

Title:

**Dual polymeric prodrug co-assembled nanoparticles with precise
ratiometric co-delivery of cisplatin and metformin for lung cancer
chemoimmunotherapy**

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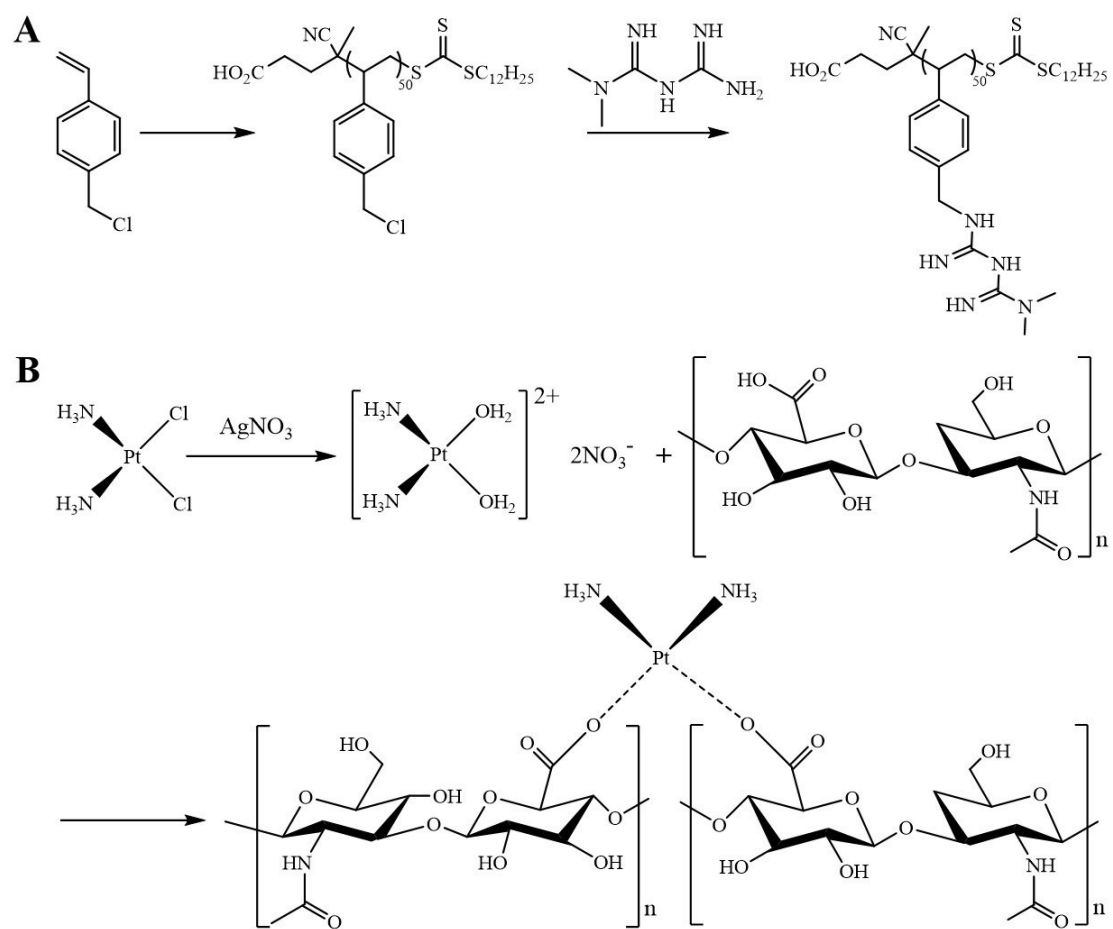
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Scheme S1. Synthesis of PMet (A) and HA-CDDP (B) polymeric prodrugs.

