Electronic Supplementary Material (ESI) for Polymer Chemistry.


**Supplementary information for**

# Sustained drug release from an ultrathin hydrogel film

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## Experimental details

### Materials

Oligo(ethylene glycol) diol (OEG, Aladdin, $M_n$ = 600 g/mol) was dried by azeotropic distillation in the presence of dry toluene. Mercaptosuccinic acid (MSA, 98 %, Aladdin), maleic acid (MA, 98 %, Aladdin), 3-mercaptopropyl trimethoxysilane (MPTMS, 99 %, Sigma) and camptothecin (CPT, 99 %, Shanxi Herbchem Biotech Co., Ltd) were used without further purification. The single-side polished silicon wafer and quartz wafer were purchased from LiJing Co., Ltd and GuangLiang High technology Co. Ltd, respectively. Scandium trifluoromethanesulfonate [$Sc(OTf)_3$] was synthesized according to our previous report.[1] Other reagents were purchase from Shanghai Chemical Reagent and used as received.

### Characterization

$^1$H NMR spectra were measured on a Bruker Avance DMX500 spectrometer in $CDCl_3$ with tetramethylsilane as internal standard under room temperature. Molecular weights and molecular weight distributions were determined by gel permeation chromatography (GPC) equipped with Waters 208 apparatus equipped with Waters 2410 RI detector (set at 25 °C) using THF as eluent with a flow rate of 1.0 mLmin$^{-1}$. UV-vis absorption spectra were conducted with UV-vis spectroscopy (UV-2450, Shimadzu) at 25 °C. Film thickness measurements were performed using a GES 5E spectroscopic ellipsometer (Semilab) on Si wafers. Measurements were performed between 190 nm to 990 nm at an angle of 60°. The refractive indexes of the films were set to 1.50 for all the films and three different measurements were performed for each five bilayers.

### Synthesis of poly[oligo(ethylene glycol) mercaptosuccinate] (POEGMS)

OEG diol (60.0 g, $M_n$ = 600, 0.1 mol), MSA (15.0 g, 10.0 mmol) and $Sc(OTf)_3$ (0.492 g, 1.0 mmol) were added into 250 mL three-necked flask immersed in oil bath preheated to 80 °C under the nitrogen atmosphere with vigorous stirring to esterification until the melt system turned into transparent. Then condensation polymerization was started at 90 °C with a pressure below 30 mmHg. After 2 h, the reduced pressure was gradually increased to 0.3-3 mmHg and maintained for 10 h to complete the polycondensation. The crude product was dissolved in methylene chloride and passed through an aluminum column to remove the catalyst. The resulting solution was concentrated and precipitated into cold diethyl ether for three times. The final product was dried in a vacuum oven for 48 hours. Yield: 63.7 g (87 %). POEGMS was characterized by $^1$H NMR (Fig. S1) and GPC (Fig. S2).

**Synthesis of acryl-CPT**

CPT (1.00 g, 2.87 mmol) and triethylamine (0.87 g, 8.61 mmol) was dispersed in anhydrous methylene chloride and cooled by an ice bath. The acryloyl chloride (0.78 g, 8.61 mmol) were added to the solution dropwise via a funnel. The reaction was continued for 24 h at room temperature. Afterward, the solution was washed successively with aqueous solutions of $NaHCO_3$ and NaCl. The organic phase was dried over anhydrous $MgSO_4$, filtered, evaporated to dryness, to give acryl-CPT. Yield: 0.96 g (83 %). Acryl-CPT was characterized by $^1$H NMR (Fig. S3).

**Synthesis of POEGMS-*g*-CPT**

POEGMS (2.00 g, 2.73 mmol of thiol), acryl-CPT (0.33 g, 0.82 mmol) and several drops of TEA were dissolved in 50 mL of methylene chloride. The solution was stirred at room temperature for 48 h, concentrated and participated in cold diethyl ether to give POEGMS-*g*-CPT. Yield: 2.1 g (90

%). POEGMS-*g*-CPT was characterized by $^1$H NMR (Fig. S4). According to the relative integral area of corresponding protons, about 30 % of thiols in POEGMS have been reacted with acryl-CPT, which matched the feeding molar ratio of acryl-CPT to POEGMS quite well, indicating the high efficiency of thiol-ene "click" reaction. The remaining 70 % of thiols could be further employed for LbL "click" chemistry.

