Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supplementary Information

Synthesis of Thermal and Oxidation Dual Responsive Polymer for Reactive Oxygen Species (ROS)-Triggered Drug Release

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Synthesis of PEGDA1k. To a solution of PEG800 (8.0 g, 10 mmol) in 150 mL of methylene dichloride was added 10 g of K_2CO_3. The suspension was stirred at 0 °C, to which 3.0 mL of acryloyl chloride (37.1 mmol) was added dropwisely. The reaction mixture was allowed to stir at room temperature for 48 h. Subsequently, the mixture was filtrated through a shot column of basic alumina. The filtrate was concentrated by rotary evaporation and precipitated into excess cold ethyl ether. The white solid was obtained after filtration and dried under reduced pressure. Yield 5.1 g (56%). The structure of PEGDA1k was characterized by ^{1}H NMR (300 MHz) and MALDI-TOF MS. Both the ^{1}H NMR and MALDI-TOF MS spectra confirmed the successful synthesis of PEGDA1k (Figure S1). The molecular weight calculated from ^{1}H NMR spectrum was 1054.4 g/mol, while that from MALDI-TOF MS (data was analyzed by Bruker Daltonics flexAnalysis 3.3.80 and PloyTools V1.0 software) was 1015 g/mol (PDI=1.02). The molecular weight obtained from both ^{1}H NMR and MALDI-TOF MS characterizations were slightly higher than the theoretical value (M_n = 822 + 108 = 930 g/mol) of the product generated from PEG800 and acryloyl chloride. This should be ascribed to the possible loss of low molecular weight polymers during the precipitation procedure. Based on these characterizations, the resulting PEGDA was finally denoted as PEGDA1k.

