Supplementary Material for

Programmed Hydrolysis in Designing Paclitaxel Prodrug for Nanocarrier Assembly

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ς Deceased

≅ This paper is dedicated to the memory of Professor Feng Liu, PhD, 1955-2014 University of North Carolina at Chapel Hill

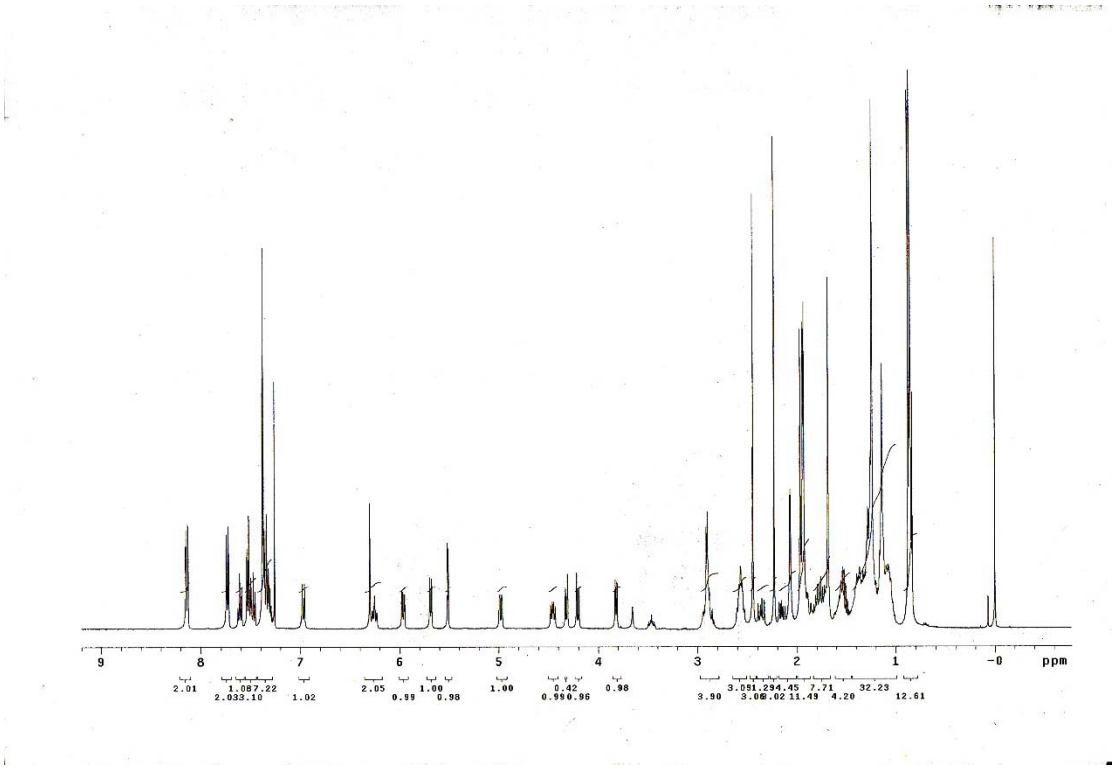

Fig. S1. ^{1}H NMR (400 MHz) spectrum of PTX-Ve in D_2O at 25°C.

