Supporting Information

Calculation of DP and $M_{n,NMR}$ from the NMR results.

The number-average molecular weight ($M_{n,NMR}$) and degree of polymerization (DP) of GMA unit were calculated from the integral values of the methylene of PEG chain proton signal (4 × 113 protons) in the range of 3.74-3.48 ppm and that of the methylene in epoxide (1× DP protons) in the range of 3.36-3.16 ppm.

Taking PEG-$PGMA_{51}$ as an example, amplifying the integral of the methylene signal (3.74-3.48 ppm) of PEG chain proton to 452 (the methylene proton number on the PEG), the integral of the methylene in epoxide (3.36-3.16 ppm) was 51.36, meaning there was 51 epoxide groups in a PEG-PGMA copolymer. So the DP of GMA should be 51 in the PEG-$PGMA_{51}$. The $M_{n,NMR}$ of the PEG-$PGMA_{51}$ could be calculated using the following formulation: 5000+51*142=12242.

Calculation of drug content from the ^{1}H NMR results.

The degree of DOX conjugation could be calculated with the following formulation:

$$\text{degree of DOX conjugation} = \frac{y}{x+y} \times 100\%$$

where x is the integral of H signal at 8.22~8.50 ppm (-CH=N-), y is the integral of H signal at 9.93~10.10 ppm (-CHO).

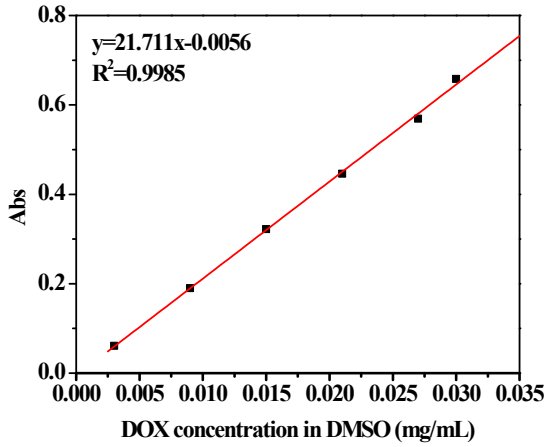
Taking the PEG-P(GMA-CBA)$_{51}$-DOX as an example: x=0.47, y=1. The degree of DOX conjugation was calculated as $\frac{0.47}{1+0.47} \times 100\% = 32\%$

So the drug content (wt%)$=\frac{n \bullet 32\% \bullet M_{DOX}}{n \bullet (M_{GMA} + M_{CBA}) + n \bullet 32\% \bullet M_{DOX} + M_{PEG}} \times 100\% = 32.47\%$

where n is the degree of polymerization of the relevant polymer, and M_{DOX}, M_{GMA}, M_{CBA}, and M_{PEG} is the molar mass of DOX, GMA, CBA and PEG, respectively.

Calculation of drug contents from the UV-vis results.

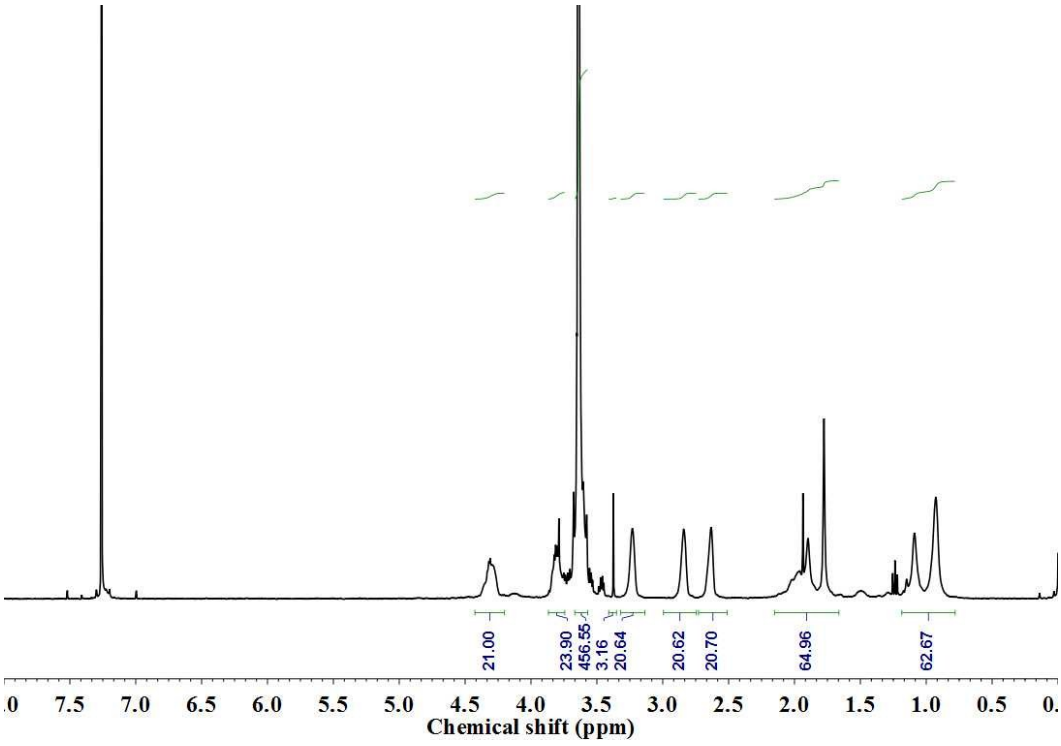
5.0 mg of PEG-P(GMA-CBA)$_n$ -DOX was dissolved in 15 mL of DMSO. The solution was measured by UV-vis spectrometry at 480 nm, and the amount of DOX was calculated from a standard calibration curve obtained from a series of DOX solution in DMSO, as following:



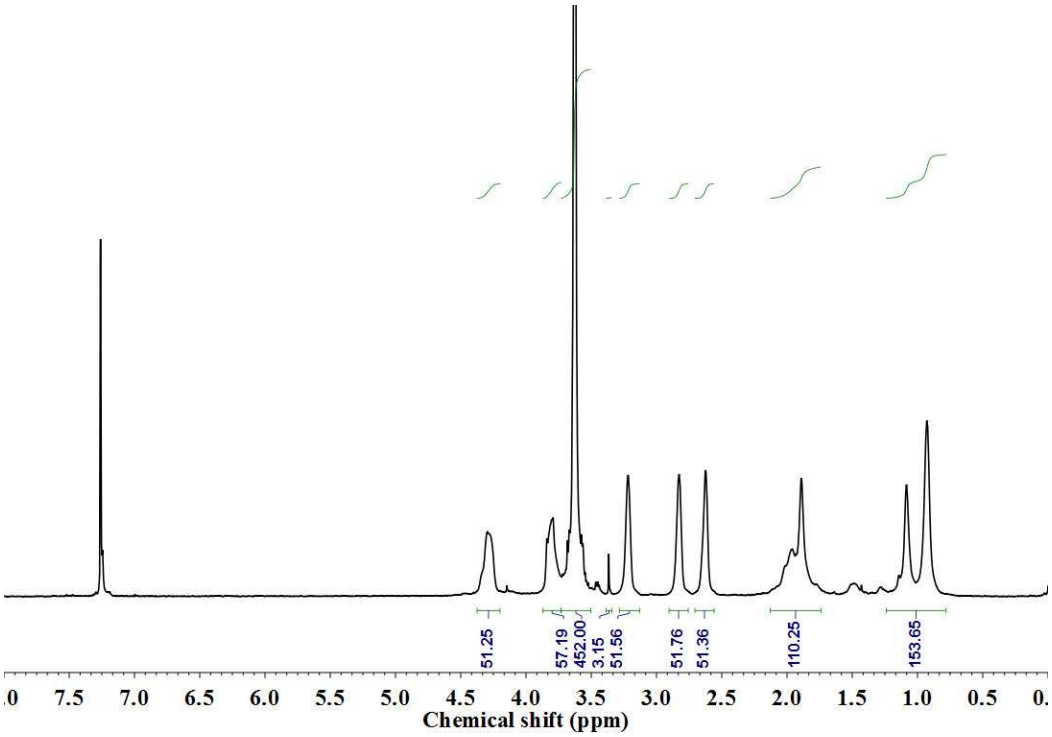
Then the drug content was calculated, as following:

$$\text{drug content (wt\%)} = \frac{W_{DOX}}{W_{PEG-P(GMA-CBA)-DOX}} \times 100\%$$