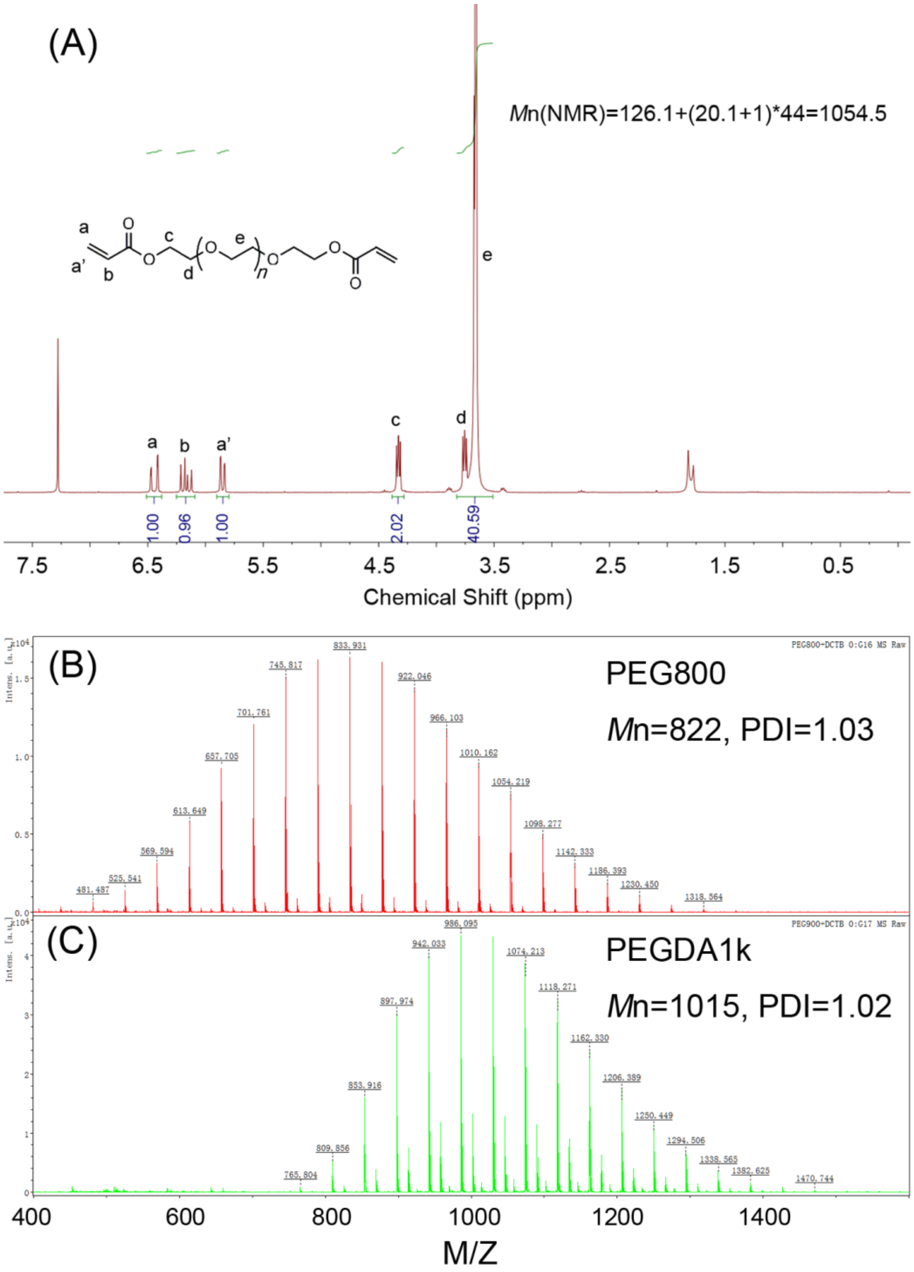

Figure S1. (A)^{1}H NMR spectrum of PEGDA1k in $CDCl_3$, and MALDI-TOF MS of PEG800 (B) and PEGDA1k (C).

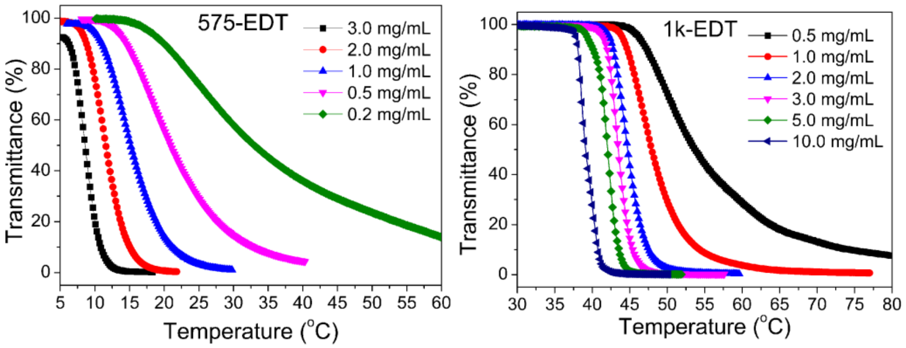

Figure S2. Temperature-dependent transmittance of 575-EDT and 1k-EDT in deionized water with different concentrations.

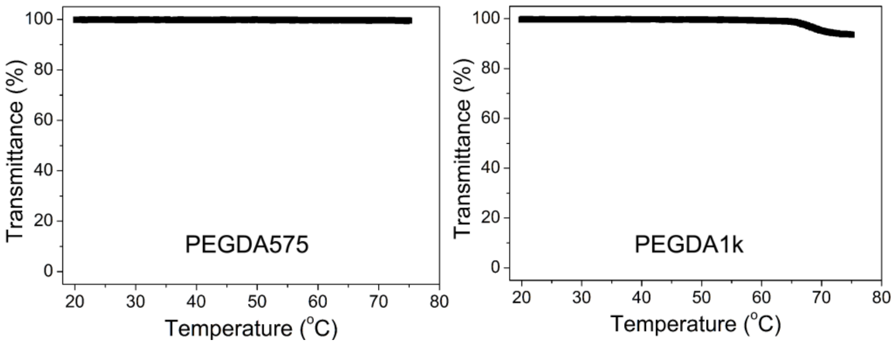

Figure S3. Temperature-dependent transmittance of PEGDA monomers in deionized water (5.0 mg/mL).

