Injectable, Self-Healing and degradable Dynamic Hydrogels with Tunable Mechanical and Stability Properties by Thermal-induced Micellization

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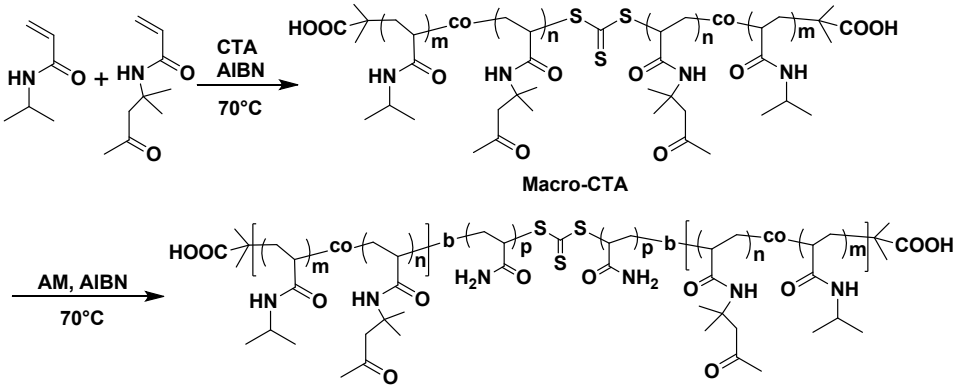
Synthesis route of ABA triblock copolymers P(NIPAM-*co*-DAAM)-*b*-PAM-*b*-P(DAAM-*co*-NIPAM)

RAFT polymerization was employed to prepare ABA triblock copolymers. As shown in Scheme S1, NIPAM and DAAM were firstly copolymerized to form difunctional macro-CTAs. And then AM was polymerized to form the triblock copolymers P(NIPAM-*co*-DAAM)-*b*-PAM-*b*-P(DAAM-*co*-NIPAM).



Scheme S1. Synthesis Route of the Macro-CTA and P(NIPAM-*co*-DAAM)-*b*-PAM-*b*-P(DAAM-*co*-NIPAM) ABA Triblock Copolymer.

^{1}H NMR spectra of macro-CTAs

Fig. S1 is the ^{1}H NMR spectra of macro-CTAs in CD_3Cl. The signals at 0.7-1.7 ppm is the protons of CH_2 in main chains and $(CH_3)_2C$ in DAAM side chain). The signals at 3.7-4.1 ppm is the protons of CH in NIPAM units. The signals at 3.4-3.6 ppm is the protons of CH_2 in DAAM units. The other protons assigned to the two units can be seen in the 1H NMR spectra. Based on the integration the intensity ratio of NIPAM units and DAAM units, the molar ratio of DAAM and NIPAM units could be calculated by formula (S1):

$$C_{DAAM}: C_{NIPAM}=A_6: 2A_3 \qquad \text{(s1)}$$

where C_{DAAM} and C_{NIPAM} were the molar ratios of DAAM and NIPAM; A_6 and A_3 were the integral ratio of the corresponding signals, respectively. The component parameters of the copolymers are listed in Table S1. One can find that the final composition of macro-CTAs was slightly different from the preset ratios due to the steric effect.

