Supporting Information

Smart-Responsive Carrier-Free Nanoassembly of SN38 Prodrug as Efficient Chemotherapeutic Nanomedicine

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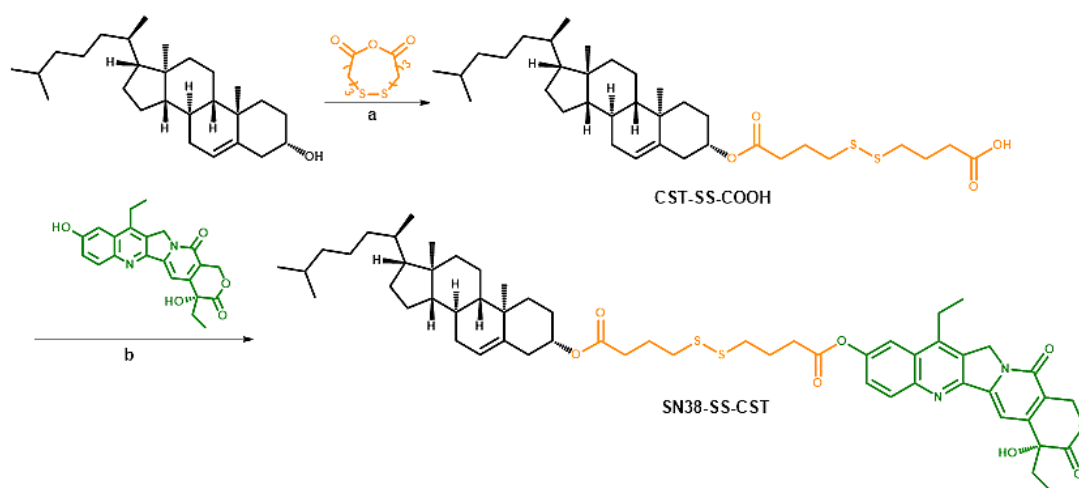[*]Correspondence: hezhgui_student@aliyun.com (Z. He); sunbingjun_spy@sina.com (B. Sun)

