Supplementary Materials

Biodegradable copper-metformin nanoscale coordination polymer for enhanced chemo/chemodynamic synergistic therapy by reducing oxygen consumption to promote H_2O_2 accumulation

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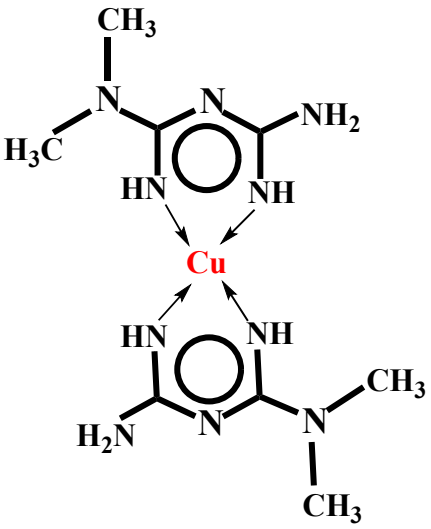

Fig. S1. The coordination interaction between copper ions and the imines groups of Met to form Cu−N bonds.

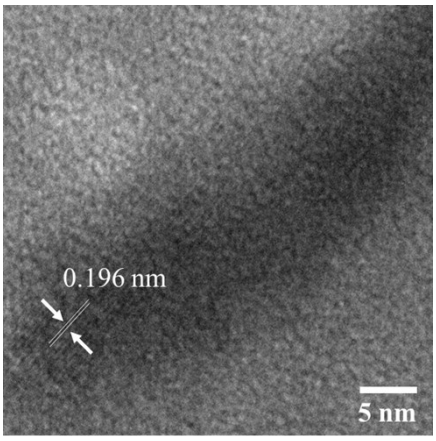

Fig. S2. The high-resolution TEM (HRTEM) of Cu-Met NPs.

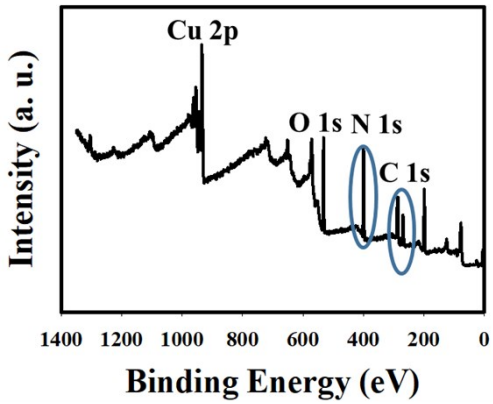

Fig. S3. XPS result of Cu-Met NPs.

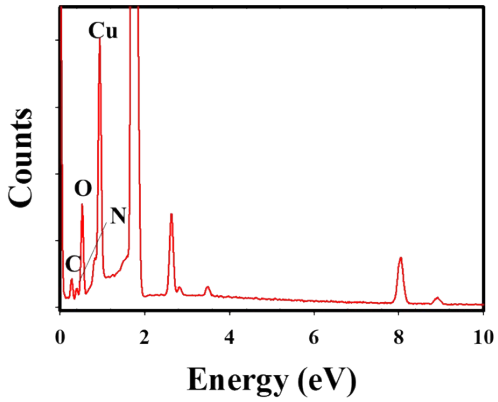

Fig. S4. EDS spectrum of Dox@Cu-Met NPs.

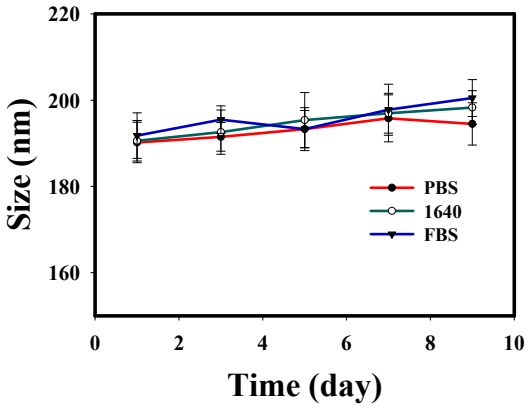

Fig. S5. The size of Dox@Cu-Met NPs during 9-day socking in simulated PBS, 1640 medium and fetal bovine serum (FBS). Error bars indicate standard deviation (n = 3).

