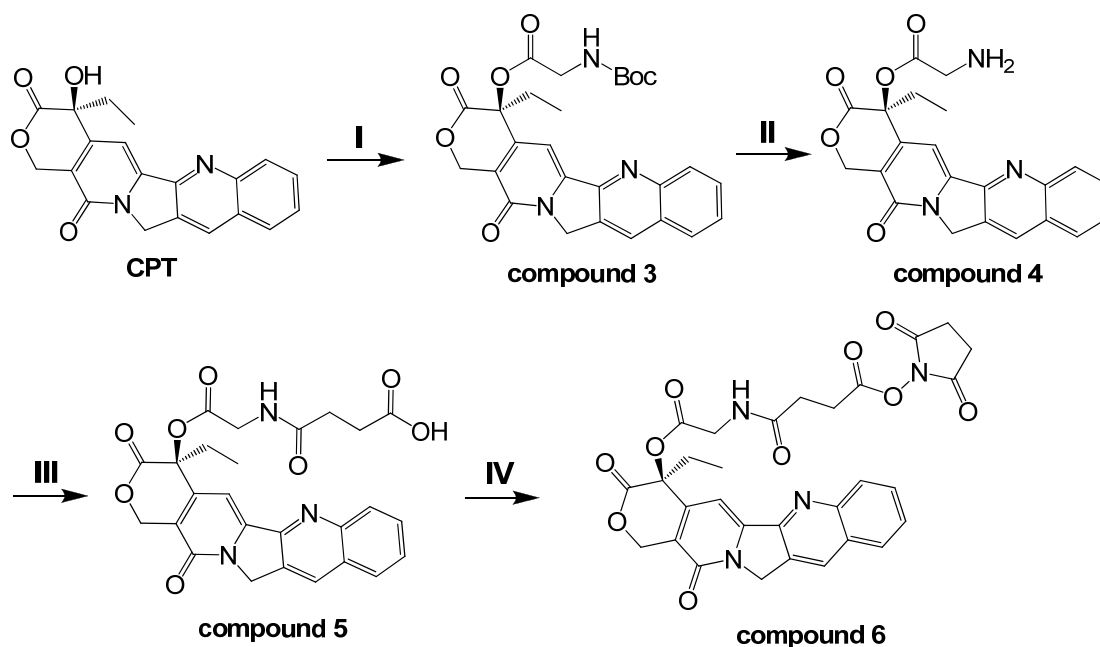


Supporting Information

Syntheses and characterization:

Compound **6** was synthesized according to Scheme S-1



Scheme S-1. I: N-Boc-Gly, DIC, DMAP, DCM, 0 °C, r.t., over night; II: TFA, DCM, r.t., 1h. III: Succinic anhydride, DIEA, DCM, r.t., over night; IV: DCC, DMAP, NHS, DCM, r.t., 2d.

(1) N-Boc-glycine (1.5 g, 8.61 mmol) was dissolved in 600mL of anhydrous methylene chloride at room temperature and to this solution were added DIC (1.34 mL, 8.61 mmol), DMAP (706 mg, 5.74 mmol) and camptothecin (1.0 g, 2.87 mmol) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred over night. The solution was washed with 0.1 N HCl, dried and evaporated under reduced pressure to yield a white solid, which was recrystallized from methanol to give camptothecin-20-ester of Boc-glycine (Compound **3**, CPT-G-Boc);

(2) Compound **3** (1.05 g, 2.08 mmol) was dissolved in a mixture of methylene chloride (10 mL) and TFA (10 mL) and stirred at room temperature for 1 h. Solvent was removed and the solid was recrystallized from methylene chloride and ether to give 970 mg white solid (Compound **4**, CPT-G-N·HCl); ¹H NMR (300 MHz,

3.99-4.20 (dd, J1=17.94, J2=68, 2H), 2.44-2.47 (m, 2H), 2.35-2.40 (m, 2H), 2.13-2.17 (m, 2H), 0.90-0.94 (t, J=7.36, 3H).