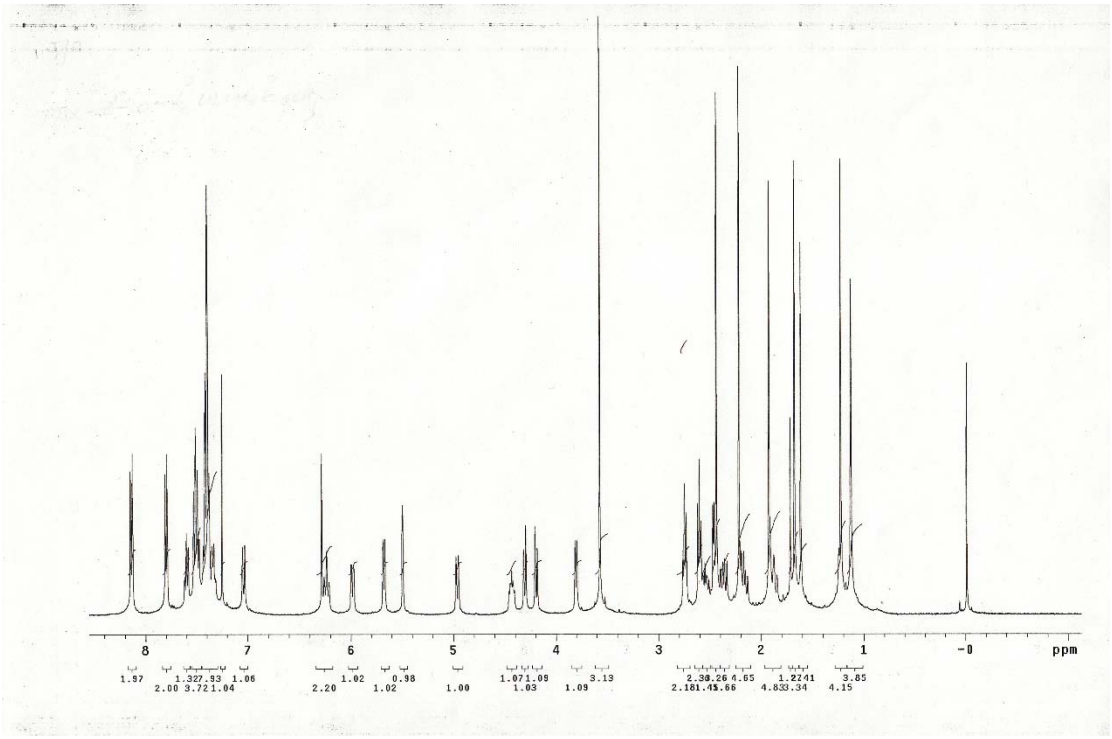

Fig. S2. ^{1}H NMR (400 MHz) spectrum of PTX-SEE in D_2O at 25°C.

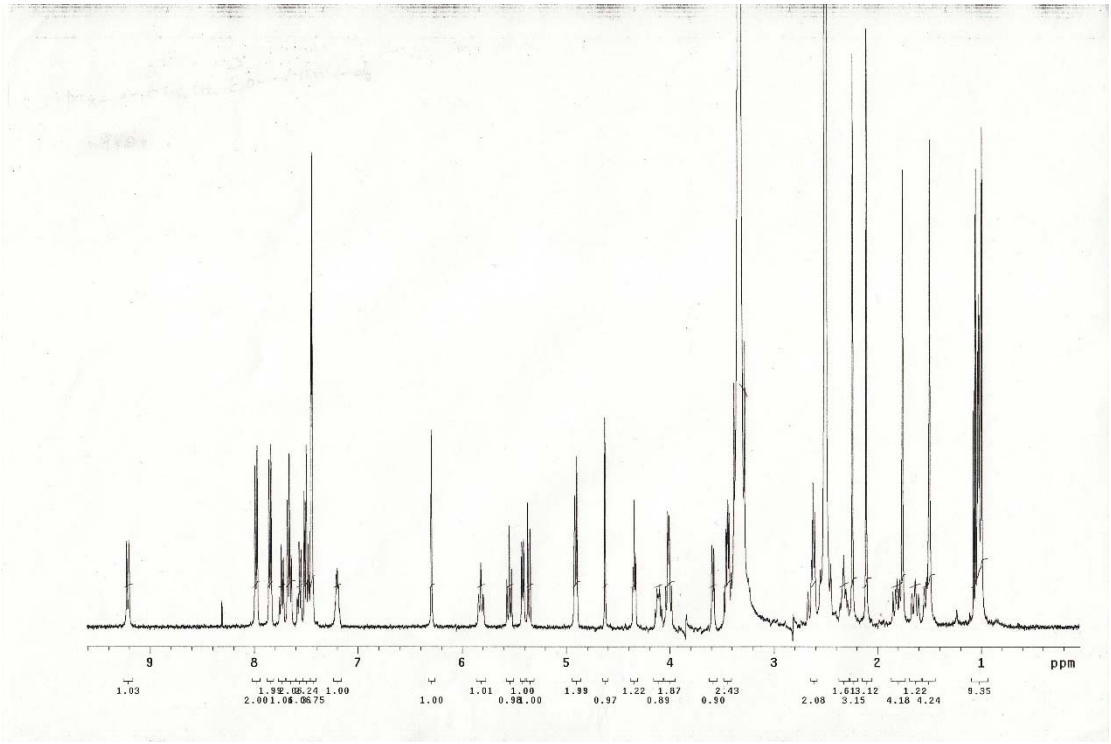

Fig. S3. ^{1}H NMR (400 MHz) spectrum of PTX-SA in D_2O at 25°C.

