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Electronic Supplementary Information (ESI)

Bridged Bis(*β*-Cyclodextrin)s-Based Polysaccharide Nanoparticle for Controlled Paclitaxel Delivery

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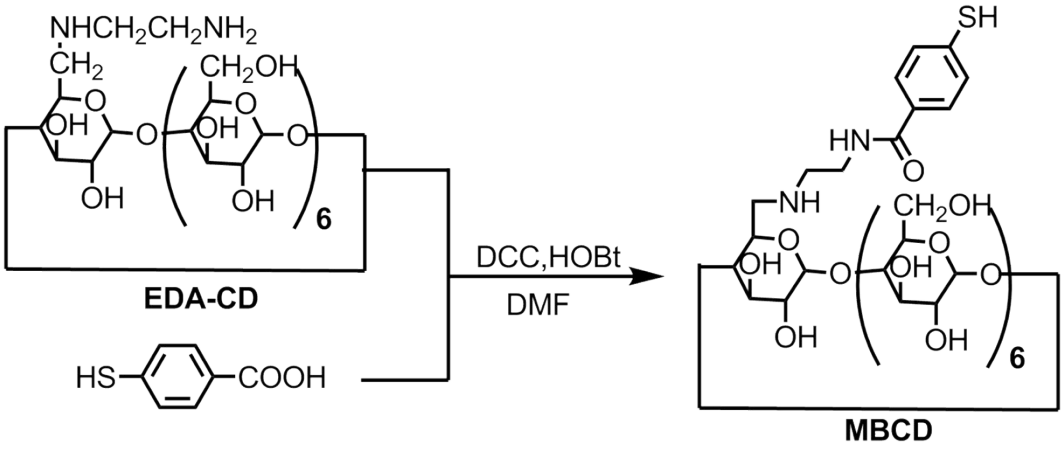
Materials. All the chemical reagents were commercially available and used as received. Mono-6-deoxy-6-ethylenediamino-*β*-CD (EDACD) was synthesized according to the reported procedures.[1] Crude *N*,*N*-dimethylformamide (DMF) was stirring in calcium hydride for three days and then distilled under reduced pressure prior to use. Milli-Q water (18.2 MΩ) was prepared using Milli-Q Synthesis System (BARNSTEAD EASYPURE II Thermo Scientific, USA). Column chromatography was performed on 200−300 mesh silica gel. All other reagents and solvents were of analytical grade and used as received.

Instruments. NMR spectra were recorded on a Bruker AV400 instrument. Mass spectra were performed on a VG ZAB-HS GC-MS. Elemental analyses were performed on a Perkin-Elmer-2400C instrument. UV/Vis spectra were recorded in a conventional quartz cell (light path 10 mm) by using a Shimadzu UV-3600 spectrophotometer equipped with a PTC-3348WI temperature controller to keep the temperature at 25 °C. TEM images were obtained on a JEOL JEM-2010FEF high-resolution transmission electron microscope with an accelerating voltage of 200 kV. The samples were prepared by placing a drop of solution onto copper grid and air-dried. For AFM measurements, a drop of sample solution was dropped onto newly clipped mica and then air-dried, then examined by using an atomic force microscope (Veeco Company, Multimode, Nano IIIa) in tapping mode in air at room temperature. The sample solutions for DLS experiments were prepared by filtering each solution through a 450 nm syringe-driven filter (JET BIOFIL) into a clean scintillation vial. The samples were examined on a laser light scattering spectrometer (BI-200SM, BROOKHAVEN Company) equipped with a digital correlator (BI-9000AT) at λ = 636 nm at 25 °C. All DLS measurements were performed at the scattering angle of 90°.



Scheme S1. Synthetic routes of compound MBCD.