**Synthesis of poly[oligo(ethylene glycol) maleate] (POEGM)**

The synthesis and purification procedures of POEGM were similar to that of POEGMS, using maleic acid as monomer. Yield: 62.8 g (90 %). POEGM was characterized by $^1$H NMR (Fig. S5) and GPC (Fig. S6).

**Preparation of ultrathin hydrogel films**

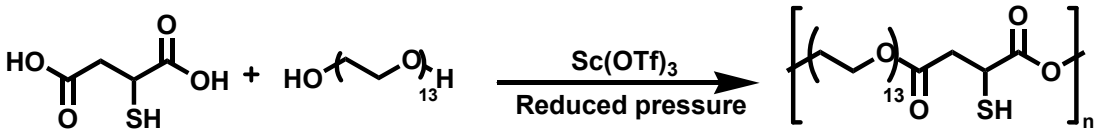
The substrates (silicon or quartz slides) were cut into 1 cm × 2 cm pieces, sonicated in ethanol for 30 min, and rinsed with deionized water. The clean substrates were hydroxylated by treating in a 30: 70 (v/v) mixture of $H_2O_2$ and $H_2SO_4$ at 80 °C for 1 h. The resulting substrates were dried under a nitrogen stream. Then MPTMS in toluene at a concentration of 1 % was prepared in a nitrogen atmosphere. The substrates were immersed into MPTMS solution at room temperature for 30 min in nitrogen atmosphere, then successively washed with toluene, ethanol and deionized water, and finally dried in a nitrogen stream. The substrates modified by thiols were alternately immersed in phosphate buffer solutions (PBS, pH 7.4) of POEGM and POEGMS-*g*-CPT at the concentration of 1 % for 10 min with intermediate water rinsing and nitrogen drying. Multilayer films can be formed by repeating these two steps in a cyclic fashion. Finally, the hydrogel films on the substrates were frozen-dried.

***In vitro* CPT release from ultrathin hydrogel film**

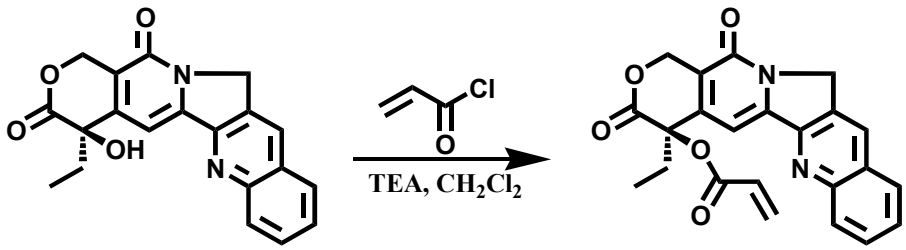
The silicon slides coated with CPT-conjugated hydrogel films were immersed into 20 mL of PBS (10 mM, pH 7.4) in electric-heated thermostatic water bath set at 37 °C. At a predetermined time interval, 10 mL of PBS was taken out and replenished with an equal volume of fresh PBS. The PBS with released CPT was frozen-dried, and the residual solid was dissolved in DMF. The amount of CPT released in the PBS was determined by measuring the UV absorbance of the solutions at 365 nm. The standard curve of CPT in DMF is:

$$A=58.831C+0.0136$$

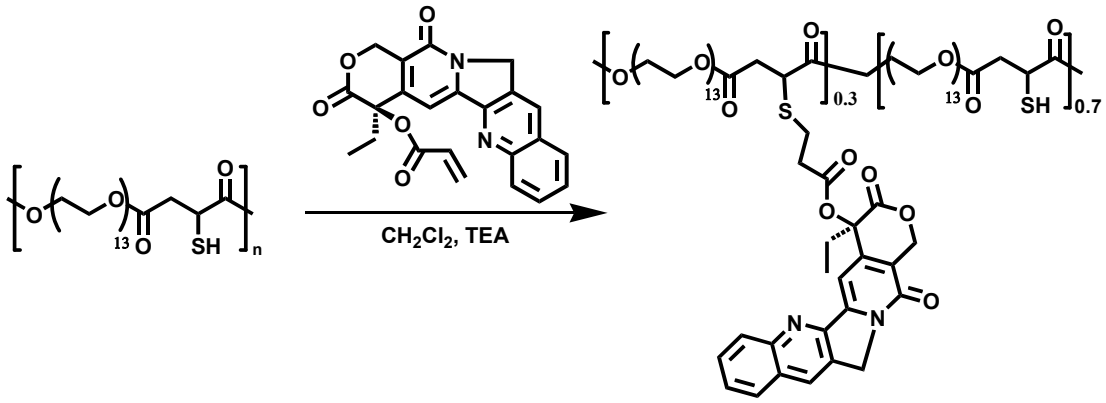
, where A is the UV absorption of CPT, C (mg/L) is the concentration of CPT in DMF. All release measurements were conducted in triplicate.



