Supporting Information

Polymeric Micelles with Ionic Cores Containing Biodegradable Cross-Links for Delivery of Chemotherapeutic Agents

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Methods

Fourier-transform infrared (FT-IR) analysis

The FT-IR spectra of freeze-dried PEO-*b*-PMA, *cl*-micelles/ED and *cl*-micelles/Cys were measured by using a NICOLET IR200 FT-IR spectrometer (Thermo Fisher Scientific Co.). Infrared spectra were analyzed using OMNI software.

Legends:

Figure S1. The typical ^{1}H NMR spectra of **(A)** DOX, **(B)** DOX-labeled PEO-*b*-PMA and **(C)** PEO-*b*-PMA copolymer in D_2O.

Figure S2. The typical ^{1}H NMR spectra of **(A)** *cl*-micelles/ED and **(B)** *cl*-micelles/Cys micelles at pH 10 in D_2O. Targeted degree of cross-linking is 0%, 20%, 30%, 40% and 60% from bottom to top.

Figure S3. IR spectra of **(A)** PEO-*b*-PMA block copolymer, **(B)** *cl*-micelles/ED and **(C)** *cl*-micelles/Cys.

Figure S4. Tapping-mode AFM images (**A, B**) and TEM images (**C, D**) of *cl*-micelles/ED (**A, C**) and cl-micelles/Cys (**B, D**). *cl*-micelles were deposited on APS mica from aqueous solutions at pH 7 and dried on the mica. Targeted degree of cross-linking is 20%. Scan size of AFM images (**A, B**) is 2 μm. Bar in TEM images (**C, D**) equals 100 nm.

Figure S5. Tapping-mode AFM images (**A, B**) and TEM images (**C, D**) of DOX-loaded *cl*-micelles/ED (**A, C**) and DOX-loaded *cl*-micelles/Cys (**B, D**). Targeted degree of cross-linking is 20%. Scan size of AFM images (**A, B**) is 2 μm. Bar in TEM images (**C, D**) equals 100 nm.

Figure S6. In vitro degradation of **(A)** *cl*-micelles/Cys and **(B)** *cl*-micelles/ED in the presence of DTT in PBS buffer (0.14 M NaCl, pH 7.4). (○) without DTT as control, (△) DTT 0.1 mM, (▲) DTT 0.5 mM, (□) DTT 5.0 mM, (■) DTT 25 mM. Targeted degree of cross-linking of both *cl*-micelles is 70%.

Figure S7. *In vitro* cytotoxic effect of DOX-loaded *cl*-micelles in A2780 ovarian carcinoma cells. (■) free DOX, (□) DOX-loaded *cl*-micelles/Cys after incubation with DTT 25 mM for 24hr at 37°C, (□)DOX-loaded *cl*-micelles/Cys and (▲) DOX-loaded *cl*-micelles/ED; n=8.