Figure S1. Synthetic scheme of SN38-SS-CST. a) DMAP, 25 ℃, 12 h. b) EDCI, HOBT, DMAP, 25 ℃, 24 h.
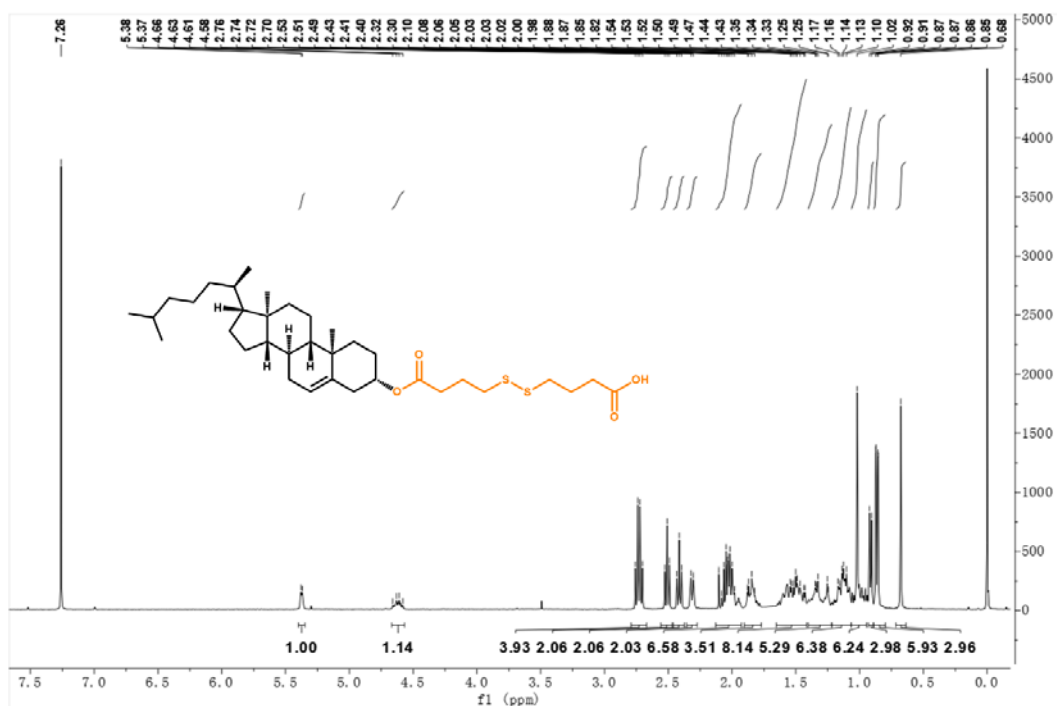
Figure S2. ^{1}H NMR of CST-SS-COOH. ^{1}H NMR (400 MHz, Chloroform-d) δ 5.37 (d, J = 4.4 Hz, 1H), 4.67 – 4.57 (m, 1H), 2.73 (q, J = 7.3 Hz, 4H), 2.51 (t, J = 7.2 Hz, 2H), 2.41 (t, J = 7.3 Hz, 2H), 2.31 (d, J = 7.7 Hz, 2H), 2.13 – 1.93 (m, 7H), 1.90 – 1.77 (m, 4H), 1.65 – 1.42 (m, 8H), 1.40 – 1.22 (m, 5H), 1.14 (dt, J = 13.8, 7.5 Hz, 6H), 1.02 (s, 6H), 0.91 (d, J = 6.5 Hz, 3H), 0.86 (dd, J = 6.6, 1.8 Hz, 6H), 0.68 (s, 3H).
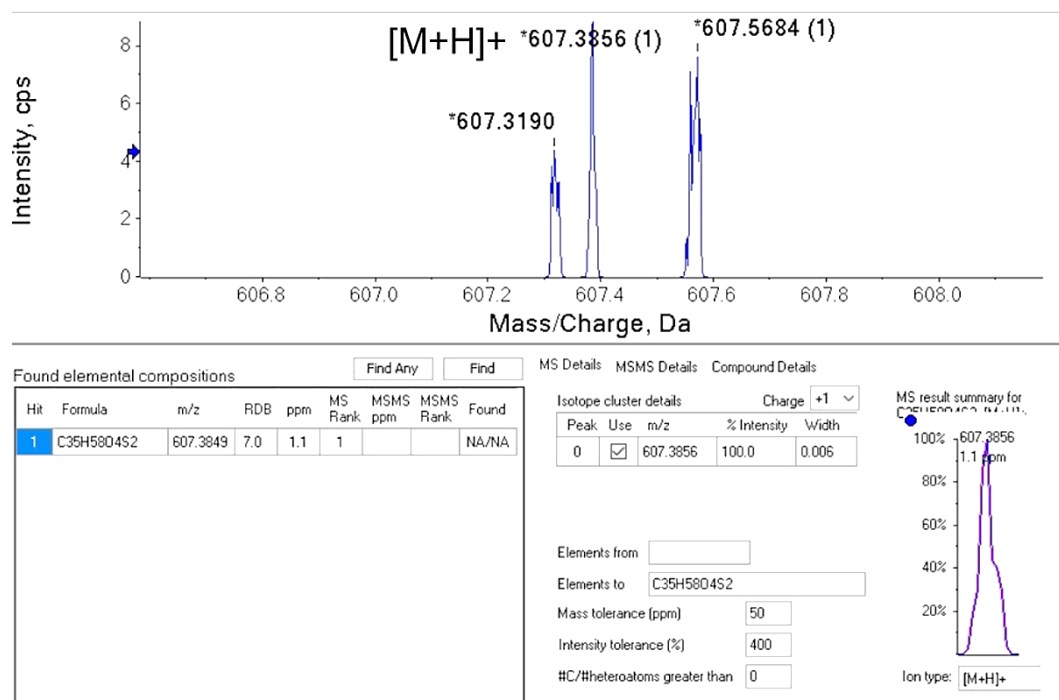
