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Supporting Information

Preparation of photo-cross-linked pH-responsive polypeptide nanogels as potential carriers for controlled drug delivery

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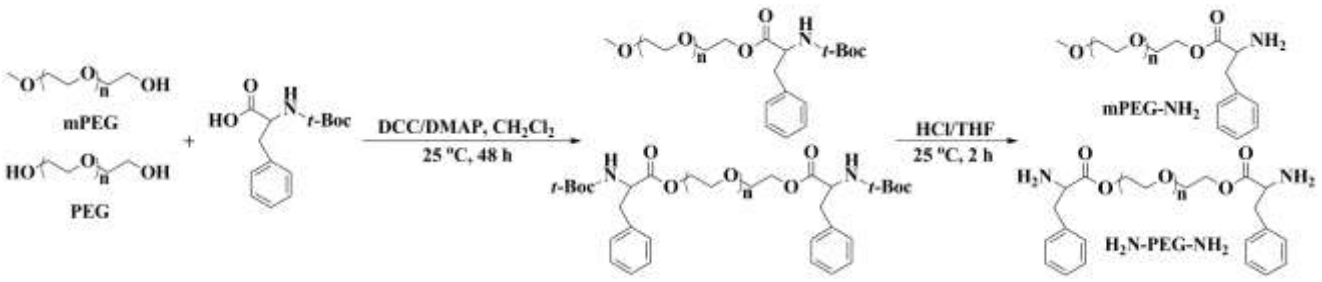
Scheme S1 Synthesis procedure for P(LGA/CLG)-*b*-PEG-*b*-P(LGA/CLG).

Synthesis of amino group terminated poly(ethylene glycol) monomethyl ether (mPEG-NH_2) and poly(ethylene glycol) (H_2N-PEG-NH_2) macroinitiator

$mPEG_{113}$-NH_2 and H_2N-PEG_{104}-NH_2 were synthesized by condensation reaction with dicyclohexylcarbodiimide (DCC)/4-*N*,*N*-dimethylaminopyridine (DMAP) as the coupling reagents and then the deprotection of *tert*-butoxycarbonyl (*t*-Boc) group as depicted in Scheme S2. Briefly, mPEG (M_n = 5000, 10.0 g, 2.0 mmol), *N*-(*tert*-Butoxycarbonyl)-L-phenylalanine (0.53 g, 2.0 mmol) and DMAP (24.43 mg, 0.2 mmol) were dissolved in 50 mL dry methylene chloride (CH_2Cl_2) in a flame-dry flask, then DCC (2.06 g, 10.0 mmol) in CH_2Cl_2 was added slowly to the solution with stirring and the reaction was conducted at room temperature for 48 h. The by-product dicyclohexylurea (DCU) precipitate was removed by filtration. Then, the solution was precipitated into excessive diethyl ether. The obtained product was further washed twice with diethyl ether and dried under vacuum at room temperature for 24 h (Yield: 96%). Subsequently, mPEG-NH-*t*-Boc (9.0 g, 1.72 mmol) was dissolved in 50 mL tetrahydrofuran (THF) at 25 ^oC in a flask. After 10 mL HCl/THF saturated solution was added, the solution was slowly stirred at 25 ^oC for 2 h and then the final product was precipitated into excessive diethyl ether and washed twice with diethyl ether. The precipitate was collected and dried under vacuum to a constant weight at room temperature. The yield was approximately 97%. The chemical structure of $mPEG_{113}$-NH_2 and H_2N-PEG_{104}-NH_2 were characterized by ^1H NMR and ^{13}C NMR, as shown in Fig. S1 and S2.



Scheme S2 Synthesis procedures for mPEG-NH_2 and H_2N-PEG-NH_2.

