Supporting Information

Dual Redox-Responsive PEG-PPS-cRGD Self-Crosslinked Nanocapsules for Targeted Chemotherapy of Squamous Cell Carcinoma

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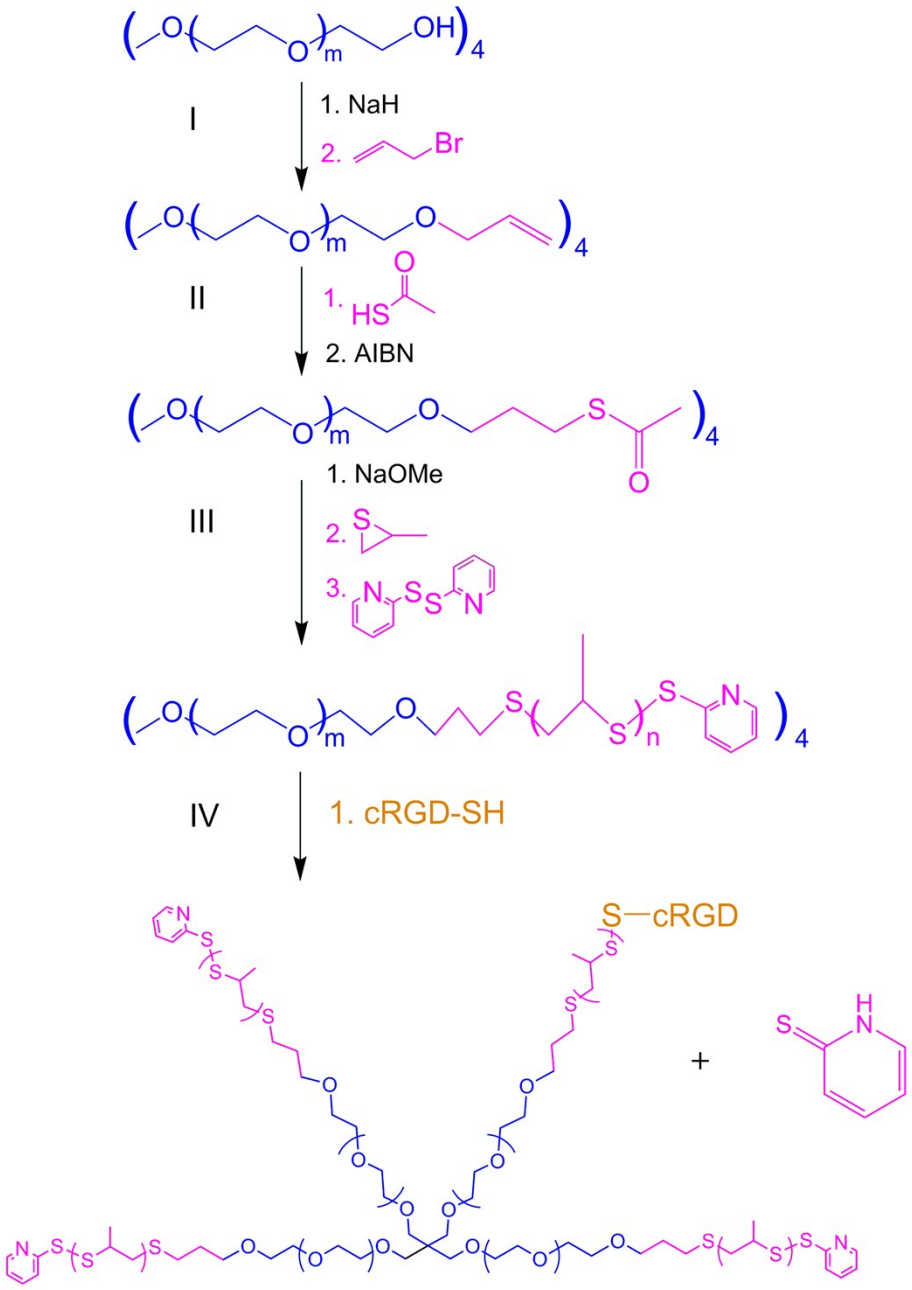


Fig. S1 Synthetic route of four-arms poly(ethylene glycol)-poly(propylene sulfide)-cRGD (PEG-PPS-cRGD).

