Supporting Information

Cu-Phytic acid Nanozyme-Induced Cuproptosis Therapy for Inhibition of Tumor Growth

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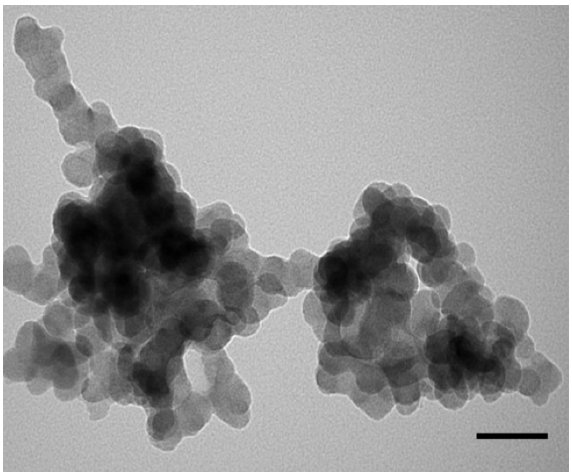


Figure S1. The TEM image of CPW (Scale bar: 100 nm).

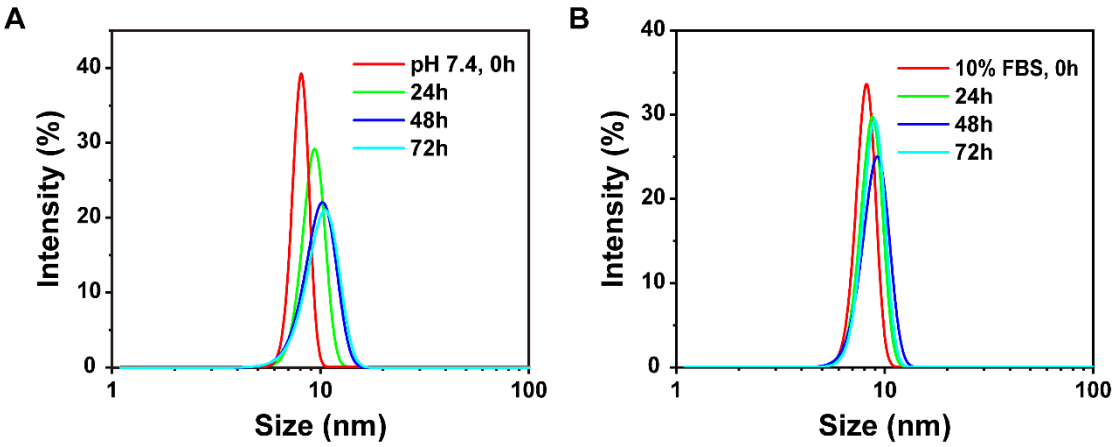
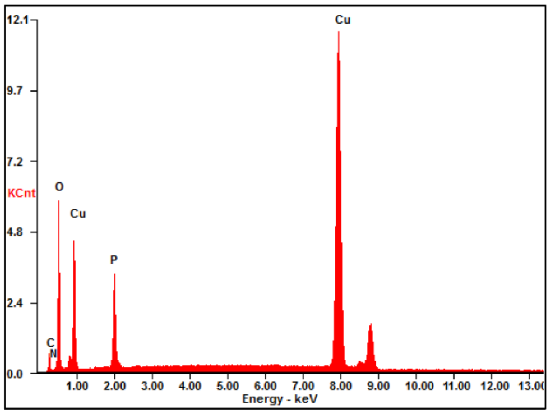


Figure S2. Short-term stability of CP dispersed in different solution, including pH 7.4 PBS solution (A) and 10% FBS (B) at different time points within 72 h.



Element	*Wt%*	*At%*
CK	07.10	17.86
NK	00.80	01.73
OK	23.21	43.84
PK	07.59	07.41
CuK	61.30	29.16
Matrix	Correction	ZAF

Figure S3. The EDS spectra of CP, as well as the Wt % and At % of various elements.