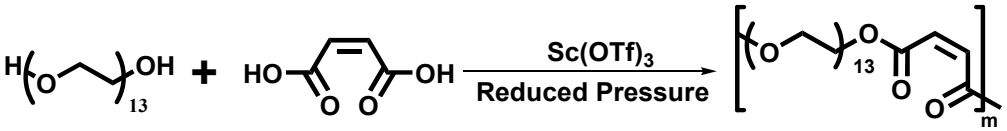

**Scheme S1** Synthesis of POEGMS.




**Scheme S2** Synthesis of acryl-CPT.




**Scheme S3** Sythesis of POEGMS-*g*-CPT.




**Scheme S4** Sythesis of POEGM.

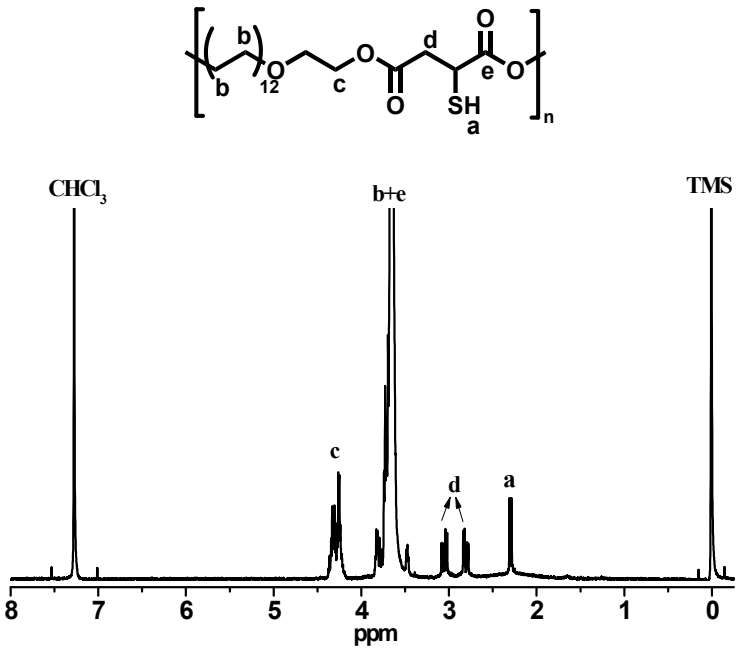



**Fig. S1** $^{1}$H NMR spectrum of POEGMS.

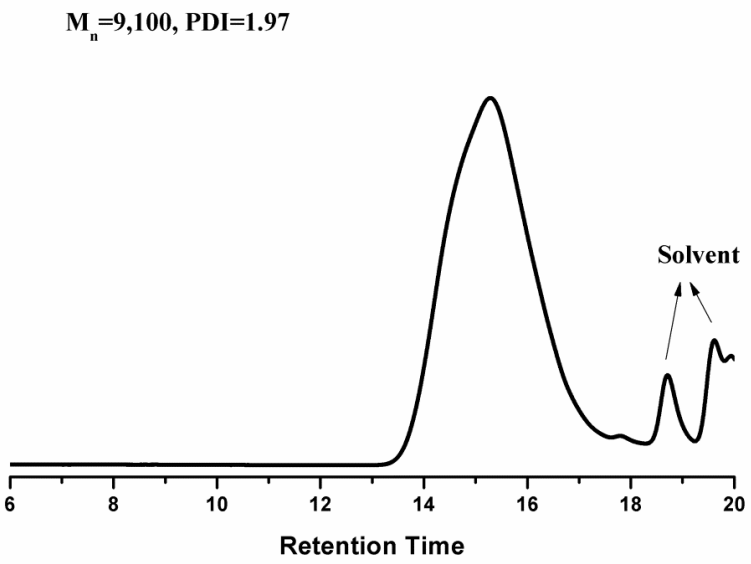



