Electronic Supplementary Information (ESI)

Temperature-Regulated Aggregation-Induced Emissive Self-Healable Hydrogel for Controlled Drug Delivery

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S1. Synthesis of TPE-2OH.

First, TPE with two phenolic hydroxyl groups (TPE-2OH) was synthesized according to literature.[1] 4-hydroxybenzophenone (2.0 g, 10 mmol) and Zinc dust (2.9 g, 44 mmol) were put into a 250 mL, two-necked, round-bottom flask equipped with a condenser. The oxygen in flask was removed under vacuum and filled with nitrogen for three cycles. After addition of 100 mL anhydrous THF, the mixture was cooled to 0 °C and 2.5 mL $TiCl_4$ (22 mmol) was slowly injected to the flask. The mixture was warmed gradually to room temperature and then refluxed overnight. The reaction was quenched by 10% K_2CO_3 solution and the product was extracted with CH_2Cl_2 three times. The organic phase was washed with saturated NaCl solution 3 times and dried by anhydrous $MgSO_4$ overnight. After solvent evaporation, the crude product was purified on a silica-gel column using petroleum ether/ethyl acetate (v/v 1:1) as eluent. A yellow solid of TPE-2OH was obtained with about 75% yield (1.38 g). ^{1}H NMR (400 MHz, DMSO-d6): 7.04-7.17 (m, 6H), 6.92-6.97 (m, 4H), 6.70-6.75 (m, 4H), 6.47-6.53 (m, 4H).

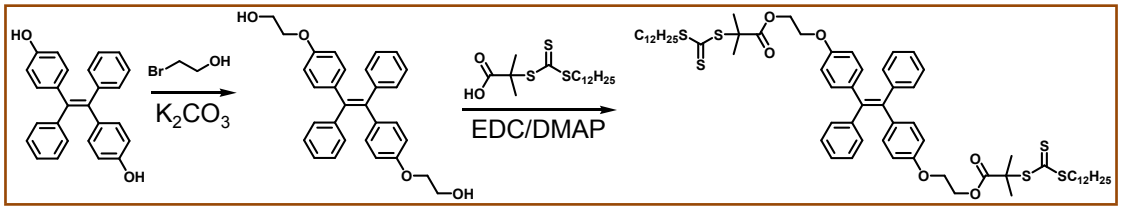
S2. Synthesis of TPE diethanol.

Then TPE-2OH(1.456 g, 4.0 mmol) was reacted with 2-bromoethanol to prepare TPE diethanol as illustrated in Scheme 1.[2] TPE-2OH (1.09g, 3 mmol) and 2-bromoethanol (1.48 g, 12 mmol) were dissolved in 20 mL DMF in a 50 mL flask, then 1.66 g (12 mmol) K_2CO_3 was added into the flask and the oxygen inside the flask was removed with nitrogen. Then the flask was immersed into a 60 ^{o}C oil bath and the reaction was performed for 24 h. After the mixture was cooled to room temperature, saturated NaCl solution was added to dissolve the K_2CO_3 and the solution was extracted with CH_2Cl_2 (20 mL×5). The organic phase was combined and washed extensively 5 times with saturated NaCl solution to remove 2-bromoethanol. Then the organic phase was dried by anhydrous $MgSO_4$ overnight. The excess solvent was removed by rotary evaporator, and the crude product was purified on a silica-gel column using petroleum ether/CH_2Cl_2 (1/1) (1.08g, ~60% yield). ^{1}H NMR (600 MHz, $CDCl_3$): 7.12-7.05 ppm (m, 4H), 6.93-7.05 ppm (m, 4H), 6.90-6.85 ppm (m, 2H), 6.58-6.53 ppm (m, 2H), 3. 92 ppm (t, 2H), 3.54 ppm (t, 2H).

S3. Synthesis of TPE-2DDMAT.

The TPE-2DDMAT was prepared by condensation of TPE diethanol and DDMAT with DMPA as catalyst and EDC.HCl as dehydrant (Scheme S1).[3] 0.90 g (2.0 mmol) TPE diethanol and 2.18 g DDMAT (12 mmol) were dissolved in 25 mL anhydrous CH_2Cl_2. Then 20 mg DMAP was added as catalyst and 1.15 g EDC.HCl was added as dehydrant. The

mixture was stirred for 24 h at room temperature. The product was washed with $NaHCO_3$ solution 5 times. After dried by anhydrous $MgSO_4$, the organic phase was concentrated on a rotary evaporator and purified by silica column with petroleum ether/ethyl acetate (7/3) as eluent. TPE-2DDMAT was obtained as range liquid after dried under vacuum (1.48 g ~65% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.12-6.75 (m, 18H, CH(ph)), 5.30 (t, 4H, CH_2OCO), 4.72 (t, 4H, OCH_2), 3.29 (t, 4H, SCH_2), 1.80 (s, 12H, $C(CH_3)_2$).



