Supplementary Information for:

Supramolecular Crafting of Self-Assembling Camptothecin Prodrugs with Enhanced Efficacy against Primary Cancer Cells

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Drug loading calculation

The drug loading of the SAPD is calculated by the following equation

$$Drug\ loading\ (\%)\ =\frac{n\times M_{CPT}}{M_{SAPD}}\times 100\%$$

where n is the number of CPT molecules per SAPD, M_{CPT} is molecular weight of the CPT (348.35 g/mol) and M_{SAPD} is the molecular weight of the SAPD.

dCPT-K$_2$ $drug\ loading$ (%) = (2 × 348.35 /1592.84) × 100% = 43.74%

dCPT-OEG$_5$-K$_2$ $drug\ loading$ (%) = (2 × 348.35 /1884.18) × 100% = 36.98%

dCPT-Sup35-K$_2$ $drug\ loading$ (%) = (2 × 348.35 /2411.64) × 100% = 28.89%
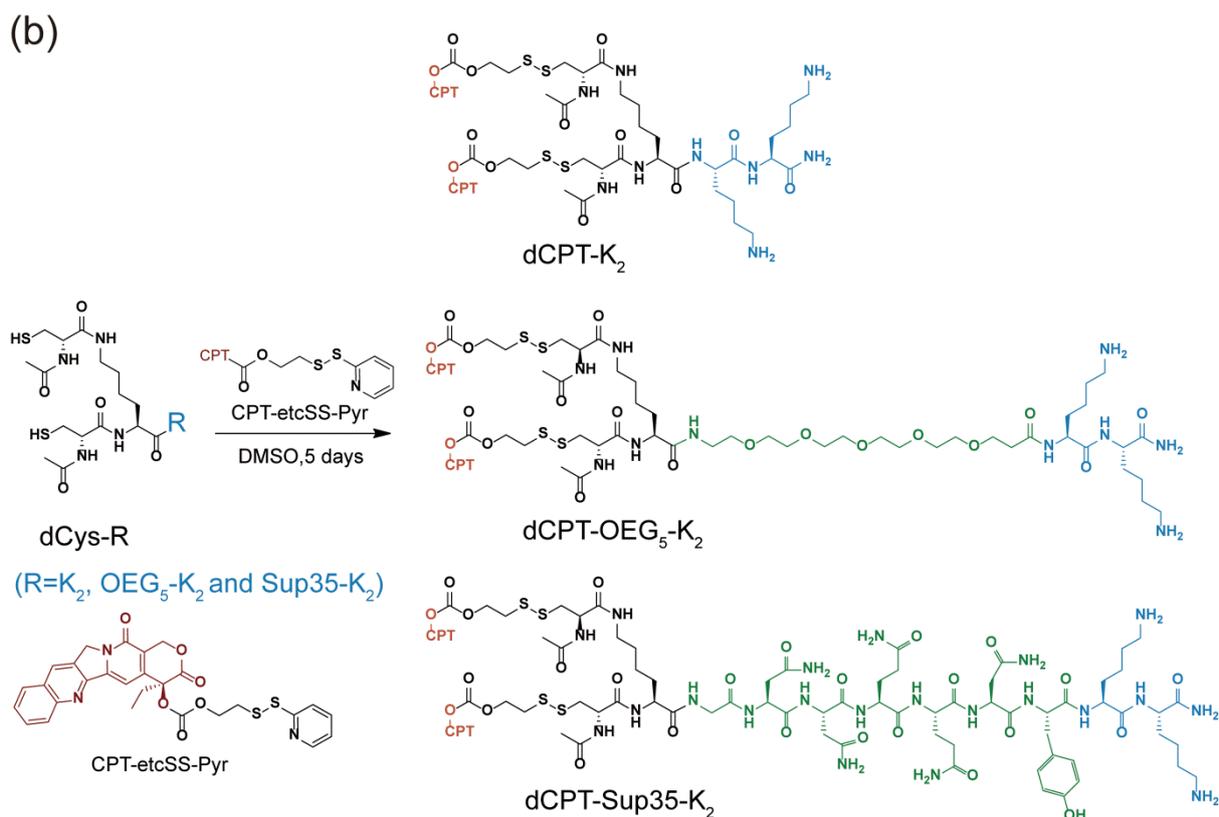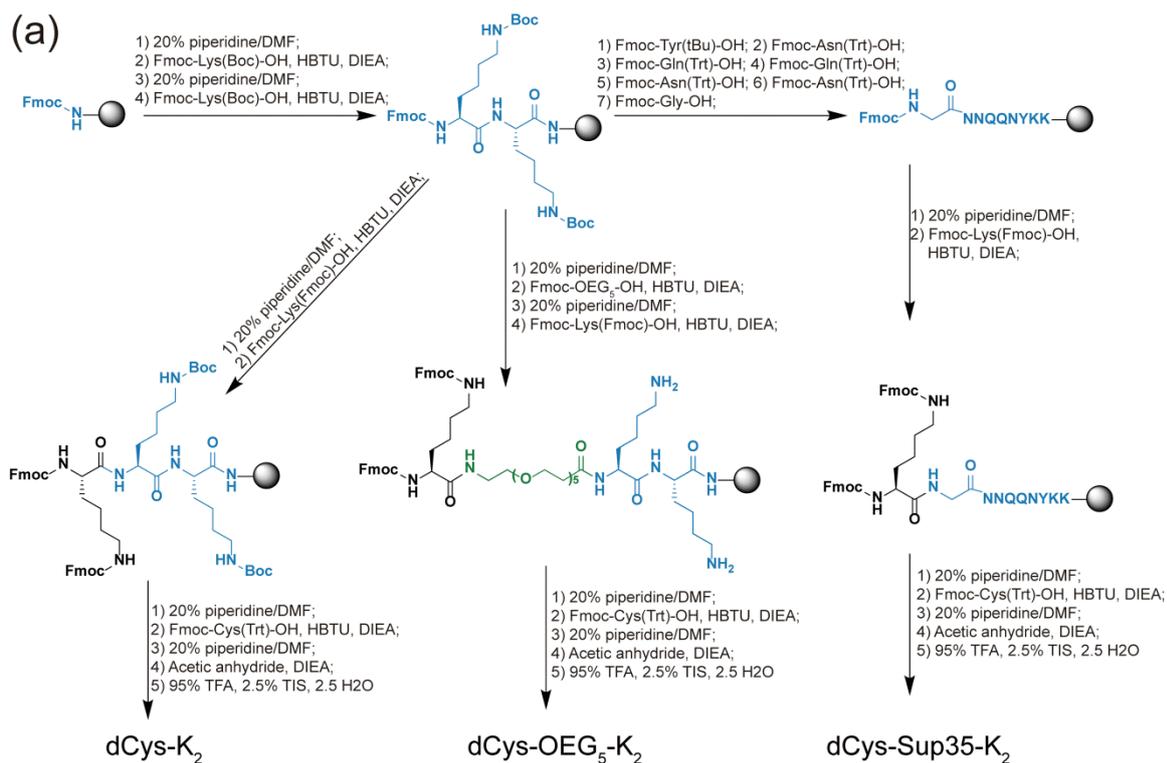
Scheme S1. (a) Synthetic routes of peptide segments (dCys-K$_2$, dCys-OEG$_5$-K$_2$ and dCys-Sup35-K$_2$) using standard Fmoc solid phase peptide techniques and (b) synthesis of self-assembling prodrugs by mixing peptide segments synthesized in (a) with CPT-etcSS-Pyr in DMSO.
