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Supporting Information

Redox/pH dual-sensitive hybrid micelles for targeting delivery and overcoming multidrug resistance of cancer

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ABBREVIATION LIST

BDD, 1,4-butanediol diacrylate;

C6, coumarin 6;

CLSM, confocal laser scanning microscopy;

CMC, critical micelle concentration;

Cy5, Cyanine5 amine;

DAPI, 4',6-diamidino-2-phenylindole,

DCM, dichloromethane;

DLE, drug loading efficiency;

DLS, dynamic light scattering;

DMAP, 4-dimethylamino pyridine;

DMF, N,N-dimethyl formamide;

DMSO, dimethyl sulfoxide;

DTT, DL-dithiothreitol;

EE, encapsulation efficiency;

F127, Pluronic F127;

F127-FA, folate-modified F127;

FA, folate;

FBS, fetal bovine serum;

FR, FA receptors;

HPLC, high performance liquid chromatography;

H&E, hematoxylin-eosin;

IC_{50}, concentration resulting in 50% inhibition of cell growth;

i.v., intravenously;

MDR, multidrug resistance;

MFI, mean fluorescent intensity;

MPS, mononuclear phagocyte system;

MTT, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide;

PBAE, poly(β-amino ester);

PBAE-*g*-TPGS, poly(β-amino ester)-*g*-D-α-tocopherol polyethylene glycol succinate;

PBS, phosphate buffer saline;

PEG, polyethylene glycol;

PI, propidium iodide;

P-gp, P-glycoprotein;

PNC, 4-nitrophenyl chloroformate;

PTX, paclitaxel;

PTX@PST, PTX loaded PBAE-*g*-TPGS/F127 hybrid micelles;

PTX@PST-FA, folate-targeted micelles;

RES, reticuloendothelial system;

Rh123, rhodamine 123;

SPF, specific pathogen-free;

s.c., subcutaneously;

TDP, 4,4'-trimethylenedipiperidine;

TEA, triethylamine;

TEM, transmission electron microscope;

TIR, tumor inhibition rate;

TPGS, D-α-tocopherol polyethylene 1000 glycol succinate;

TPGS-PNC, PNC activated TPGS;

TUNEL, terminal deoxynucleotidetransferase (TdT)-mediated dUTP nick-end labeling.

SUPPLEMENTARY FIGURES

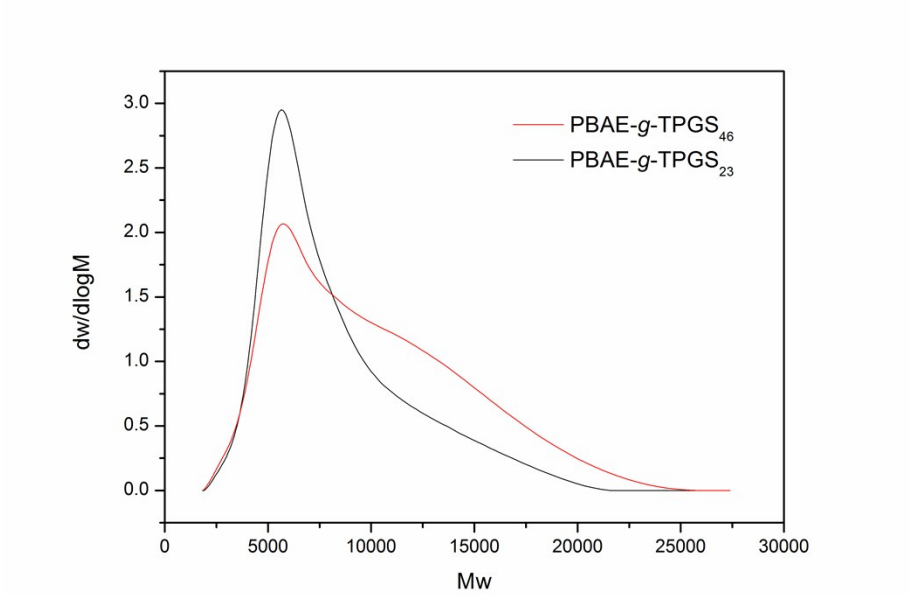

Figure S1. GPC results of PBAE-*g*-TPGS$_{46}$ and PBAE-*g*-TPGS$_{23}$ copolymers. THF was used as the mobile phase.

