

Supporting Information

Mitochondrial-Targeted Triphenylphosphonium–Hydroxycamptothecin Conjugate and Its Nano-formulations for Breast Cancer Therapy: *in vitro* and *in vivo* Investigation

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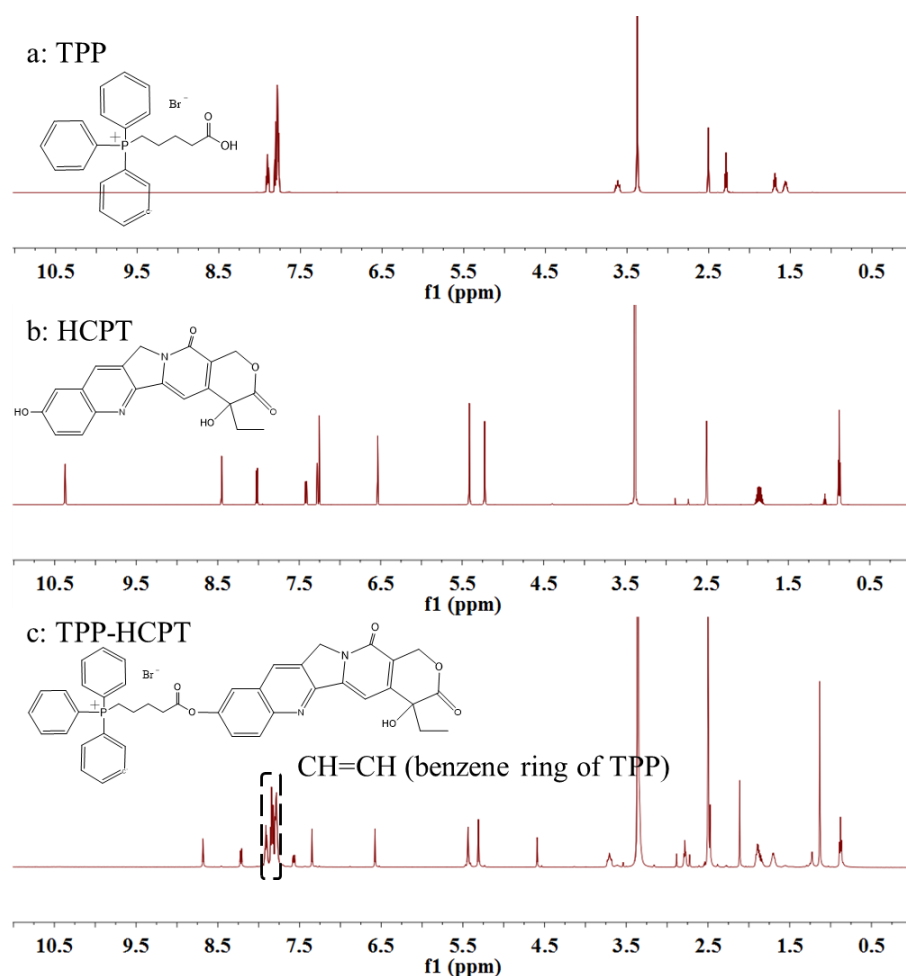


Figure S1. Proton NMR spectra of TPP(a), HCPT(b) and TPP-HCPT conjugate (c).