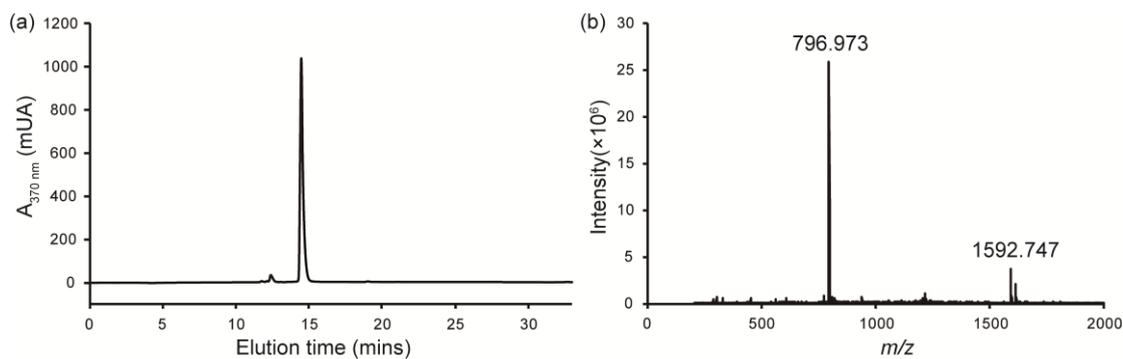
Figure S1. RP-HPLC (a) and ESI-MS spectrum (b) of dCPT-K_2. The peaks at 796.973 and 1592.747 correspond to $[M+2H]^{2+}$ and $[M+H]^+$, respectively.
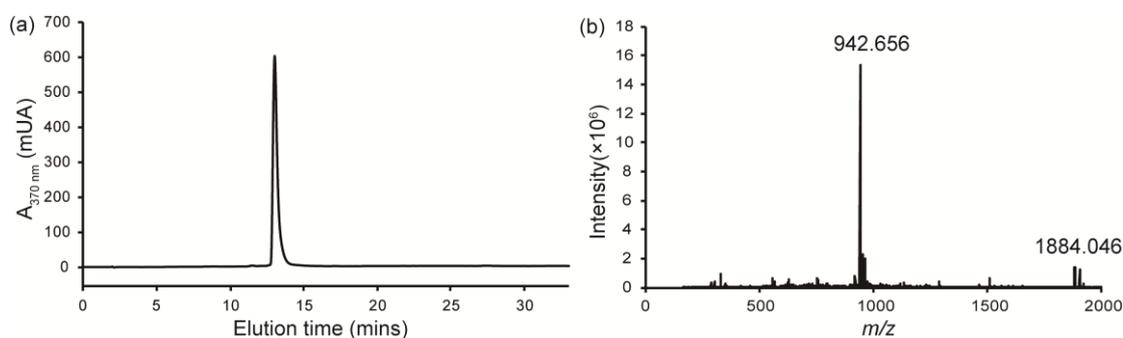
Figure S2. RP-HPLC (a) and ESI-MS spectrum (b) of dCPT-OEG_5-K_2. The peaks at 942.656 and 1884.046 correspond to $[M+2H]^{2+}$ and $[M+H]^+$.
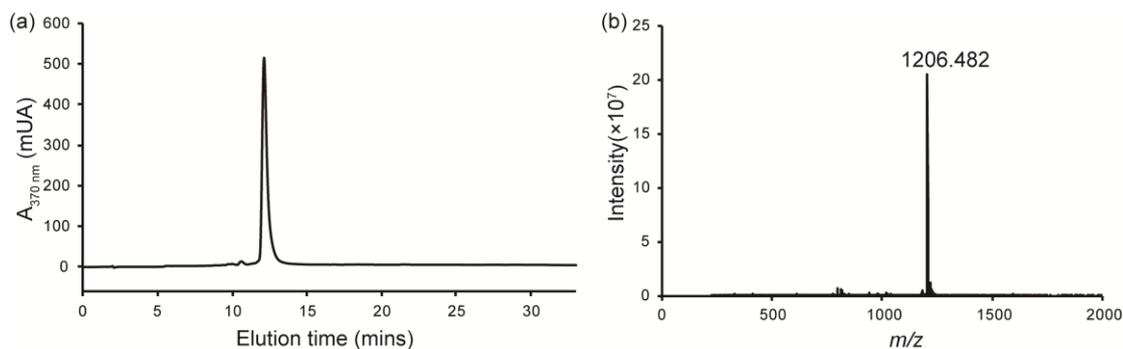
Figure S3. RP-HPLC (a) and ESI-MS spectrum (b) of dCPT-Sup35-K_2. The peaks at 1206.482 correspond to $[M+2H]^{2+}$.