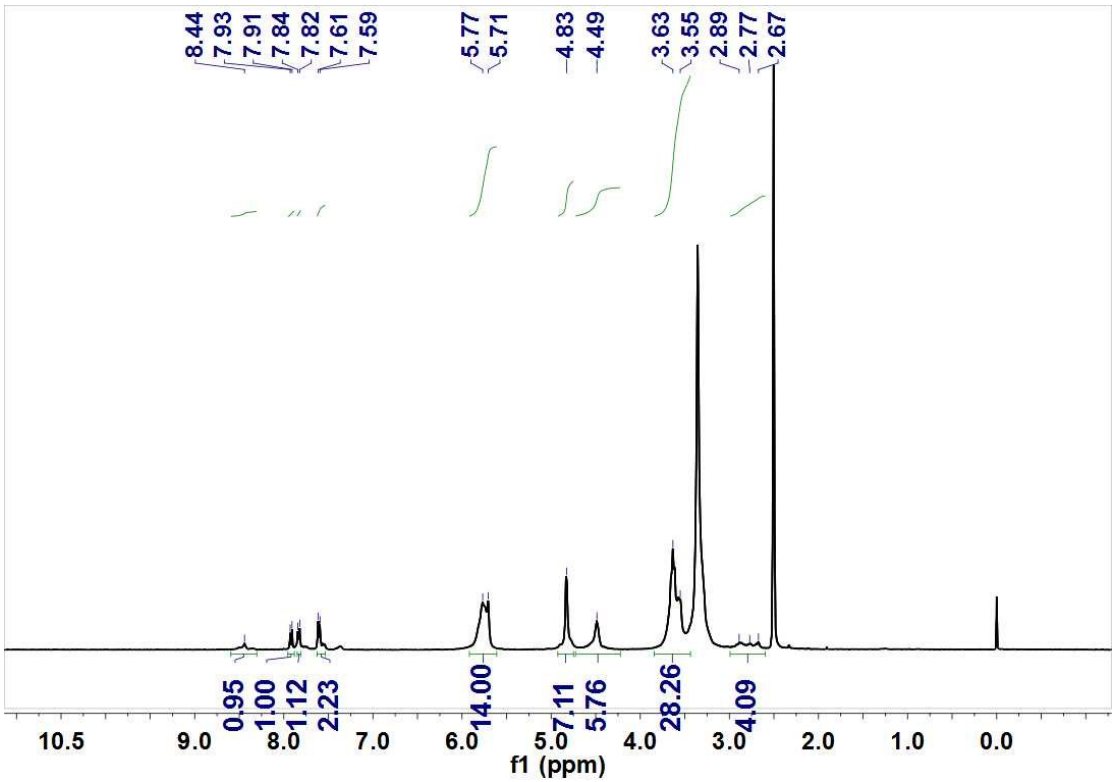


Fig. S1 ^{1}H NMR (400 MHz) spectrum of MBCD in DMSO-d_6 at 25 °C.

