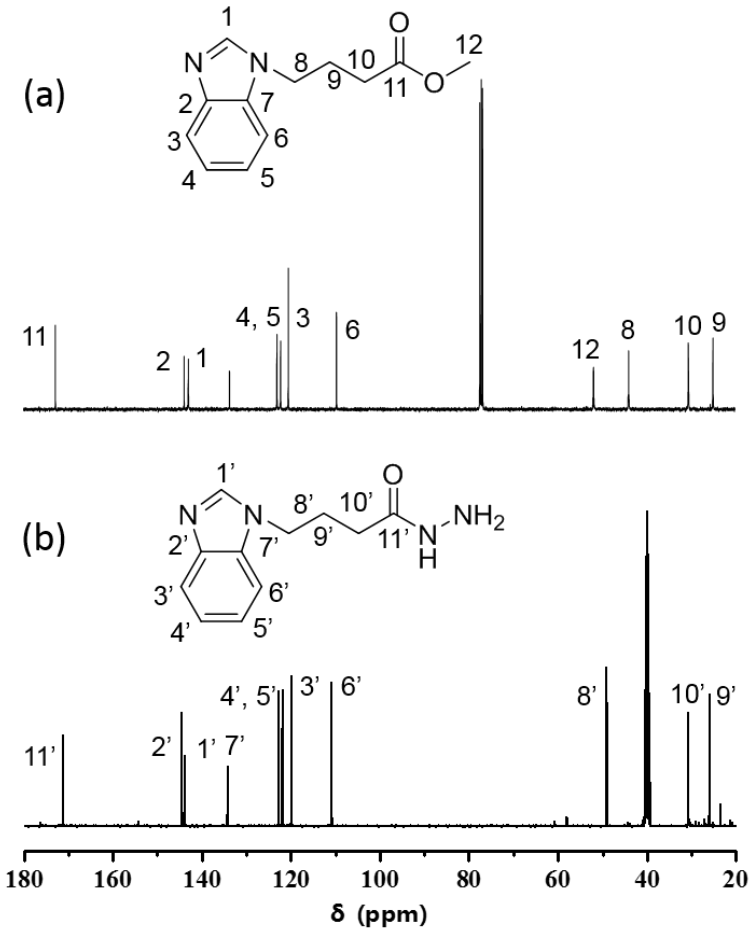


Figure S10 ^{13}C-NMR spectra of BM-ES (a) and BM-AH (b).

6.3 Synthesis of BM-DOX

44mg BM-AH and 83mg DOX·HCl (molar ratio was 2: 1) were dissolved in 10mL methanol and was heated to reflux for 12h at 75°C under stirring condition. The organic solvent was removed and redundant BM-AH was removed by sedimentation in ethyl acetate repeatedly. Yields: 85%. ^{1}H-NMR (DMSO-d_6, δ, ppm): 1.17 (C**H**$_3$-CH-); 3.91 (C**H**$_3$-O-CH-); 4.85-5.01 (-C-CH$_2$(O**H**), **H**O-C-); 5.30 (-CH-CH(O**H**)-CH-); 7.35-7.58 (-CH-C**H**-C**H**-CH-); 7.67-7.90 (-C-C**H**-CH-CH-C**H**-C-); 8.10 (-N=C**H**-N-); 9.06 (-C-N**H**-N=C-); 13.21 (-C-CH(O**H**)-C-).

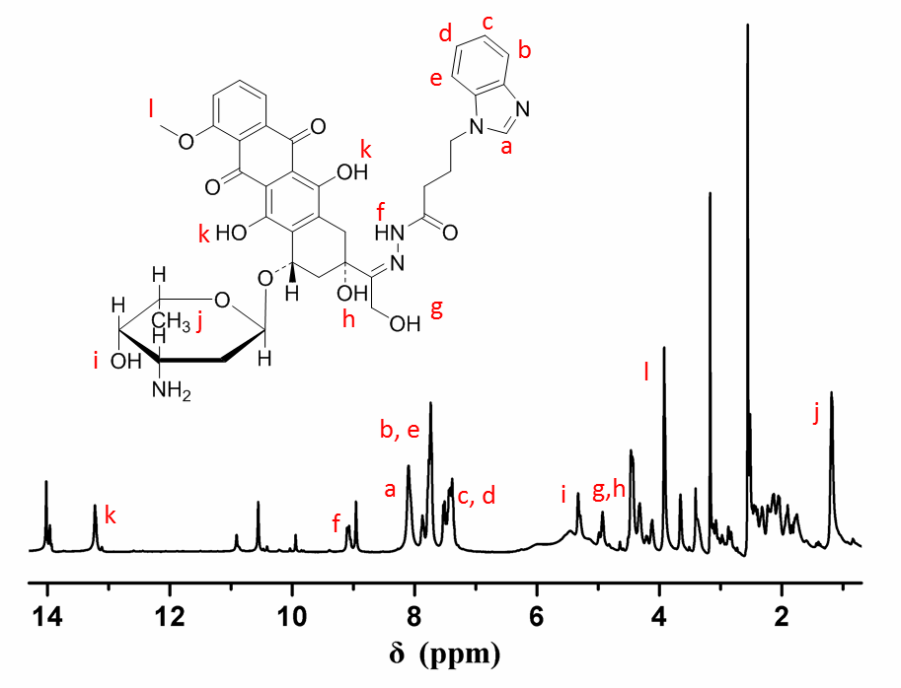


Figure S11 ^{1}H-NMR spectra of BM-DOX.