Scheme S1. Synthesis procedure of TPE-2DDMAT.

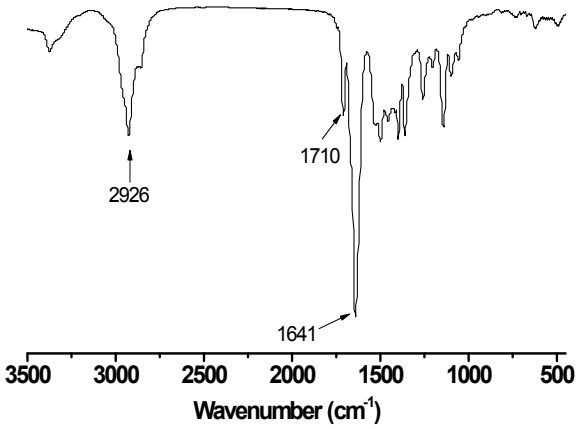


Fig. S1 FT-IR spectrum of TPE-[P(DMA_{94}-*stat*-DAA_{30})]$_2$ (casted on KBr pellet).

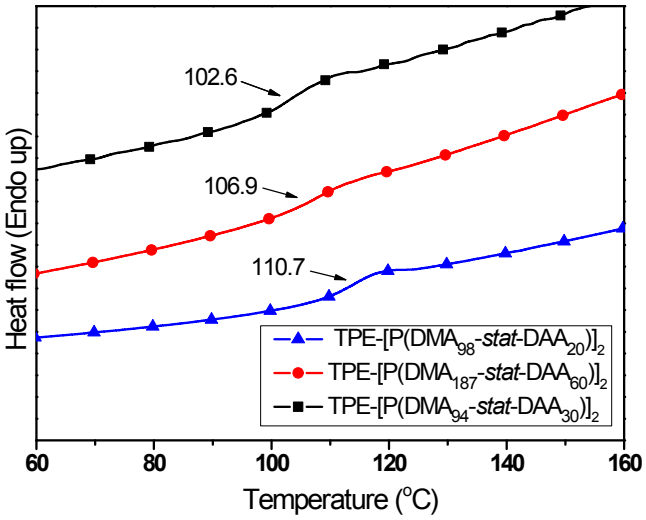


Fig. S2 DSC Curves of the TPE-[P(DMA-*stat*-DAA)]$_2$.

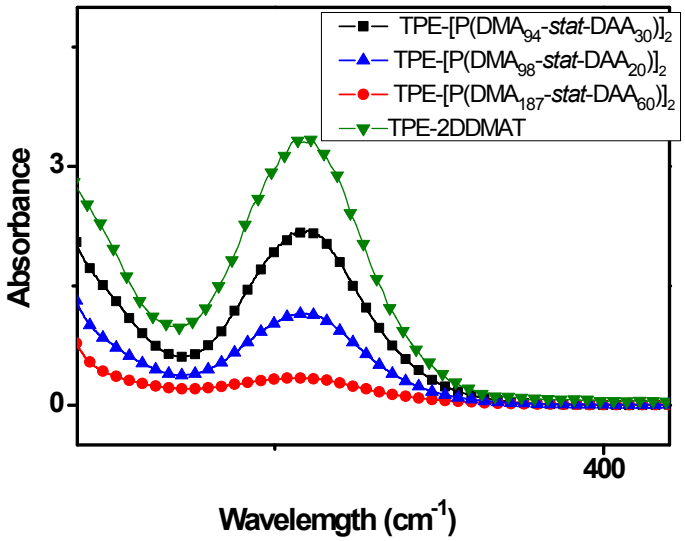


Fig. S3 UV spectra of TPE-2DDMAT solution (in CH_2Cl_2) and TPE-[P(DMA-*stat*-DAA)]$_2$ water solution.