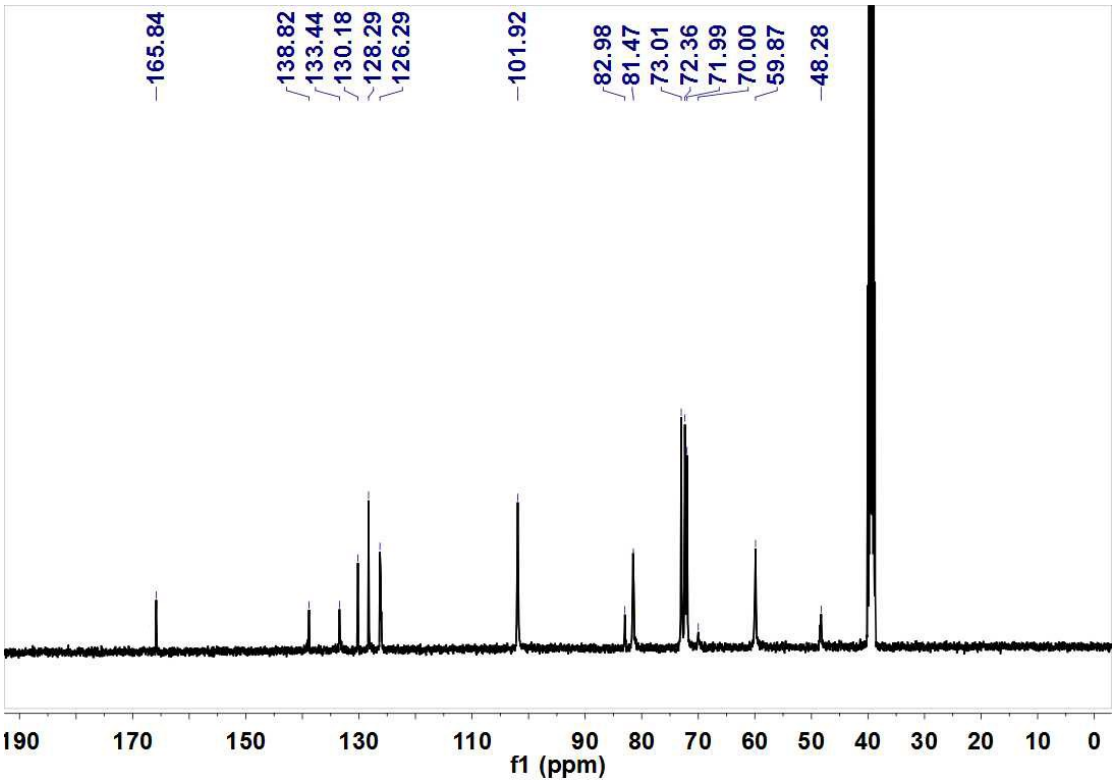


Fig. S2 ^{13}C NMR (100 MHz) spectrum of MBCD in DMSO-d_6 at 25 °C.

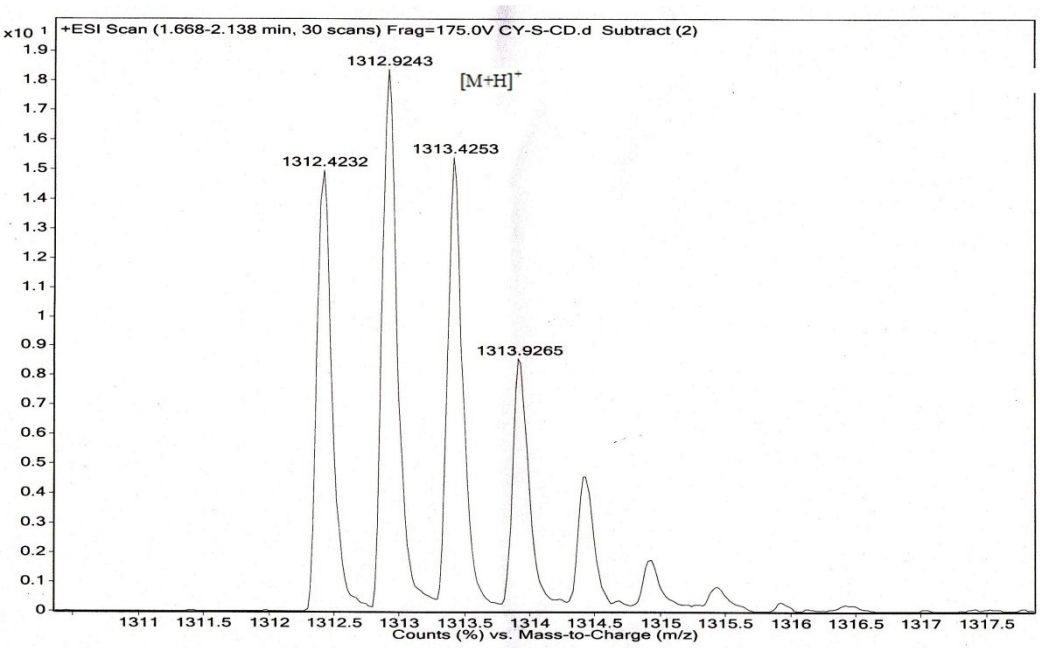


Fig. S3 ESI-MS spectrum of MBCD.