Figure S3. MS of CST-SS-COOH. Calcd for $C_{35}H_{58}O_4S_2$, 607.3849; found, 607.3856 $[M+H]^+$.
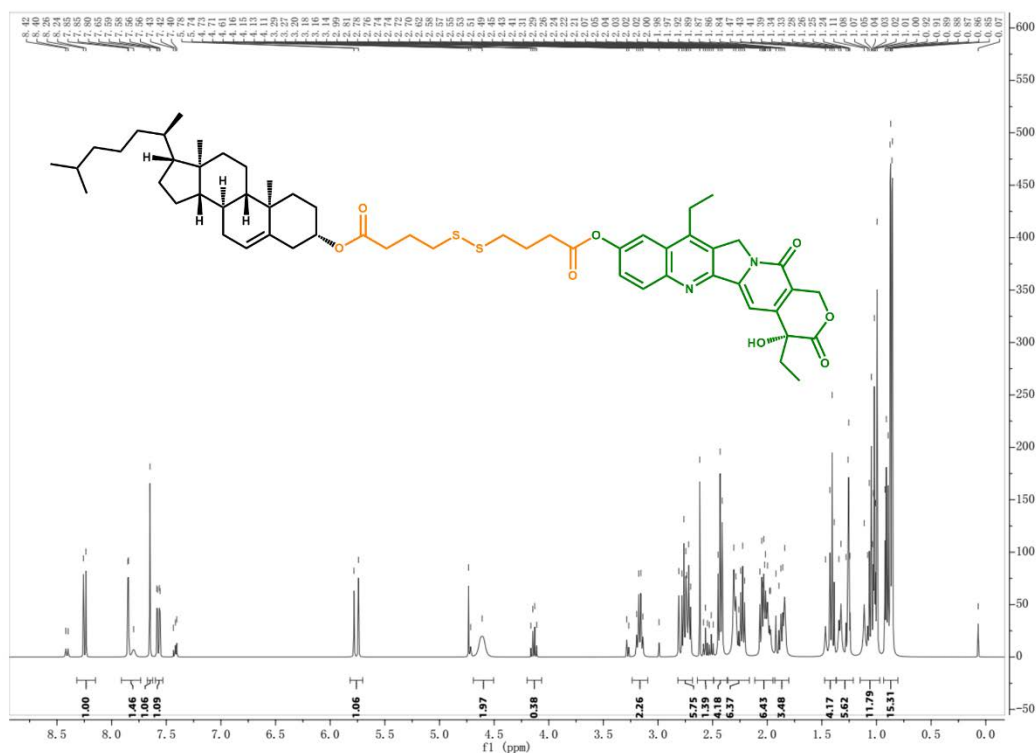
Figure S4. [^1]H NMR of SN38-SS-CST. [^1]H NMR (400 MHz, Chloroform-*d*) δ 8.25 (d, *J* = 9.2 Hz, 1H, Ar-H), 7.85 (d, *J* = 2.5 Hz, 1H, Ar-H), 7.65 (s, 1H, Ar-H), 7.57 (dd, *J* = 9.1, 2.5 Hz, 1H, Ar-H), 5.76 (d, *J* = 16.3 Hz, 1H, -CH), 4.59 (s, 3H), 4.17-4.11 (m, 1H, -CH), 3.17 (q, *J* = 8.3 Hz, 2H), 2.85 - 2.74 (m, 6H, -CH$_2$), 2.64 - 2.48 (m, 3H), 2.42 (q, *J* = 7.6 Hz, 4H), 2.27 (d, *J* = 32.4 Hz, 6H), 2.05 (s, 6H), 1.92 (s, 3H), 1.41 (s, 4H), 1.25 (s, 6H), 1.03 (dd, *J* = 19.5, 8.7 Hz, 12H), 0.95 - 0.83 (m, 15H, -CH$_3$).