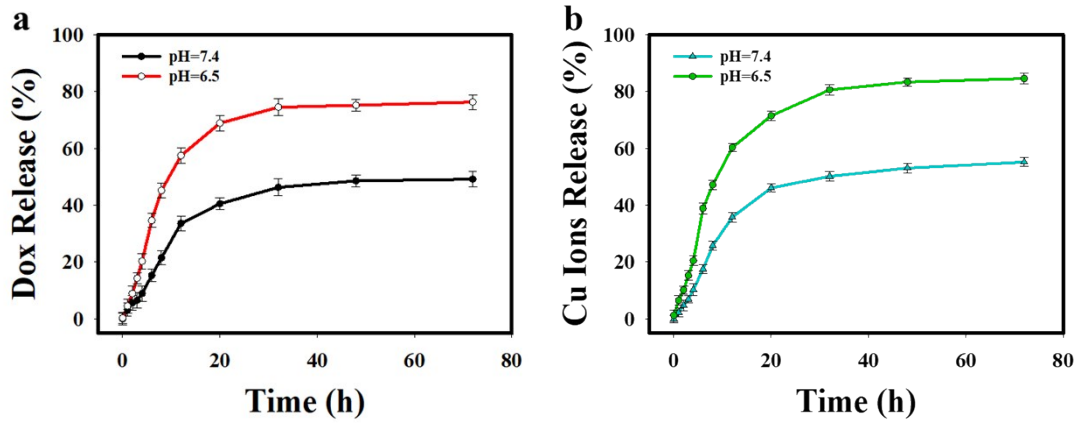

Fig. S6. Accumulated releasing Dox (a) and Cu ions (b) from Dox@Cu-Met NPs (200 μg/mL) at different pH value with 5 mM GSH.

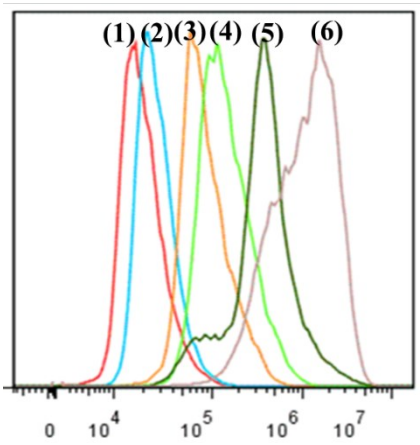

Fig. S7. Flow cytometry analysis of ROS production in MCF-7 cells after treatment with treated with (1) PBS, (2) Dox, (3) Met, (4) Dox@Cu-Met NPs + BSO (100 μM), (5) Cu-Met NPs, or (6) Dox@Cu-Met NPs.

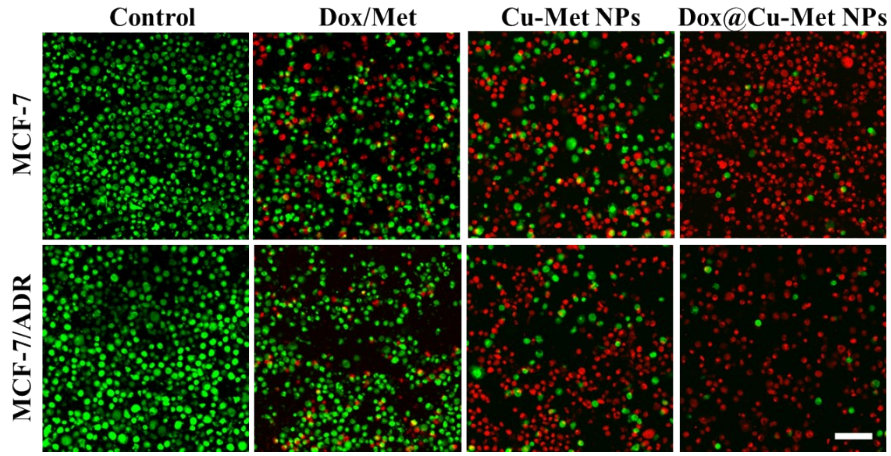

Fig. S8. Live/Dead cell staining of MCF-7 cells and MCF-7/ADR after incubation with Dox (2 μg/mL) /Met (0.2 mg/mL), Cu-Met NPs (50 μg/mL), and Dox@Cu-Met NPs (50 μg/mL). Scale bar = 100 μm.