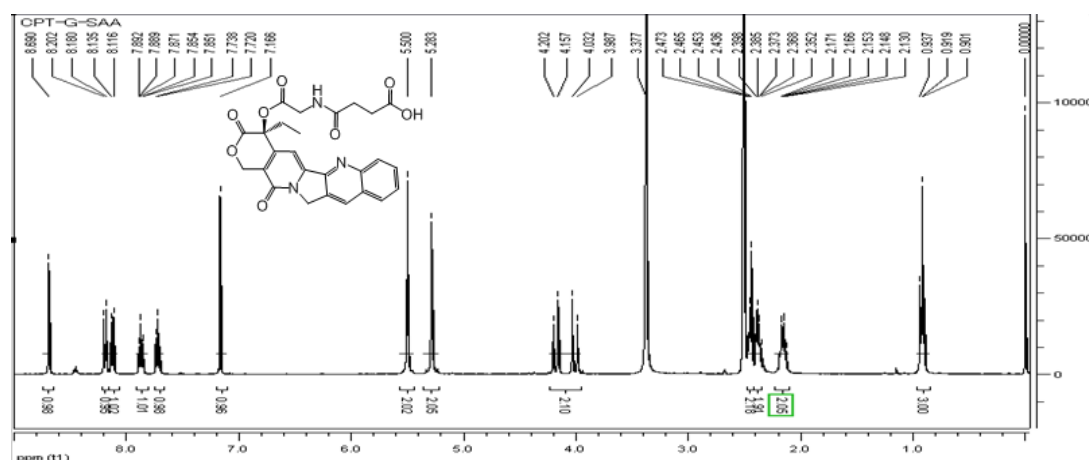


Fig. S-3. ^1H NMR of compound **5**

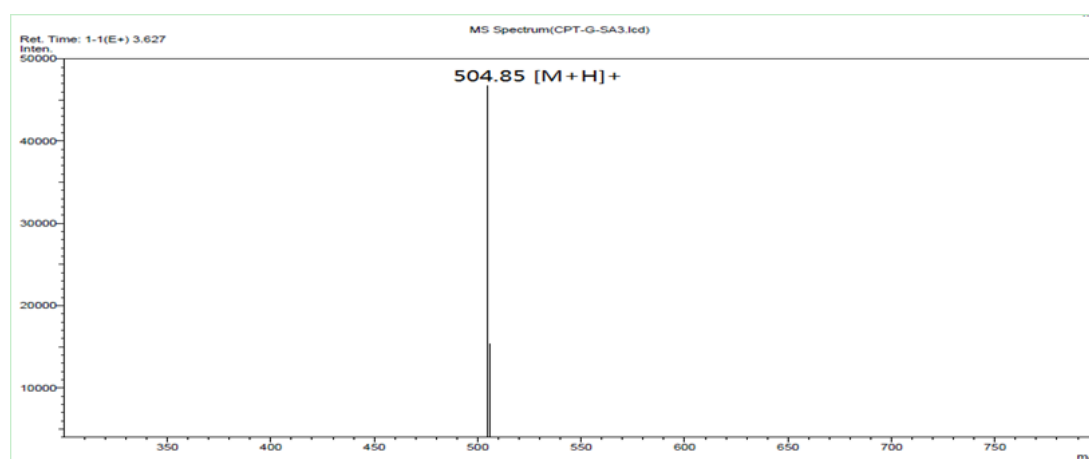


Fig. S-4. MS of compound **5**

(4) Compound **5** (850 mg, 1.68 mmol) was dissolved in DCM (300 mL) and stirred at r.t. for 1h, added NHS (207 mg, 1.85 mmol), DCC (416 mg, 2.02 mmol) and A catalytic amount of DMAP. Stirred at r.t. for 2 days, Cooled to -20°C and filtered to remove precipitation, dried and evaporated under reduced pressure to yield a yellow to white solid (743 mg, 1.23 mol, Compound **6**, CPT-G-SA-OSu).

^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.71 (s, 1H), 8.13-8.21 (dd, J1=8.23, J2=25.34, 2H), 7.86-7.89 (t, J=7.10, 1H), 7.71-7.75 (t, J=7.25, 1H), 7.81 (s, 1H), 5.50 (s, 2H), 5.31 (s, 2H), 4.20-4.25 (d, J=18.05, 1H), 4.01-4.06 (d, J=17.94, 1H), 3.39-4.46 (m, 3H),

2.88-2.91 (t, J=7.06, 2H), 3.78 (s, 4H), 2.13-2.19 (dd, J₁=7.54, J₂=15.31, 2H),
1.04-1.07 (t, J=7.00, 2H), 0.90-0.93 (t, J=7.36, 3H).