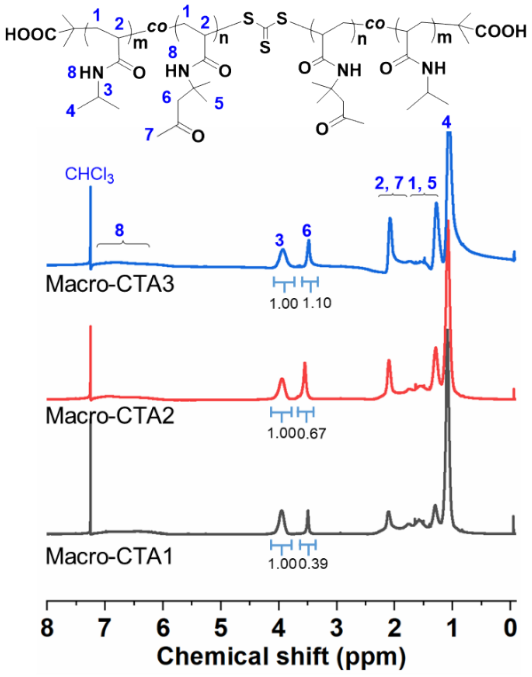


Fig. S1 ^{1}H NMR spectra of macro-CTAs

Table S1. Physical parameters of macro-CTAs measured by ^{1}H NMR and GPC

Macro-CTAs	Feed ratio (mol %)		Final composition [a] (mol%)		Theoretical $M_{n,theo}$ (g·mol^{-1})	M_n (g· mol^{-1}) [b]	M_w/M_n (PDI) [b]
	NIPAM	DAAM	NIPAM	DAAM			
Macro-CTA1	90.0	10.0	83.9	16.1	24,002	23,010	1.14
Macro-CTA2	80.0	20.0	74.9	25.1	25,122	24,972	1.18
Macro-CTA3	70.0	30.0	64.5	35.5	26,242	25,020	1.12

[a] Expected number-average molecular weight from polymerization stoichiometry

[b]Determined by GPC

The molecule weights (MWs) and polydispersity index of macro-CTAs and triblock copolymers

The $M_{n,GPC}$ and polydispersity index (PDI) of the macro-CTAs were determined by GPC. As shown in Figure S2 and Table S1, the PDI was is lesser than 1.20, indicating that the molecule weights (MWs) of copolymers has a relative narrow distribution. $M_{n,GPC}$ is close to the theoretical molecule weight ($M_{n,\ theo}$), and thus $M_{n,GPC}$ was used as the molecule weight of macro-CTAs.

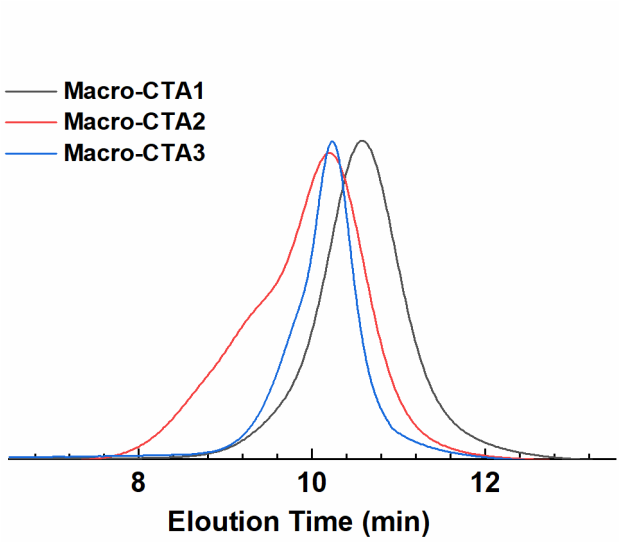


Fig. S2 GPC traces of precursor polymers

Fig. S3 is the GPC chromatogram for the copolymers. The GPC data was listed in Table 1.

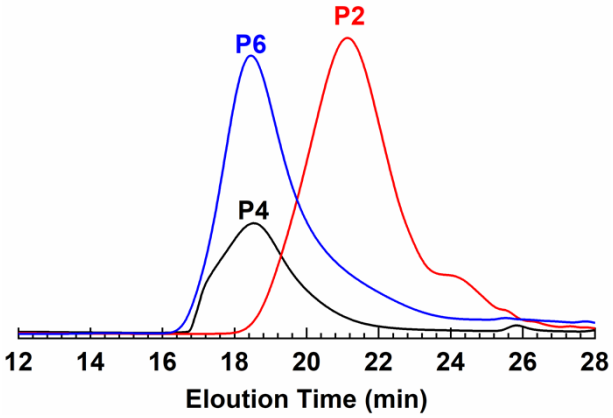


Fig. S3 GPC traces of ABA triblock copolymers

SEM of hydrogels at 37 ºC

The microstructure of hydrogels at 37 ºC was observed by SEM. One can find that the network structure of hydrogels was similar to that of at 5 ºC.