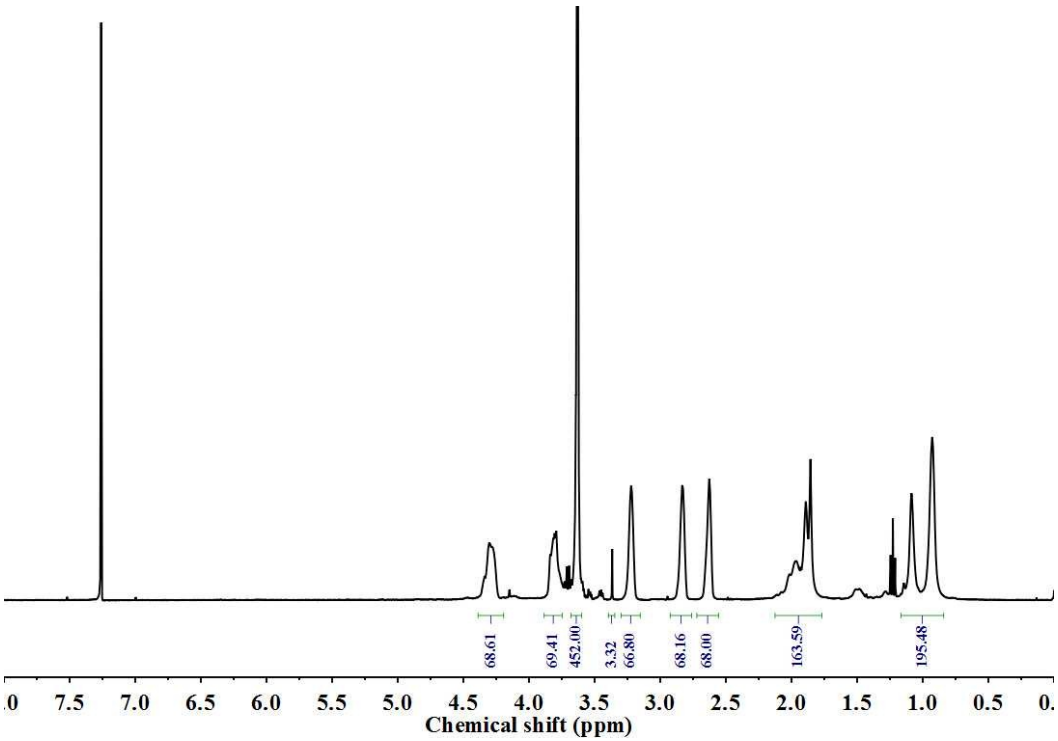
where W_{DOX} is the weight of DOX in PEG-P(GMA-CBA)-DOX, and $W_{PEG\text{-}P(GMA\text{-}CBA)\text{-}DOX}$ is the weight of PEG-P(GMA-CBA) -DOX.



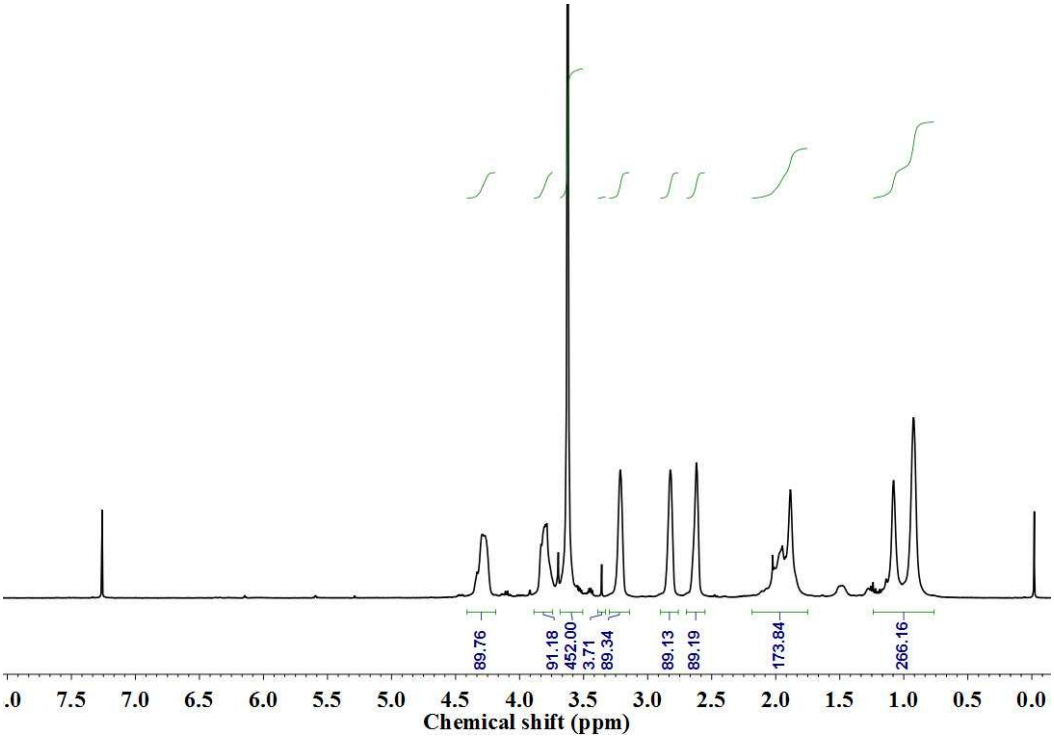
PEG-PGMA$_{21}$



PEG-PGMA$_{51}$



PEG-PGMA$_{68}$



PEG-PGMA$_{89}$

Fig. S1. ^{1}H NMR of PEG-PGMA in $CDCl_3$.