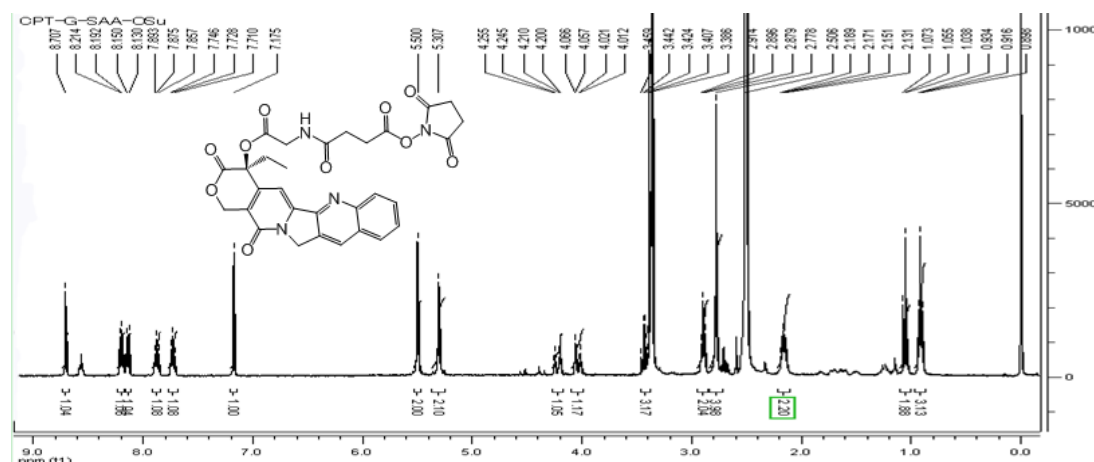


Fig. S-5. ^1H NMR of compound 6

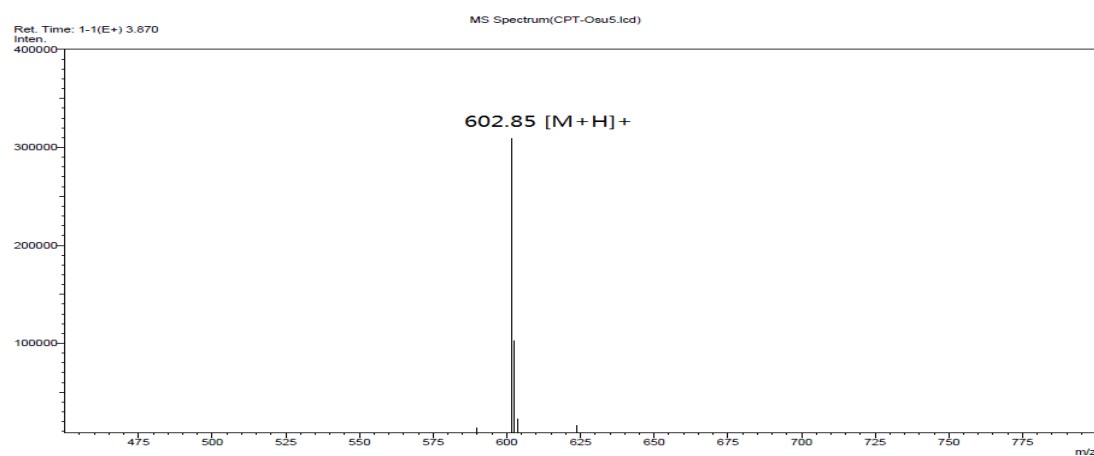


Fig. S-6. MS of compound 6

Peptide synthesis. Peptide of FFYGE-SS-EEE (Compound 7) was prepared by standard Fmoc solid-phase peptide synthesis (SPPS) using 2-chlorotrityl chloride resin and the corresponding N-Fmoc protected amino acids with side chains properly protected by a tert-butyl group. The first amino acid (Fmoc-Glu(OtBu)-OH) was loaded on the resin at the C-terminal with the loading efficiency about 1 mmol/g. 20% piperidine in anhydrous N,N'-dimethylformamide (DMF) was used during the deprotection of Fmoc group. Then the next Fmoc-protected amino acid was coupled to the free amino group using HBTU as the coupling reagent. The growth of the

peptide chain was according to the standard Fmoc SPPS protocol. After the last coupling step, 20% piperidine in anhydrous DMF was used during the deprotection of Fmoc group. excessive reagents were removed by a single DMF wash for 5 minutes (5 ml per gram of resin), followed by five steps of washing using dichloromethane (DCM) for 2 min (5 ml per gram of resin). The peptide derivatives were cleaved from the resin by cleave reagent (TFA: Tis: H₂O=95:2.5:2.5) and the mixture was evaporated under reduced pressure and poured into ice-cold diethylether, successively. The resulting precipitate was centrifuged for 10 min at 0-4 °C at 10,000 rpm. Afterward the supernatant was decanted and the solid was dissolved in DMSO for HPLC purification. ¹H NMR (300 MHz, DMSO-d₆) δ 8.56-8.63(m, 1H) , 8.38-8.42 (t, J=5.77, 1H), 7.99-9.19 (m, 5H), 7.08-7.29 (m, 7H), 6.98-7.00 (m, 2H), 6.61-6.64 (d, J=8.38, 2H), 4.53-4.67 (m, 2H), 3.13-4.26 (m, 4H), 3.96 (s, 1H), 3.80 (s, 1H), 3.57-3.60 (m, 2H), 3.30-3.38 (m, 6H), 2.73-3.11 (m, 4H), 2.54-2.67 (m, 6H), 2.20-2.34 (m, 2H), 1.67-1.99 (m, 9H). MS: calc. M⁺ = 1282.45, obsvd. (M+H)⁺ = 1283.20.