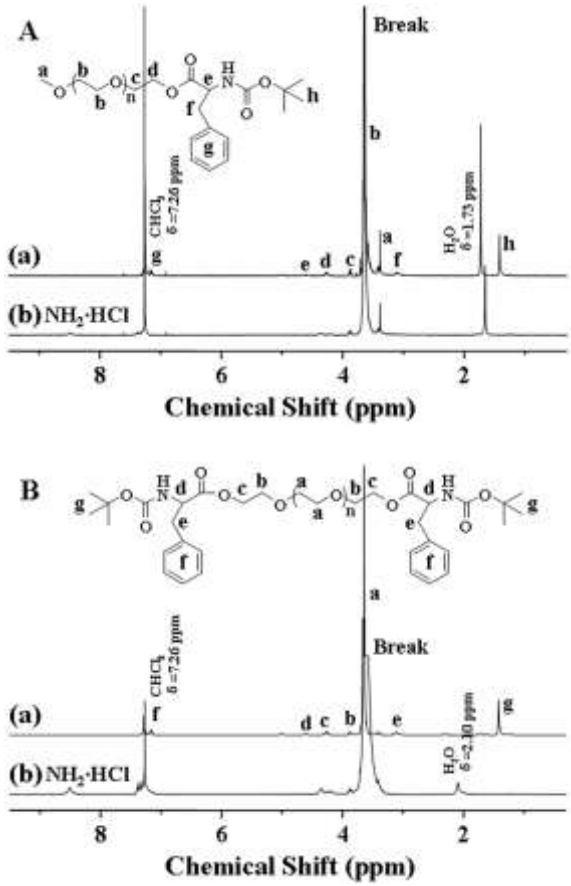


Fig. S1 ^{1}H NMR of macroinitiators before (a) and after (b) deprotection, $mPEG_{113}$ (A), and PEG_{104} (B) (in $CDCl_3$).

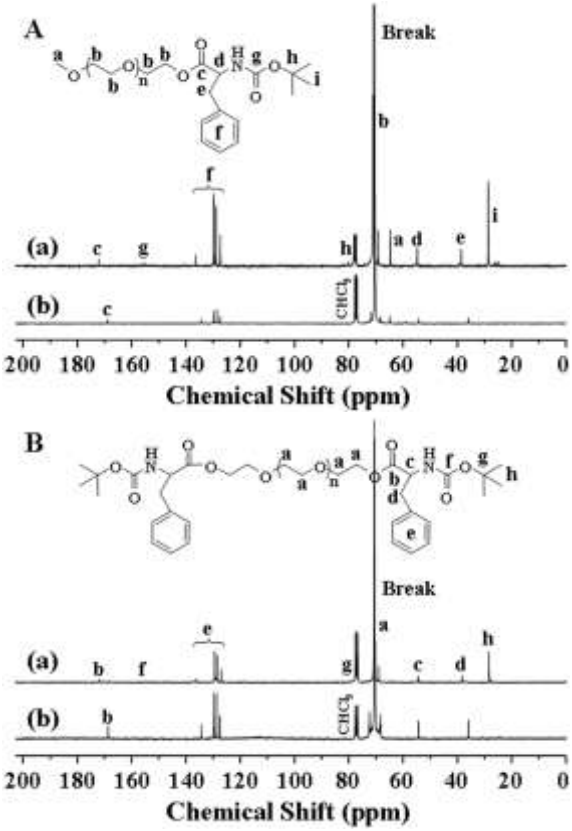


Fig. S2 ^{13}C NMR of macroinitiators before (a) and after (b) deprotection, $mPEG_{113}$ (A), and PEG_{104} (B) (in $CDCl_3$).

