

Supporting Information

A pH-Sensitive Nano Drug Delivery System from Doxorubicine-conjugated Amphiphilic Polyrotaxane-based Block Copolymers

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Synthesis of 2-bromopropionyl terminated Pluronic F127 (Br-F127-Br)

Pluronic F127 was converted to the corresponding ATRP macroinitiator by the end-capping reaction with a four-fold molar excess of 2-bromopropionyl bromide in CH_2Cl_2 . In brief, in a 100 mL three-neck round-bottom flask, Pluronic F127 (12.6 g, 1 mmol) was dissolved in distilled CH_2Cl_2 (20 mL). Then 4-dimethylaminopyridine (DMAP) (122 mg, 1 mmol) and triethylamine (TEA) (0.42 mL, 3 mmol) was added, after which 10 mL dry CH_2Cl_2 containing 2-bromopropionyl bromide (0.92 g, 4 mmol) was added dropwise under nitrogen. The reaction continued for 2 h at 0 °C and for another 24 h at room temperature under stirring. Finally the mixture was filtered to remove the precipitated salt. The product was purified by precipitation into 500 mL anhydrous ether at 5 °C. The sequence was repeated three times. ^1H NMR analysis was used to determine the degree of esterification (higher than 95 %). Its ^1H NMR spectrum is displayed in Figure S1. ^1H NMR (DMSO-d_6): δ 4.23-4.24 (s, 4 H, $-\text{CH}_2\text{-O-C(=O)-}$), 1.02-1.04 (d, 210 H, $-\text{O-CCH}_3\text{-C-O-}$), 2.08 (d, 3H, $\text{CH}_3\text{-C-Br}$), 1.71-1.73 (d, 1 H, $-\text{CH-Br}$), 3.40-3.50 (m, $\text{CH}_2\text{CH}_2\text{O}$ of PEG and CH_2CHO of PPG) ppm.

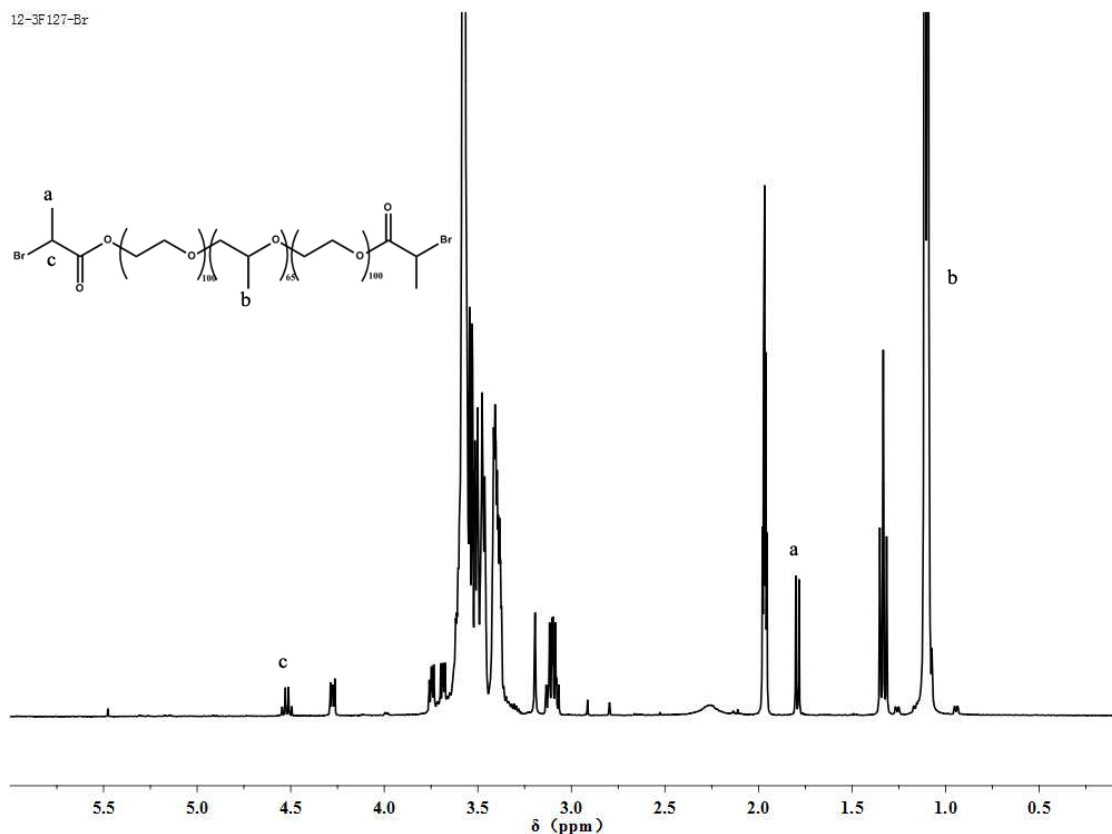


Figure S1. ¹H NMR spectrum of Br-F127-Br.