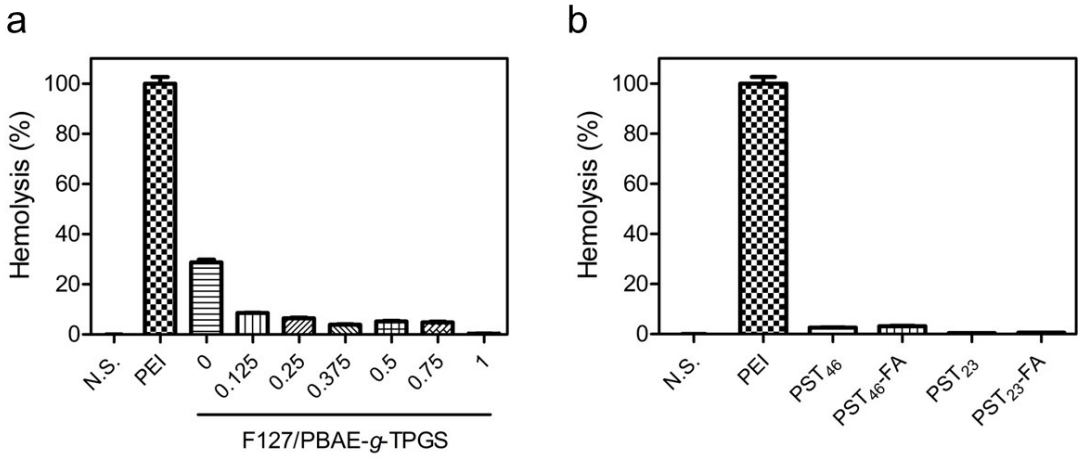

Figure S2. Hemolytic ratio of hybrid micelles in different (a) components of F127/PBAE-*g*-TPGS (n:n) and (b) materials.

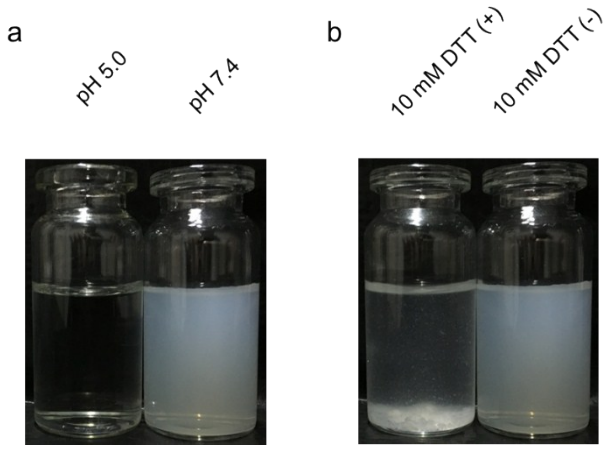

Figure S3. Representative pictures of PST micelle solutions under different (a) pH value and (b) reductive conditions.

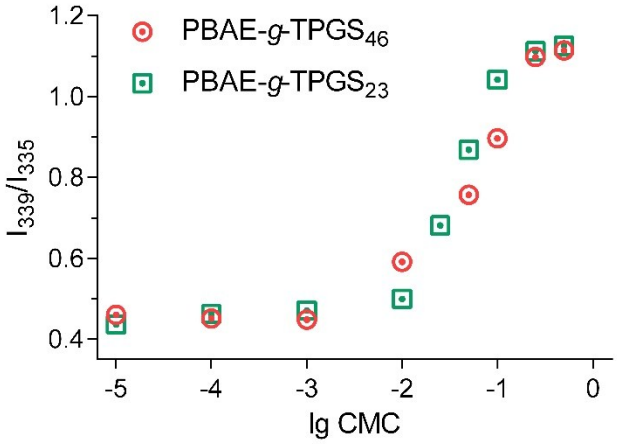

Figure S4. CMC values of PBAE-*g*-TPGS$_{46}$ and PBAE-*g*-TPGS$_{23}$ copolymers.

