Supporting Information

Polydopamine-Modified ROS-responsive Prodrug Nanoplatform with Enhanced Stability for precise treatment of breast cancer

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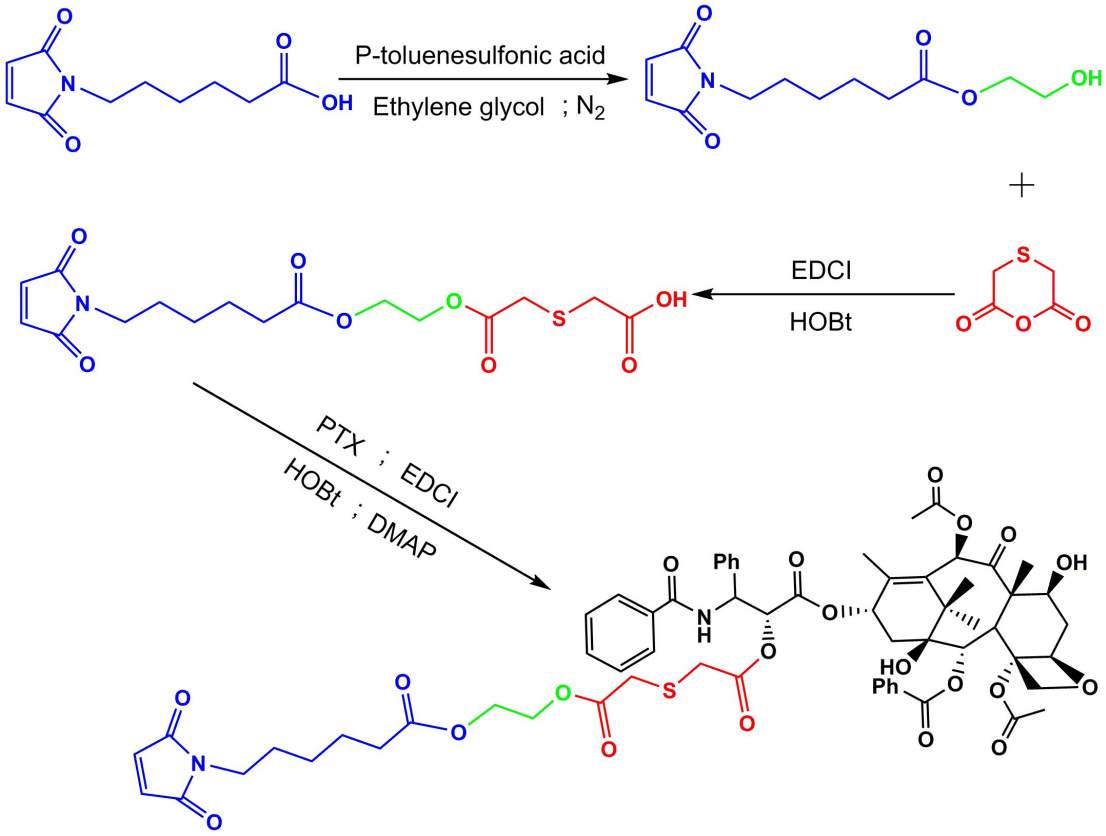
Synthesis the prodrug of PTX