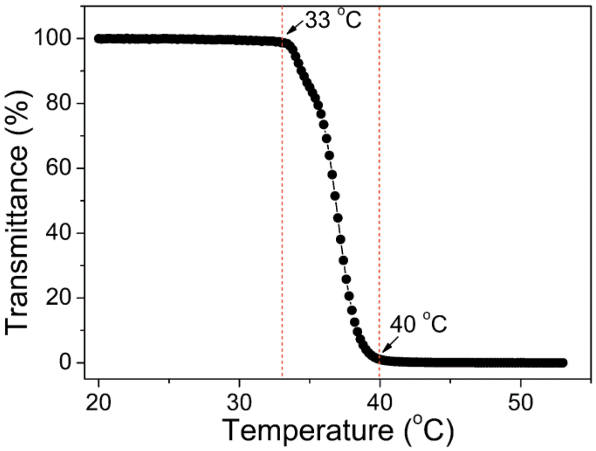

Figure S4. Temperature-dependent transmittance of 1k-EDT in D_2O (5.0 mg/mL).

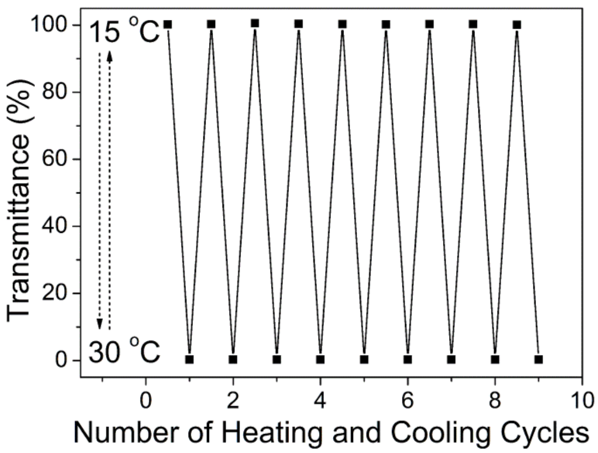

Figure S5. Light transmittance variation of 700-EDT in deionized water (3.0 mg/mL) under repeated heating and cooling cycles.

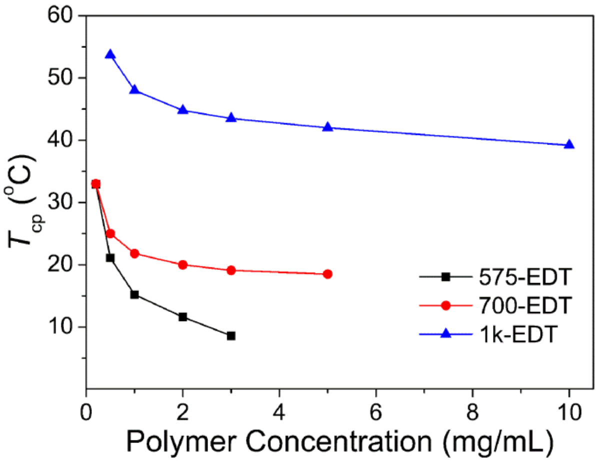

Figure S6. Plots of cloud point temperature (T_{cp}) as function of polymer concentration in deionized water.

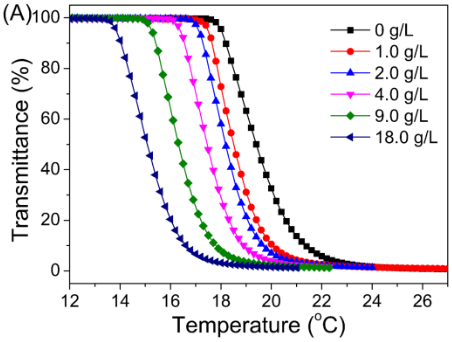

Figure S7. Turbidimetric assay of 700-EDT in deionized water (2.0 mg/mL), with the presence of NaCl.