Synthesis of PR-based triblock copolymer *via* ATRP of PEGMA in aqueous solution

A typical protocol for the polyrotaxane synthesis *via* the ATRP of poly(ethylene glycol)methyl ether methacrylate (PEGMA) was as follows. In a sealable Pyrex reactor, an aqueous solution containing a predetermined amount of β-CD was added to 1 mL aqueous solution of Br-F127-Br (0.39 g, 0.03 mmol), followed by vigorous stirring at room temperature for 24 h to form a PPR. PEGMA (1.32 g, 1.2 mmol) and N,N,N',N'',N''-pentamethyldiethylenetriamine (PMDETA) (12.6 mg, 0.072 mmol) were then added to the resulting suspension of PPR. After quenched in the liquid nitrogen, Cu(I)Cl (6.0 mg, 0.06 mmol) was added, followed by three times of degassing using a nitrogen purge. The reactor was sealed under vacuum and the reaction started and maintained for 6.0 h at 25 °C. The polymerization stopped after breaking the Pyrex reactor. The crude product was directly freeze-dried before dissolved in 15 mL DMF, and then the solution was dialyzed using a dialysis bag (MWCO 3500) for 48 h with water changing every 12 hours, in which the whole dialyzing bag was put into a 60 °C water bath for 16 h. All the content was freeze-dried. The crude product was again dissolved in DMF and fractionally precipitated with anhydrous ether. The purified product was dried under vacuum. Their FTIR spectra are depicted in Figure S2.

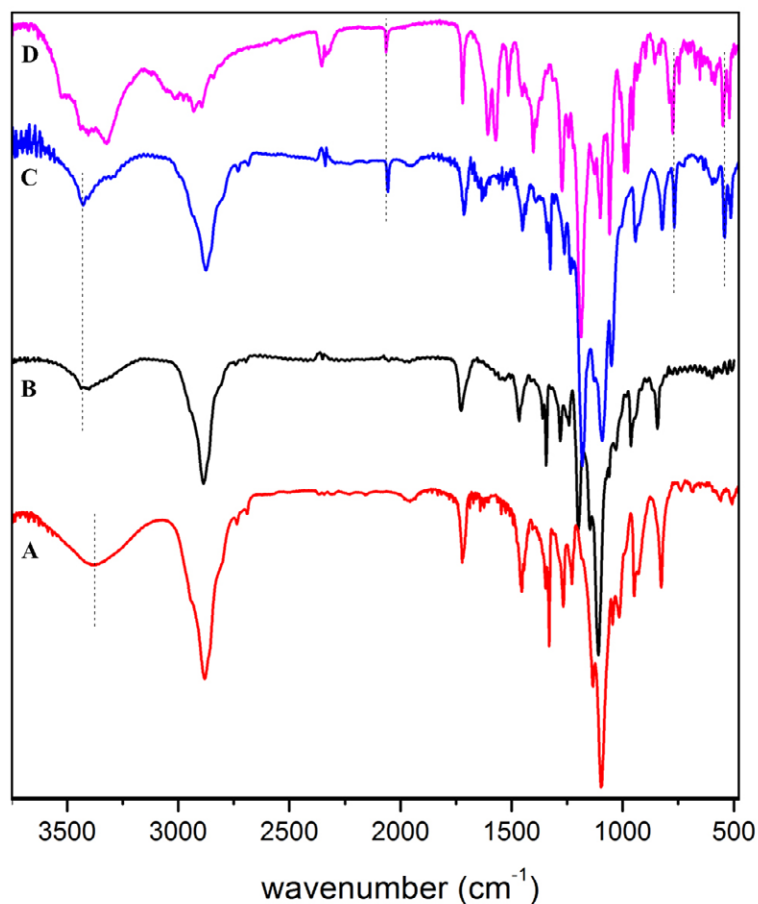


Figure S2. FTIR spectra of (A) DOX, (B) F-30-20-DOX7, (C) F-30-20-EDA and (D) F-30-20.

TOF-MS spectrum of DOX-CA

The TOF-MS spectrum of DOX-CA displays the expected pseudomolecular ions at m/z 700 ($M+H$), 722 ($M + Na$) and 738 ($M + K$) (Figure S3).