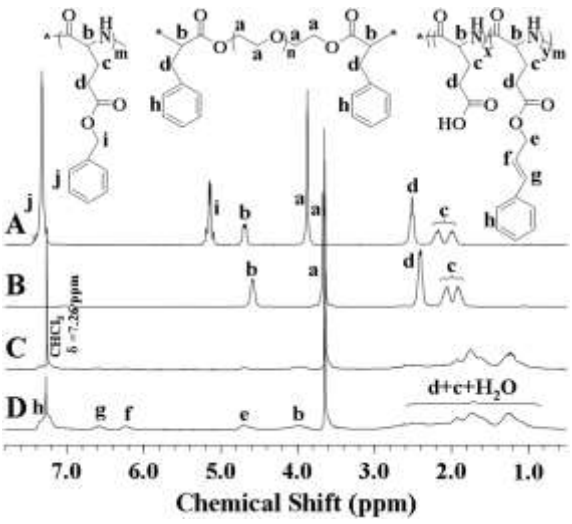


Fig. S3 ^{1}H NMR spectra of $PBLG_{106}$-*b*-PEG_{104}-*b*-$PBLG_{106}$ (A), PLG_{106}-*b*-PEG_{104}-*b*-PLG_{106} (B), $P(LGA_{87}/CLG_{19})$-*b*-PEG_{104}-*b*-$P(LGA_{87}/CLG_{19})$ **2** (C) and $P(LGA_{68}/CLG_{38})$-*b*-PEG_{104}-*b*-$P(LGA_{68}/CLG_{38})$ **3** (D) (in CF_3COOD+$CDCl_3$ (1/1, v/v) for (A), CF_3COOD for (B), and $CDCl_3$ for (C) and (D)).

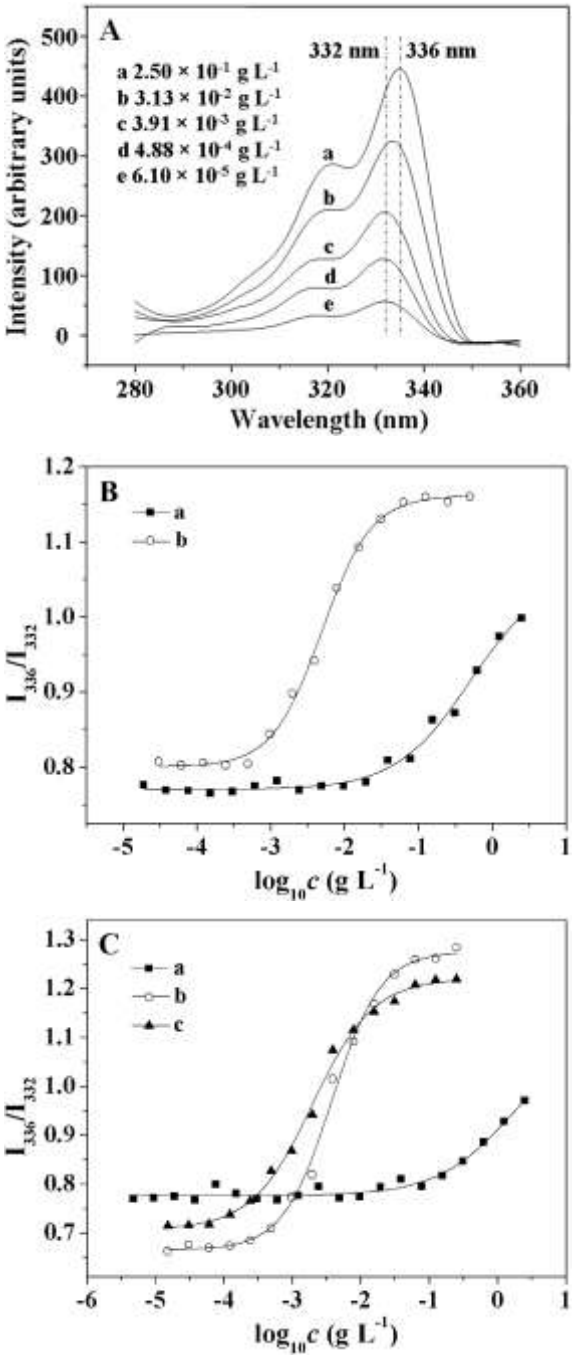


Fig. S4 Excitation spectra of pyrene in aqueous solution of mPEG$_{113}$-*b*-P(LGA$_{73}$/CLG$_{37}$) at different concentrations (λ_{em} = 390 nm) (A), the intensity ratio (I_{336}/I_{332}) as a function of concentration of mPEG$_{113}$-*b*-PLGA$_{110}$ (a) and mPEG$_{113}$-*b*-P(LGA$_{73}$/CLG$_{37}$) (b) (B), and PLGA$_{106}$-*b*-PEG$_{104}$-*b*-PLGA$_{106}$ (a), P(LGA$_{87}$/CLG$_{19}$)-*b*-PEG$_{104}$-*b*-P(LGA$_{87}$/CLG$_{19}$) (b) and P(LGA$_{68}$/CLG$_{38}$)-*b*-PEG$_{104}$-*b*-P(LGA$_{68}$/CLG$_{38}$) (c) (C).