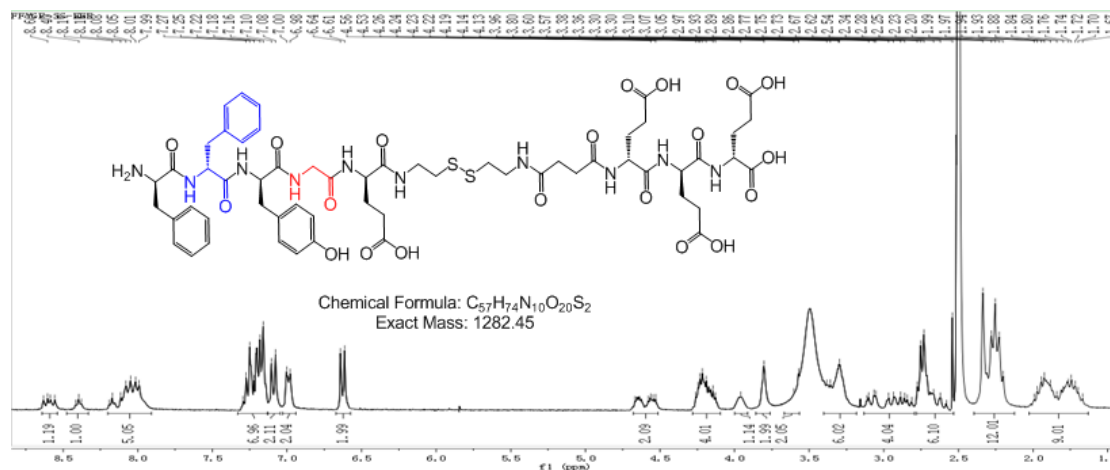


Fig. S-7. ¹H NMR of FFYGE-ss-EEE

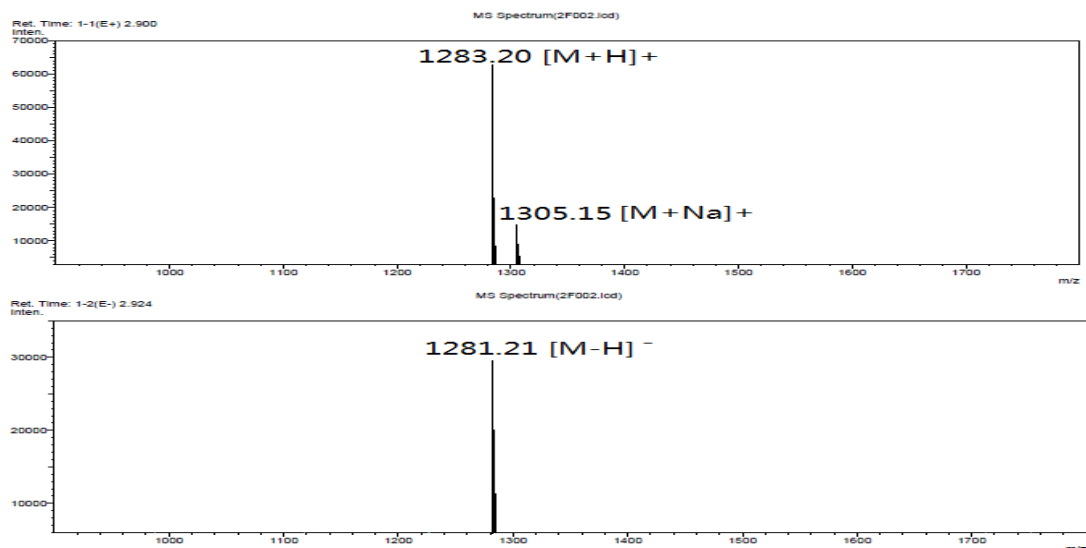


Fig. S-8. MS of FFYGE-ss-EEE

Synthesis and Characterization of CPT-G-FFYGE-ss-EEE (Compound 1). The compound **6** (124 mg, 0.2 mmol), compound **7** (257 mg, 0.2 mmol) was dissolved in 10mL DMF, added DIEA (165 μ L, 1 mmol) stirred at r.t. over night. Concentrated and evaporated under reduced pressure. HPLC purified the mixture, evaporated under reduced pressure to remove the methanol. Freeze-drying the solution to give 45 mg of compound **1** (yellow solid). ^1H NMR (400 MHz, DMSO- d_6) δ 12.13 (s, 5H), 9.16 (s, 1H), 8.69 (s, 1H), 8.42 (t, J = 5.6 Hz, 1H), 8.20 – 7.94 (m, 11H), 7.90 – 7.82 (m, 1H), 7.72 (t, J = 7.5 Hz, 1H), 7.23 – 7.06 (m, 10H), 7.01 (d, J = 8.3 Hz, 2H), 6.63 (d, J = 8.2 Hz, 2H), 5.50 (s, 2H), 5.28 (s, 2H), 4.42 (dd, J = 25.7, 17.7 Hz, 3H), 4.31 – 4.11 (m, 5H), 3.97 (dd, J = 17.9, 5.5 Hz, 1H), 3.73 (dd, J = 29.7, 16.5 Hz, 2H), 3.30 (d, J = 5.5 Hz, 3H), 3.01 – 2.83 (m, 3H), 2.73 (dd, J = 13.2, 6.3 Hz, 6H), 2.61 – 2.53 (m, 2H), 2.34 (s, 4H), 2.31 – 2.19 (m, 10H), 2.15 (d, J = 7.5 Hz, 2H), 2.03 – 1.86 (m, 4H), 1.85 – 1.64 (m, 4H), 0.90 (t, J = 7.3 Hz, 3H). MS: calc. M^+ = 1769.59, obsvd. $(M+H)^+$ = 1770.90. HR-MS: 1770.5968.