Figure S1

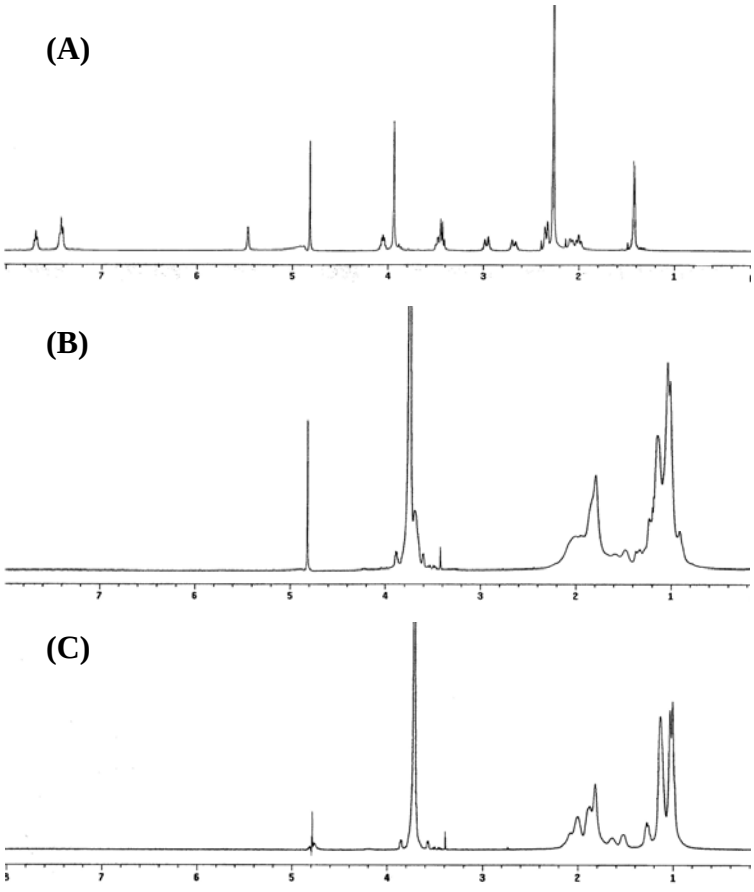


Figure S2

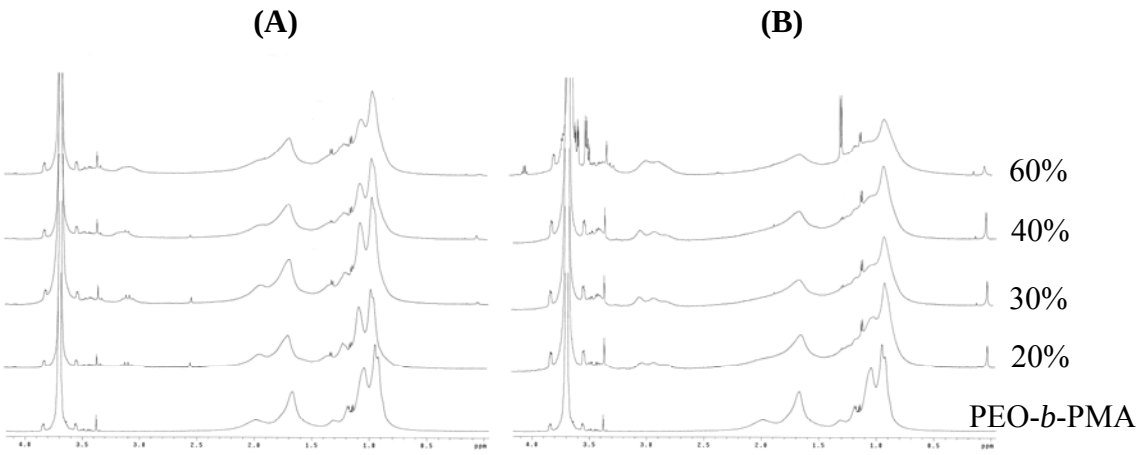


Figure S3

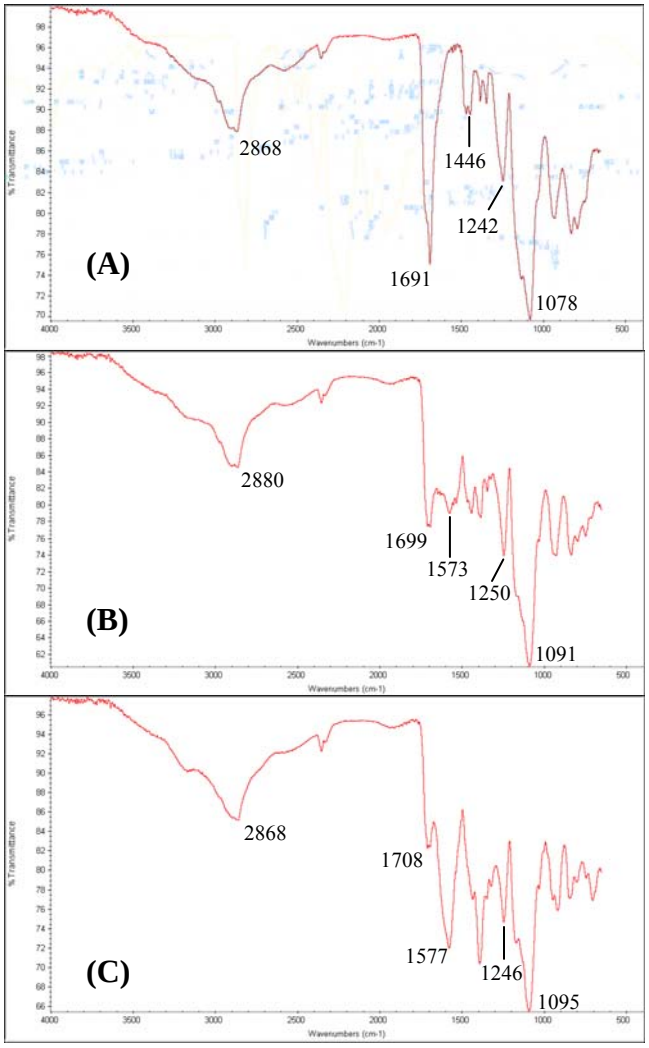

2868
1446
1242
(A)
1691
1078
2880
1699
1573
1250
(B)
1091