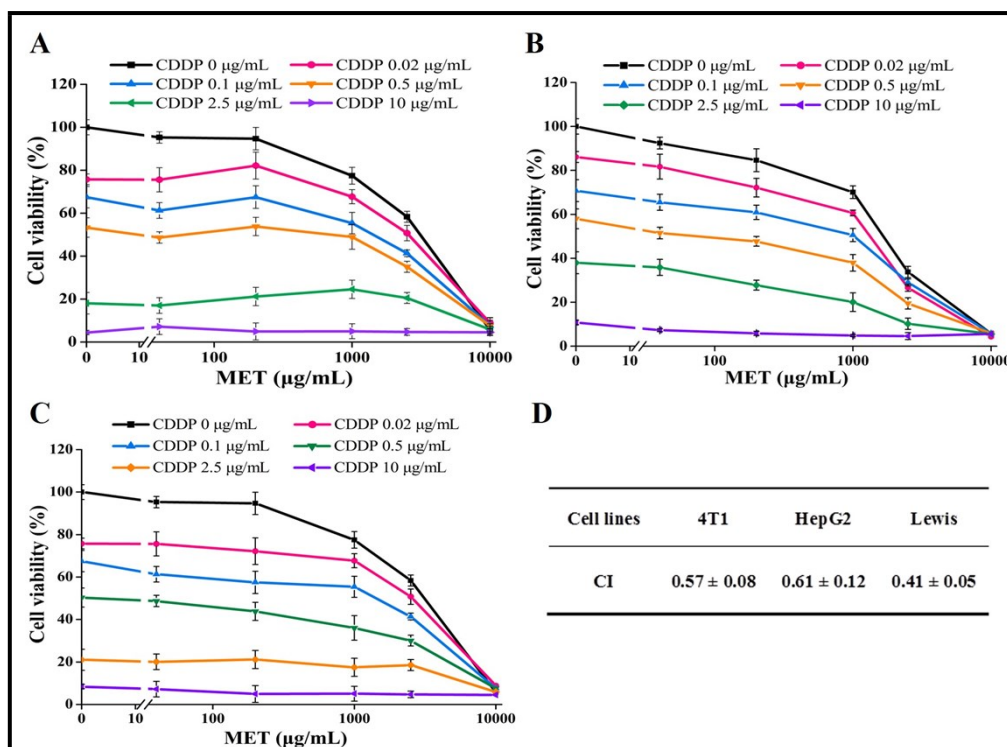


Figure S1. The cytotoxicity profiles of MET and CDDP combination treatment against 4T1 (A), HepG2 (B) and LLC (C) cell lines for 72 h. (D) Synergy of MET with CDDP was indicated by CI values.

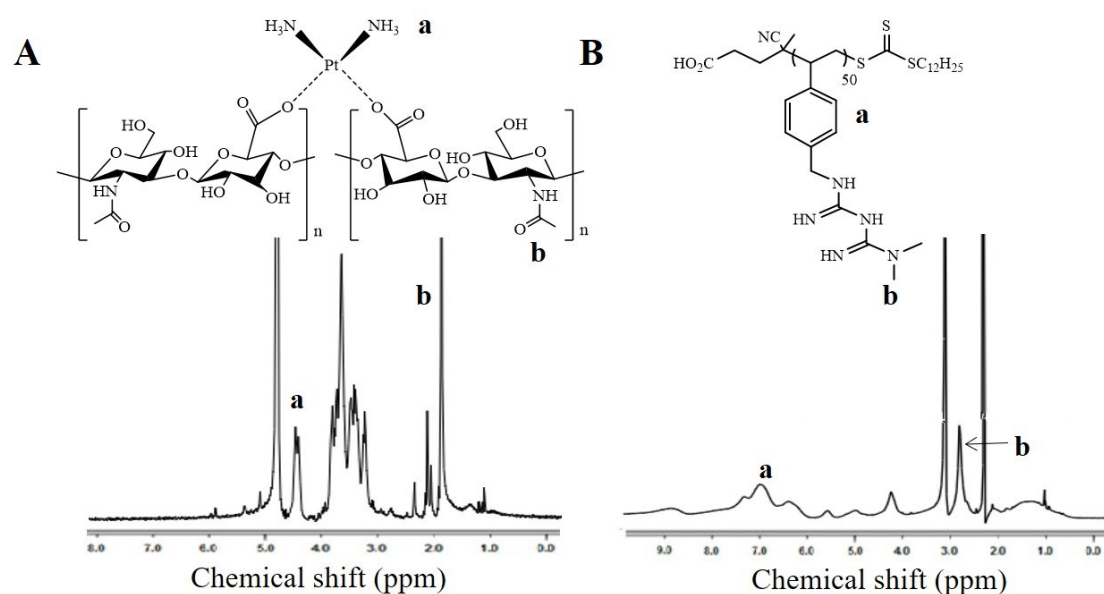


Figure S2. ^1H NMR spectra of HA-CDDP (A) in D_2O and PMet (B) in DMSO-d_6 .