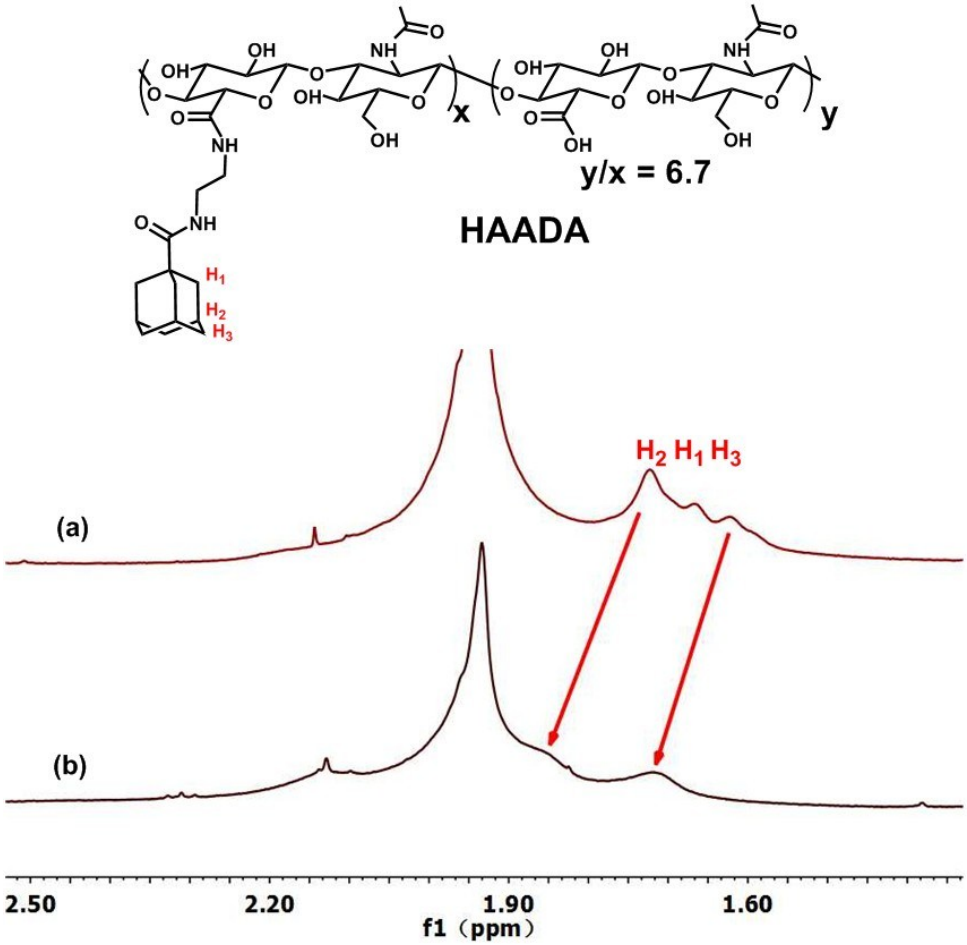


Fig. S4 ^{1}H NMR spectra of (a) HAADA and (b) DTCD·HAADA complex in D_2O at 25 ºC ([HAADA] = 1.0 mM and [DTCD] = 0.5 mM).