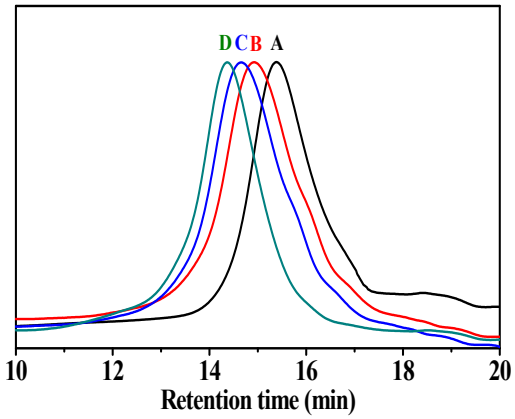
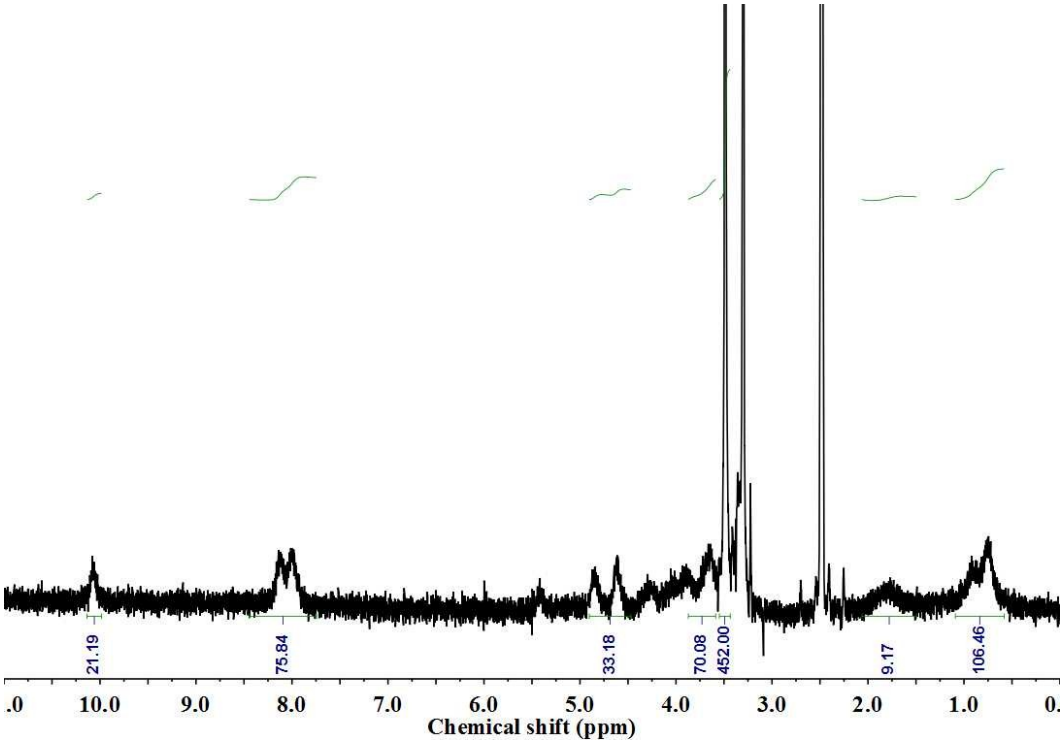
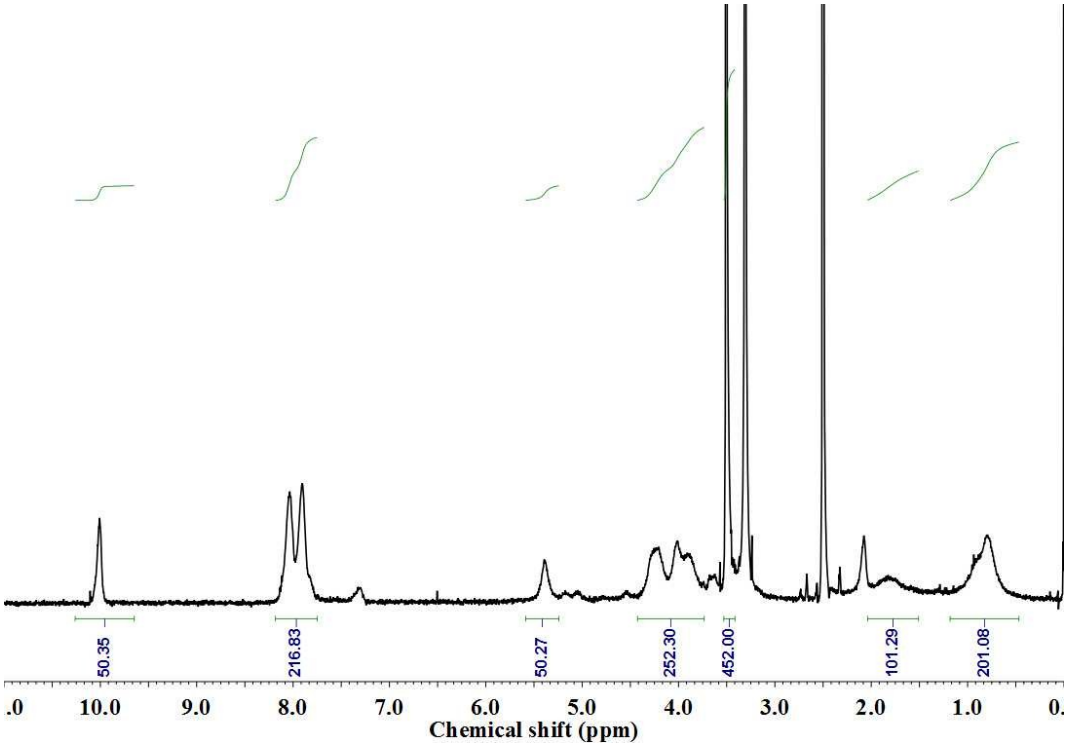