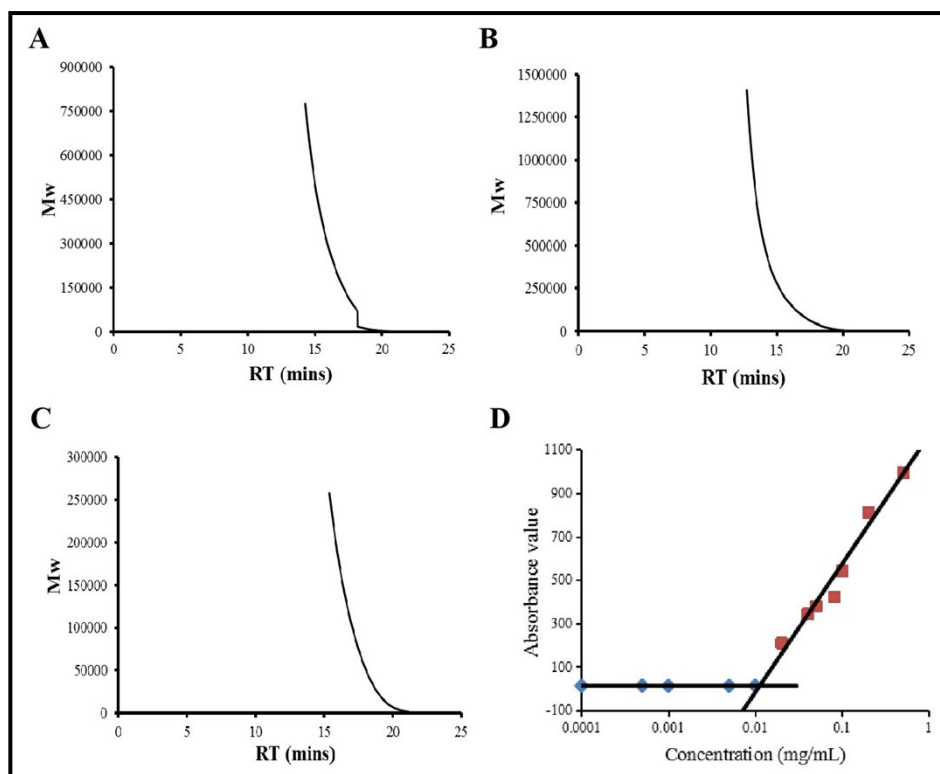


Figure S3. GPC assay of PVBC polymer (A), PMet prodrug (B) and HA-CDDP prodrug (C). Plots of fluorescence intensity of Nile red against PMet polymeric prodrug concentration (D).

Table S1 GPC parameters of polymers

Polymer	Mn	Mw	Mw/Mn	PDI
poly(4-vinylbenzyl chloride)	67690	150205	2.219	1.292
PMet	121403	287772	2.37	1.447
HA-CDDP	32356	70154	2.168	1.845

Table S2 IC₅₀ values of CDDP solution, MET solution, Free combo, HA-CDDP solution, HA/PMet NPs and HA-CDDP/PMet NPs against 4T1 cells, HepG2 cells and LLC cells after 72 h treatment (mean \pm SD, n = 3).