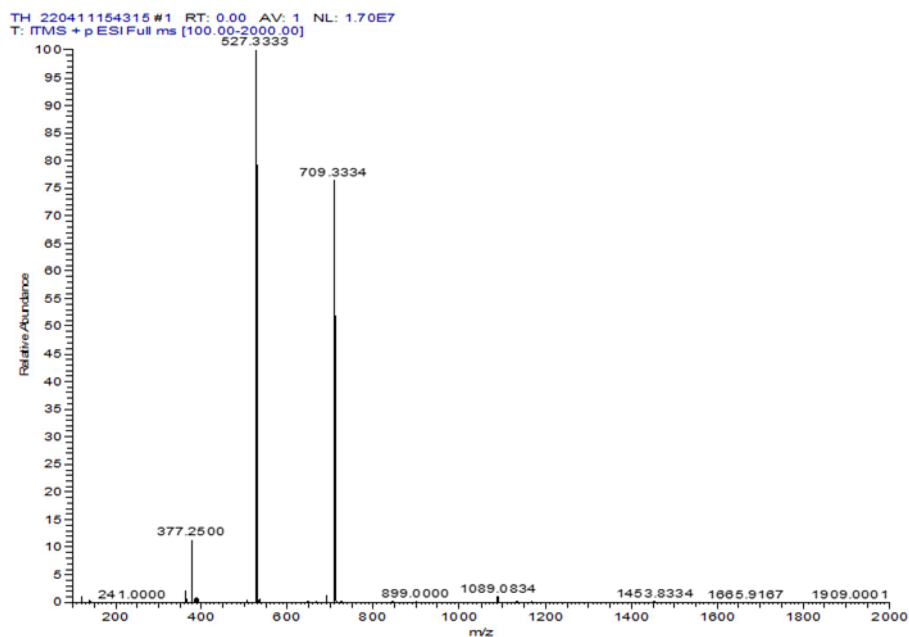


Figure S2. ESI-MS of TPP-HCPT (ESI source: I Spray Voltage: 4.50kV; Tube Lens: 110V; Capillary Temp: 275°C; Capillary Voltage: 35V; Sheath Gas Flow Rate: 5arb).

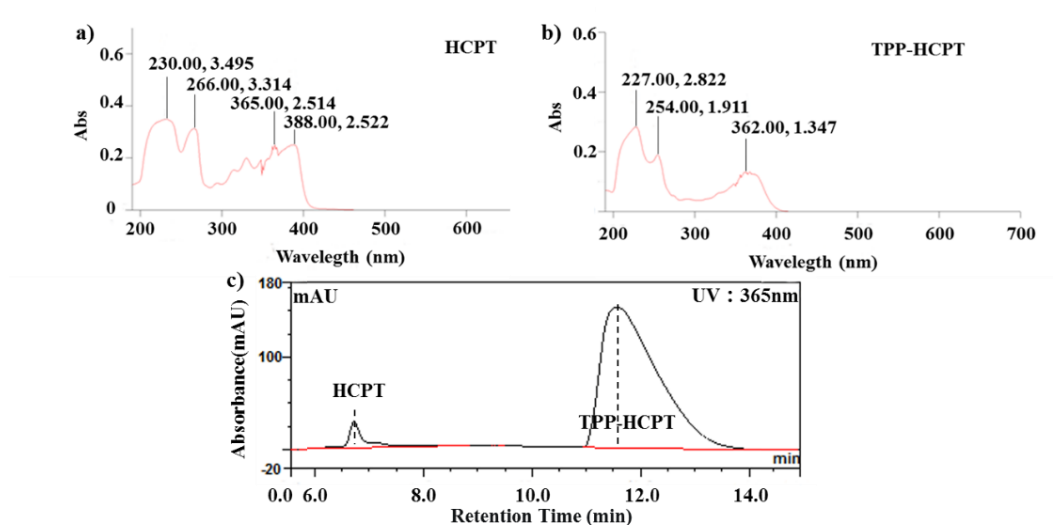


Figure S3. UV full-wavelength scanning of HCPT and TH (190nm-700nm, a and b). High performance liquid chromatography (HPLC) of HCPT and TH under the exact same chromatographic conditions (c).