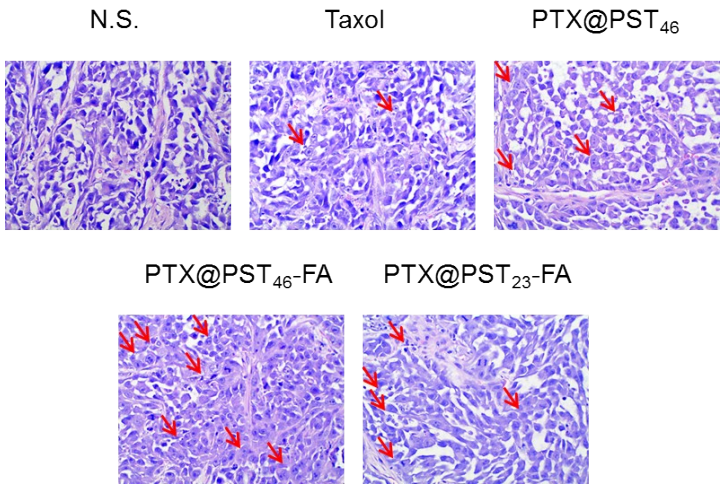

Figure S5. H&E staining of MCF-7/ADR tumors with different treatments.

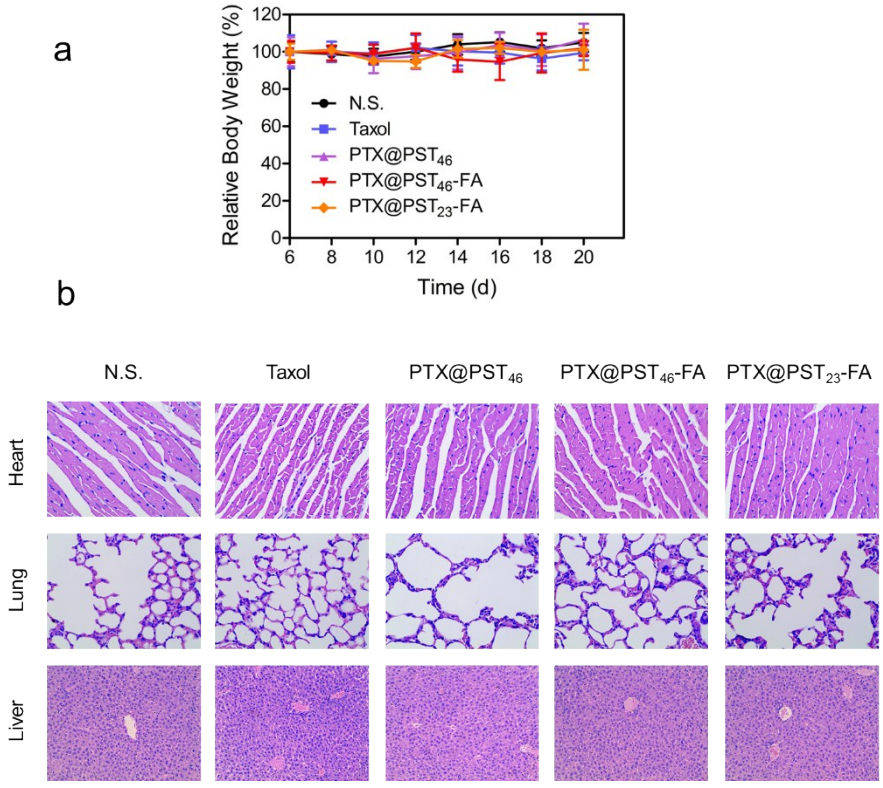

Figure S6. (a) Relative body weight and (b) H&E staining of main organs in MCF-7/ADR tumor growth inhibition experiment.