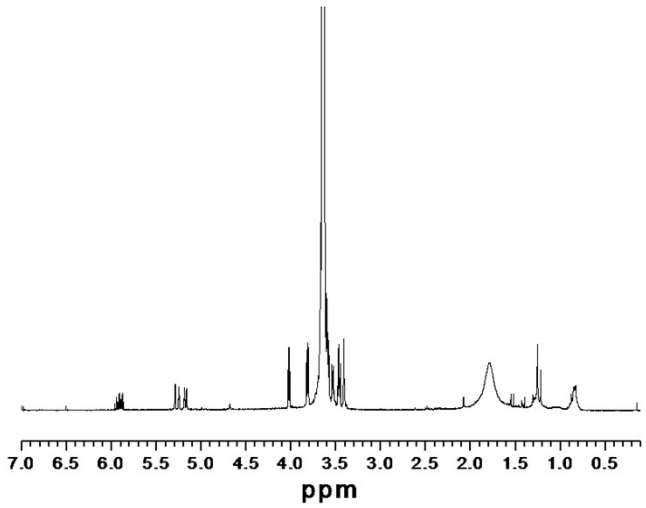


Fig. S2 ^{1}H NMR spectra of PEG-allyl ether using $CDCl_3$ as solvent. δ=3.39-3.89 (broad, PEG chain protons), 5.85-5.98 (m, 1H, -CH_2OCH2C**H**=CH_2), 5.15-5.30 (m, 2H, -CH_2OCH_2CH=C**H**$_2$).

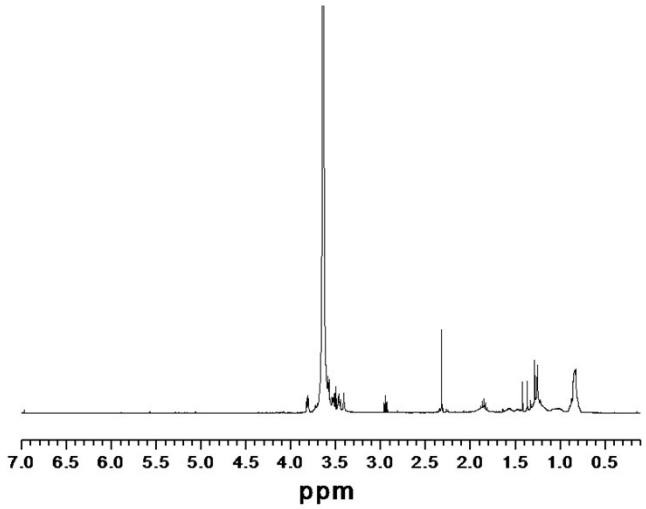


Fig. S3 ^{1}H NMR spectra of PEG-thioacetate using $CDCl_3$ as solvent. δ=1.81-1.93 (q, 2H, -OCH_2C**H**$_2CH_2$S-), 2.35 (s, 3H, -SCOC**H**$_3$), 2.92-2.97 (t, 2H, -OCH_2CH_2C**H**$_2$S-), 3.39-3.89 (broad, PEG chain protons).