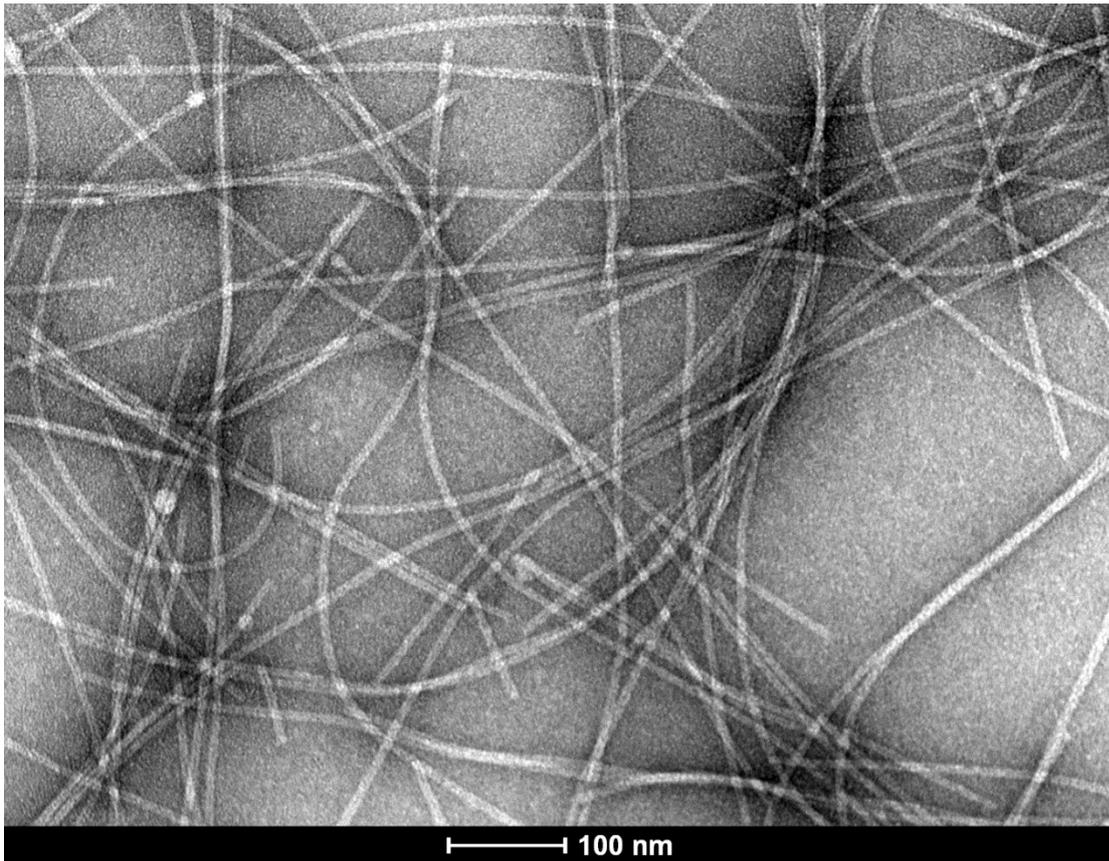
Figure S4. TEM image of nanotubes formed by dCPT-K$_2$ in water at $100 \, \mu$ M.