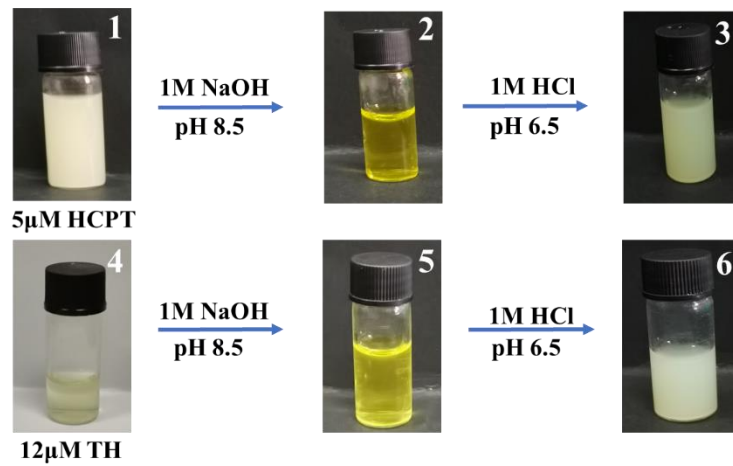


Figure S4. HCPT and TH in deionized water (1 and 4), dissolved in alkaline solution (pH8.5) (2 and 5), and the subsequent aggregation when acidified to pH 6.5 using 1M HCl.

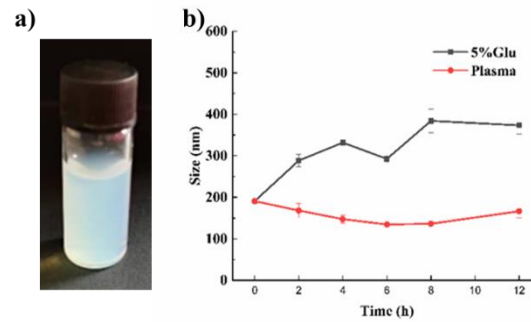


Figure S5. HCPT-loaded TH nanoparticles (a) and their particle size change in 5% glucose and plasma after HA coating (b).

Table S1. Particle size and PDI of TH solution at different concentrations.

Concentration	Size(nm)	PDI	Zeta(mV)
1mg/ml	203.2±12.34	0.312	+0.026
5mg/ml	440.7±32.17	0.264	+1.335
10mg/ml	580.9±13.62	0.330	+3.452

Table S2. Particle size, PDI and zeta potential of HCPT-loaded TH nanoparticles and HA coated HCPT-loaded TH nanoparticles.

Concentration	Size(nm)	PDI	Zeta(mV)
HCPT-loaded TH nanoparticles	155.5±9.96	0.312	+5.62
HA coated HCPT-loaded TH NPs	190.8±6.25	0.208	-3.71

Table S3. The particle size and PDI value of TH nanoparticles (containing 1mg/mL of TH) made from different pharmaceutical adjuvants.

Antisolvent precipitation	Mass ratio of TH:materials	Size (nm)	PDI
P188	1:4	758.5±31.77	0.482
TPGS	2:1	367.9±17.44	0.482
TPGS	1:2	249.3±14.31	0.398
DSPE-PEG ₂₀₀₀	4:1	580.9±26.31	0.540
DSPE-PEG ₂₀₀₀	1:4	248.5±13.24	0.438
PEG ₅₀₀₀ -PCL ₄₈₀₀	4:1	156.8±10.28	0.418
PEG ₅₀₀₀ -PCL ₄₈₀₀	1:1	134.1±17.28	0.528
PEG ₅₀₀₀ -PCL ₄₈₀₀	1:4	113.4±6.54	0.435
PEG ₃₀₀₀ -PLGA ₅₀₀₀	4:1	312.5±6.97	0.311
PEG ₃₀₀₀ -PLGA ₅₀₀₀	1:1	234.1±11.25	0.387
PEG ₃₀₀₀ -PLGA ₅₀₀₀	1:2	213.1±13.60	0.412
PEG ₃₀₀₀ -PLGA ₅₀₀₀	1:3	133.2±8.63	0.352
PEG ₃₀₀₀ -PLGA ₅₀₀₀	1:4	86.41±5.93	0.256
chol-PEG _{1k}	4:1	234.7±8.55	0.387
chol-PEG _{1k}	1:4	146.1±6.87	0.347
hyaluronic acid _{3-10k}	4:1	422.3±13.14	0.294
hyaluronic acid _{3-10k}	1:4	295.3±7.25	0.384
hyaluronic acid _{40-50k}	4:1	346.6±18.30	0.786
hyaluronic acid _{40-50k}	1:4	292.3±6.91	0.098