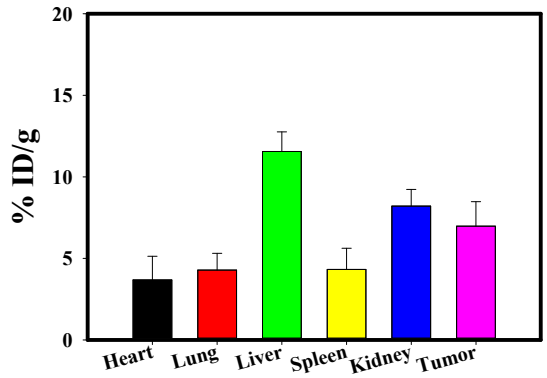

Fig. S9. The distribution content of Cu in the major organs (heart, liver, spleens, lungs, and kidney) and tumors of breast tumor-bearing mice after intravenous injection Dox@Cu-Met NPs for 24 h. Error bars indicate standard deviation (n = 3).

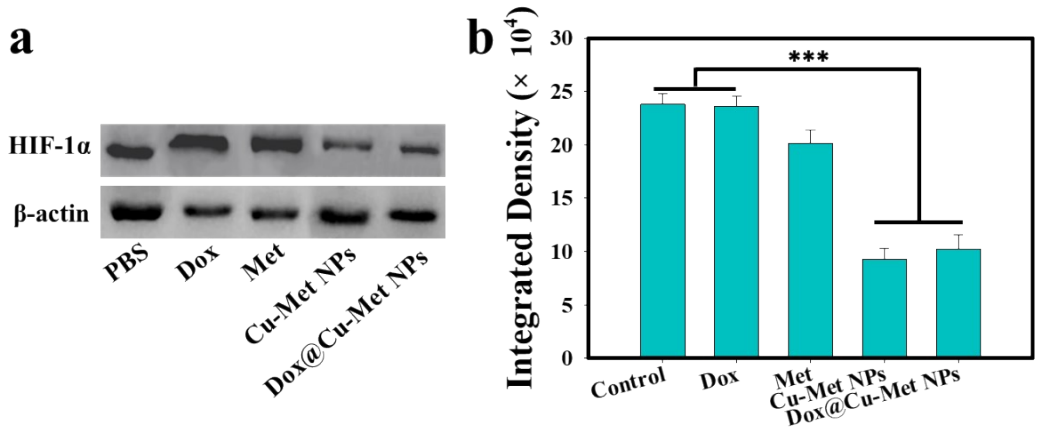

Fig. S10. (a) Western blot assay of HIF-1α levels in tumor tissues of mice after treated with Dox, Met, Cu-Met NPs, or Dox@Cu-Met NPs. (b) Quantitative analysis of relative HIF-1α expression in tumor tissues of mice according to (a).

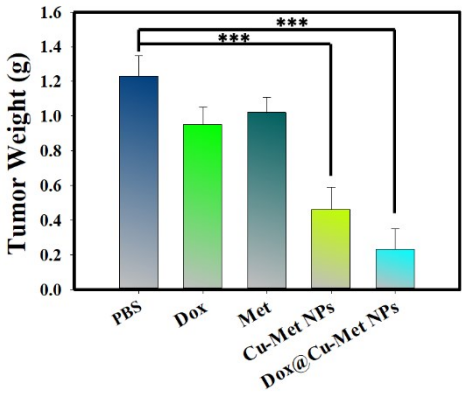

Fig. S11. Tumor weight of breast tumor-bearing mice intravenous injection with PBS, Dox, Met, Cu-Met NPs, and Dox@Cu-Met NPs after a 14-day treatment. ***$p < 0.001$, **$p < 0.01$, or *$p < 0.05$. Error bars indicate standard deviation (n = 3).