**Fig. S2** GPC trace of POEGMS.

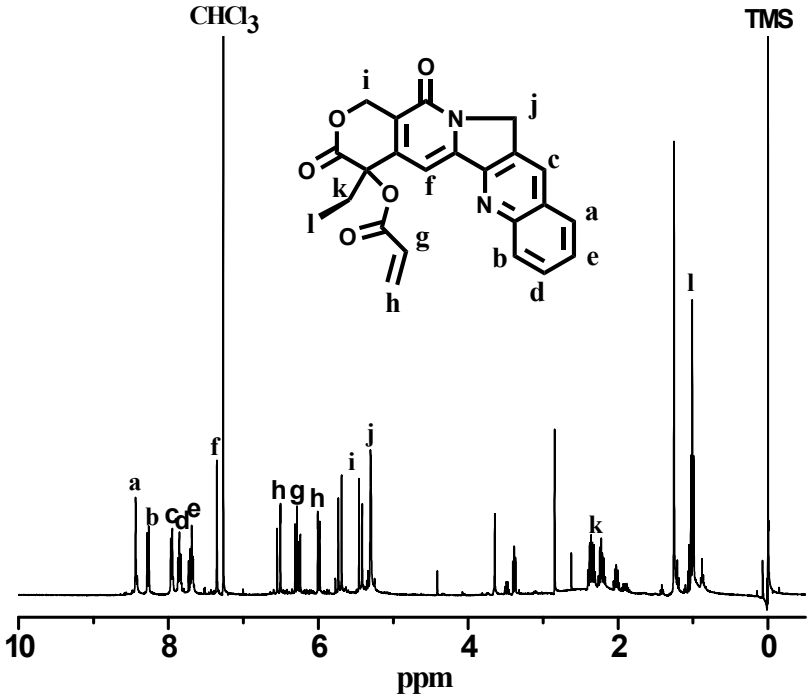



**Fig. S3** $^{1}$H NMR spectrum of acryl-CPT.

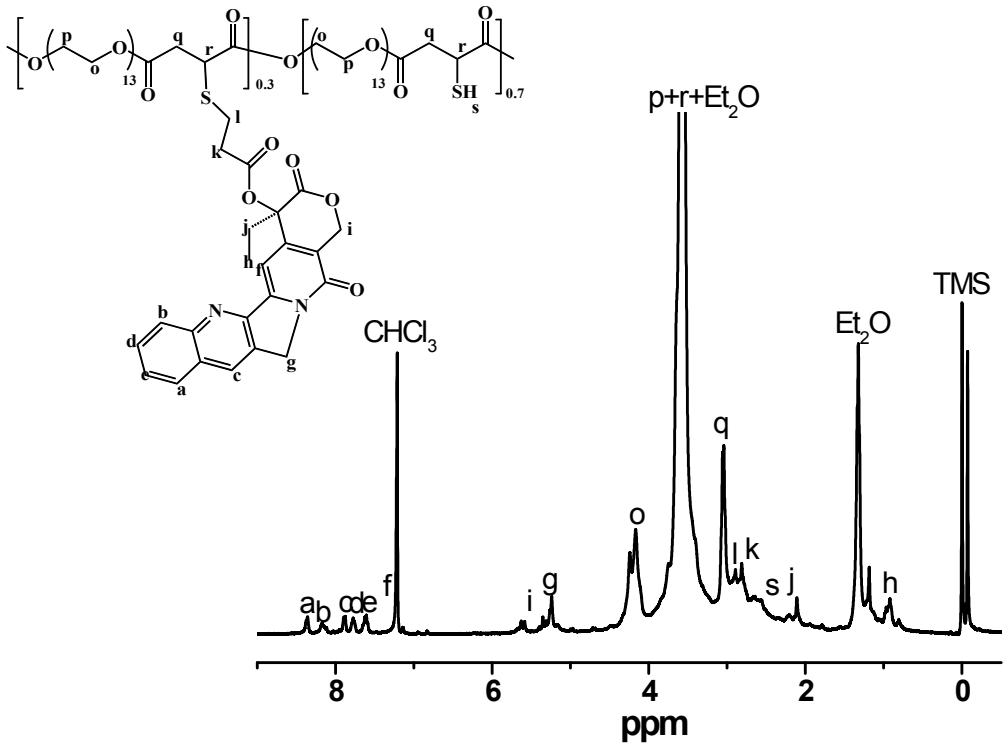



**Fig. S4** [1]H NMR spectrum of POEGMS-*g*-CPT.

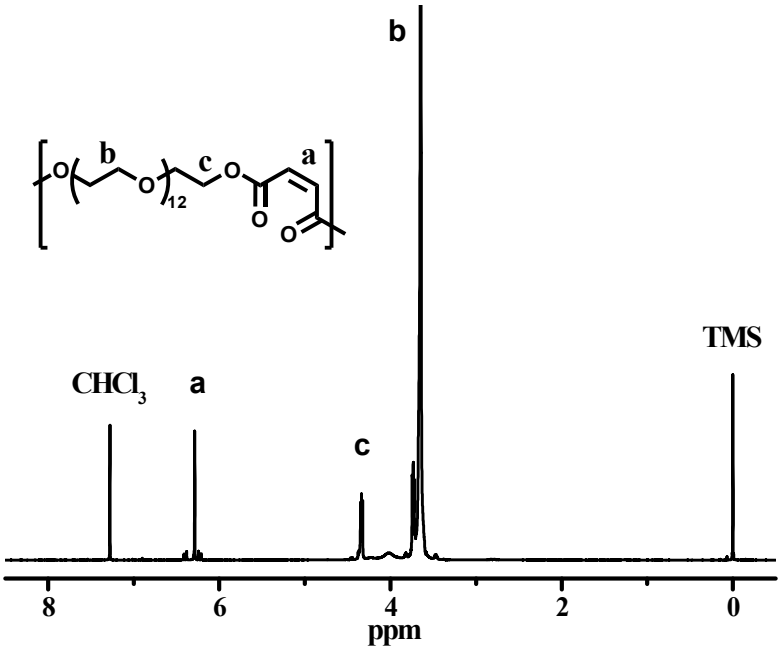