2868
1708
1577
1246
(C)
1095

Figure S4

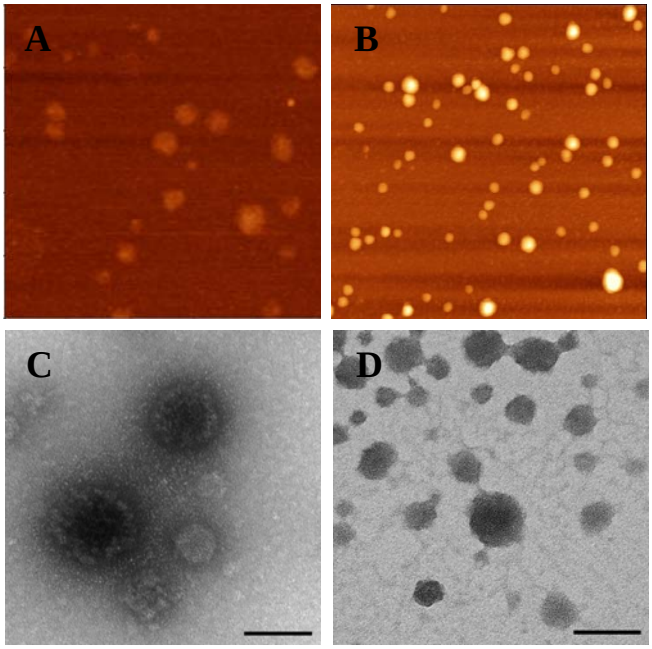


Figure S5

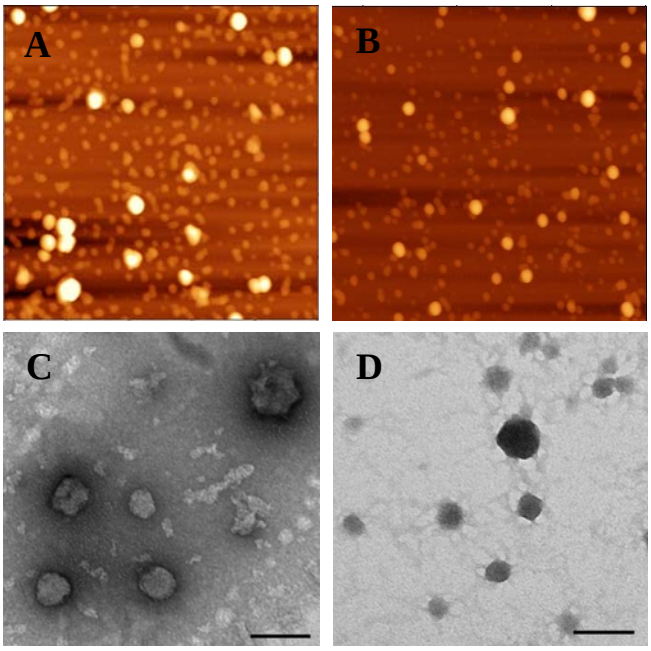


Figure S6

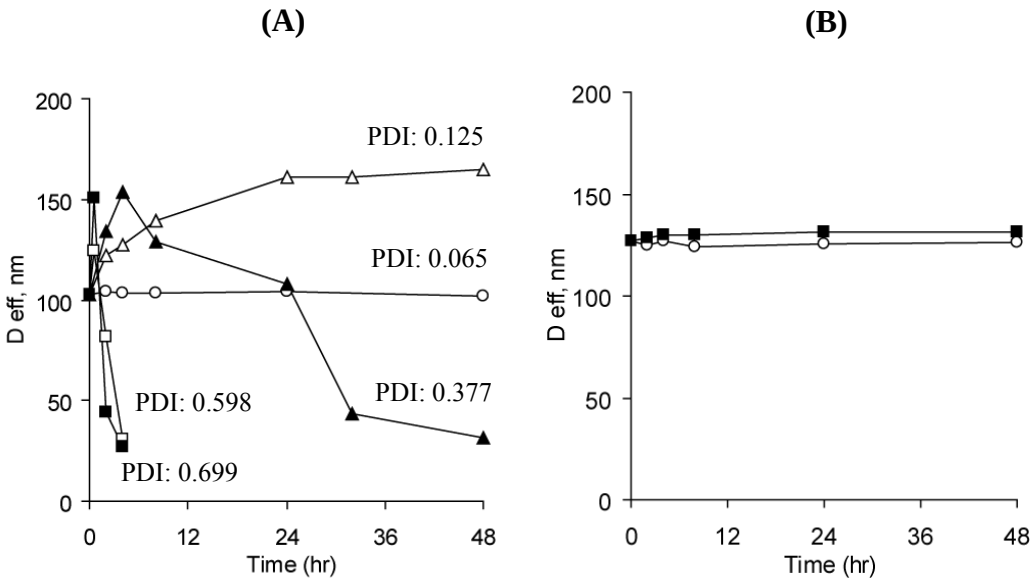
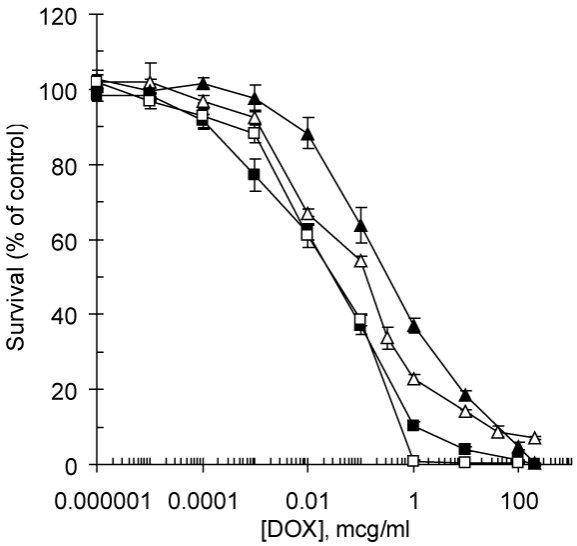

(A)
(B)
200
150
100
50
0
D eff, nm
PDI: 0.125
PDI: 0.065
PDI: 0.598
PDI: 0.377
PDI: 0.699
0
12
24
36
48
Time (hr)

Figure S7


120
100
80
60
40
20
0
Survival (% of control)
0.000001
0.0001
0.01
1
100
[DOX], mcg/ml