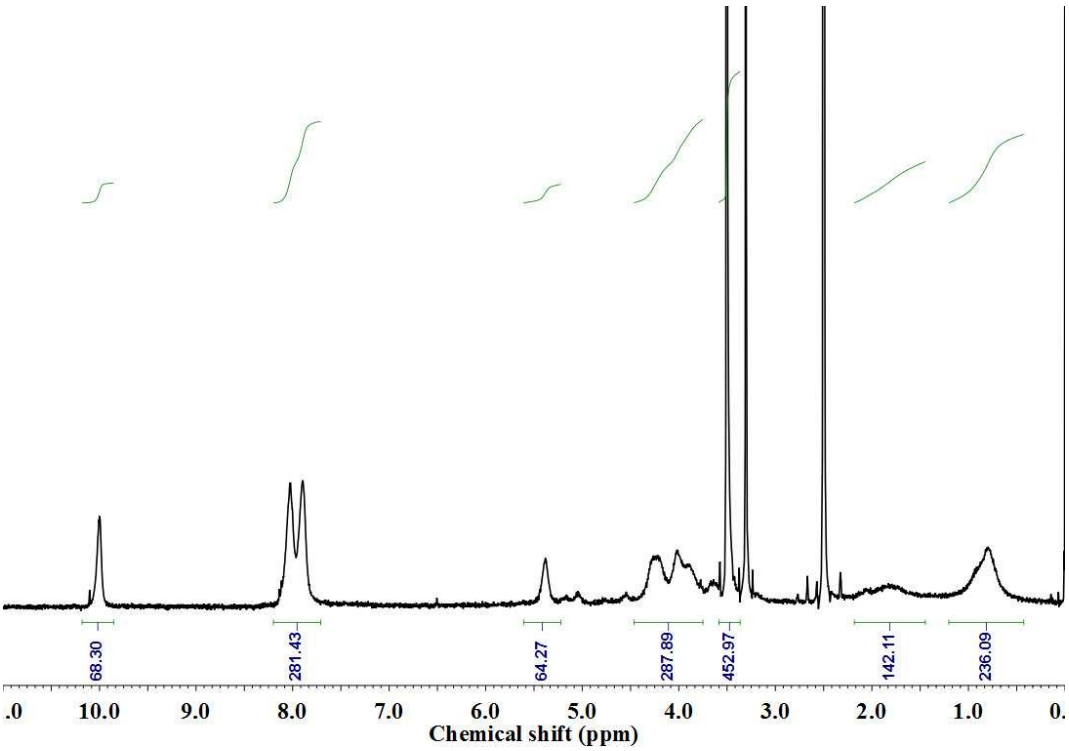
Fig. S2. GPC traces of the di-block copolymers: (A) PEG-PGMA$_{21}$, (B) PEG-PGMA$_{51}$, (C) PEG-PGMA$_{68}$, (D) PEG-PGMA$_{89}$.