Formulations	IC ₅₀ (μ g/mL)		
	4T1	HepG2	LLC
CDDP solution	3.04 \pm 0.31	1.05 \pm 0.09	2.11 \pm 0.36
MET solution	249.19 \pm 7.05	185.47 \pm 4.08	213.87 \pm 5.04
Free combo	1.77 \pm 0.02	11.33 \pm 2.01	1.03 \pm 0.07
HA-CDDP solution	1.99 \pm 0.14	1.76 \pm 0.13	1.83 \pm 0.27
HA/PMet NPs	3.58 \pm 0.35	3.34 \pm 0.21	3.58 \pm 0.39
HA-CDDP/PMet NPs	1.07 \pm 0.07	0.50 \pm 0.05	0.74 \pm 0.05

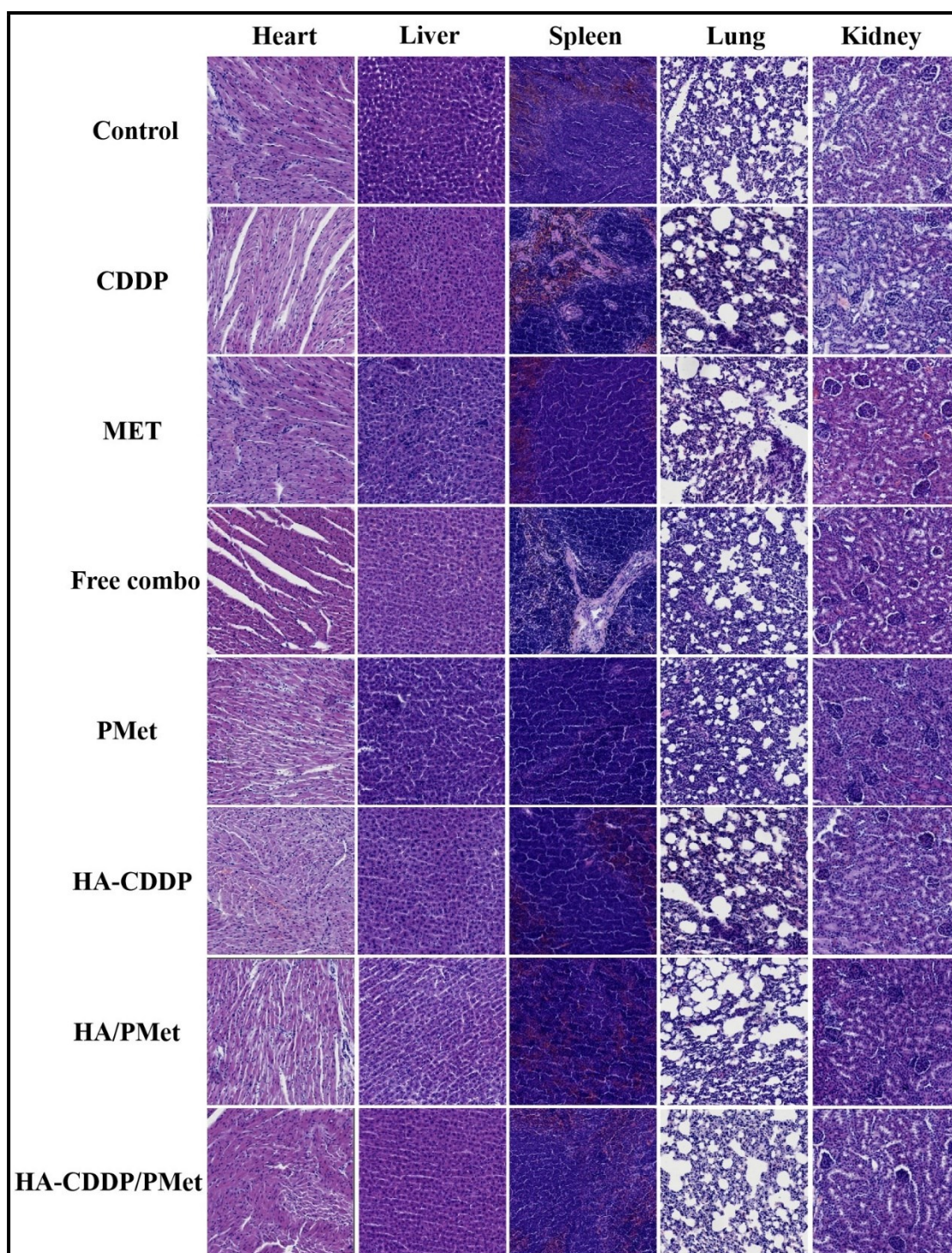


Figure S4. H&E staining of heart, liver, spleen, lung and kidney after various treatments, scale bar = 50 μ m.