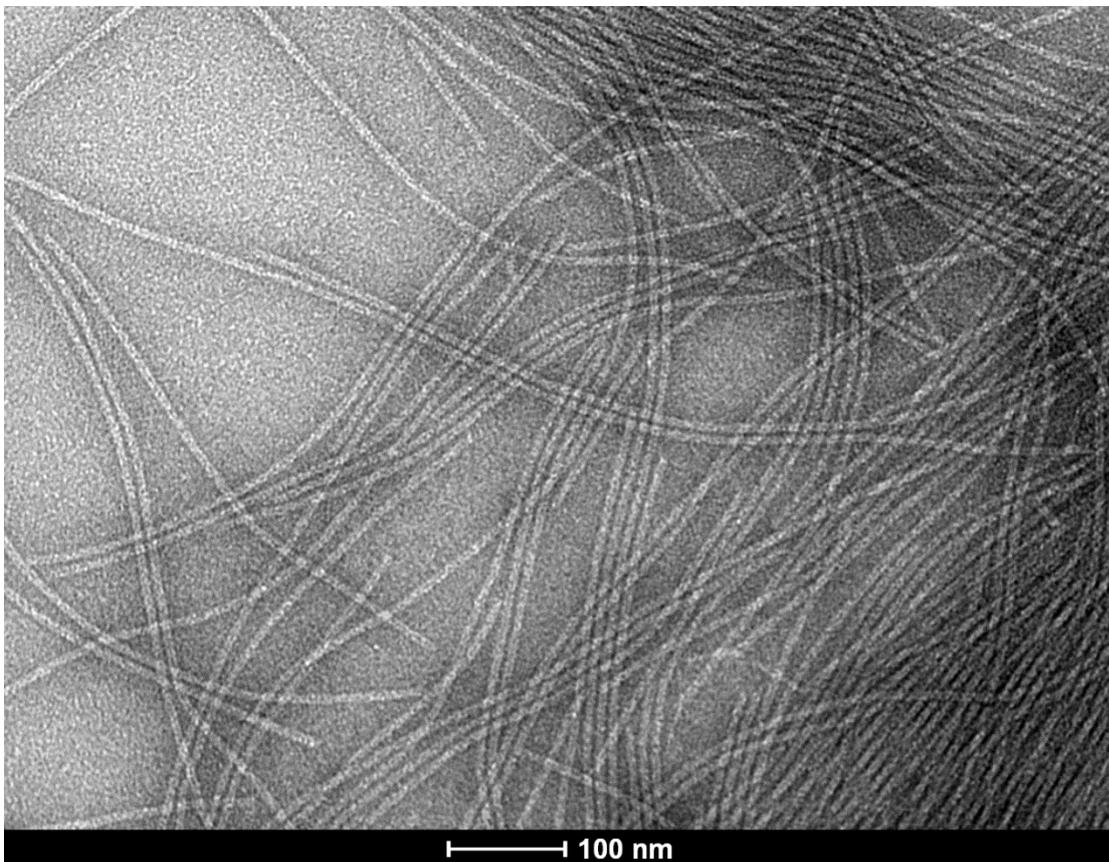
Figure S5. TEM image of nanotubes formed by dCPT-OEG$_5$-K$_2$ in water at $100 \, \mu$M.
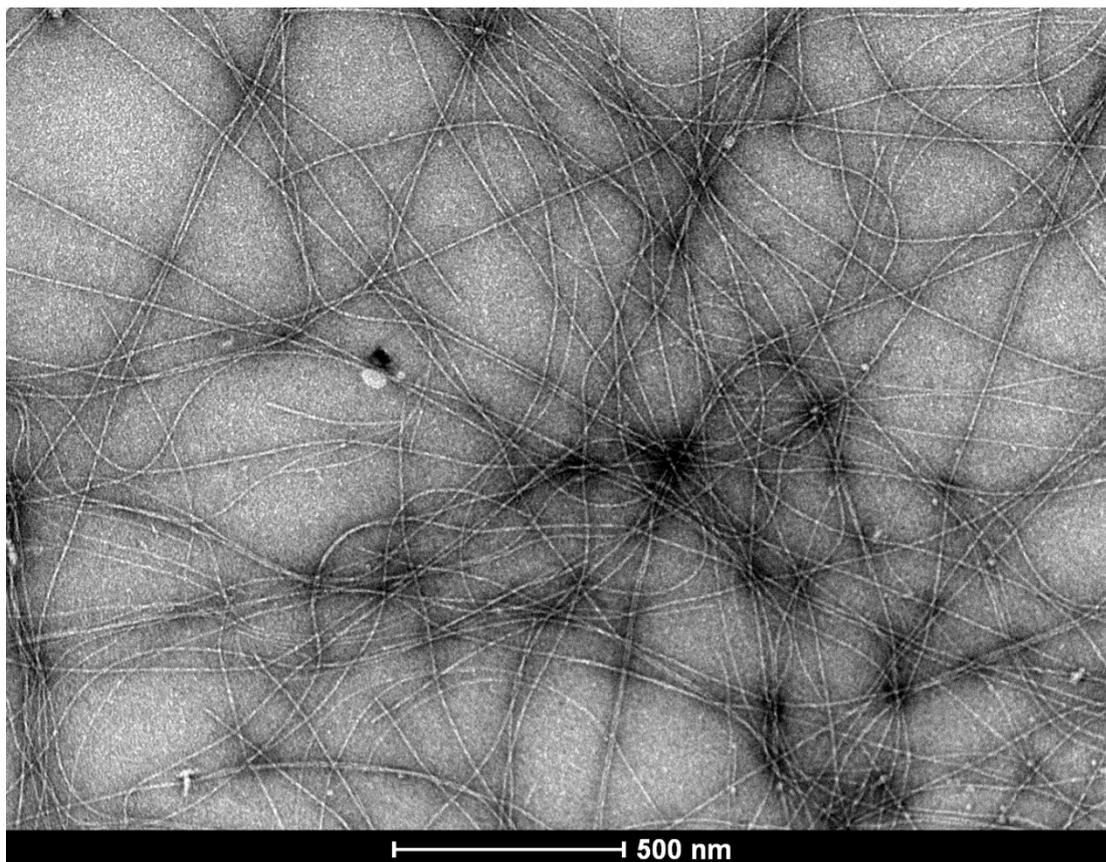
Figure S6. TEM image of nanofibers formed by dCPT-Sup35-K_2 in water at 100 μM.