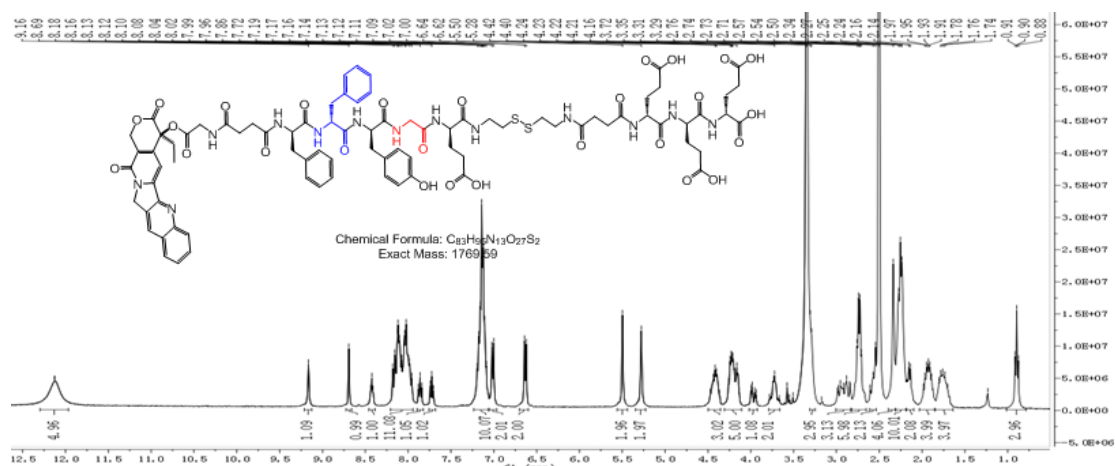


Fig. S-9. 1H NMR of CPT-G-FFYGE-ss-EEE

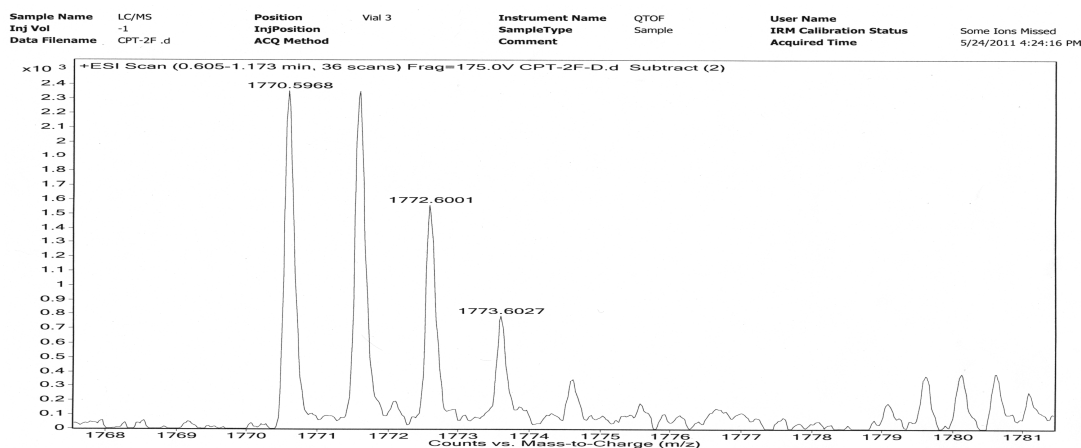


Fig. S-10. HR-MS of CPT-G-FFYGE-ss-EEE

CPT gel preparation: 2 mg of compound **1** (1.13 μ mol) was dissolved in 270 μ L of ultrapure water containing 0.48 mg (4 equiv. to **4**) of Na_2CO_3 and 3.07 mg of GSH in 100 μ L of ultrapure water containing 0.85 mg (0.8 equiv. to GSH) of Na_2CO_3 to neutralize GSH to make the final pH value to 7.4. And then 22.6 μ L of ultrapure water containing 0.69 mg of GSH (2.26 μ mol, 2 equiv. to **4**) was added. Gel was formed after being kept at room temperature for about 20 min.