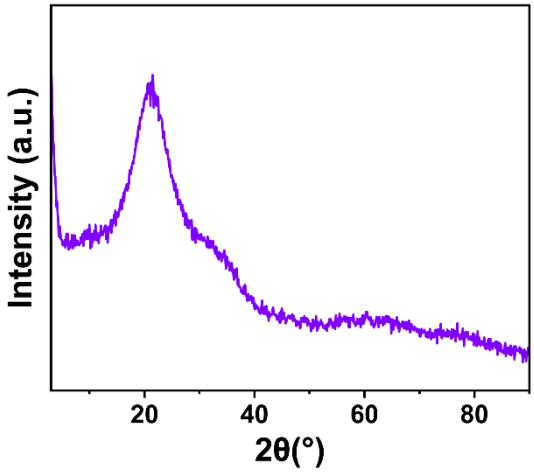


Figure S4. The powder XRD pattern of CP.

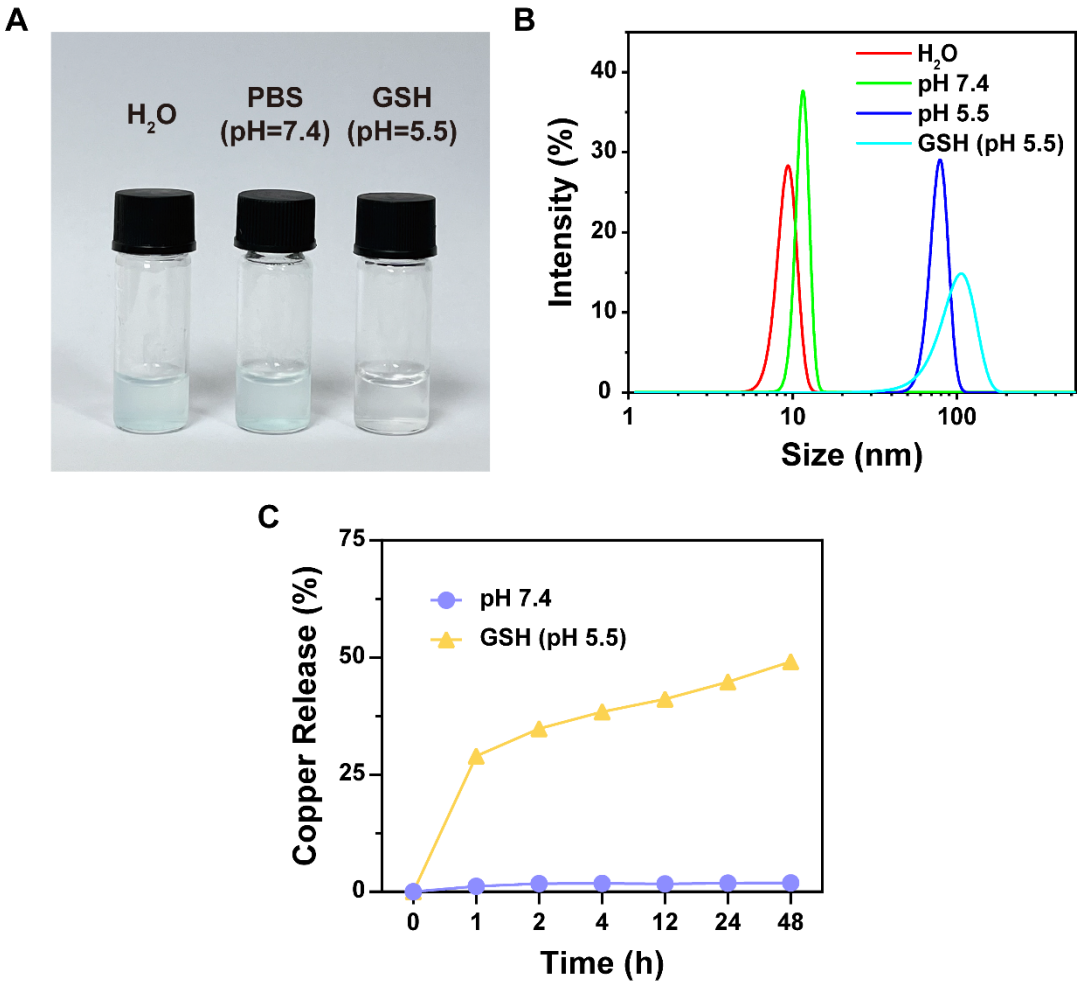


Figure S5. Evaluation on pH/GSH dual response of CP. (A)The photographs of CP dispersed in H_2O, PBS (pH 7.4) and GSH (10 mM, pH 5.5) solution for 48 h, respectively. (B) Size distribution change of CP after dispersed in different solution. (C) Copper release profiles from CP under different conditions.