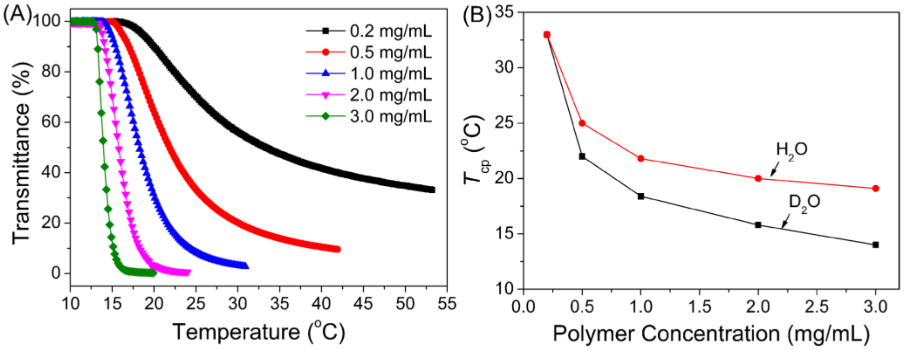

Figure S8. Turbidimetric assay of 700-EDT in D_2O at varied concentrations.

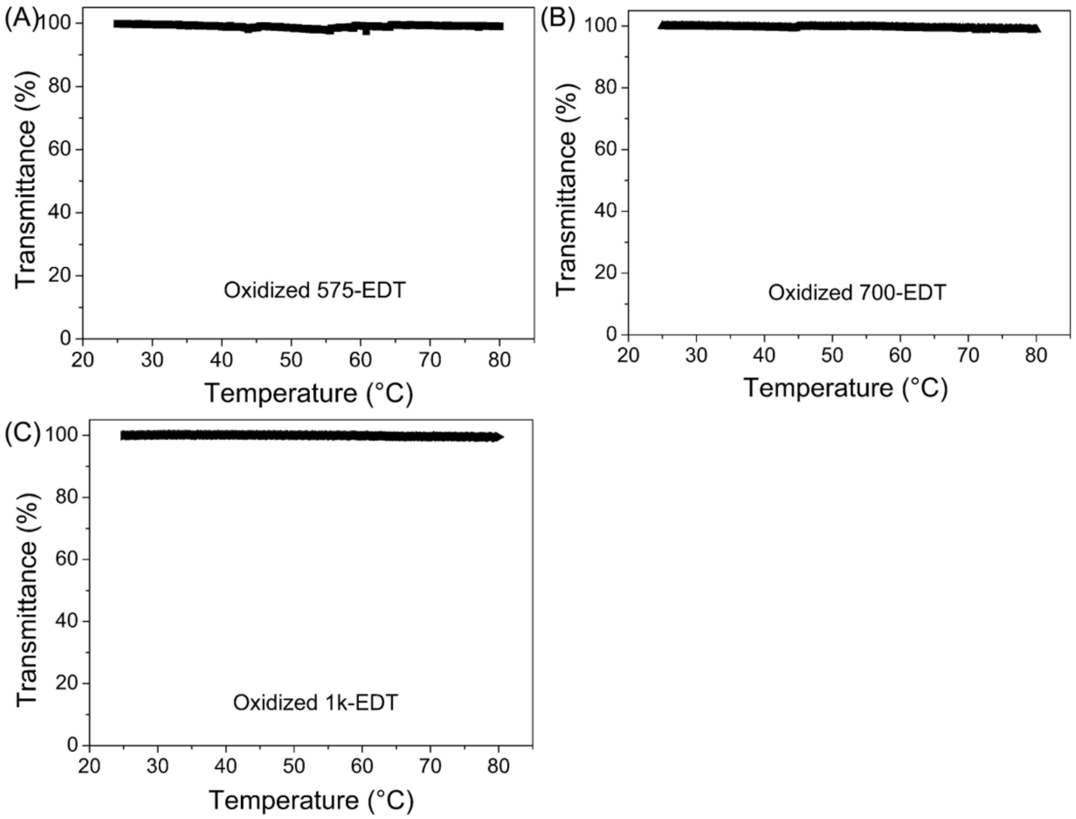

Figure S9. Turbidimetric assay of oxidized PEG-EDT copolymers in deionized water (2.0 mg/mL). The oxidized PEG-EDT copolymers were obtained by incubation of PEG-EDT copolymers solution (2.0 mg/mL) with H_2O_2 at a $[H_2O_2]/[S] = 4.0$ for 24 h (37 °C).