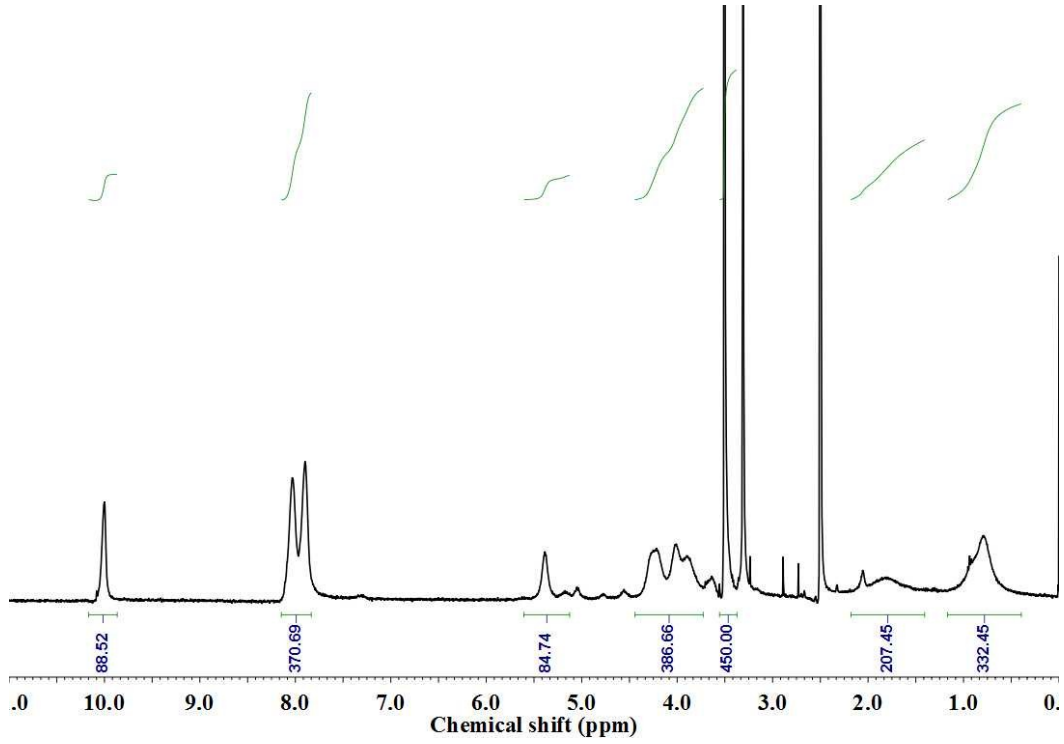
$PEG\text{-}P(GMA\text{-}CBA)_{21}$



$PEG\text{-}P(GMA\text{-}CBA)_{51}$



PEG-P(GMA-CBA)$_{68}$



PEG-P(GMA-CBA)$_{89}$

Fig. S3. ^{1}H NMR of PEG-P(GMA-CBA) in DMSO-d_6.

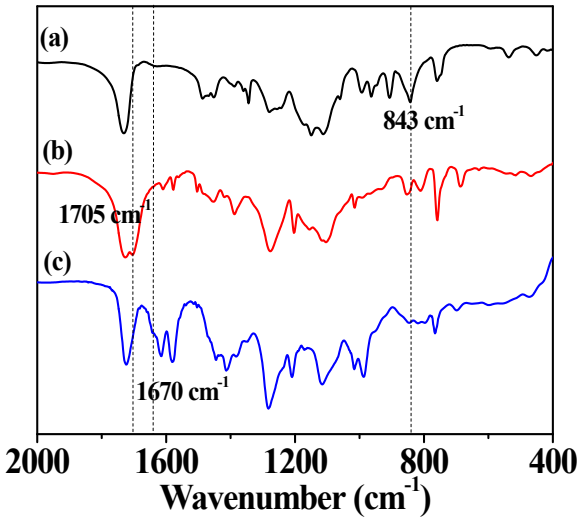
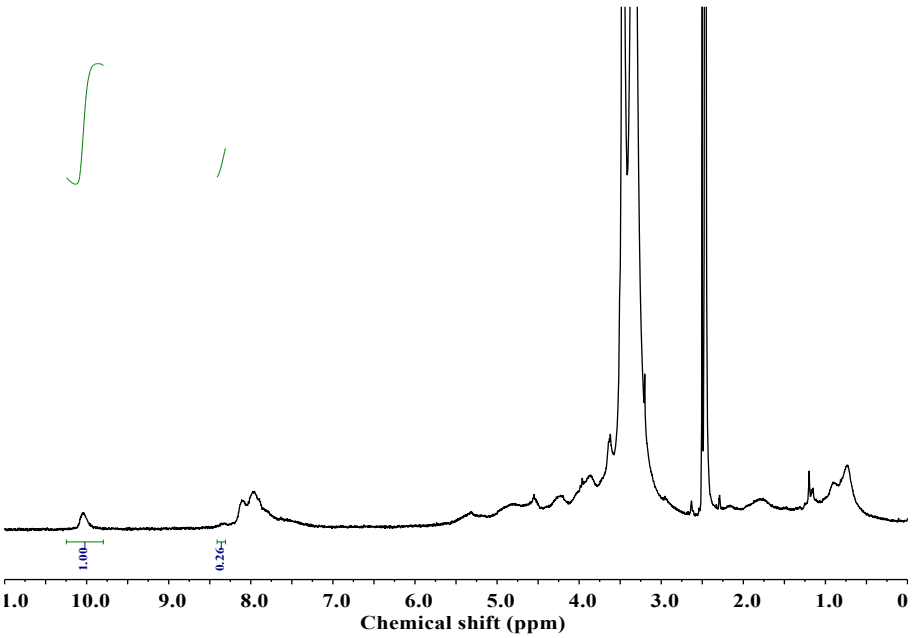
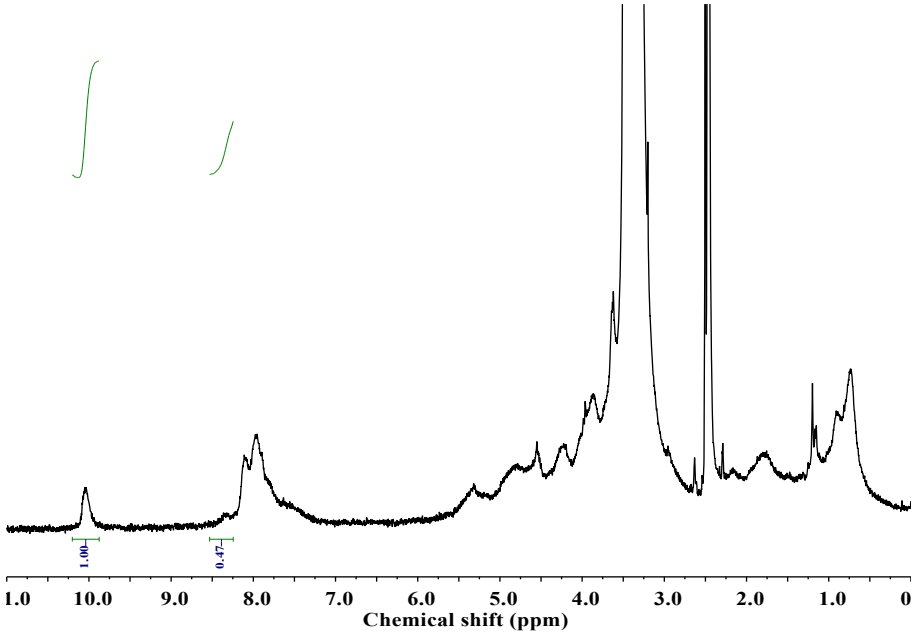