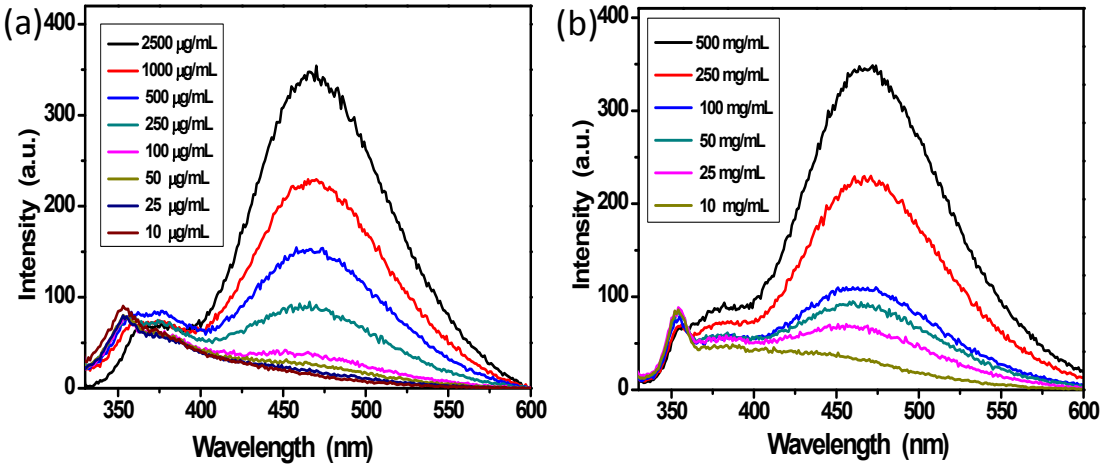


Fig. S4 Fluorescence spectra of polymer TPE-[P(DMA_{187}-*stat*-DAA_{60})]$_2$ (a) and TPE-[P(DMA_{98}-*stat*-DAA_{20})]$_2$ (b) at various concentration.

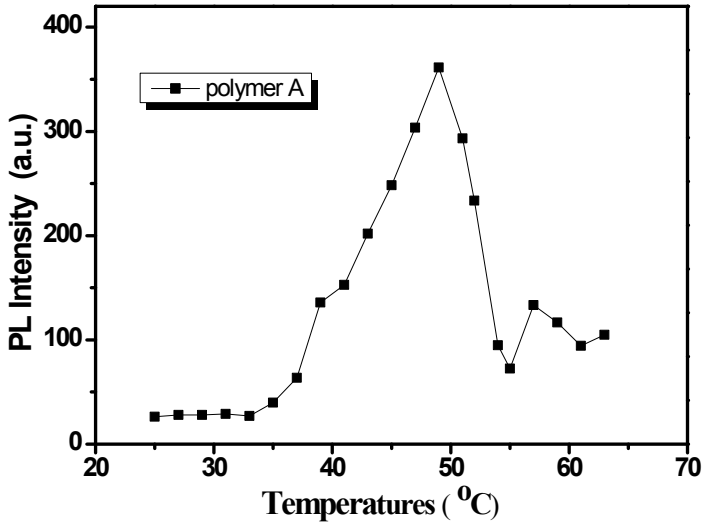


Fig. S5 PL intensity of 1% TPE-[P(DMA_{94}-*stat*-DAA_{30})]$_2$ solution with increasing temperatures.

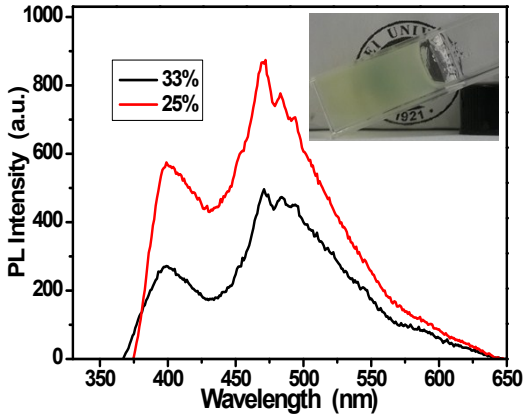


Fig. S6 Fluorescence spectra of hydrogels prepared from TPE-[P(DMA$_{94}$-*stat*-DAA$_{30}$)]$_2$ with low ratio of DTDPH cross-linking (the insert is optical image of 25% ratio of cross-linking).