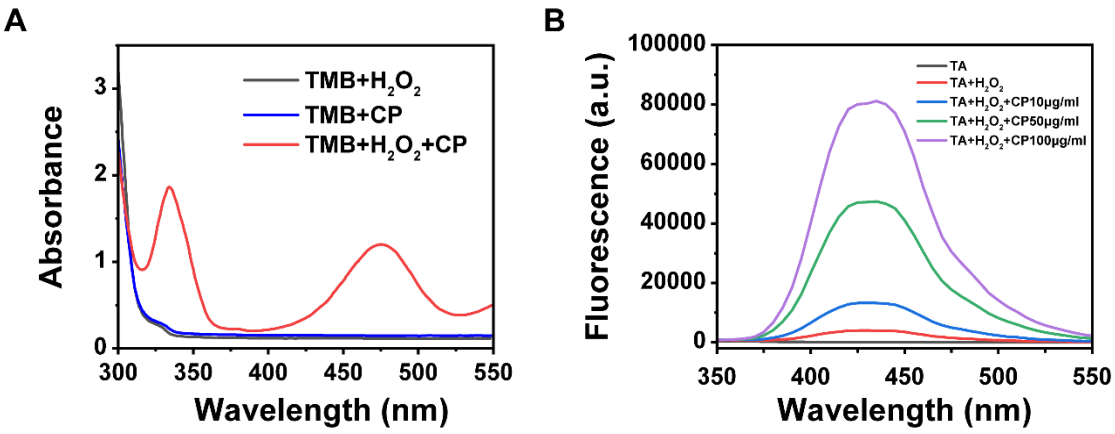


Figure S6. Evaluation on POD-like activity of CP. (A)The UV-vis absorption spectra of TMB catalytic oxidation under different conditions. (B) Fluorescent spectra of TA after reaction with H_2O_2 at different concentrations of CP.

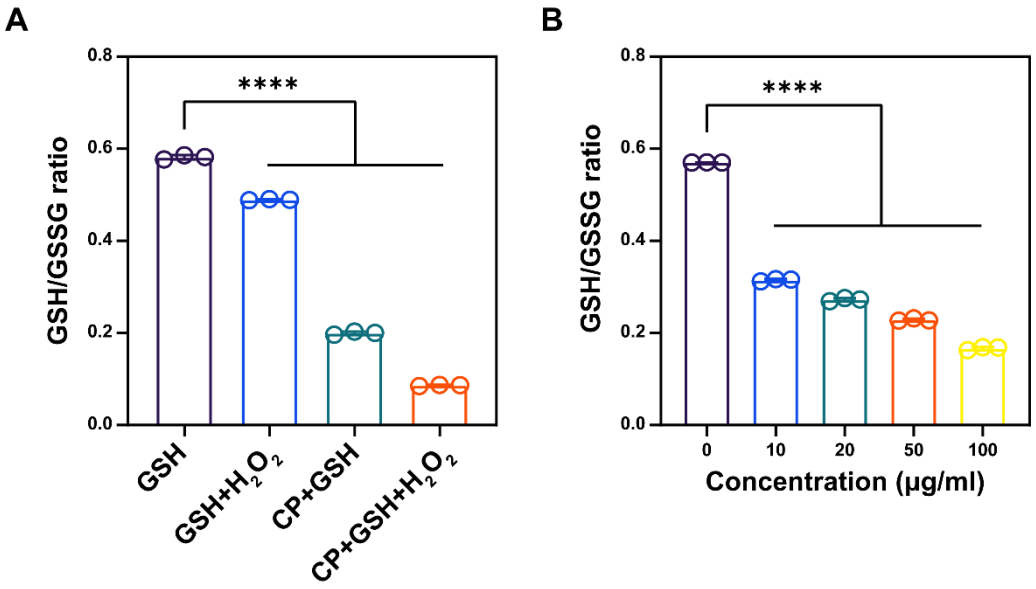


Figure S7. CP-induced variation of GSH/GSSG ratio. (A) The GSH/GSSG ratio was used to evaluate the GPx-like activity of CP. (B) The GSH/GSSG ratio in GSH depletion experiment under different concentrations of CP conditions. One-way analysis of variance (ANOVA): ****P<0.0001.