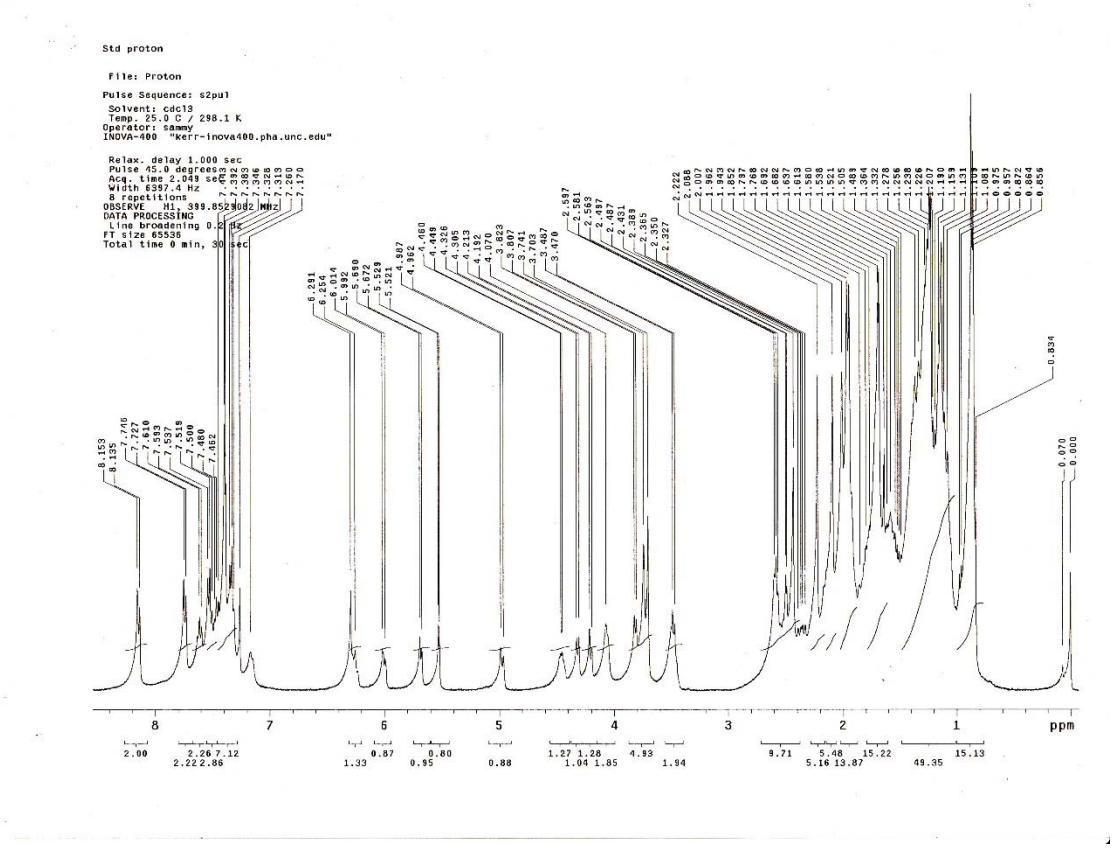

Fig. S4. ^{1}H NMR (400 MHz) spectrum of PTX-S-S-Ve in D2O at 25°C.