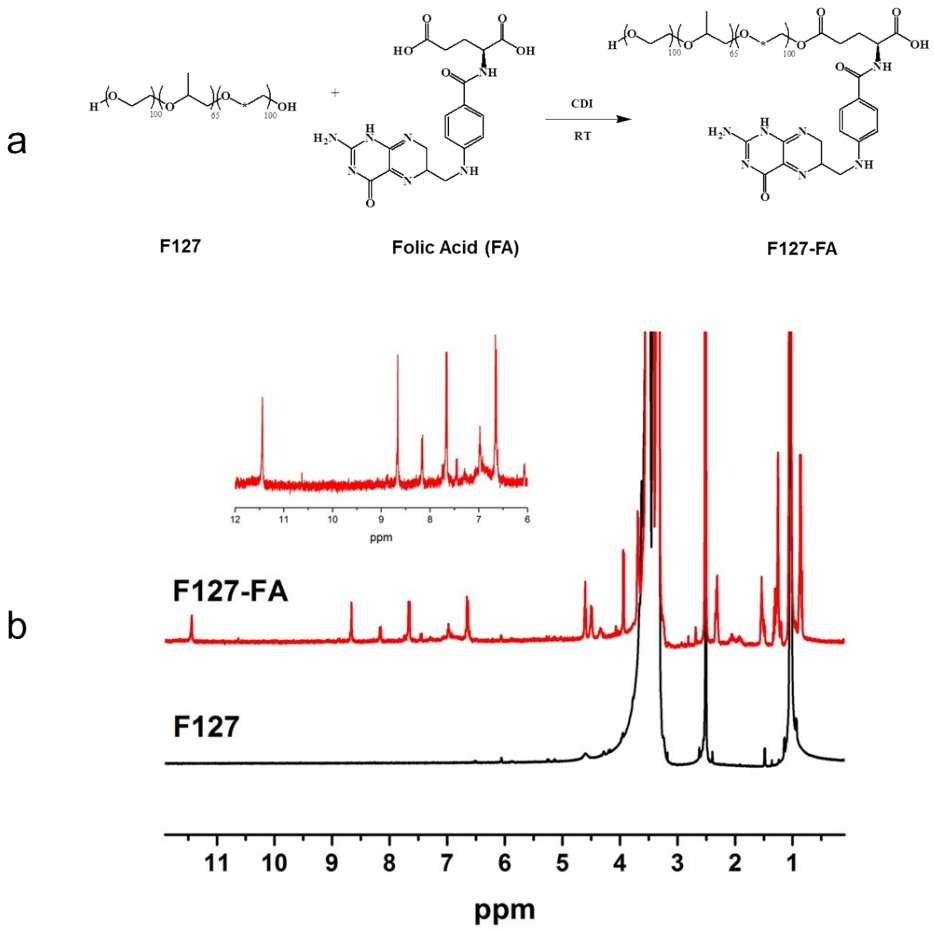

Figure S7. Synthesis and characterization of folate-F127 conjugation. ^{1}H-NMR uses $CDCl_3$ as the solvent.

SUPPLEMENTARY TABLE

Table S1. Characterization of PTX-loaded hybrid micelles.

Micelles	Size/nm[a]	PDI[a]	ζ Potential/mV[a]	EE%[b]
PTX@PST_{46}	170.4±3.5	0.121	-15.3±2.3	84.2
PTX@PST_{46}-FA	177.5±1.8	0.133	-14.3±1.8	77.2
PTX@PST_{23}	175.4±3.2	0.125	-10.3±3.6	99.8
PTX@PST_{23}-FA	179.2±4.4	0.147	-10.0±2.6	99.1

[a] Detected by DLS; [b] detected by HPLC.

SUPPLEMENTARY EXPERIMENTAL SECTIONS

Synthesis of folate modified F127

Folate (FA) was first activated by N,N'-carbonyldiimidazole (CDI). Briefly, FA (0.1 mmol, 44.1 mg) and CDI (0.2 mmol, 32.4 mg) were dissolved in DMSO and stirred overnight. Then, F127 (0.05 mmol, 630 mg) was added. After the reaction for 72 h, the resultant slution was dialyzed against alkaline water (pH=8) for 4 days to remove excess FA and distilled water for another day. Folate-F127 conjugation was collected after lyophilization.