Supporting information

Redox/Ultrasound Dual Stimuli-Responsive Nanogels for Precisely Controllable Drug Release

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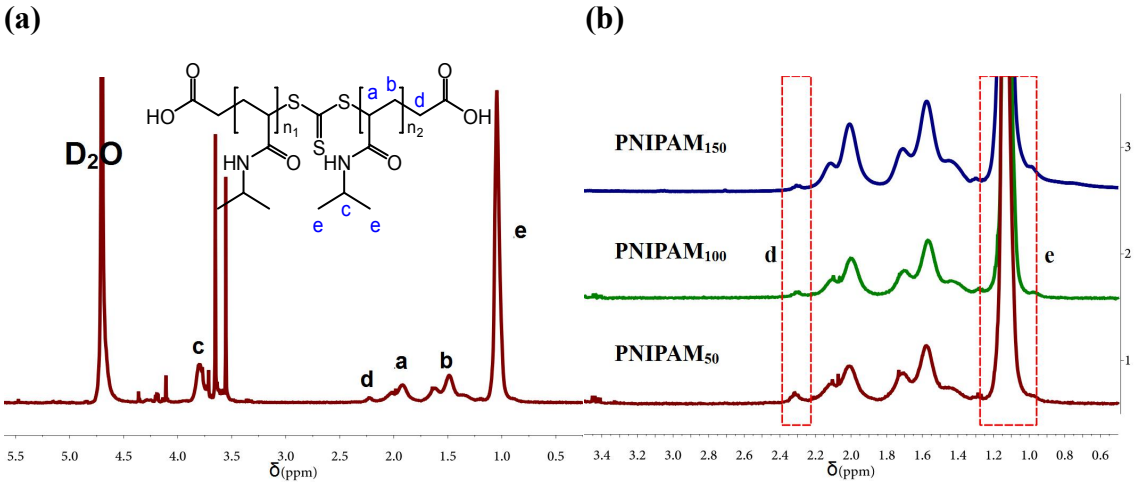

Fig. S1 ^{1}H NMR of HOOC-PNIPAM$_n$-COOH polymers.

A series of HOOC-PNIPAM$_n$-COOH polymers were synthesized via the reversible addition-fragmentation chain transfer (RAFT) polymerization and the chemical structure was confirmed by ^{1}H NMR spectroscopy. In the ^{1}H NMR spectra of HOOC-PNIPAM-COOH polymers (Fig. S1a), the chemical shifts at ~1.92 ppm (**a**) and ~1.49 ppm (**b**) were assigned to methine (-CH) and methylene (-CH_2) in repeat units, respectively. The chemical shift at ~3.80 ppm (**c**) was assigned to methine (-CH) link to amido. The chemical shift at ~2.22 ppm (**d**) was assigned to methylene (-CH_2) link to carbonyl group. The chemical shift at ~1.14 ppm (**e**) was assigned to symmetrical two methyls (-CH_3). The molecular weights (Mn) of the PNIPAM were calculated from the ratio of these two integrals and shown in Table S1.

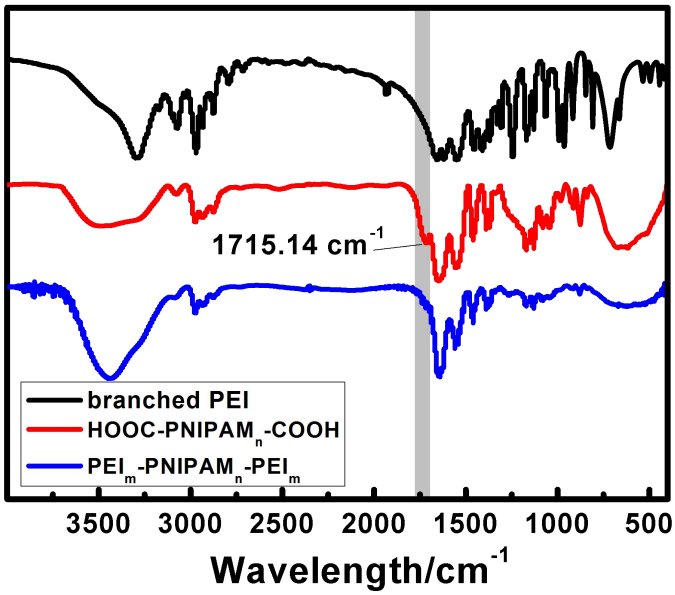

Fig. S2 FTIR spectra of PEI, HOOC-PNIPAM$_n$-COOH and PEI$_m$-PNIPAM$_n$-PEI$_m$.