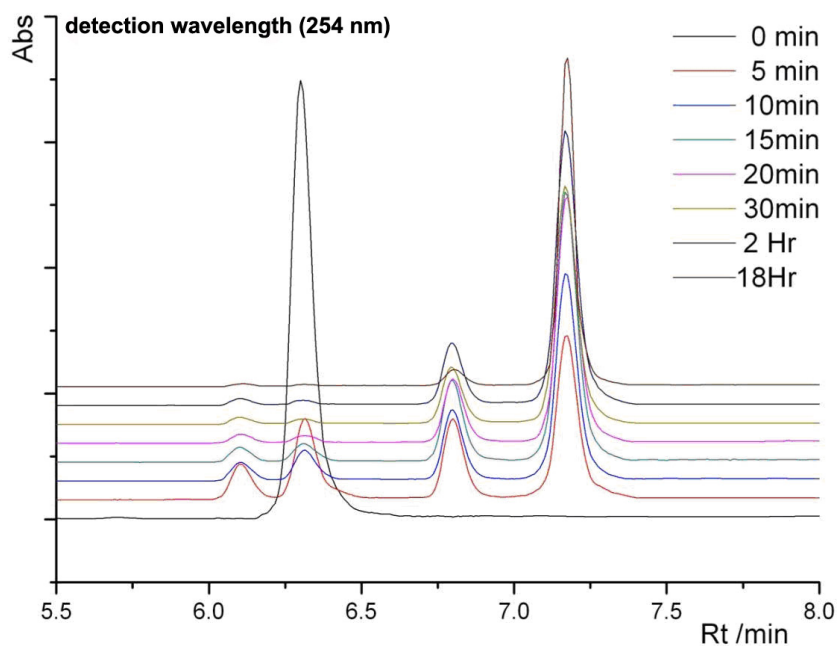


Fig. S-11. HPLC traces of PBS solutions of **1** after the addition of 2 equiv. of GSH at different time points (HPLC analysis were performed on Waters 600E Multi-solvent Delivery System using a C₁₈ RP column with acetonitrile (0.1% of TFA) and water (0.1% of TFA) as the eluents)

Table S-1. The percentage of different components in solution and the gel at different time points

Compounds	GSH (2 equiv.)	1	2	Dimer of 2
0min	--	100%	--	--
5min	8.83	22.81	20.38	47.98
10min	5.18	8.89	20.07	65.85
15min	3.45	4.51	19.84	72.20
20min	2.40	1.91	18.39	77.29
30min	1.90	1.15	16.96	80.00
2Hr	1.66	1.00	16.36	80.98
18Hr	0.85	0.45	5.34	93.36

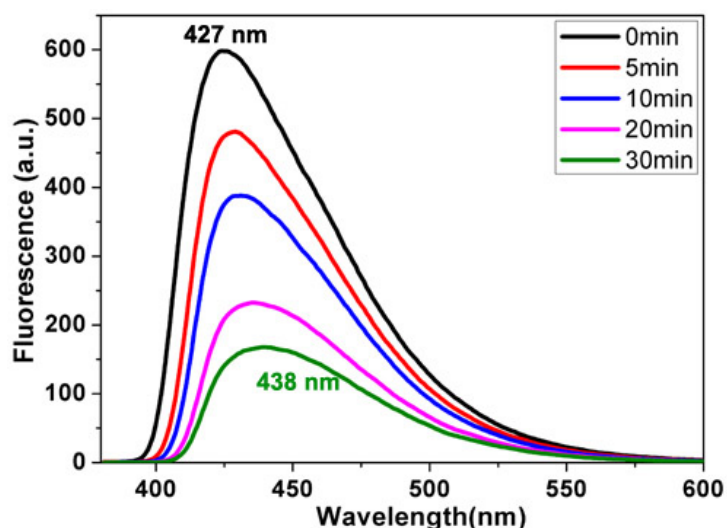


Fig. S-12. Emission spectra of PBS solutions of **1** after the addition of 2 equiv. of GSH at different time points (Emission spectra were recorded on a Perkin-Elmer LS-55 luminance spectrometer at excitation wavelength of 370 nm)

Rheology:

Rheology was performed at $37.0 \pm 0.1^\circ\text{C}$ using an AR 2000ex rheometer (TA company, America) by 40 mm parallel plates. A solution containing 1 wt% of **1** with 2 equiv. of GSH was transferred to the plate. Dynamic time sweep was firstly performed at 1.0 rad/s frequency and 1.0% strain for 1 hour. Dynamic strain sweep was then conducted at the frequency value of 1 rad/s. Dynamic frequency sweep was finally performed in the range of 0.1–100 rad/s at strain value of 1.0%.

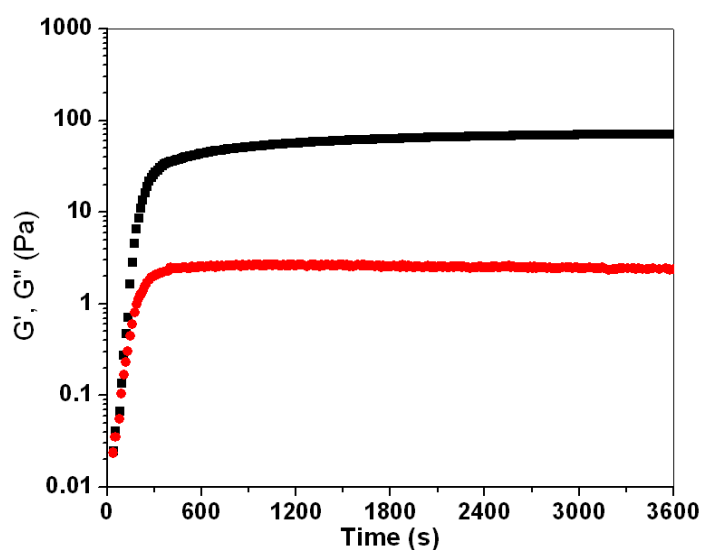


Fig. S-13. Rheological measurement with the mode of dynamic time sweep of solution of **1** with 2 equiv. of GSH at the frequency of 1 rad/s and strain of 1%