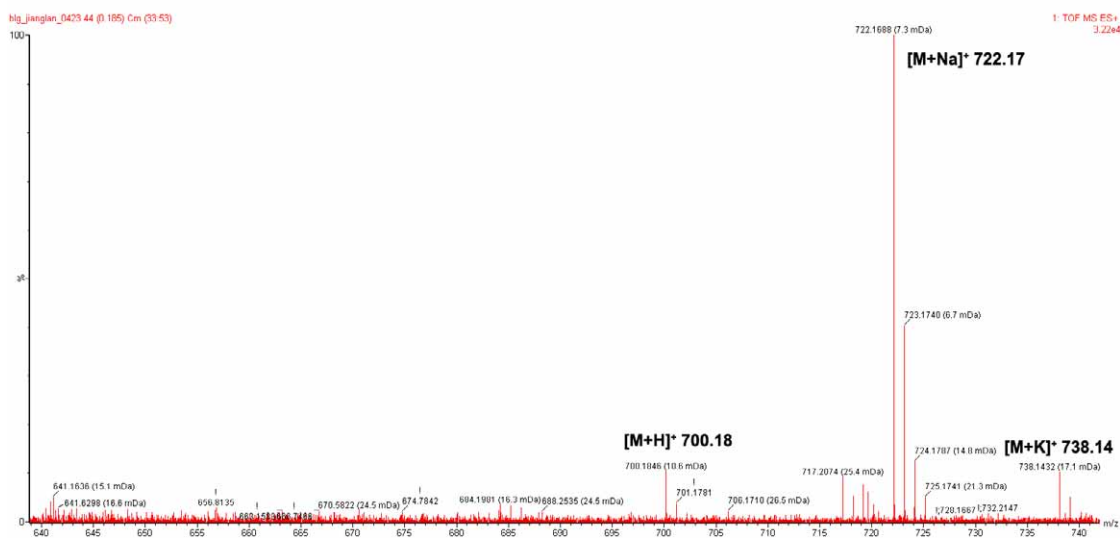


Figure S3. TOF-MS spectrum of DOX-CA.

A standard line of DOX in the buffered solution at pH 5.0

The DOX with different concentration was dissolved in the buffered solution at pH 5.0, and determined by the UV-vis spectroscopy at 480 nm. The standard line was created after linear fitting and is shown in Figure S4.

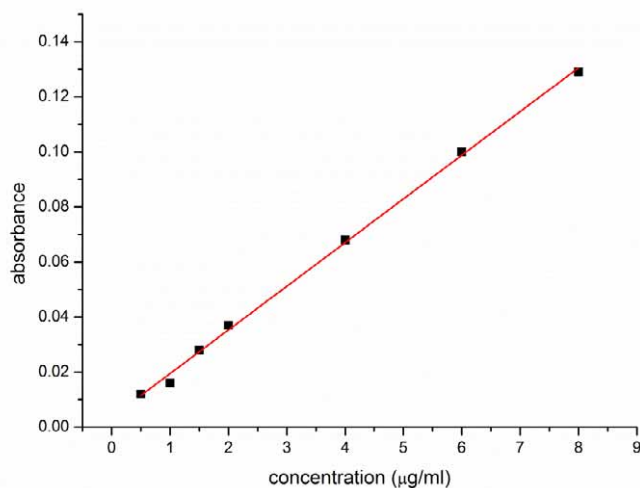


Figure S4. The standard line in the buffered solution at pH 5.0 obtained from a series of solutions with different DOX concentrations.

A standard line of DOX in the buffered solution at pH 7.4

The DOX with different concentration was dissolved in the buffered solution at pH 7.4, and determined by the UV-vis spectroscopy at 480 nm. The standard line was created after linear fitting and is shown in Figure S5.

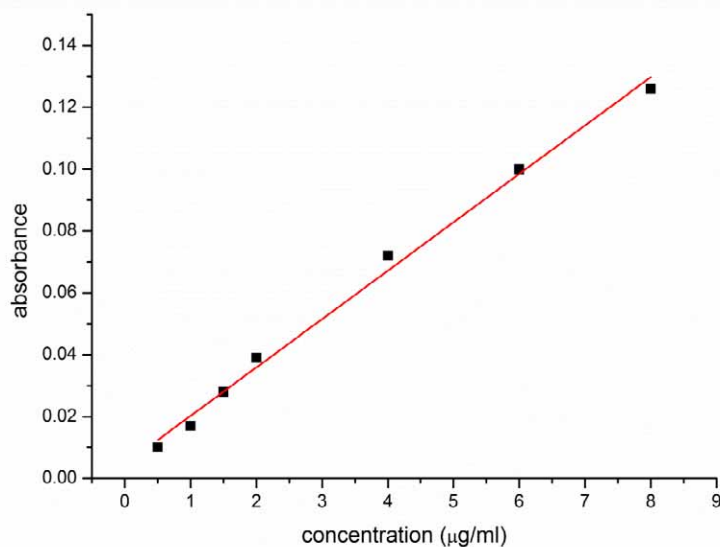


Figure S5. The standard line in the buffered solution at pH 7.4 obtained from a series of solutions with different DOX concentrations.