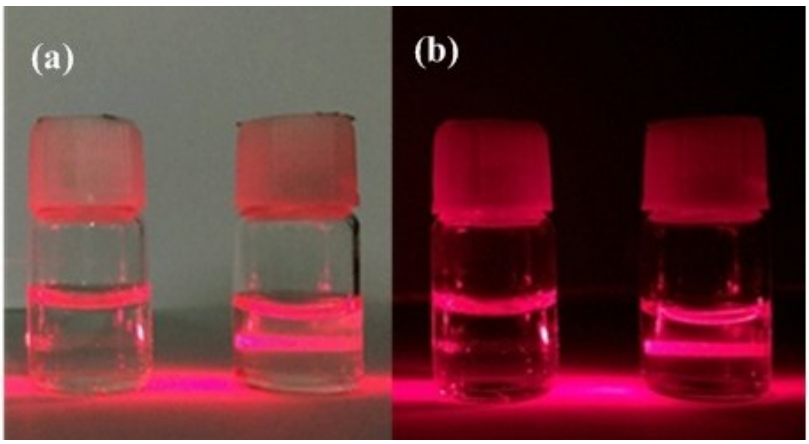


Fig. S5 Tyndall effect of HAADA (left bottle) and DTCD·HAADA complex (right bottom) in the (a) bright and (b) dark fields.

Table S1. Nanoparticle size distribution of DTCD·HAADA assembly at different concentrations.

[DTCD][a]	2.5×10^{-4} M	2.5×10^{-5} M	2.5×10^{-6} M
[HAADA][a]	2.0 mg/mL	0.2 mg/mL	0.02 mg/mL
Inclusion efficiency	80%	50%	15%
Particle size	231 nm	186 nm	163 nm

[a]The molar ratio between β-CD unit in DTCD and adamantyl unit in HAADA was fixed at 1:1. The inclusion efficiency was calculated according to the binding constant between β-CD and adamantane (4×10^4 M^{-1}).[2]

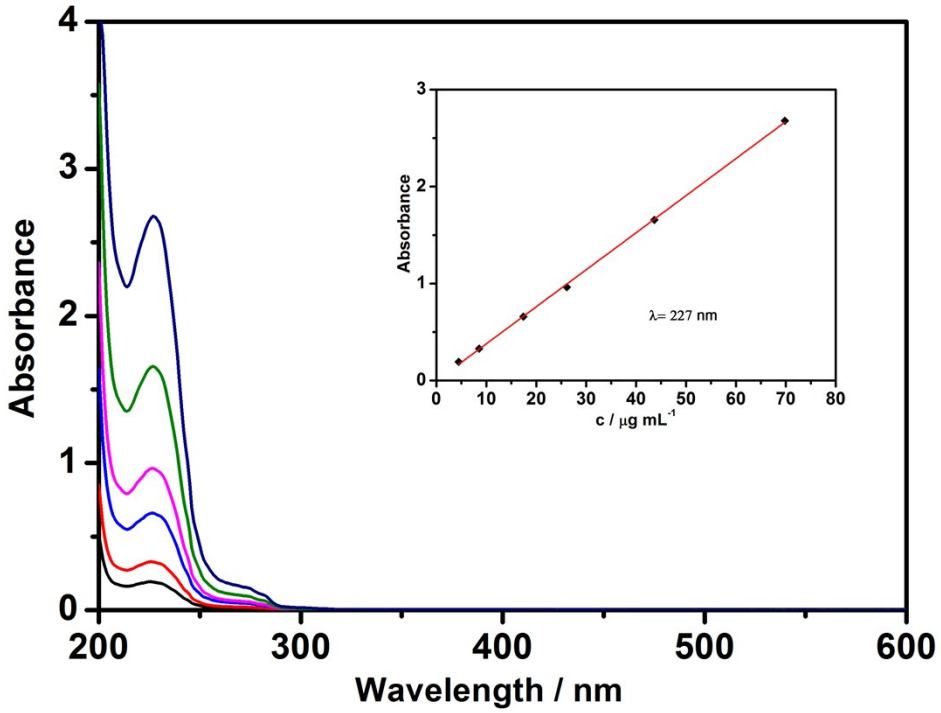


Fig. S6 UV/Vis spectra of PTX at 4.5, 8.6, 17.5, 26.1, 43.67 and 69.8 μg·mL^{-1} in acetonitrile.