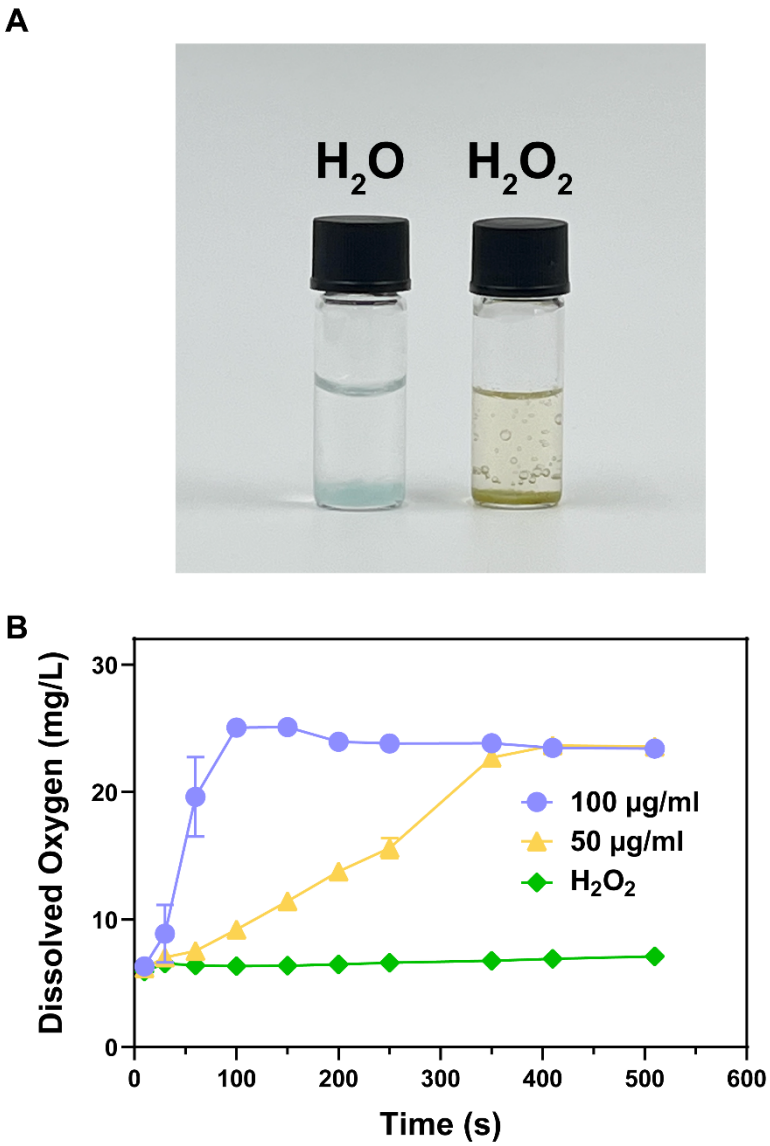


Figure S8. Evaluation on CAT-like activity of CP. (A) The photographs of CP dispersed in H_2O and 30% H_2O_2 solution. (B) Oxygen production of CP at different concentration.