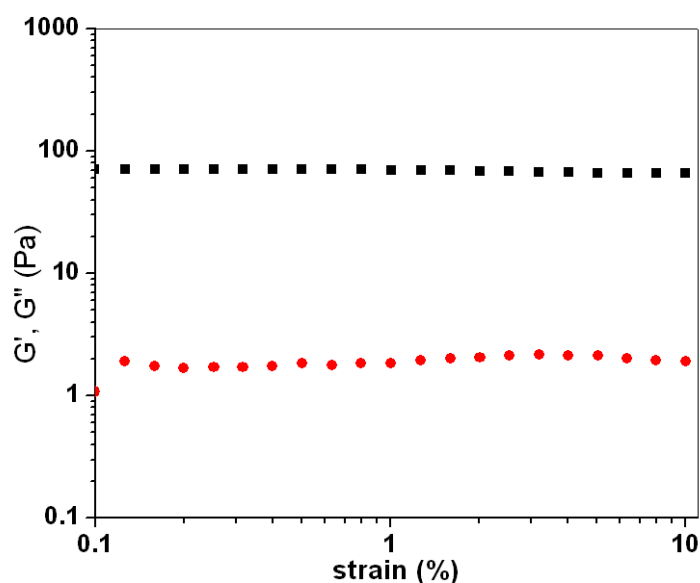


Fig. S-14. Rheological measurement with the mode of dynamic strain sweep of the gel at 2h time point at the frequency of 1 rad/s

Determination of IC₅₀ values:

The IC₅₀ values of compounds were measured by the MTT cell viability test. The cells were seeded in 96-well plates at a density of 5,000 cells per well with a total medium volume of 75 μ L and incubated for 24 hours. 25 μ L of the solutions containing serials of concentrations of compounds were then added into the cells. 48 hours later, the medium was replaced with fresh medium supplemented with 15 μ L of MTT reagent (5 mg/mL). 4 hours later, the medium containing MTT was removed and DMSO (100 μ L/well) was added to dissolve the formazan crystals. The optical density of the solution was measured at 490 nm, using a microplate reader (Bio-RAD iMark™, America). Cells without the treatment of the compounds were used as the control. The experiment was repeated for 3 times. The cell viability percentage was calculated by the following formula: The cell viability percentage (%) = $\text{OD}_{\text{sample}}/\text{OD}_{\text{control}} \times 100\%$. Prism 5.0 software was used to calculate the IC₅₀.