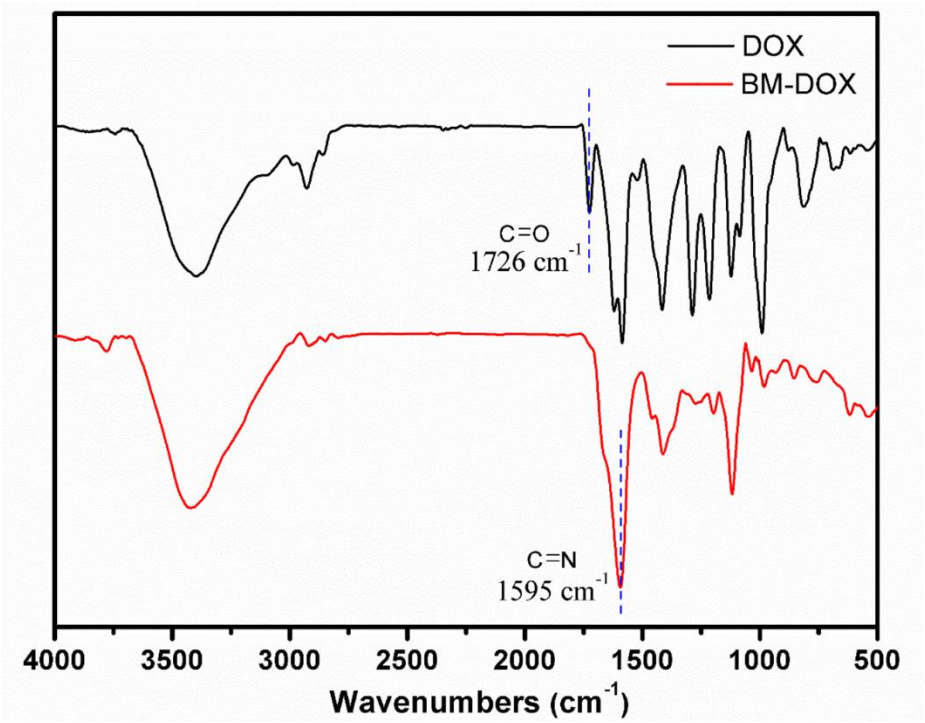


Figure S12 FTIR spectra of BM-DOX.

7 Synthesis of TSPCs- andSPCs-based self-assemblies

13.7 mg LA-PEG-CD and 3 mg BM-DOX (molar ratio was 1: 1) were dissolved in 2 ml deionized water for 12h at room temperature under stirring

condition. The mixture was dialyzed in water for 12 h (molecular weight cut off: 500 D), Yields: 85%.^{1}H-NMR (D_2O-d_6, δ, ppm):1.25 (-CH-C**H**$_3$);2.11 (-CH-C**H**$_2$-CH-); 3.3-3.6 (protons in backbone of CD and PEG); 4.54 (protons related –O-C**H**$_n$- in LA); 7.10-7.44 (protons in benzene of BM); 7.98 (-C-C**H**-N-)

12.3 mg mPEG-CD and 3 mg BM-DOX (molar ratio was 1: 1) were dissolved in 2 ml deionized water for 12h at room temperature under stirring condition. The mixture was dialyzed in water for 12 h (molecular weight cut off: 500 D), Yields: 90%.^{1}H-NMR (D_2O-d_6, δ, ppm): 1.25 (-CH-C**H**$_3$);2.11 (-CH-C**H**$_2$-CH-); 3.3-3.6 (protons in backbone of CD and PEG); 7.10-7.44 (protons in benzene of BM); 7.98 (-C-C**H**-N-).

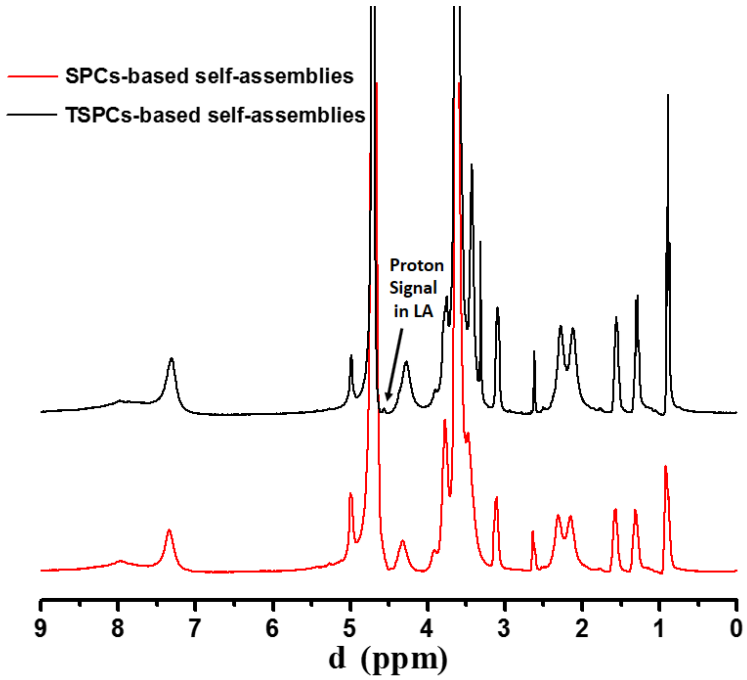


Figure S13 ^{1}H-NMR spectra ofTSPCs- and SPCs-based self-assemblies.