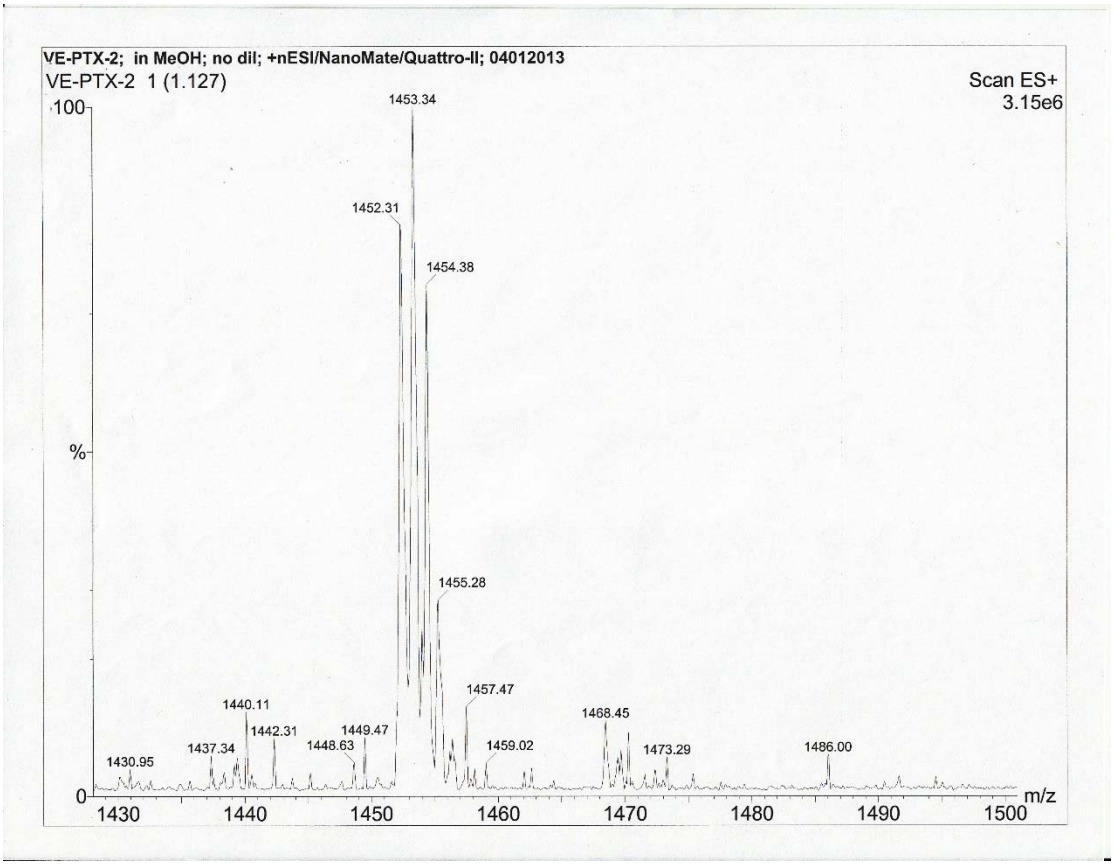

Fig. S5. ESI mass spectrum of PTX-S-S-Ve.

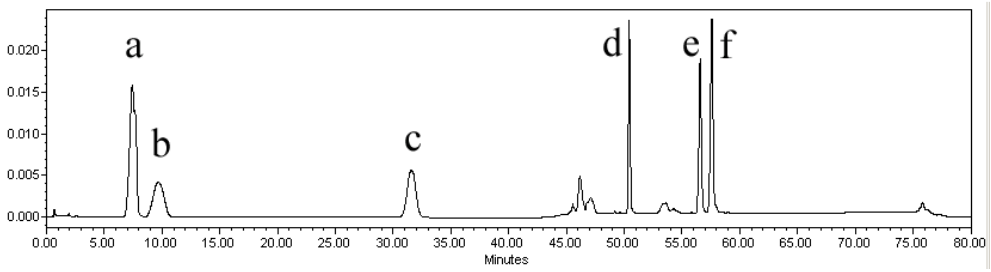

Fig. S6. Chromatogram for PTX and its prodrugs. The retention time was 6.70, 9.29, 31.67, 50.98, 57.72 and 58.83 min for PTX-SA (a), PTX (b), PTX-SEE (c), PTX-C16-Br2 (d), PTX-Ve (e), and PTX-S-S-Ve (f), respectively.