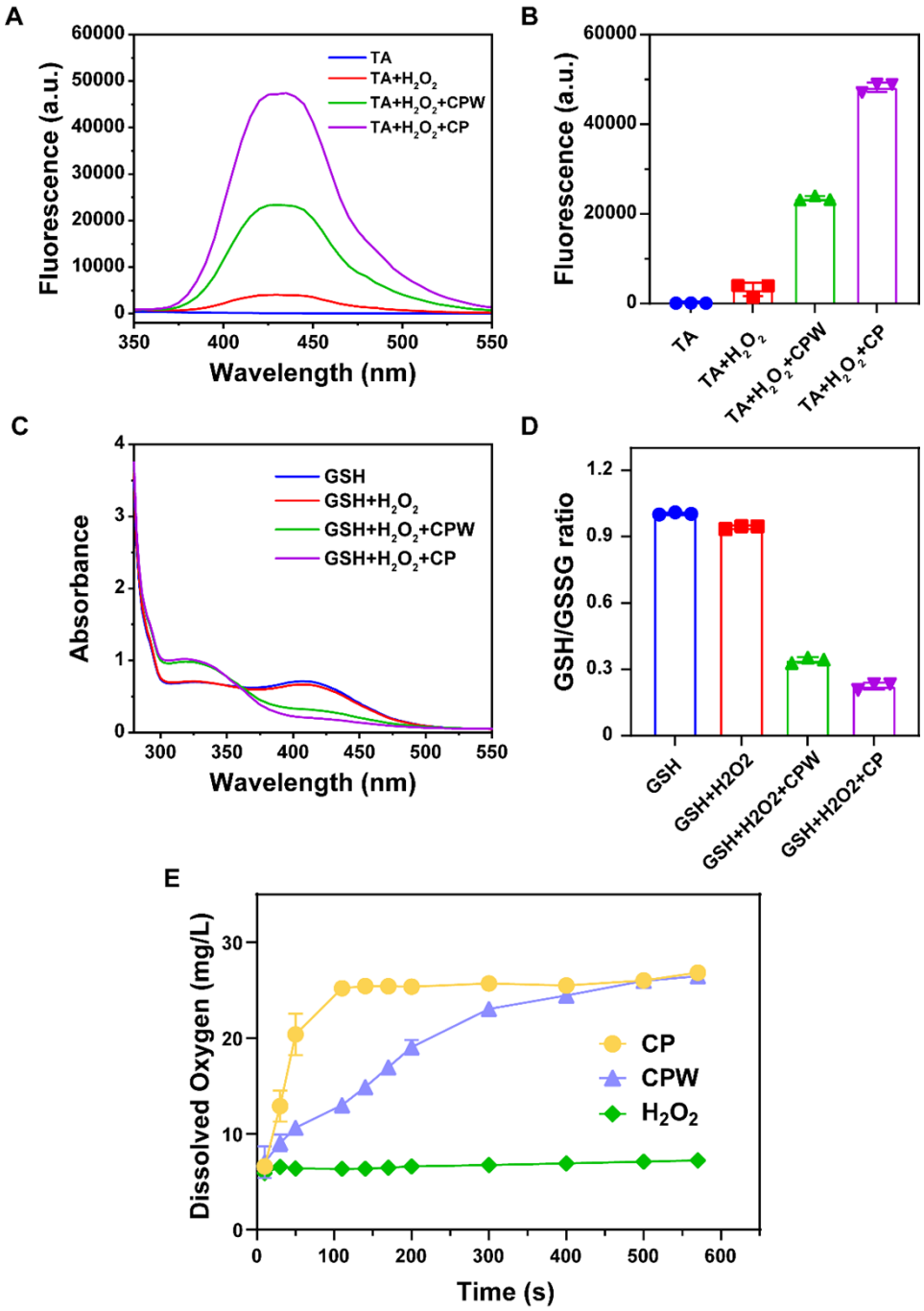


Figure S9. The influence of HA modification on catalytical activity of CP. (A)Fluorescent spectra of TA after reaction with H_2O_2 in the presence of CPW or CP. (B) The quantified results from fluorescent comparison experiment. (C)The UV-vis absorption spectra of GPx-like capacity of CP in the presence of CPW or CP. (D) The GSH/GSSG ratio from comparison experiment. (E) Oxygen production of CP in the presence of CPW or CP. (mean±s.d., n=3).