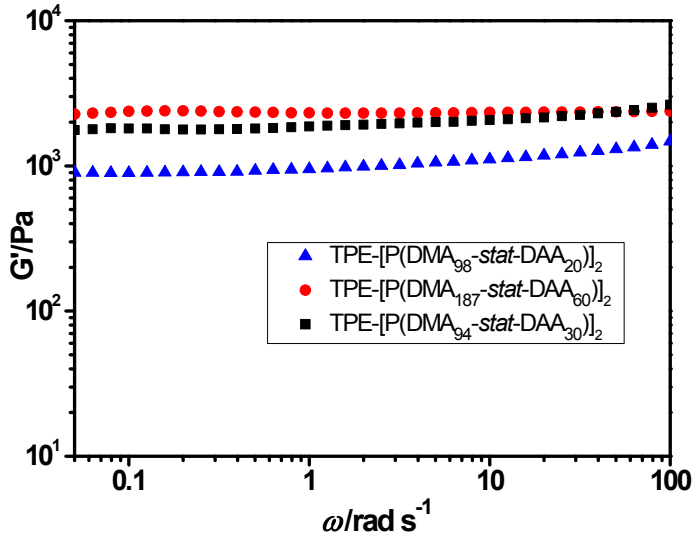


Fig. S7 Comparison of G′ of the hydrogels prepared from different copolymers with POE$_{23}$ DH cross-linking.

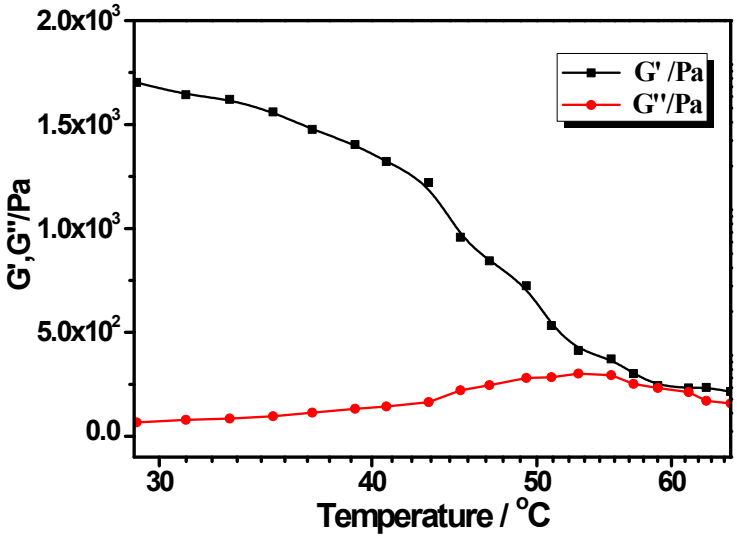


Fig. S8 Rheology curve of POE_{23} DH cross-linked TPE-[P(DMA_{94}-*stat*-DAA_{30})]$_2$ hydrogel under temperature scan.

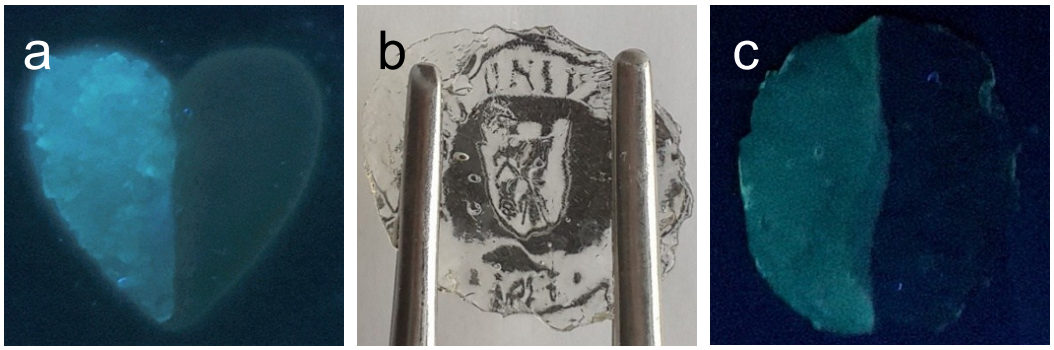


Fig. S9 TPE-[P(DMA_{94}-*stat*-DAA_{30})]$_2$ hydrogel with PEO_{23} DH cross-linking was cut into small particles and put into the heart shaped mould with half hydrogel prepared from P(DMA_{93}-*stat*-DAA_{30}) (a); self-healed hydrogel disk prepared from TPE-[P(DMA_{98}-*stat*-DAA_{20})]$_2$ with P(DMA_{93}-*stat*-DAA_{30}) hydrogel under room light (b) and 365 nm UV exposure (c).