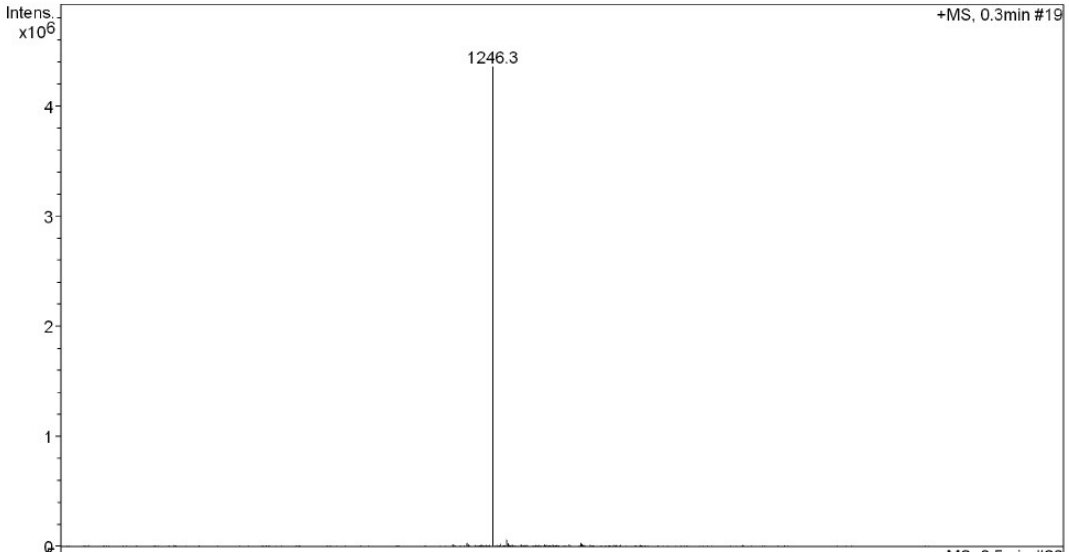
As illustrated in Fig. S1, the maleimide-bearing prodrugs (PTX-S-MAL) were synthesized by conjugating 6-Maleimidocaproic acid 2-hydroxyethyl ester to PTX via inserting a thioether bond linker. The chemical structure of PTX-S-MAL was confirmed by mass spectrum and 1H NMR spectroscopy (Fig. S2 -S3).

PTX-S-MAL ^{1}H-NMR (400MHz, $CDCl_3$):

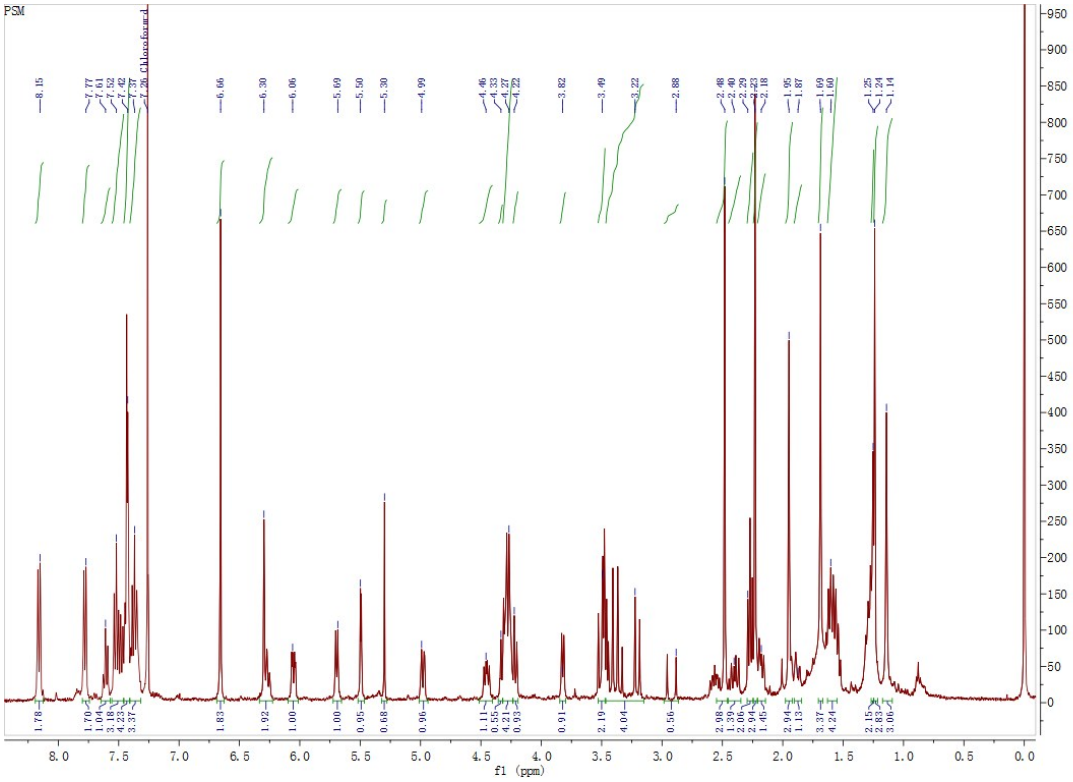
^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.15 (d, 2H), 7.77 (d, 2H), 7.61 (m, 1H), 7.52 (m, 3H), 7.42 (d, 4H), 7.37 (m, 3H), 6.66 (s, 2H, -COCH=CHCO-), 6.30 (t, 2H, 10-H, 13-H), 6.06 (dd, 1H, J=5.7 Hz, J=2.1 Hz, 3'-H), 5.69 (d, 1H, J=5.4 Hz, 2-H), 5.50 (d, 1H, J=2.4 