**Fig. S5** [1]H NMR spectrum of POEGM.

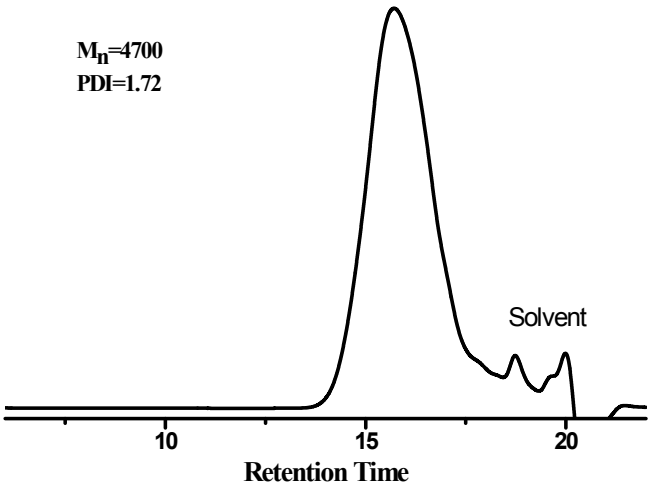



**Fig. S6** GPC trace of POEGM.

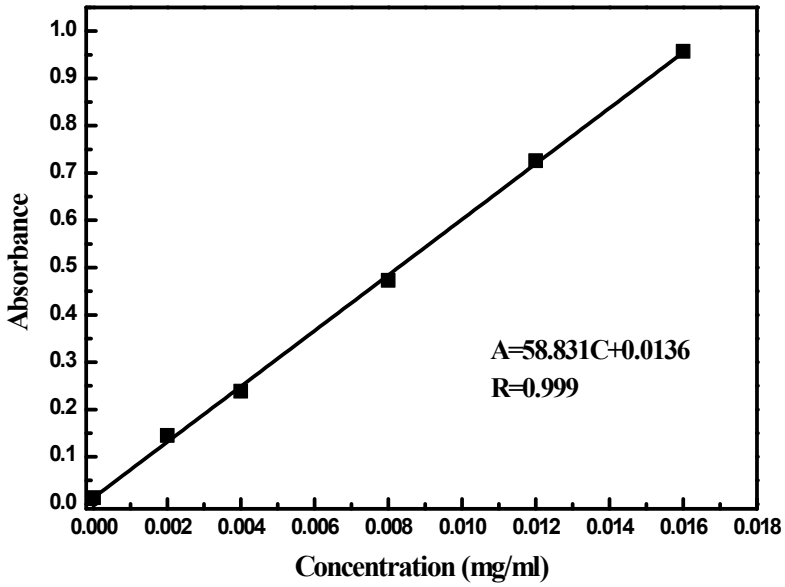



**Fig. S7** Calibration curve of CPT in DMF by UV-vis at 365 nm.

**References**

1 K. Zhang, Y. Wang, W. P. Zhu, X. D. Li and Z. Q. Shen, *J. Polym. Sci. Pol. Chem.*, 2012, 50, 2045-2052.