Monoisotopic Mass, Even Electron Ions
1426 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 57-57   H: 77-77   N: 0-11   O: 0-37   Na: 0-3   S: 2-2
12
221210-2-14-6-2-cst 76 (0.441)   1: TOF MS ES+
                                                                                                          3.46e+002
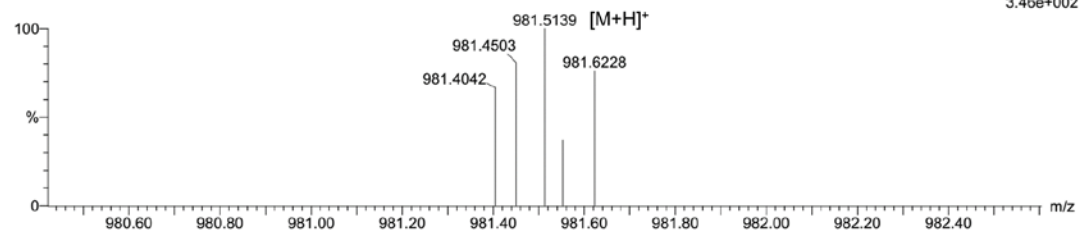

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Minimum:                        -1.5
Maximum:             5.0   20.0   50.0

Mass         Calc. Mass  mDa   PPM   DBE    i-FIT   Norm   Conf(%)  Formula
981.5139     981.5121    1.8   1.8   20.5   43.7    n/a    n/a      C57 H77 N2 O8 S2
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Figure S5. MS of SN38-SS-CST. Calcd for $C_{57}H_{76}N_2O_8S_2$, 980.5043; found, 981.5121 $[M+H]^+$.
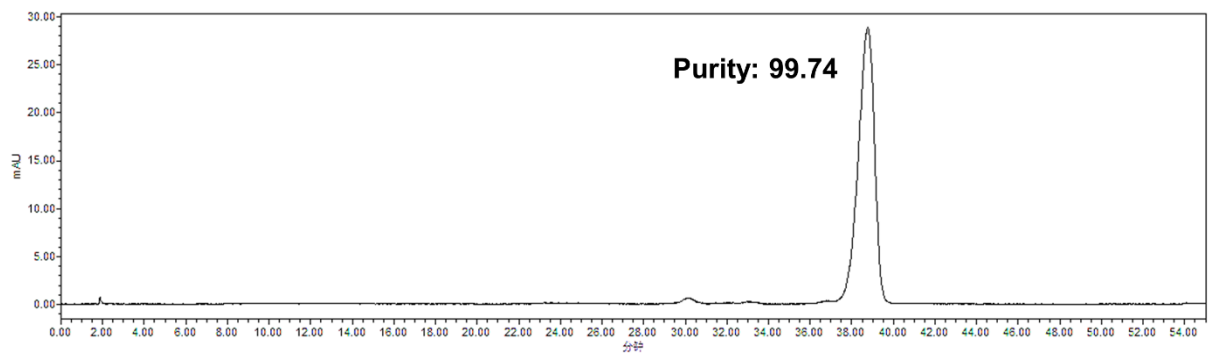
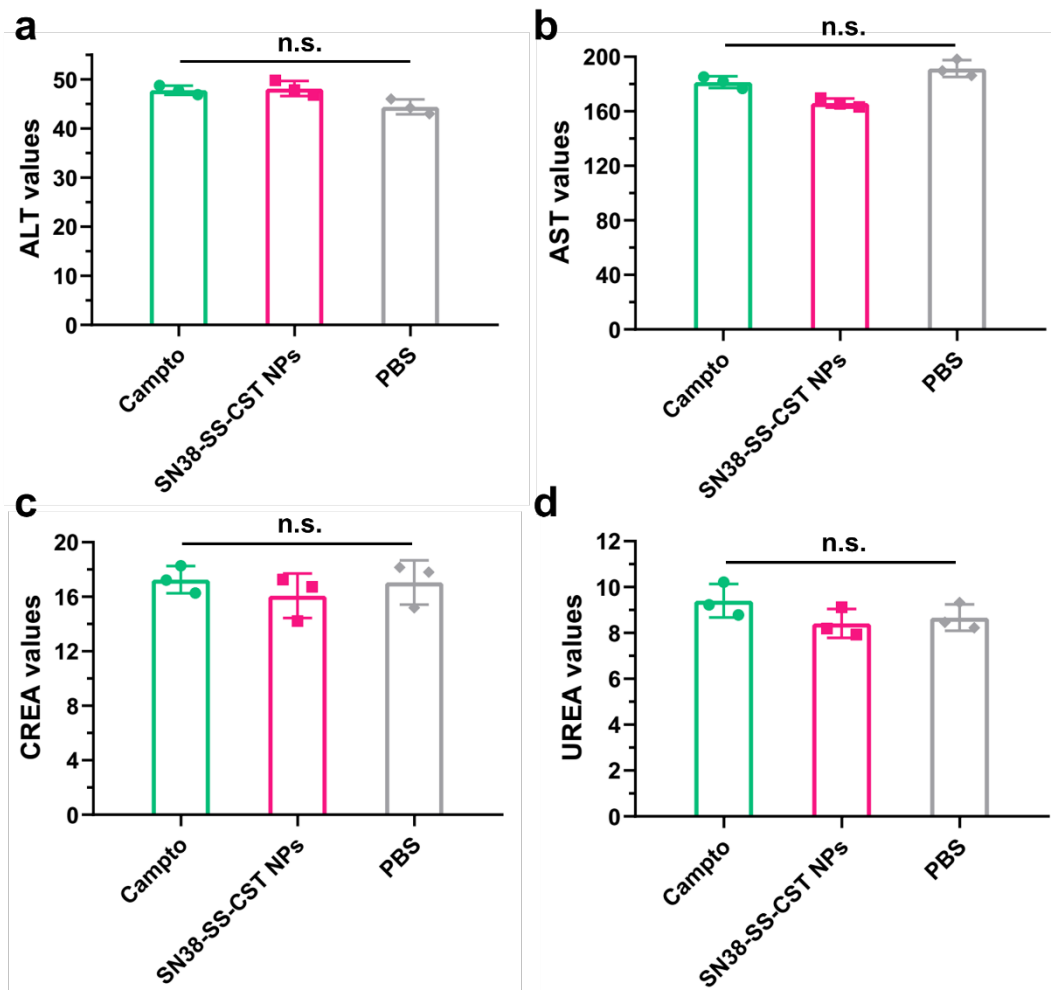**Figure S6.** HPLC spectra of SN38-SS-CST. Purity: 99.74%.