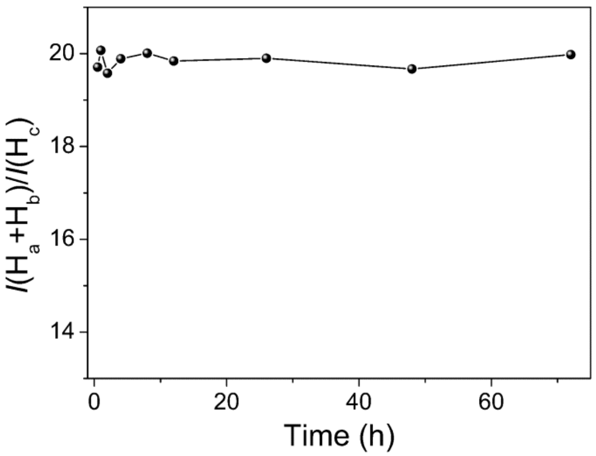

Figure S10. Plot of integral ratio of methylene *a* + *b* to methylene *c* vs. time. $[H_2O_2]/[S] = 4.0$.

Discussion. If the ester bond scissions occurred during the oxidation of 1k-EDT by H_2O_2, the integral of methylene *c* (−C*H*$_2$OC(O)−) would decrease and the integral of methylene *a* + *b* (attributed to the ethylene groups in PEG segment) would increase, which led to an increase of integral ratio of methylene *a* + *b* to methylene *c*. However, as shown in Figure S9, the integral ratio of methylene *a* + *b* to methylene *c* almost remained constant during the whole oxidation process. And the integral ratio of methylene *a* + *b* to methylene *c* is 19.98 at 72 h, which is close to value (20.09) that calculated from Figure S1 A. All these results demonstrated that there was no detectable ester bond scissions occurred during the oxidation of 1k-EDT by H_2O_2.

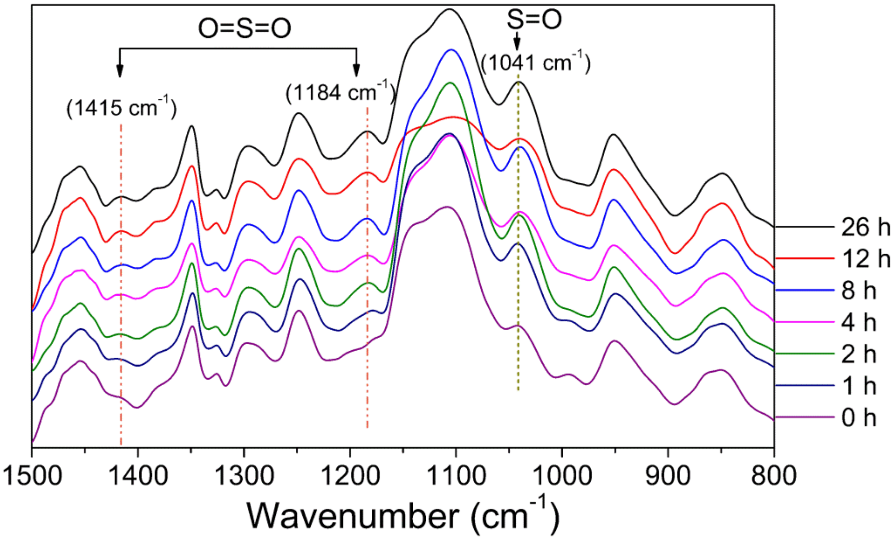

Figure S11. FT-IR spectra of 1k-EDT after oxidation with H_2O_2 in water at 37 °C. $[H_2O_2]/[S] = 4.0$. The present data were normalized against C-H stretching bend (methylene) at 1868 cm^{-1}.[1]