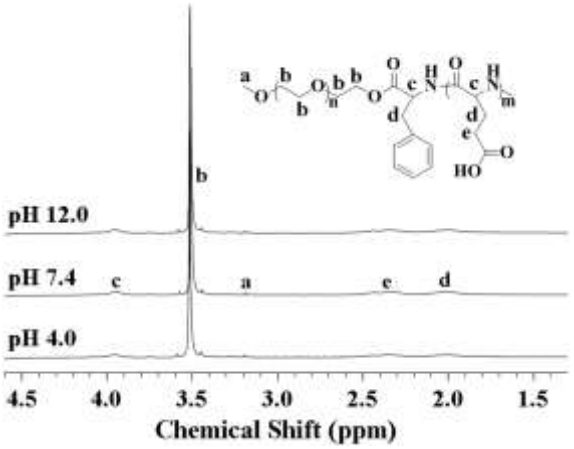


Fig. S5 ^{1}H NMR spectra of mPEG$_{113}$-*b*-PLGA$_{110}$ at pH 4.0, 7.4, and 12.0 (in D_2O).

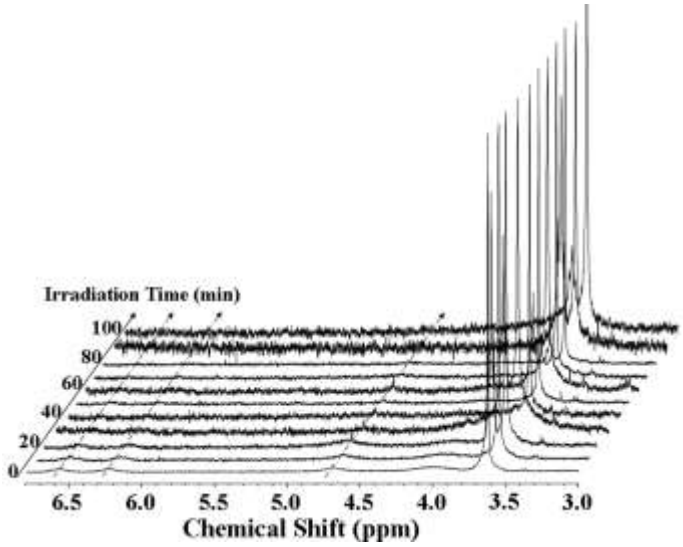


Fig. S6 Change in the ^{1}H NMR spectra of mPEG$_{113}$-*b*-P(LGA$_{73}$/CLG$_{37}$) **1** as a function of irradiation time (in $CDCl_3$) (nanogels were prepared in aqueous solution at pH 7.4).