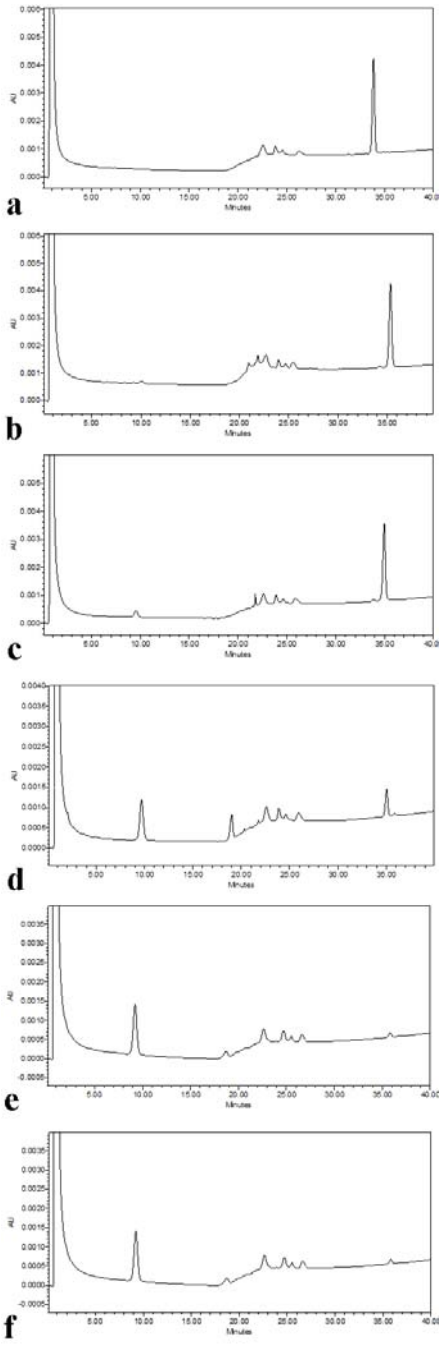

Fig. S7. Chromatograms for PTX-VE (a), and PTX-S-S-VE after the treatment of glutathione at 0 h (b), 4 h (c), 8 h (d), 24 h (e), and 48 h (f) below. The retention time was 9.3, 34.0, and 35.2 min for PTX, PTX-VE, and PTX-S-S-VE, respectively.

Sample Name:	PTX-Ve emulsion 1		
SOP Name:	mansettings.nano		
File Name:	QIANG FU.dts	**Dispersant Name:**	Water
Record Number:	10	**Dispersant RI:**	1.330
Material RI:	1.59	**Viscosity (cP):**	0.8872
Material Absorbtion:	0.01	**Measurement Date and Time:**	Friday, August 09, 2013 3:17:54 PM

Temperature (°C):	25.0	**Duration Used (s):**	60
Count Rate (kcps):	486.4	**Measurement Position (mm):**	1.05
Cell Description:	Disposable sizing cuvette	**Attenuator:**	4

			Size (d.nm):	**% Intensity**	**Width (d.nm):**
Z-Average (d.nm):	135.2	**Peak 1:**	164.7	100.0	76.56
PdI:	0.161	**Peak 2:**	0.000	0.0	0.000
Intercept:	0.919	**Peak 3:**	0.000	0.0	0.000

Result quality : Good

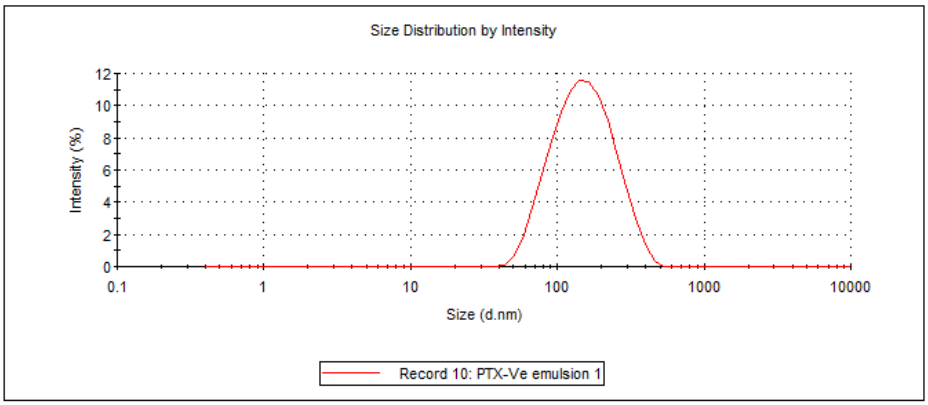

Fig. S8. Particle size distribution for PTX-Ve/Ve NES.