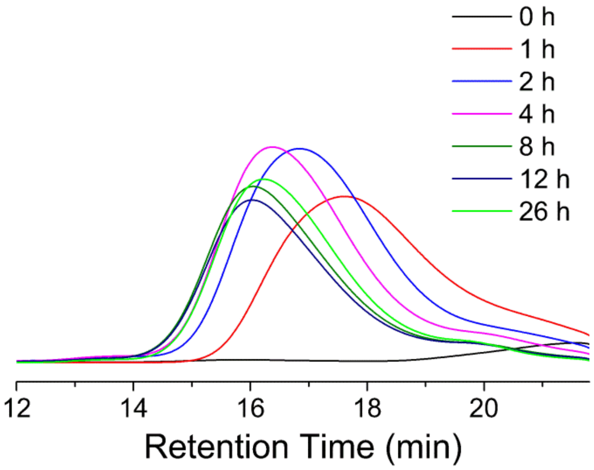

Figure S12. Aqueous GPC curves of 1k-EDT after oxidation with H_2O_2 in water at 37 °C. $[H_2O_2]/[S] =$ 4.0.

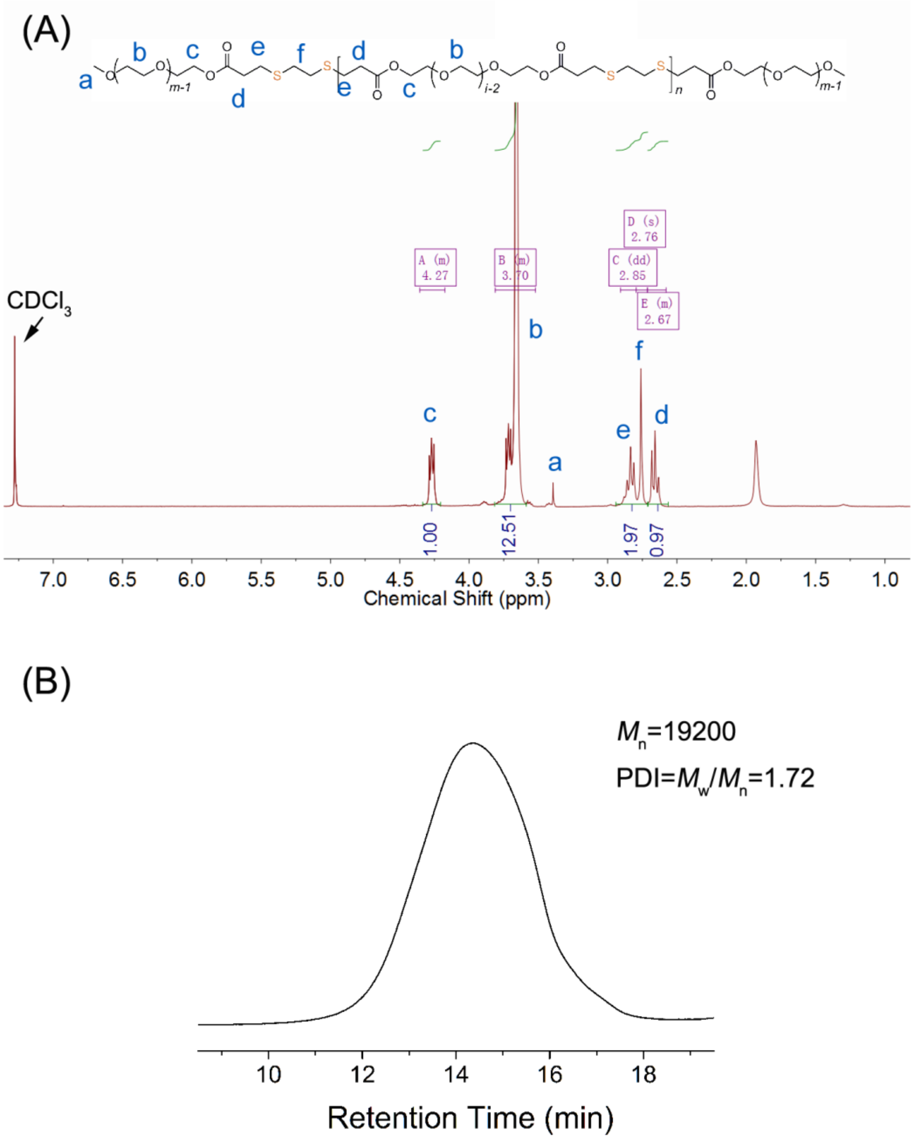

Figure S13. (A) ^{1}H NMR spectrum and (B) GPC trace in $CHCl_3$ (1.0 mL/min, at 35 °C) of mPEG-*b*-575EDT-*b*-mPEG.