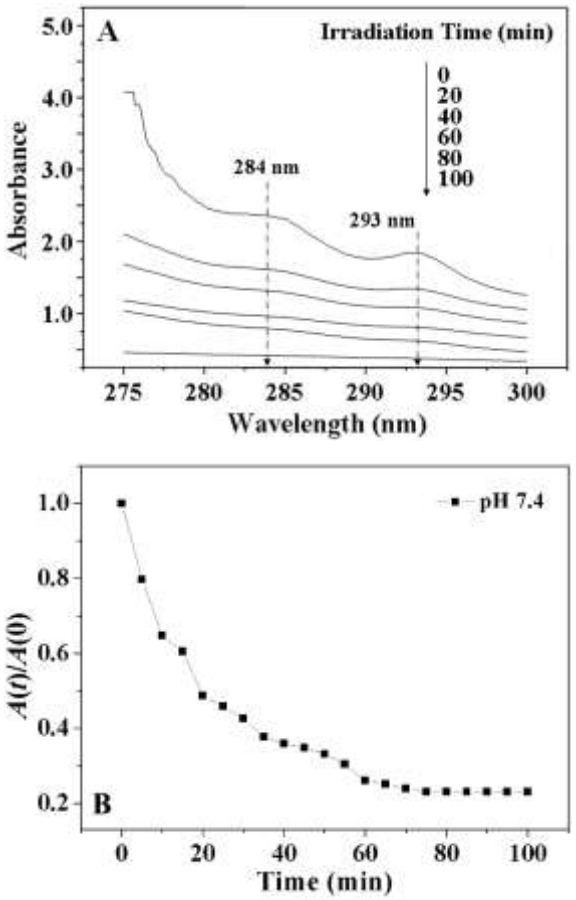


Fig. S7 UV-vis spectra of P(LGA$_{87}$/CLG$_{19}$)-*b*-PEG$_{104}$-*b*-P(LGA$_{87}$/CLG$_{19}$) aqueous solution of 0.5 g L^{-1} at pH 7.4 subjected to UV irradiation at λ = 254 nm as a function of irradiation time (A), decrease in $A(t)/A(0)$ for the cinnamyl residues determined from the UV-vis absorption spectra at pH 7.4 plotted as a function of irradiation time (B).

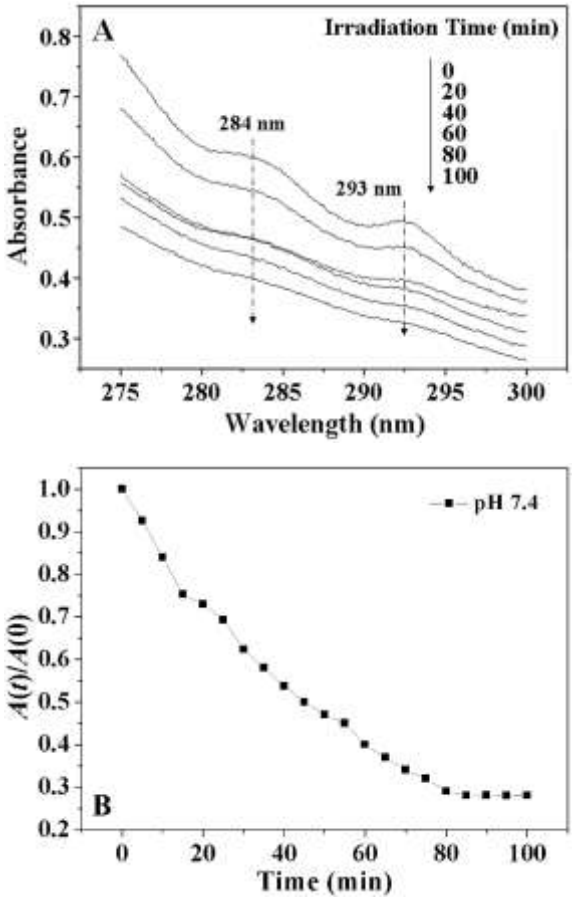
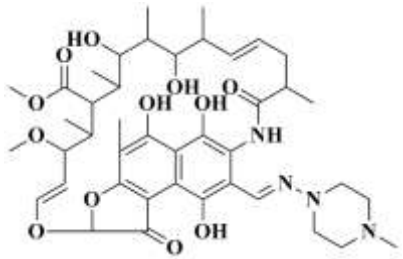


Fig. S8 UV-vis spectra of P(LGA$_{68}$/CLG$_{38}$)-*b*-PEG$_{104}$-*b*-P(LGA$_{68}$/CLG$_{38}$) aqueous solution of 0.5 g L^{-1} at pH 7.4 subjected to UV irradiation at λ = 254 nm as a function of irradiation time (A), decrease in $A(t)/A(0)$ for the cinnamyl residues determined from the UV-vis absorption spectra at pH 7.4 plotted as a function of irradiation time (B).



Scheme S3 Chemical structure of rifampin.

The rifampin chemical structure was used to explain the release behavior as an ancillary factor.