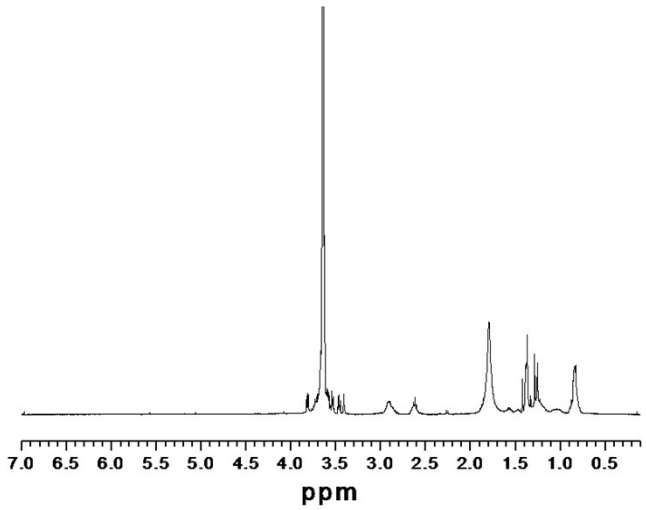
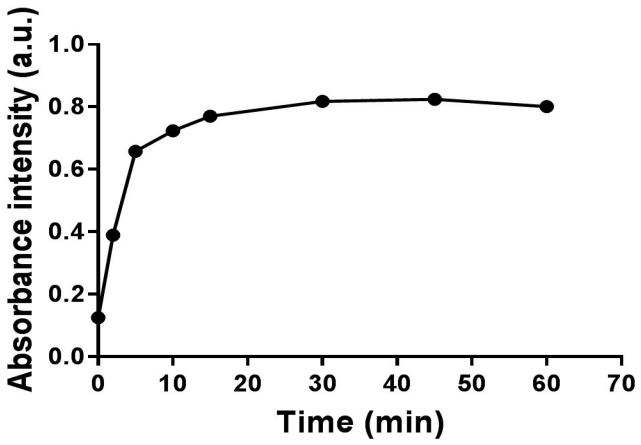


Fig. S4 ^{1}H NMR spectra of PEG-PPS using $CDCl_3$ as solvent. δ=1.35-1.45 (d, CH_3 in PPS chain), 1.81-1.9 (q, 2H, -OC**H**$_2$$CH_2CH_2S$), 3.6-3.7 (broad, PEG chain protons).



$$\frac{\Delta A_{342nm}}{8080} \times \frac{\text{Mw of Polymer}}{\text{mg/mL of Polymer}} = 0.334$$

Fig. S5 The raise in UV absorption intensity of pyridine thione (absorbance at 342 nm) during the modification of cRGD-SH onto PEG-PPS via a disulfide exchange reaction. The degree of modification of cRGD was calculated using the above formulation. The reaction reached a plateau after 1 h and the coupling efficiency of cRGD on four-arm PEG-PPS was ~8.35%.