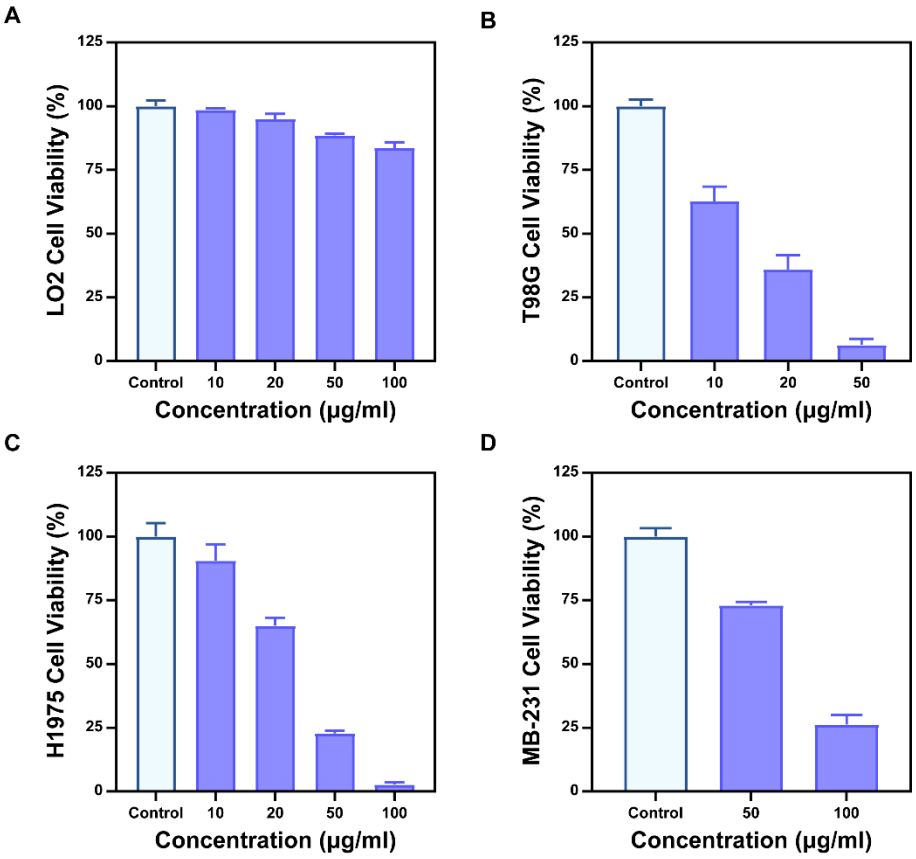


Figure S10. Cell viability of different types of cells treated with CP at different concentrations. (A) LO2 cells, (B) T98G cells, (C) H1975 cells, (D) MDA-MB-231 cells. (mean±s.d., n=3).

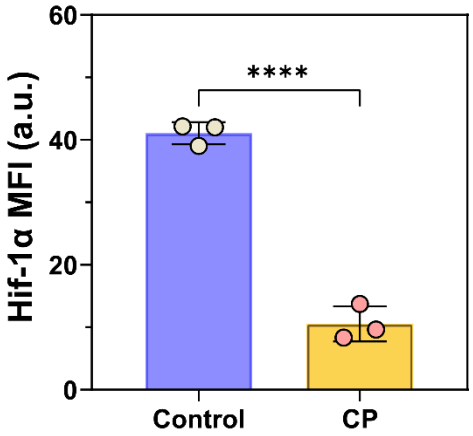


Figure S11. Relative fluorescent intensity analysis of HIF-1α based on the data from Figure 3F, using Image-J software. Student's t test: ****P<0.0001.

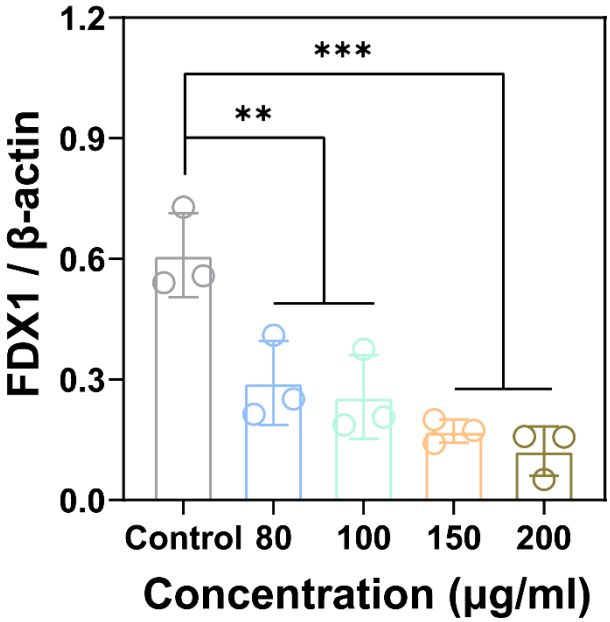


Figure S12. Semiquantitative analysis of FDX1 expression based on the data from Figure 4E. One-way analysis of variance (ANOVA): **P<0.01, ***P<0.001.