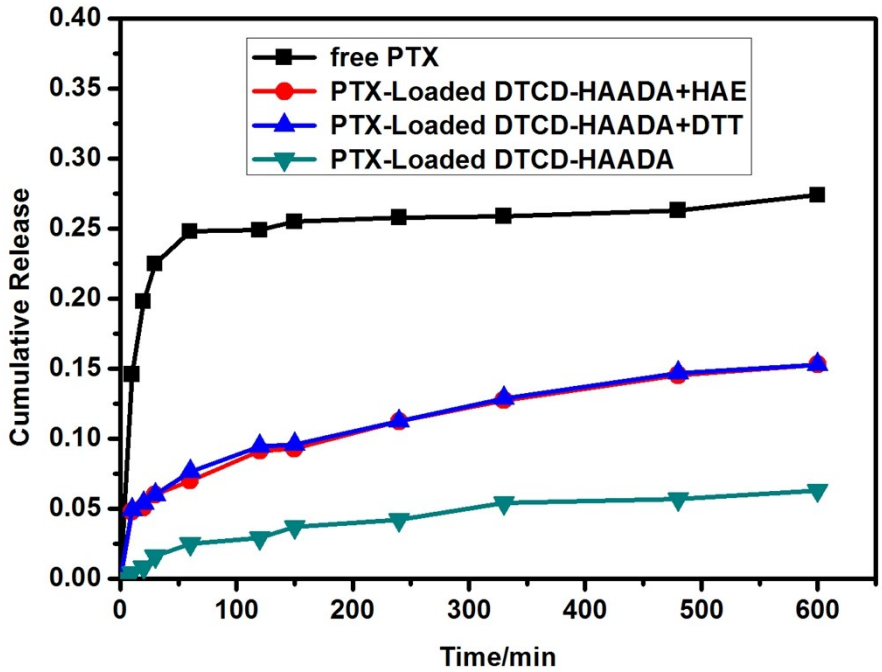


Fig. S7 *In vitro* release profiles of free PTX and PTX from the DTCD·HAADA nanoparticles with and without DTT or HAE in PBS (pH = 7.2, I = 0.01 M) at 37 °C ([PTX] = 0.024 mg mL^{-1}, [DTCD·HAADA] = 0.78 mg mL^{-1}, [DTT =10 mM, and [HAE] = 0.5 IU mL^{-1}).

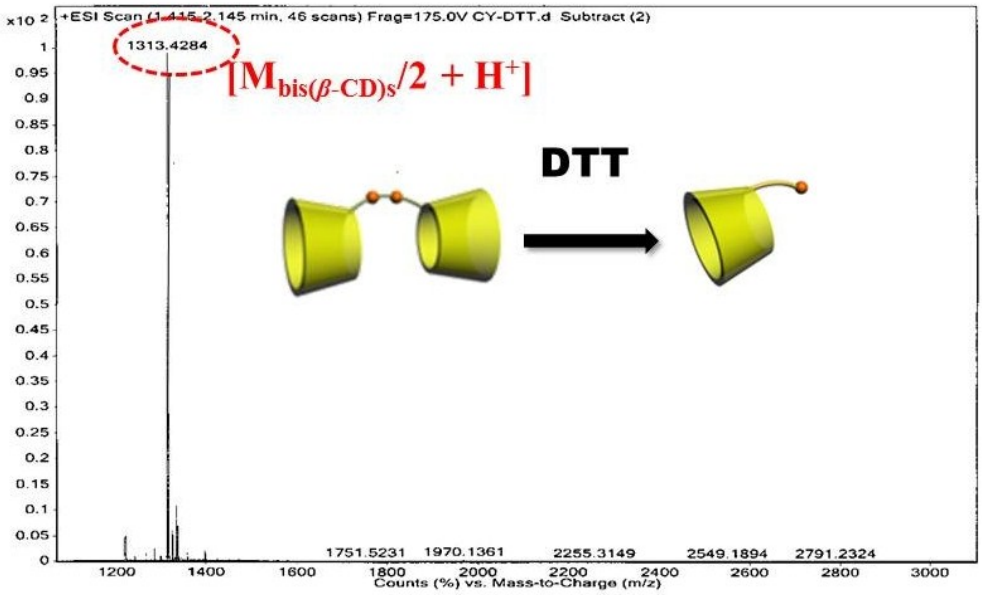


Fig. S8 ESI-MS spectrum of DTCD in the presence of DTT.