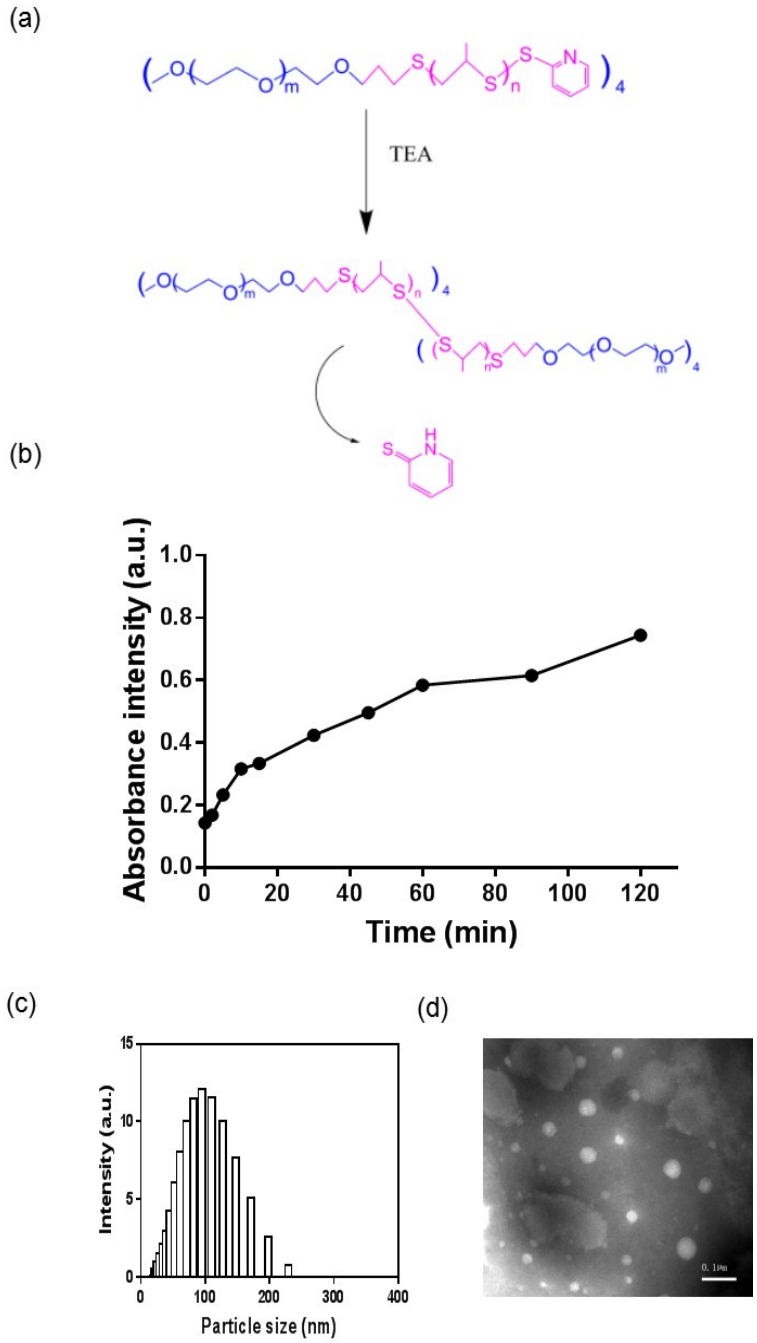


Fig. S6 (a) The self-crosslinked mechanism of PEG-PPS via disulfide exchange reaction of pyridine dithione groups with initiation of TEA. (b) The raise in UV absorption intensity of pyridine thione (absorbance at 342 nm) during the self-crosslinked process of PEG-PPS. (c) Particle size distribution of self-crosslinked PEG-PPS nanocapsules. (d) TEM image of PEG-PPS self-crosslinked nanocapsules (the sample negatively stained using 1% phosphotungstic acid solution).

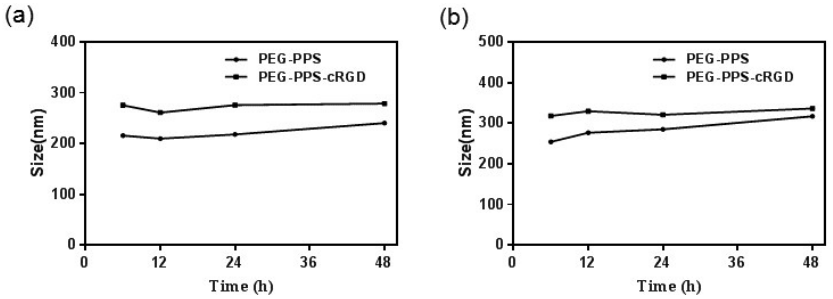


Fig. S7 Average particle sizes of DOX-loaded PEG-PPS and PEG-PPS-cRGD nanocapsules incubated in PBS (a) and DMEM medium (b) during the detection period of 48 h.

Table. S1 Hemolytic ratio after incubation with the nanocapsule (n=3).

	Hemolysis ratio (%)					
	0.25 h	0.5 h	0.75 h	1 h	2 h	3 h
PEG-PPS	0.55±0.06	0.61±0.03	0.56±0.08	0.69±0.07	0.72±0.08	0.91±0.04
DOX-loaded PEG-PPS	0.68±0.07	0.69±0.07	0.70±0.07	0.88±0.02	0.85±0.08	0.65±0.04
DOX-loaded PEG-PPS-cRGD	0.63±0.07	0.69±0.04	0.63±0.03	0.85±0.06	0.87±0.04	0.90±0.05

Table. S2 Body weight changes in KM mice (n = 10).

	Saline	DOX	PEG-PPS	DOX-loaded PEG-PPS	DOX-loaded PEG-PPS-cRGD
2d	2.35±0.41	0.84±0.58**	1.71±0.47	1.86±0.29	1.79±0.40
14d	8.75±1.25	4.82±0.17**	7.95±1.20	9.2±1.76	7.00±1.28

** $P < 0.01$, compared with saline group.