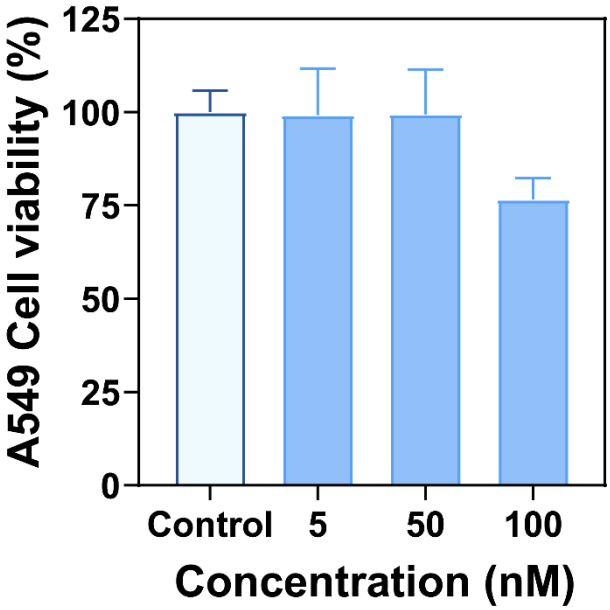


Figure S13. Cell viability of A549 cells after different concentrations of Elesclomol coupled with Cu^{2+} treatments. (mean±s.d., n=3).

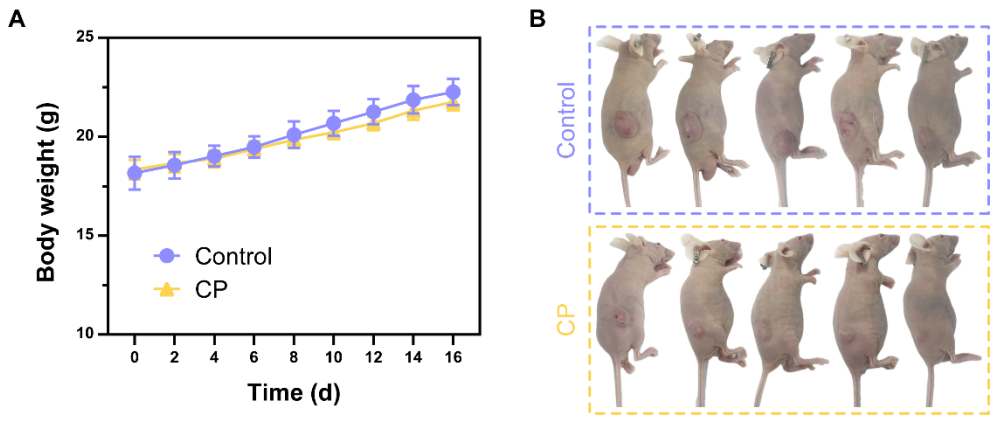


Figure S14. In vivo antitumor activity of CP. (A) Body weight curves of tumor-bearing mice after various treatments (mean±s.d., n=5). (B) The representative images of tumor-bearing nude mice in control and CP group after a period of 16 days treatments.

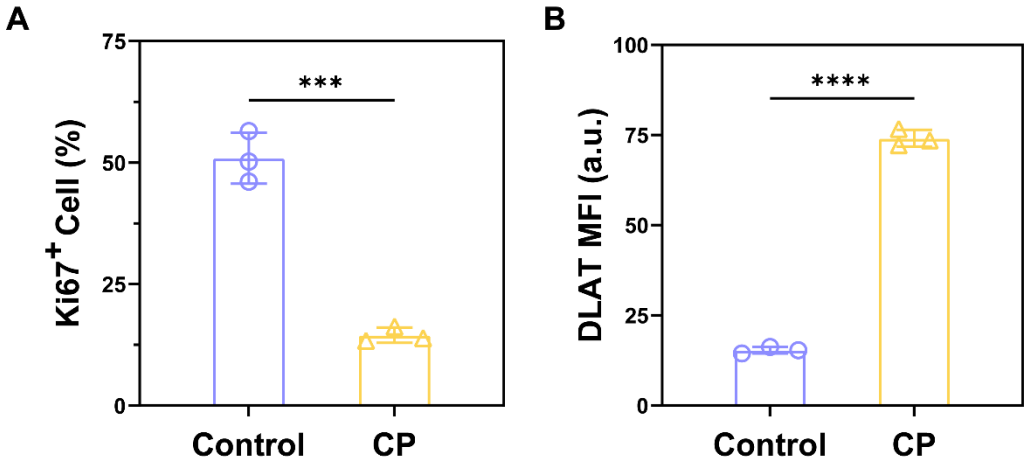


Figure S15. Quantified results of the proportion of positive signals stained by Ki67 and DLAT from control and CP group based on the data from Figure 5F and 5G. (A) Ki67 positive cells rate. (B) Mean fluorescence intensity of DLAT expression. Student's t test: ***P<0.001, ****P<0.0001.