The process of conjugation between HOOC-PNIPAM$_n$-COOH and PEI was monitored by FTIR analysis (Fig. S2). The polymerization process was monitored by the FTIR spectrum, which showed a peak at 1715 cm^{-1} corresponding to the carboxyl groups of the HOOC-PNIPAM$_n$-COOH. And then the observed bond of the carboxyl group disappeared after conjugating PEI, determining successful synthesis of copolymer.

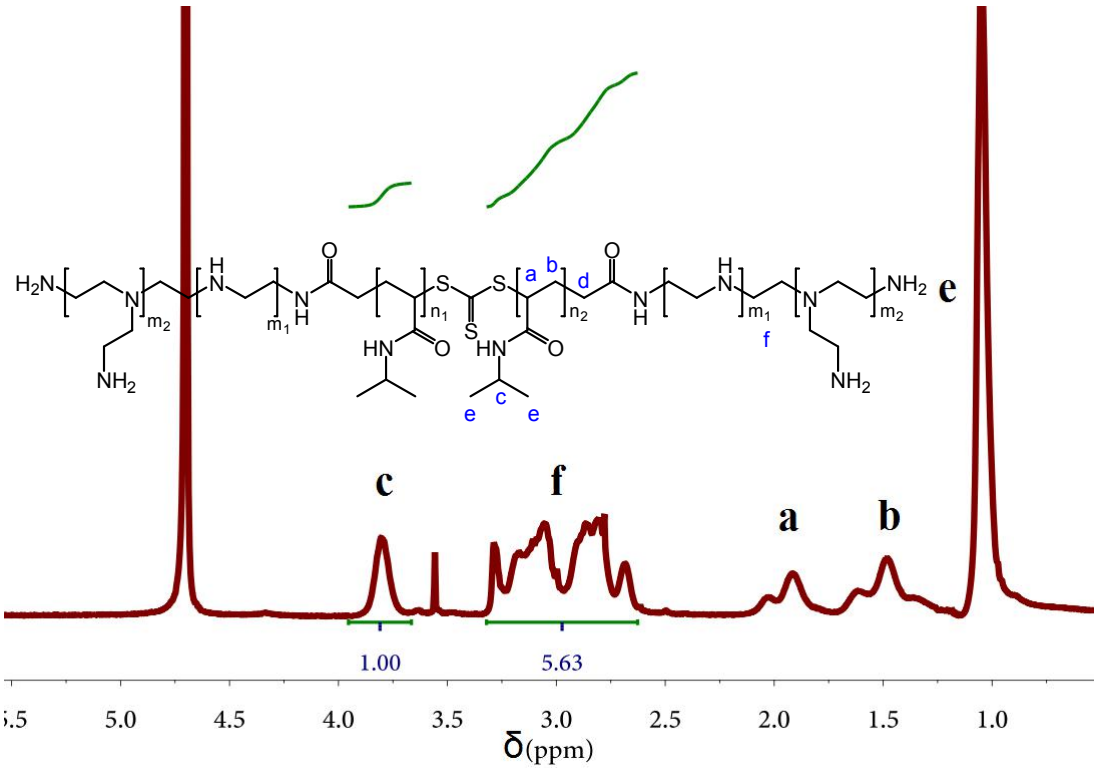

Fig. S3 ^{1}H NMR of PEI$_{42}$-PNIPAM$_{100}$-PEI$_{42}$ copolymer.

In the ^{1}H-NMR of PEI_{42}-$PNIPAM_{100}$-PEI_{42} (Fig. S3), the chemical shifts at ~1.92 ppm (a) and ~1.49 ppm (b) were assigned to methine (-CH) and methylene ($-CH_2$) in repeating units of PNIPAM, respectively. The peak at ~3.80 ppm (c) was assigned to methine (-CH) link to amido group of PNIPAM and the signals at 2.60~3.30 ppm (f) were attributed to the methylene group in PEI. We have calculated the n values of PNIPAM block from Fig. S1b and the ratio of PNIPAM: PEI was 62: 86.8, it indicated that 1 molar PNIPAM had been connected with 2.1 molar PEI. The molecular weights (Mn) of the polymers calculated from the ratio of these two integrals were shown in Table S1.[1-3]

Table S1 Properties of polymers.