Fig. S10 Group ratio triggered gel-sol-gel transition of the hydrogel prepared from TPE- TPE-[P(DMA_{94}-*stat*-DAA_{30})]$_2$ with PEO_{23} DH cross-linking. (Credit from Hebei University)

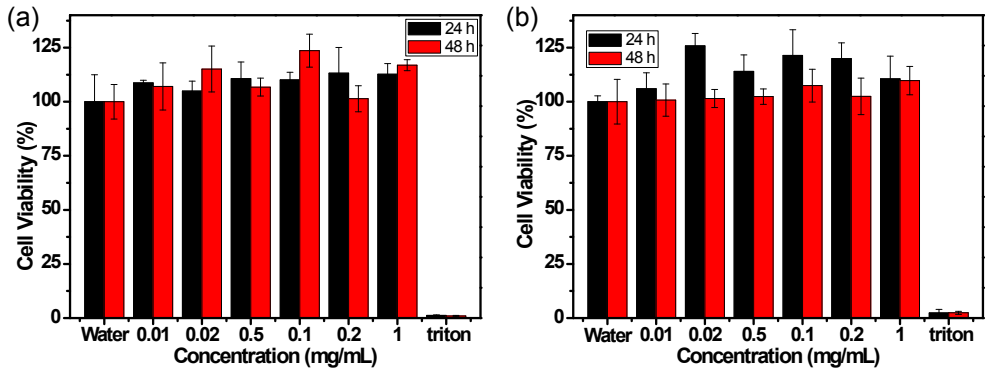


Fig. S11 In vitro cytotoxicity of TPE-[P(DMA$_{98}$-*stat*-DAA$_{20}$)]$_2$ and PEO$_{23}$ DH solution with various concentration to HeLa cell (a) and JB6 P+ cells (b).

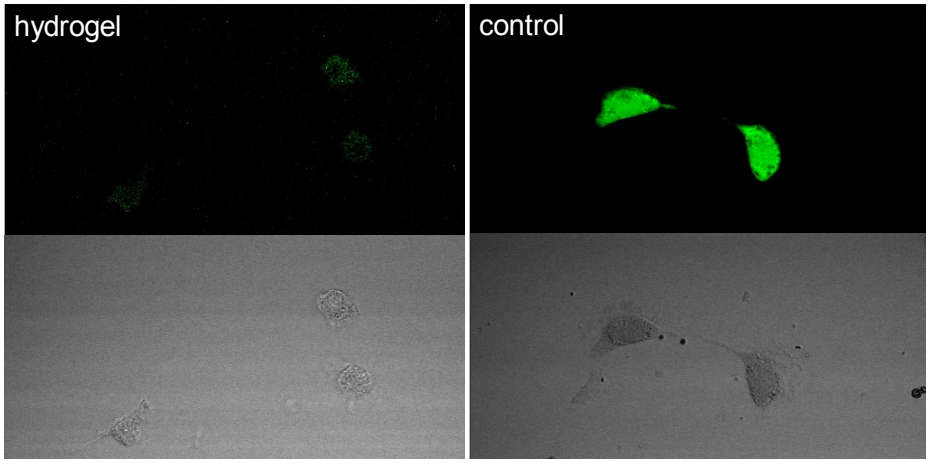


Fig. S12 Confocal microscopy images of the JB6 P+ cell in hydrogel prepared from TPE-[P(DMA$_{94}$-*stat*-DAA$_{30}$)]$_2$ with PEO$_{23}$ DH cross-linking (magnification: ×60. The control is the pure culture-medium).

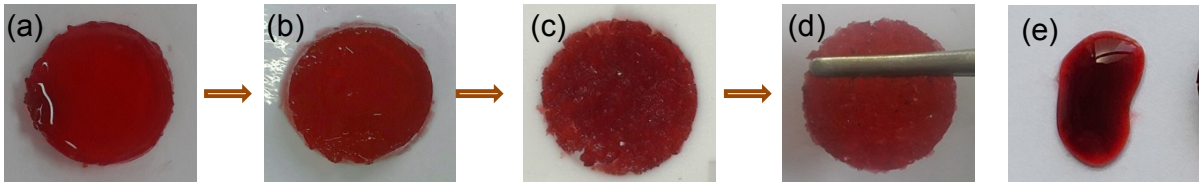


Fig. S13 Optical images of the drug loaded hydrogel before (a) and after (b) drug release; after ground into particles (c) and self-healed into a whole plate (d); and the hydrogel after drug release in pH 5.4 buffer (e).

References

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(3) Li, H.; Zhang, X.; Zhang, X.; Yang, B.; Yang, Y.; Wei, Y., Ultra-stable biocompatible cross-linked fluorescent polymeric nanoparticles using AIE chain transfer agent. *Polym. Chem.* **2014,** *5* (12), 3758-3762.