Hz, 2'-H), 5.30 (d, 1H, J=6.9 Hz, -NH-), 4.99 (d, 1H, J=6.9 Hz, 5-H), 4.46 (t, 1H, 7-H), 4.33 (d, 1H, J=6.0 Hz, 20α-H), 4.27 (s, 4H, -OCH_2CH_2O-), 4.22 (d, 1H, J=6.3 Hz, 20β-H), 3.82 (d, 1H, J=5.1 Hz, 3-H), 3.49 (t, 2H, -CH_2-N (CO) CO), 3.22 (m, 4H, -$COCH_2SCH_2CO$-), 2.88 (m, 1H, 6α-H), 2.48 (s, 3H, 4-$COCH_3$), 2.40 (m, 2H, 14α-H, 14β-H), 2.29 (t, 2H, J=5.7 Hz, -CH_2CO-), 2.23 (s, 3H, 10-$COCH_3$), 2.18 (t, 2H, J=6.9 Hz, -CH_2CO-), 1.95 (s, 3H, 18-H), 1.87 (t, 1H, 6β-H), 1.69 (s, 3H, 19-H), 1.60 (m, 4H, -$CH_2CH_2CH_2$-), 1.25 (m, 2H, -$CH_2CH_2CH_2$-), 1.24 (s, 3H, 17-H), 1.14 (s, 3H, 16-H). MS (ESI) (m/z): calcd for $C_{63}H_{71}N_2O_{21}S$: m/z 1246.3 $[M+Na]^+$; found: 1223.3.