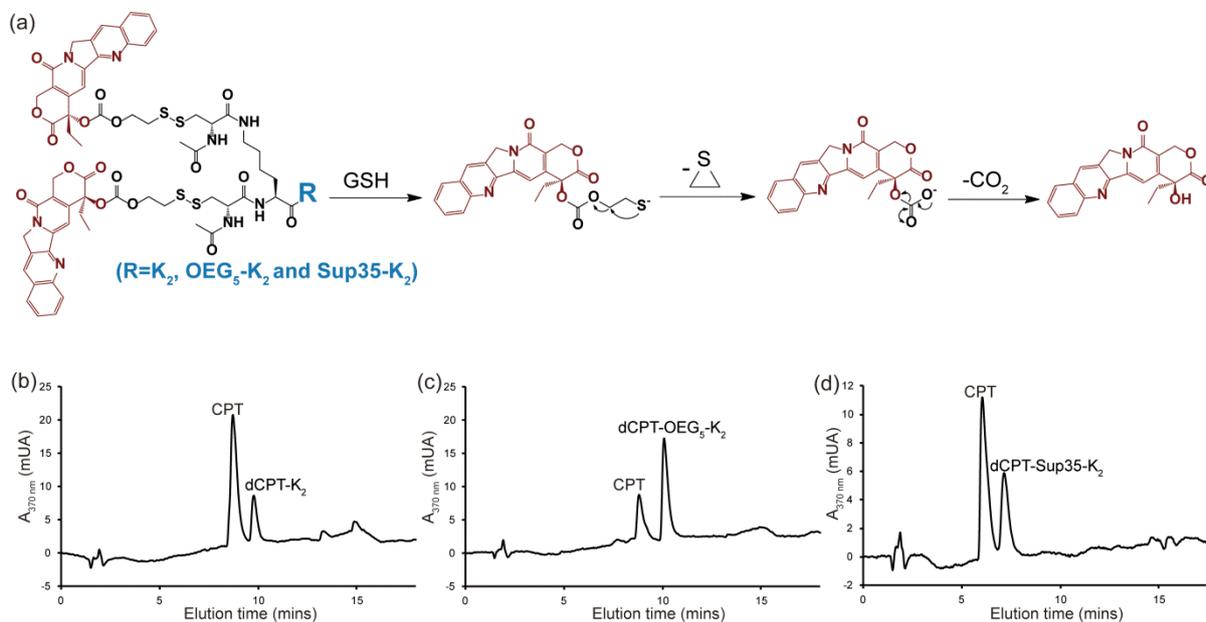
Figure S7. (a) Expected molecular mechanism of GSH-induced release of free CPT from the designed conjugates (dCPT-K_2, dCPT-OEG_5-K_2 and dCPT-Sup35-K_2). HPLC analysis of free CPT release from conjugates dCPT-K_2 after 5 minutes incubation (b), dCPT-OEG_5-K_2 after 5 minutes incubation (c) and dCPT-Sup35-K_2 after 10 minutes incubation (d). The conjugates concentrations for all the cases were 25μM, and the release experiments were carried out in the presence of 10 mM GSH in 10 mM sodium phosphate solution at 37℃.