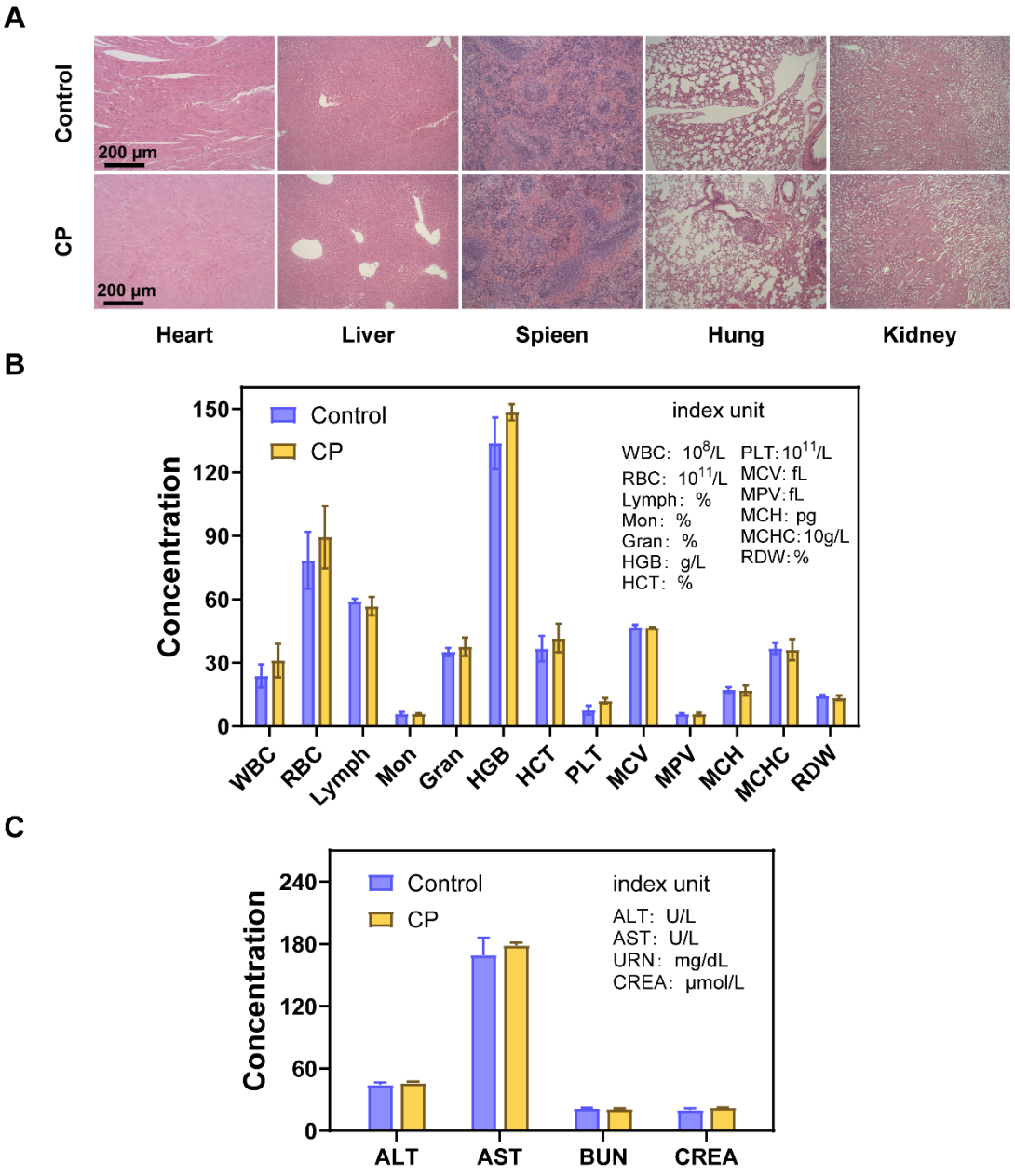


Figure S16. Biocompatibility of CP. (A) H&E staining of the major organs (heart, liver, spleen, kidney and lung) of mice in CP group and healthy mice group. (B) Hematological parameters analysis of healthy mice and tumor-bearing mice treated with CP. (C) blood biochemistry test after treatment with CP (mean±s.d., n=3).