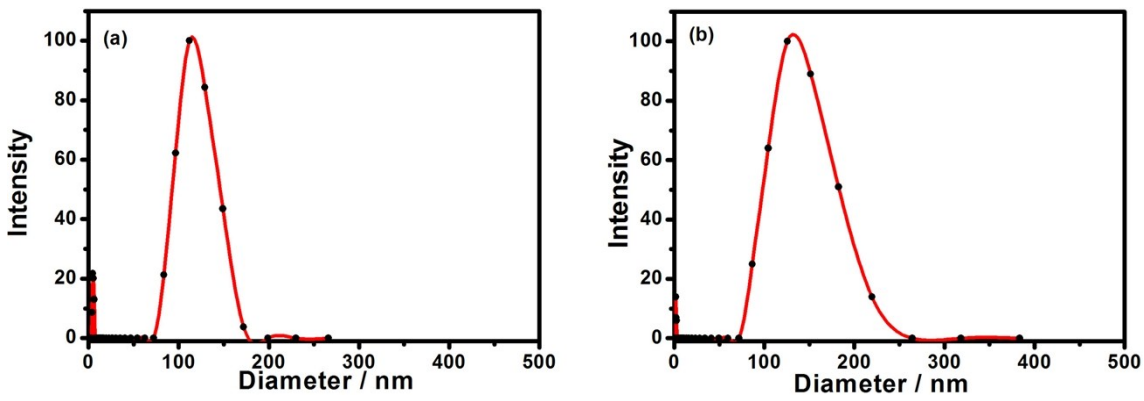


Fig. S9 DLS results of (a) MBCD·HAADA complexes and (b) DTCD·HAADA nanoparticles treated by DTT.

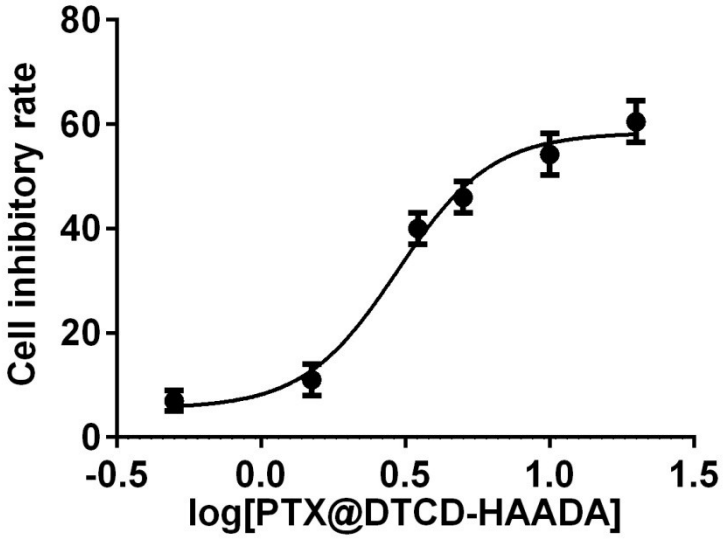


Fig. S10 The inhibitory rate of HepG2 cells at different concentrations of PTX-loaded DTCD·HAADA nanoparticle after incubation for 24 h.

References

1 B. L. May, S. D. Kean, C. J. Easton and S. F. Lincoln, *J. Chem. Soc*., 1997, **1**, 3157−3160.

2 M. R. Eftink, M. L. Andy, K. Bystrom, H. D. Perlmutter and D. S. Kristol, *J. Am. Chem. Soc*., 1989, **111**, 6765−6772.