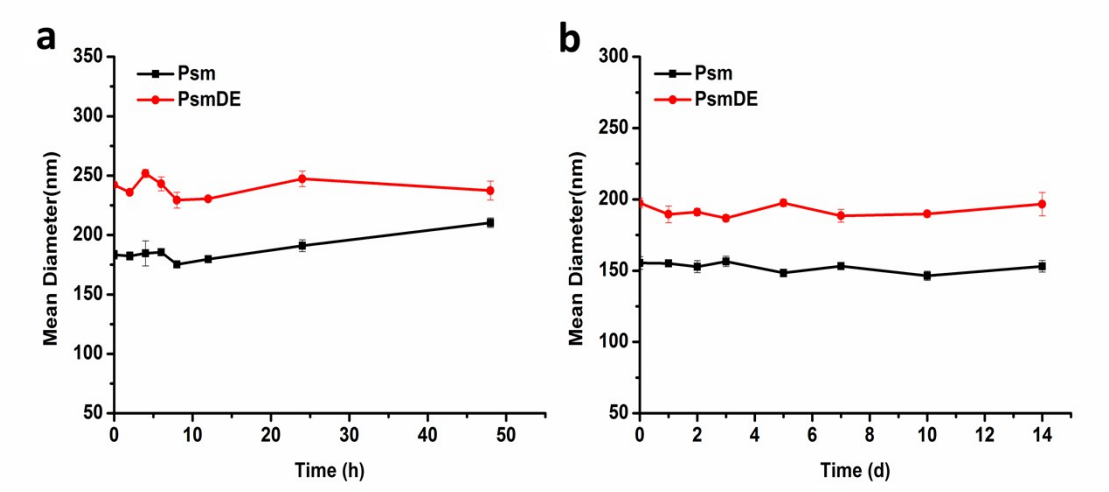
FigS1. Synthesis procedure of PTX-S-MAL



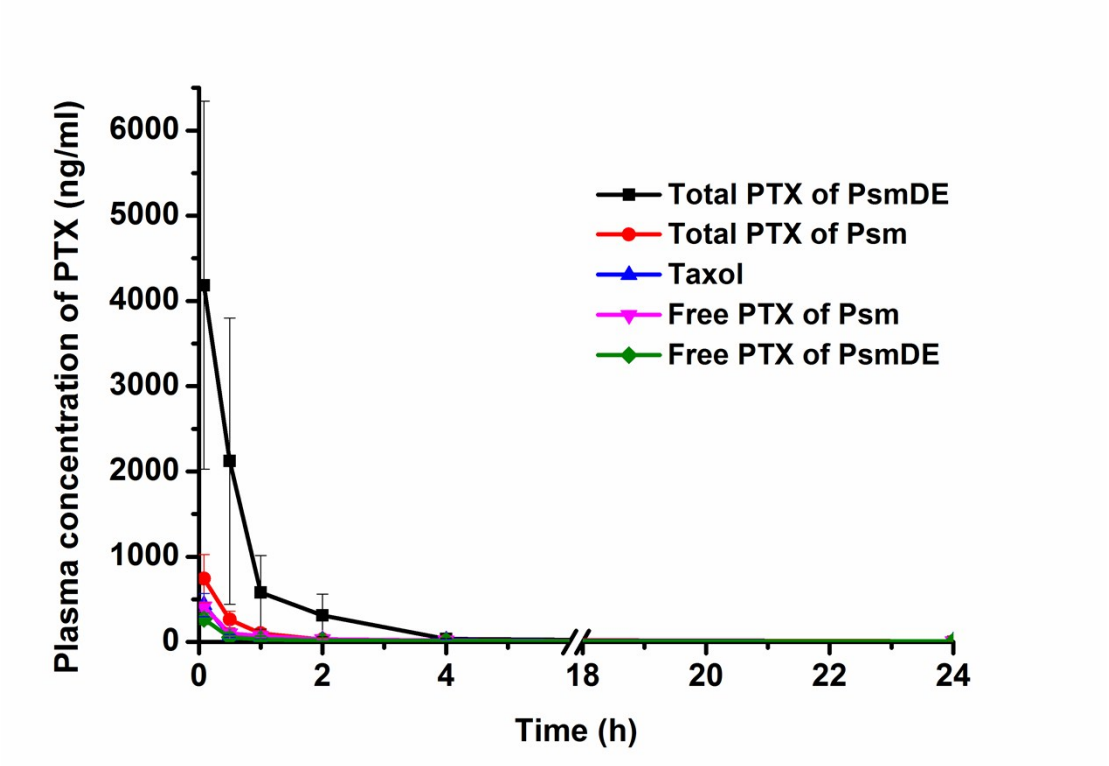
FigS2. Mass spectrum of PTX-S-MAL



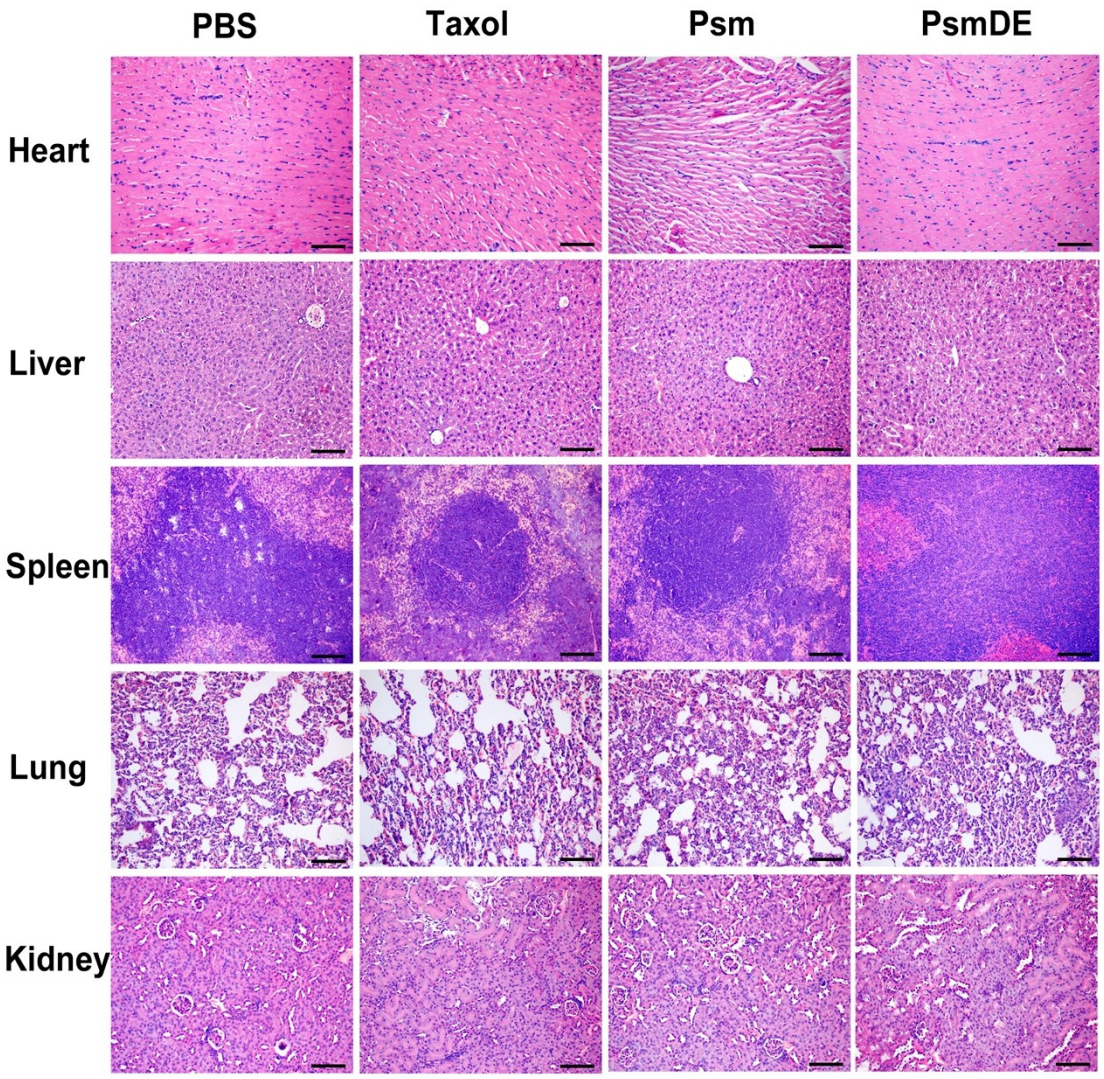
FigS3. 1H NMR spectrum of PTX-S-MAL



FigS4. (a) Colloidal stability of Psm and PsmDE after incubation in PBS (pH 7.4) supplemented with 10% FBS at 37 °C. (b) Long-term stability of Psm and PsmDE after store at 4 °C.



FigS5. *In vivo* plasma concentration-time profiles of free and total PTX in blood after Taxol, Psm, and PsmDE were intravenously injected into the mice through the tail vein at a PTX dose of 1 mg/kg. All data are presented as mean ± SD (n=5).



FigS6. H&E stained images of major organs; Heart, Liver, spleen, lung and kidney of healthy mice. The mice were sacrificed.

Table S1. Characteristics of Prodrug NPs

PPa/NPs	Size[a] (nm)	Zeta[b] (mv)	PDI[c]
Psm	165.7 ± 5.8	-20.2 ± 0.74	0.079 ± 0.018
PsmD	183.7 ± 1.3	-25.1 ± 3.07	0.066 ± 0.056
PsmDE	196.4 ± 5.8	-18.1 ± 1.56	0.099 ± 0.094

a) Mean diameters and b) Zeta potential of prodrug NPs obtained by DLS. c) Polydispersity index of the Prodrug NPs.

Table S2.In vitro cytotoxicity ((IC_{50}) values) of PTX-sol and Prodrug NPs to 4T1 cancer cells (MTT assay).

Formulations	4T1 (nM)	
	48 h	72 h
PTX-sol	59.6	21.46
Psm	59.3	30.1
PsmDE-	76.31	31.8

Table S3.In vitro cytotoxicity ((IC_{50}) values) of PTX-sol and Prodrug NPs to 3T3 cancer cells (MTT assay).

Formulations	3T3 (nM)	
	48 h	72 h
PTX-sol	245.6	148.8
Psm	511.9	344.2
PsmDE-	630.3	435.6