Sample Name:	PTX-S-S-Ve emulsion 3		
SOP Name:	mansettings.nano		
File Name:	QIANG FU.dts	**Dispersant Name:**	Water
Record Number:	15	**Dispersant RI:**	1.330
Material RI:	1.59	**Viscosity (cP):**	0.8872
Material Absorbtion:	0.01	**Measurement Date and Time:**	Friday, August 09, 2013 3:35:54 PM

Temperature (°C):	25.0	**Duration Used (s):**	60
Count Rate (kcps):	464.4	**Measurement Position (mm):**	1.05
Cell Description:	Disposable sizing cuvette	**Attenuator:**	4

			Size (d.nm):	**% Intensity**	**Width (d.nm):**
Z-Average (d.nm):	128.3	**Peak 1:**	151.0	100.0	63.46
PdI:	0.138	**Peak 2:**	0.000	0.0	0.000
Intercept:	0.923	**Peak 3:**	0.000	0.0	0.000
Result quality :	Good				

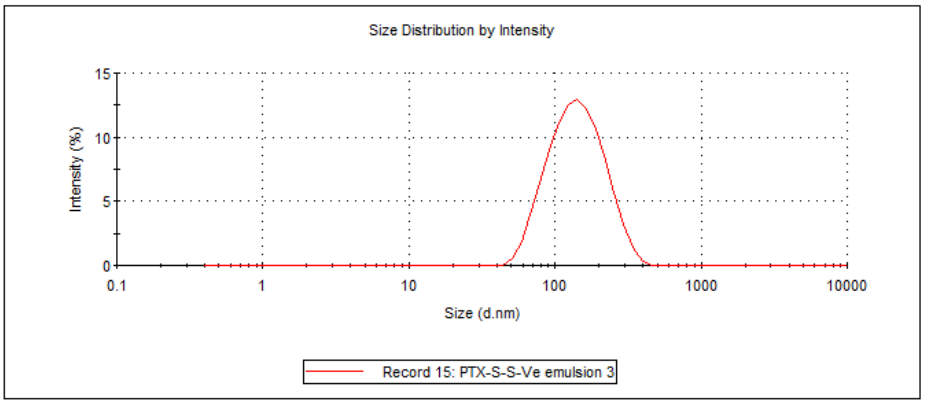

Fig. S9. Particle size distribution for PTX-S-S-Ve/Ve NES.

Table S1. The stability evaluation for PTX-S-S-VE/VE NES

Time (month)	Physical appearance	Z-average (nm)	PDI	EE (%)
0	Good	128.1 ± 0.4	0.175 ± 0.012	98.7 ± 0.3
1	Good	134.6 ± 1.8	0.189 ± 0.021	98.1 ± 0.3
2	Good	129.4 ± 3.2	0.180 ± 0.017	98.9 ± 0.4
3	Good	126.5 ± 0.9	0.174 ± 0.009	98.7 ± 0.3
6	Good	130.9 ± 1.1	0.181 ± 0.011	98.6 ± 0.2
12	Good	134.1 ± 2.0	0.181 ± 0.021	98.1 ± 0.4