Figure S7. Hepatorenal functions of CT26 bearing mice after the treatment. a) ALT values. b) AST values. c) CREA values and d) UREA values. Data are presented as means ± SD (n = 3).
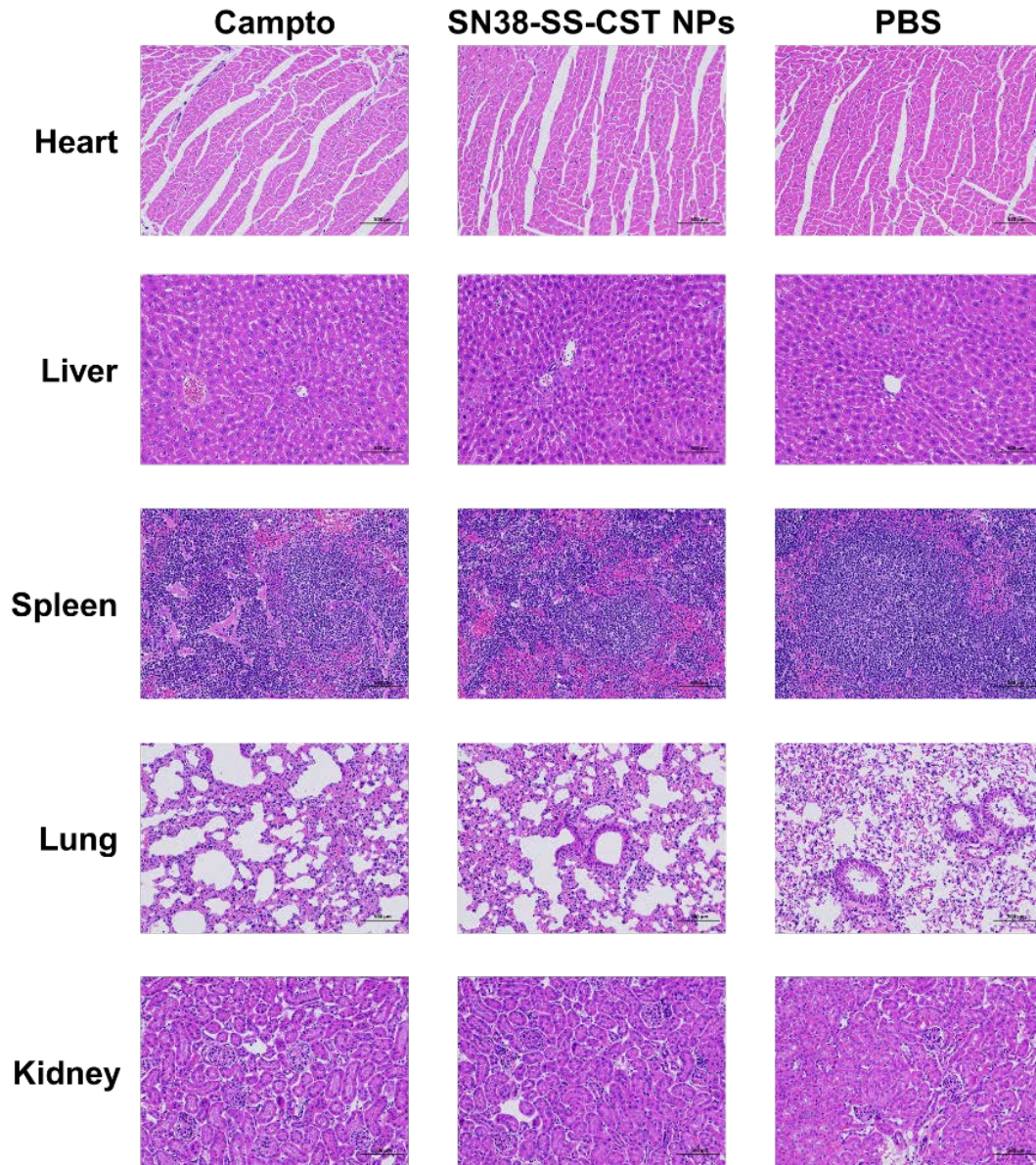
Figure S8. H&E staining of major organs of 4T1 bearing mice. Scale bar = 500 μm.

Table S1. Characterization of SN38-SS-CST NPs

Formulation	Size (nm)	PDI	Zeta potential (mV)	Drug loading (%)
SN38-SS-CST NPs	104.5±1.504	0.078±0.096	-22.3±0.068	31.94

Data are presented as mean ± SD.

Table S2. Molecular dynamics simulation diameters

Formulation	Grid Score[a]	Grid vdw energy[b]	Grid es energy[c]	Internal energy repulsive[d]
SN38-SS-CST NPs	-56.491173	-56.519341	0.028166	36.259464

a) The diameter indicates binding affinity (kcal mol^{-1}). b) The diameter indicates Van der Waals forces (kcal mol^{-1}). c) The diameter indicates electrostatic forces (kcal mol^{-1}). d) The diameter indicates repulsive affinity (kcal mol^{-1}).

Table S3. IC_{50} values of the formulations.

Formulations	IC_{50} on CT26 cell (nM)	IC_{50} on 4T1 cell (nM)
Campto	2063	2638
SN38-SS-CST NPs	291.2	335.7