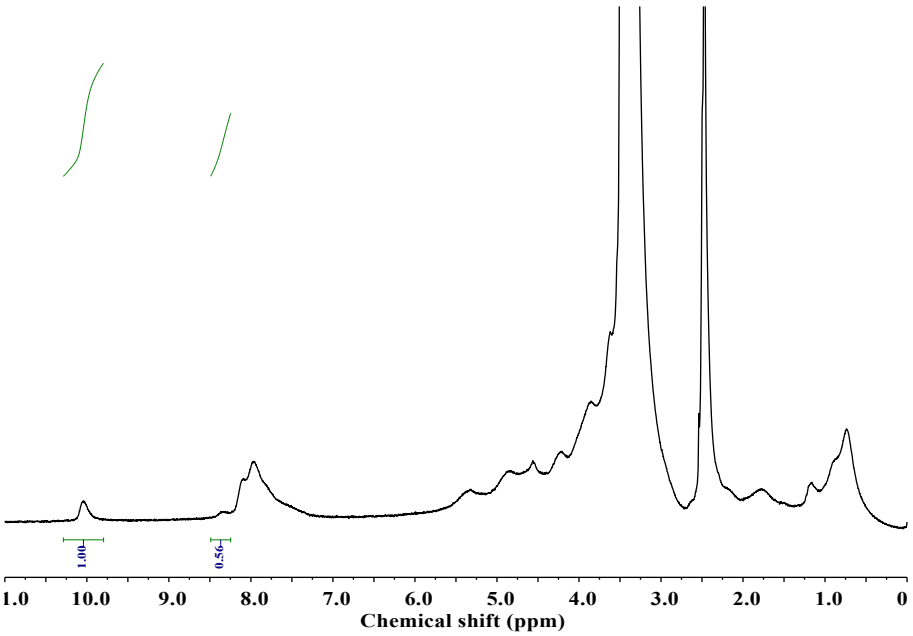
Fig. S4. FT-IR spectra of (a) PEG-PGMA$_{51}$, (b) PEG-P(GMA-CBA)$_{51}$ and (c) PEG-P(GMA-CBA)$_{51}$-DOX.



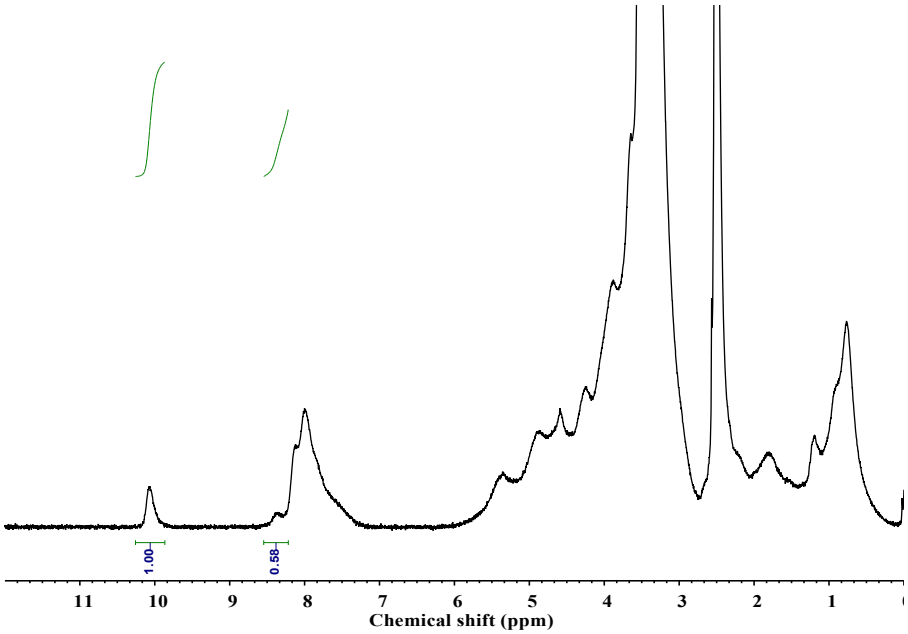
PEG-P(GMA-CBA)$_{21}$-DOX



PEG-P(GMA-CBA)$_{51}$-DOX



PEG-P(GMA-CBA)$_{68}$-DOX



PEG-P(GMA-CBA)$_{89}$-DOX

Fig. S5. ^{1}H NMR of PEG-P(GMA-CBA)$_{89}$-DOX in DMSO-d_6.