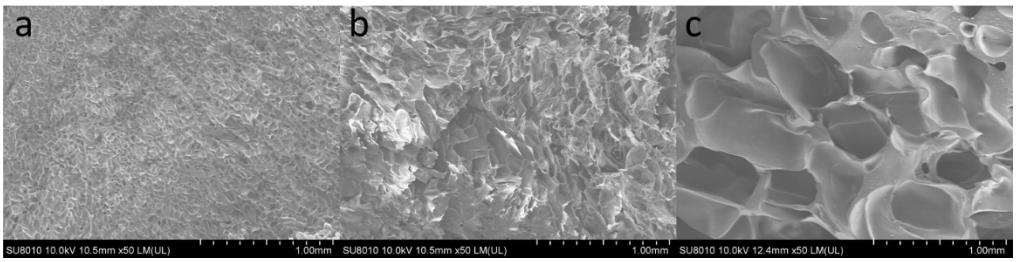


Fig. S4 SEM images of hydrogels H2 (a), H4 (b) and H6(c) at 37 ºC.

Degradation of hydrogel in solution ethanolamine

H4 samples were immersed into PBS and its buffer with ethanolamine (10 equev. to trithiocarbonate groups) at pH 7.4, respectively (Fig. S5a). The hydrogel degraded in presence of ethanolamine after 2 h, while another one was just slight swelling in absence of ethanolamine (Fig. S5b).

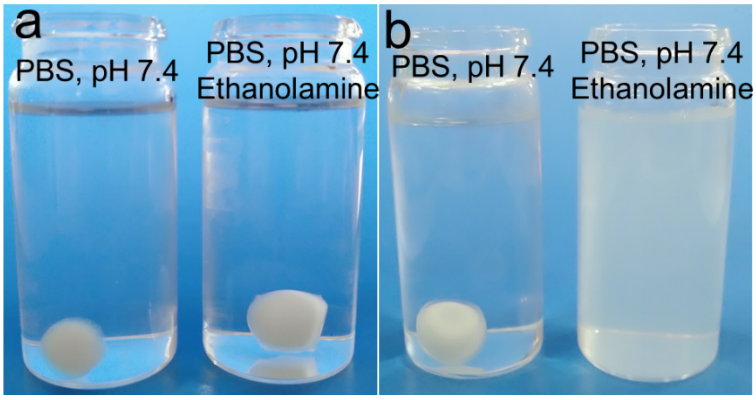


Fig. S5 Degradation of gel in pH 7.4 (a) and pH 2.5 (b) phosphate buffered saline (PBS).

The analysis of DOX release with different models

The data of DOX release from hydrogel H4 were analyzed using the zero-order, first-order, Higuchi, and Ritger-Peppas models by the Eqs. (s2)–(s5)[1], respectively.

Zero - order model : $M/Mz = kt$ (s2)

First - order model : $Mt/Mz = 1-e^{-kt}$ (s3)

Higuchi model : $Mt/Mz=kt^{0.5}$ (s4)

Ritger - Peppas model : $Mt/Mz= kt^{n}$ (s5)

where Mt/Mz represents the amount of DOX released at time t; k is the kinetic constant; and n is the diffusional exponent that characterizes the mechanism of DOX release. $n \leq 0.45$ corresponds to a Fickian diffusion, $0.45 < n < 0.89$ to a non-Fickian or anomalous diffusion, $n \geq 0.89$ to a zero-order transport[2,3]. The fitting results were listed in Table S2.

Table S2 Determined parameters of DOX released from H4 by fitting several kinetic equations.

Models	Conditions	K	R^2	n
Zero-order model	5 °C, pH 2.0	41.26	0.912	-
	37 °C, pH 2.0	2.83	0.832	-
	37 °C, pH 7.4	3.39	0.702	-
First-order model	5 °C, pH2.0	393.47	-2.835	-
	37 °C, pH 2.0	$8.61*10^{-6}$	-4.261	-
	37 °C, pH 7.4	$8.27*10^{-9}$	-4.433	-
Higuchi model	5 °C, pH 2.0	62.63	0.947	-
	37 °C, pH 2.0	12.11	0.741	-
	37 °C, pH 7.4	15.06	0.383	-
Ritger-Peppas model	5 °C, pH 2.0	66.02	0.964	0.454
	37 °C, pH 2.0	19.95	0.974	0.303
	37 °C, pH 7.4	26.10	0.880	0.264

References

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