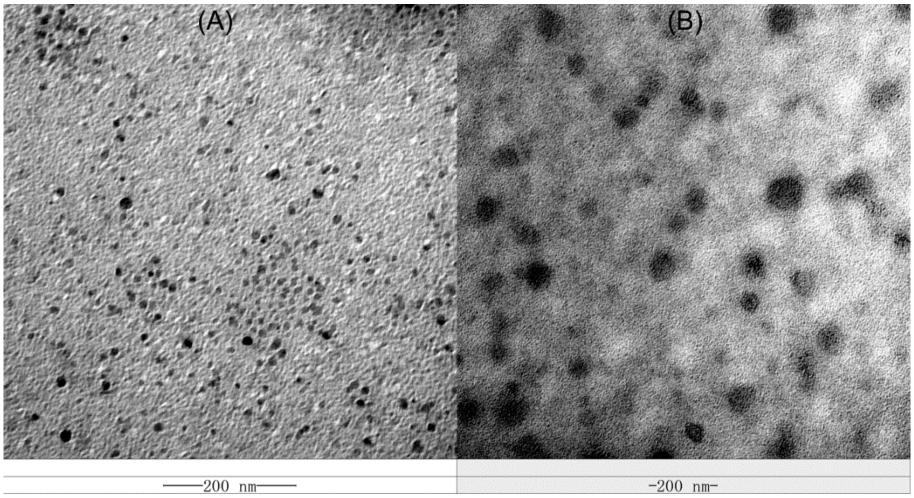

Figure S14. TEM images of mPEG-*b*-575EDT-*b*-mPEG nanoparticles at (A) 37 °C and (B) room temperature (*ca.* 16   23 °C). The polymer concentration used for fabricating the TEM samples was 0.5 mg/mL. And the sizes (diameter) of mPEG-*b*-575EDT-*b*-mPEG nanoparticles analyzed by ImageJ 1.48 software were 14.3 ± 3.23 and 76.6 ± 14.9 nm for (A) and (B), respectively. The scale bars were showed at the button of the images.

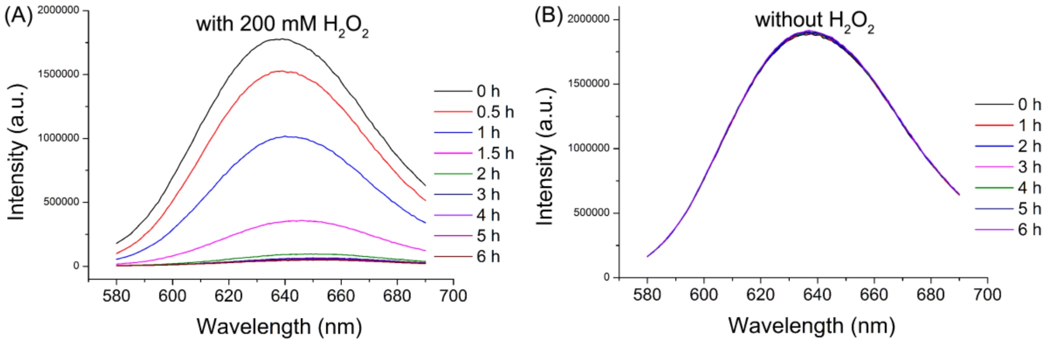

Figure S15. Changes of fluorescence intensity of Nile Red loaded nanoparticles with or without treatment with H_2O_2.

REFERENCES

(1) Carampin, P.; Lallana, E.; Laliturai, J.; Carroccio, S. C.; Puglisi, C.; Tirelli, N. *Macrom. Chem. Phys.* **2012,** 213, 2052-2061.