Smaple	**NIPAM/CTA (or PNIPAM/PEI)**		M_{HNMR}[a]	M_{GPC}[b]	**PD**[b]
	In feed (mol/mol)	**Observed(mol/mol)**[a]	**(g·mol^{-1})**	**(g·mol^{-1})**	
$PNIPAM_{50}$[c]	50/1	36/1	4113	3653	1.43
$PNIPAM_{100}$	100/1	62/1	7051	9505	1.37
$PNIPAM_{150}$	150/1	107/1	12114	16975	1.44
PEI_{14}-$PNIPAM_{100}$-PEI_{14}	1/3	1/2.2	8349	-	-
PEI_{42}-$PNIPAM_{100}$-PEI_{42}	1/3	1/2.1	10801	-	-
PEI_{232}-$PNIPAM_{100}$-PEI_{232}	1/3	1/2.0	27029	-	-
PEI_{42}-$PNIPAM_{50}$-PEI_{42}	1/3	1/2.0	7708	-	-
PEI_{42}-$PNIPAM_{150}$-PEI_{42}	1/3	1/2.0	15803	-	-

[a] Determined by ^{1}H NMR spectroscopy.

[b] Measured by GPC using DMF as eluent on the basis of polystyrene calibration curve.

[c] The *n* (50, 100 and 150) was denoted as the theoretical number of monomers.

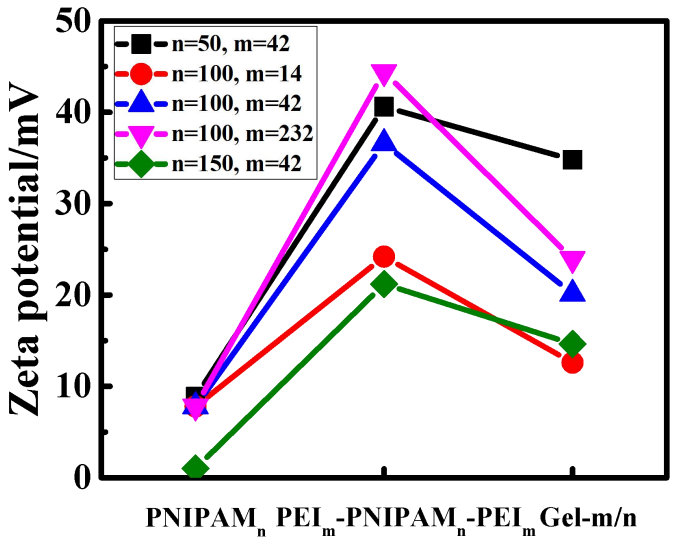

Fig. S4 Zeta potentials of polymers, copolymers and nanogels in aqueous solutions.

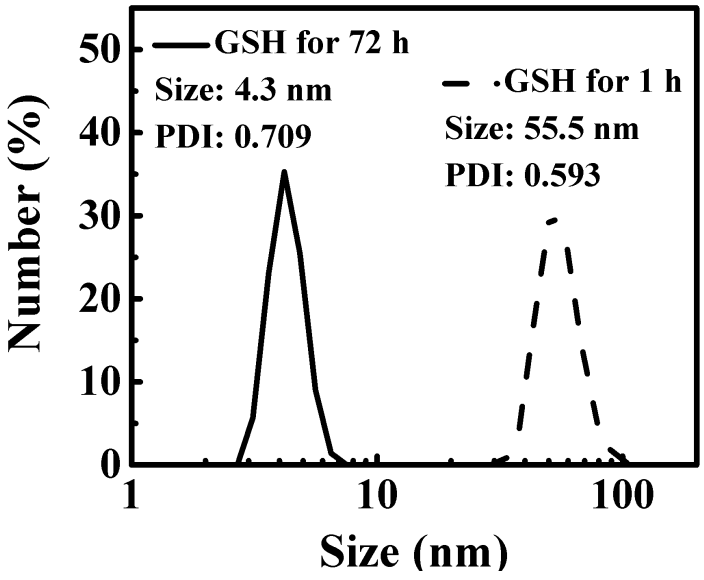

Fig. S5 Reduction-triggered size distribution changes of Gel-42/100 with time. Dashed line: 1hr; Solid line: 72 hrs.

References

1. Z. X. Lu, L. T. Liu and X. R. Qi, *International journal of nanomedicine*, 2011, 6, 1661-1673.
2. J. Yang, P. Zhang, L. Tang, P. Sun, W. Liu, P. Sun, A. Zuo and D. Liang, *Biomaterials*, 2010, 31, 144-155.
3. Ş. K. D, T. Gulinsarfraz, G. Hedström, A. Duchanoy, P. Eklund and J. M. Rosenholm,

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