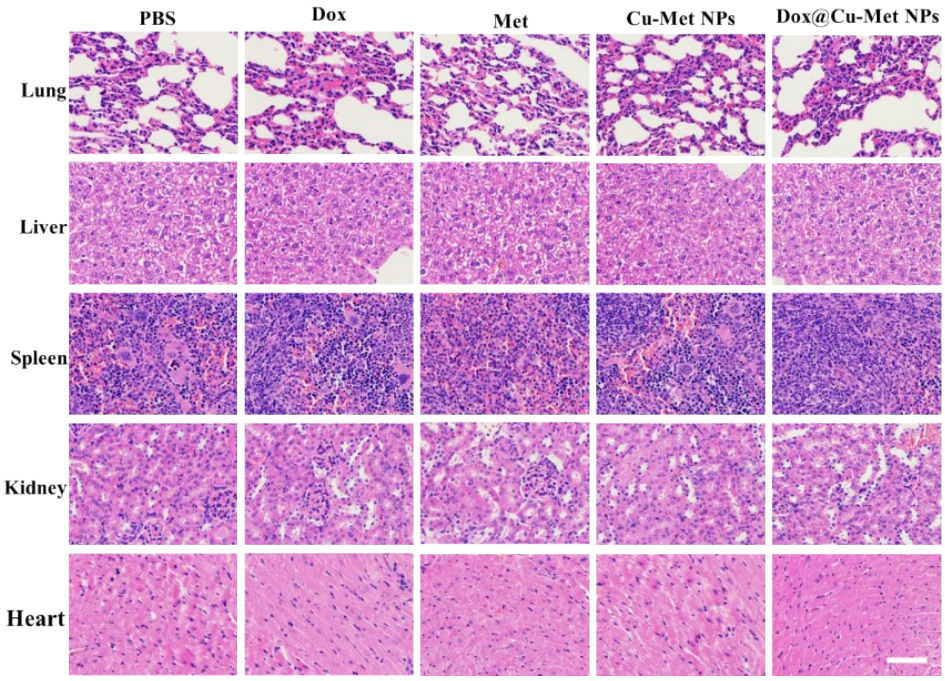

Fig. S12. H&E staining of the main organs after the mice treated with PBS, Dox, Met, Cu-Met NPs, Dox@Cu-Met NPs. Scale bar = 50 μm.

Table S1. The main hematology analysis and blood biochemistry analysis of mice treated with Dox@Cu-Met NPs after 14-day treatment.

Index	Blank	2.5mg/kg	Ratio 1	5 mg/kg	Ratio 2
WBC (10^9 L^{-1})	4.69 ± 2.13	4.57 ± 1.67	0.97	4.66 ± 3.15	0.99
RBC (10^{12} L^{-1})	11.02 ± 0.98	11.32 ± 1.11	1.03	11.23 ± 1.23	1.02
PLT (10^9 L^{-1})	778.5 ± 100.5	753 ± 103.2	0.97	761.2 ± 99.4	0.97
HGB (g/L)	167.3 ± 9.8	170.3 ± 6.5	1.01	168.56 ± 7.3	1.01
HCT (%)	0.51 ± 0.05	0.49 ± 0.042	0.96	0.52 ± 0.04	1.01
MCH (pg)	14.85 ± 0.51	14.15 ± 0.52	0.95	14.38 ± 0.49	0.97
LY (%)	89.91 ± 1.79	90.15 ± 1.15	1.00	89.73 ± 0. 92	0.99
NE (%)	1.23 ± 1.17	1.31 ± 1.21	1.07	1.29 ± 1.23	1.05
MPV (fL)	2.08 ± 3.27	2.01 ± 2.77	0.97	2.06 ± 2.69	0.99
ALB (g/L)	35.86 ± 1.54	35.15 ± 3.67	0.98	35.99 ± 1.61	1.00
TP (g/L)	60.43 ± 2.10	62.98 ± 3.21	1.04	61.33 ± 2.09	1.01
ALT(U/L)	95.68 ± 32.49	95.37 ± 30.49	0.99	95.03 ± 38.67	0.99
AST (U/L)	178.77 ± 35.01	180.26 ± 33.95	1.01	175.68± 39.46	0.98
GLO (mmol/L)	4.68 ± 2.84	4.59 ± 2.71	0.98	4.37 ± 2.64	0.93
BUN (mmol/L)	7.87 ± 1.65	7.89 ± 1.43	1.00	7.65 ± 1.38	0.97
CRE (μmol/L)	20.43 ± 5.09	20.98 ± 4.69	1.03	20.75 ± 4.77	1.02

Note: Ratio 1 = Blank/(2.5 mg/kg); Ratio 2 = Blank/(5mg/kg).

White blood cells (WBC), red blood cell (RBC), platelets (PLT), hemoglobin (HGB), hematocrit (HCT), mean corpuscular hemoglobin (MCH), lymphocyte count (LY), neutrophil count (NE), mean platelet volume (MPV), globulin (GOL), Albumin (ALB), ALB/GLOB Ratio, alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), creatinine (CREA), and total protein (TP).