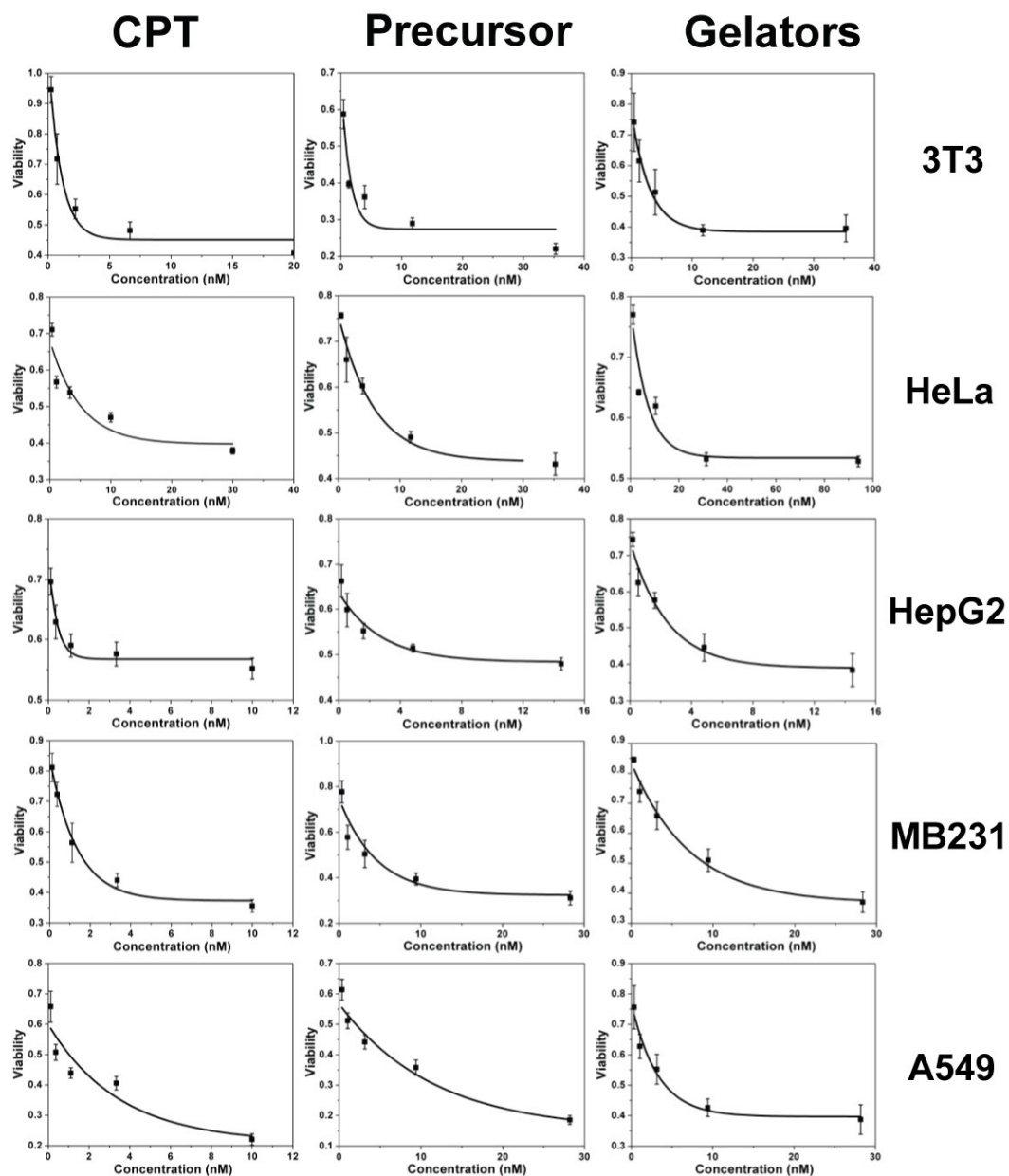


Fig. S-15. Inhibition curves of different compounds at different concentrations against different cells (gelators refer to the components in the gel at 48h time point)

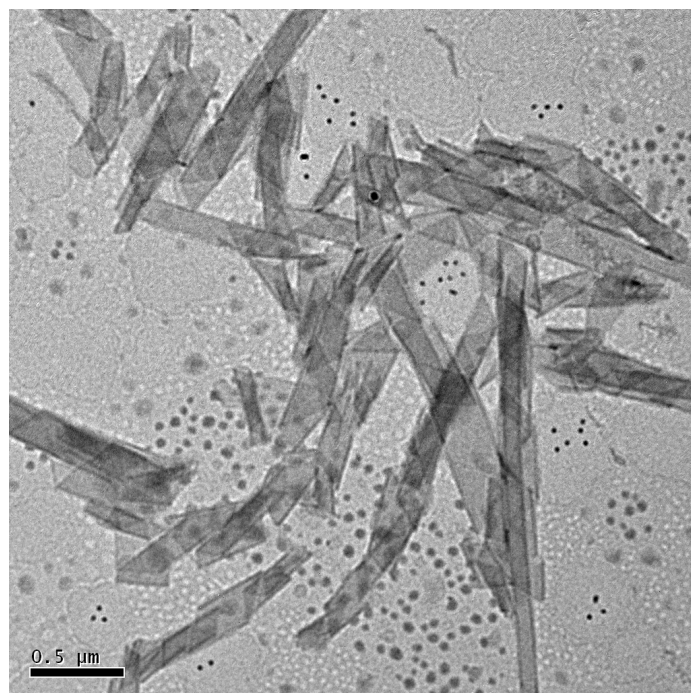


Fig. S-16. A TEM image of the gel at 2h time point (the image indicated that thin tapes rolled into tube structures)

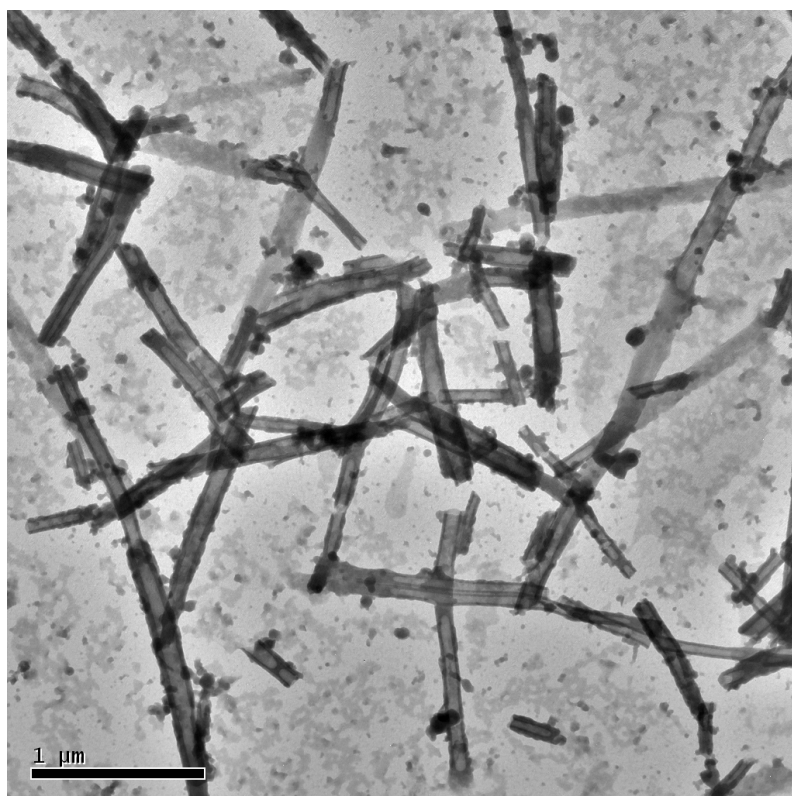


Fig. S-17. A TEM image of the gel at 48h time point to show the tubular structures