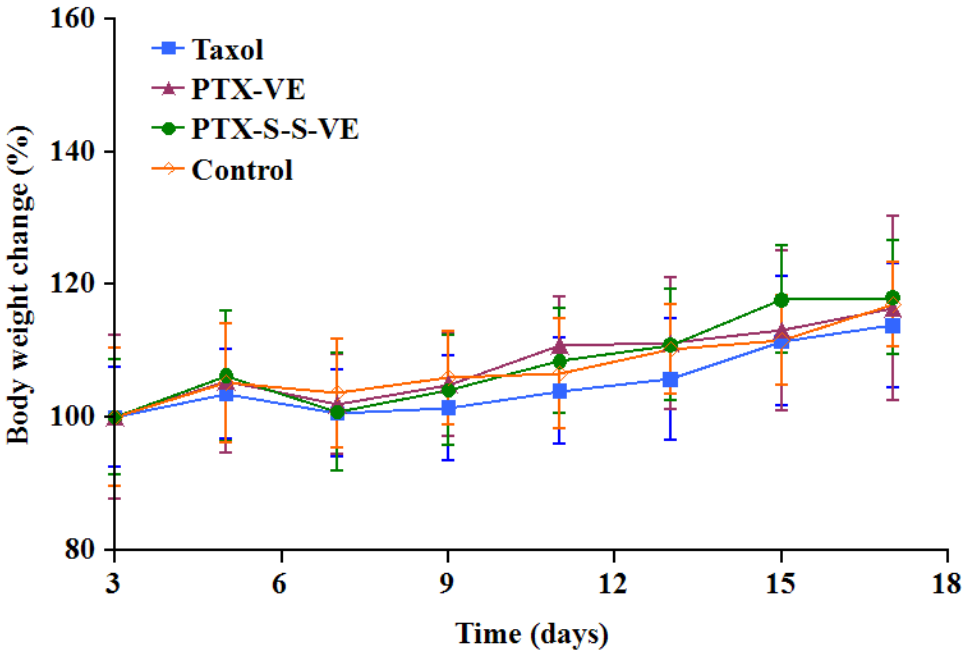

Fig. S10. Body weight change for the nude mice over 18 days after tumor inoculation treated with Taxol®, PTX-VE/VE NES, PTX-S-S-VE/VE NES, and saline. The formulations were administered intravenously at an equivalent dose of 5 mg/kg of PTX every second day for 5 injections in total (data are expressed as the mean ± SD, n=5 mice for each formulation).

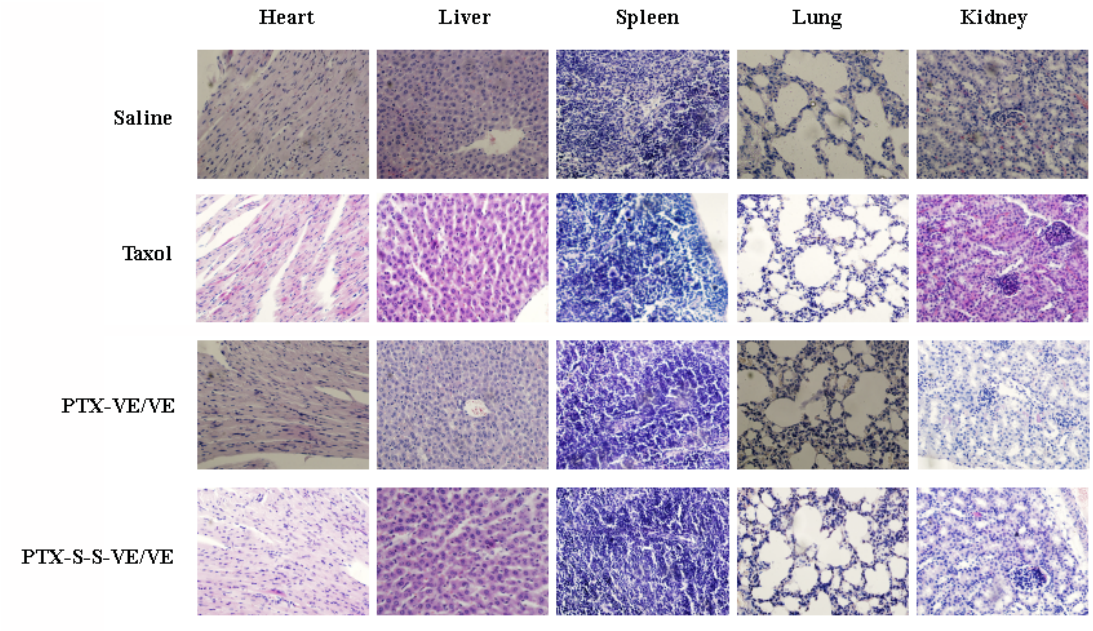

Fig. S11. Typical histopathologic images of hearts, liver, spleen, lung, and kidney after treatment with saline, Taxol®, PTX-VE/VE NES and PTX-S-S-VE/VE NES. The formulations were administered intravenously at an equivalent dose of 5 mg/kg of PTX every second day for 5 injections in total (data are expressed as the mean ± SD, n=5 mice for each formulation).