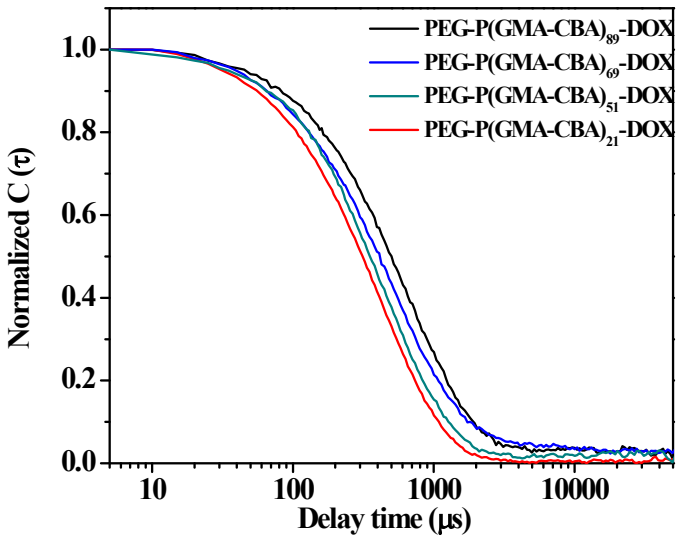
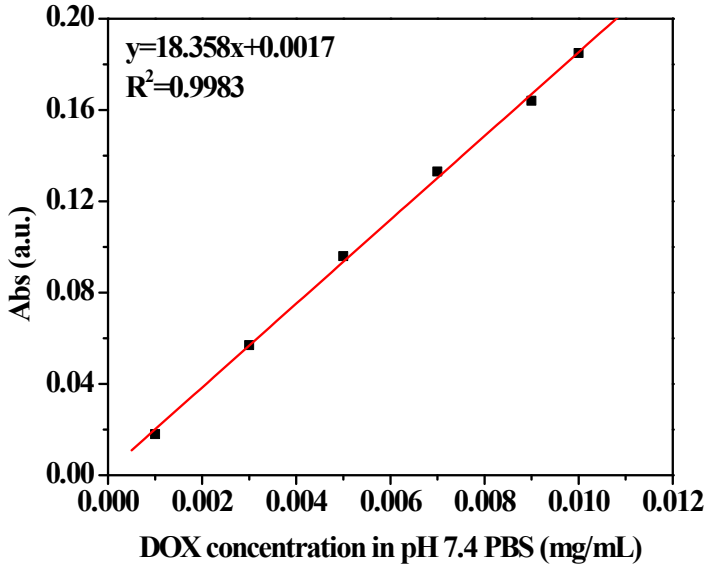


Fig. S6. Normalized ACF curves of the proposed polyprodrug nanoparticles.



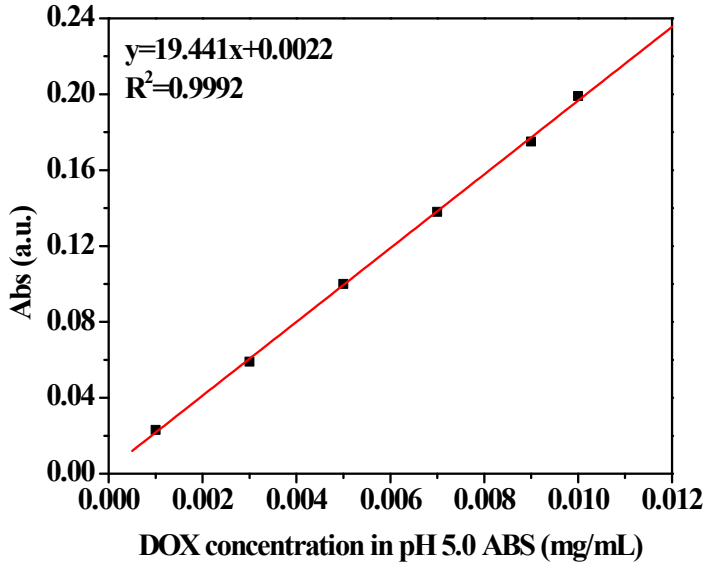


Fig. S7. The standard calibration curves of DOX in pH 7.4 PBS and pH 5.0 ABS measured by UV-vis spectra at 480 nm.