

Supporting information of

Highly stable, coordinated polymeric nanoparticles loading
copper(II) diethyldithiocarbamate for combinational
chemo/chemodynamic therapy of cancer

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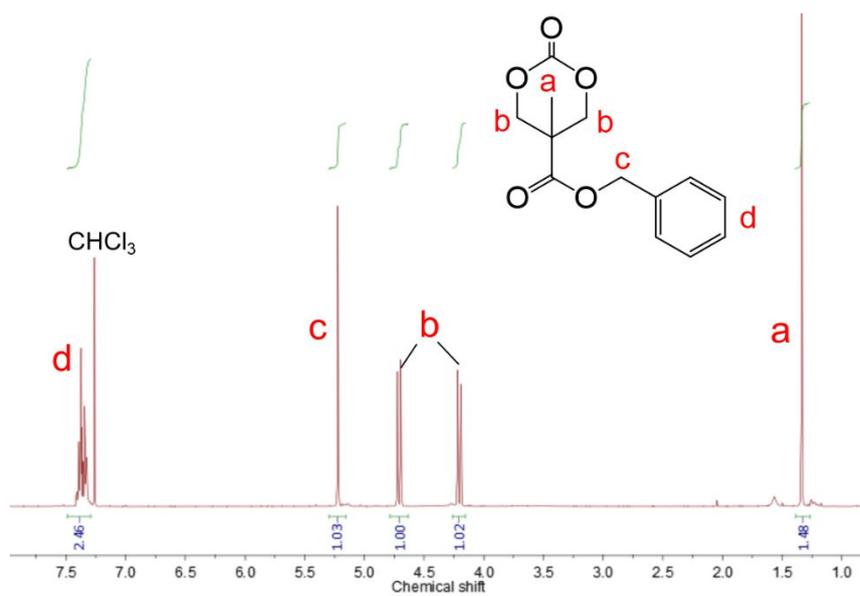


Figure S1. ^1H NMR spectrum of monomer MTC-OBn in CDCl_3 .

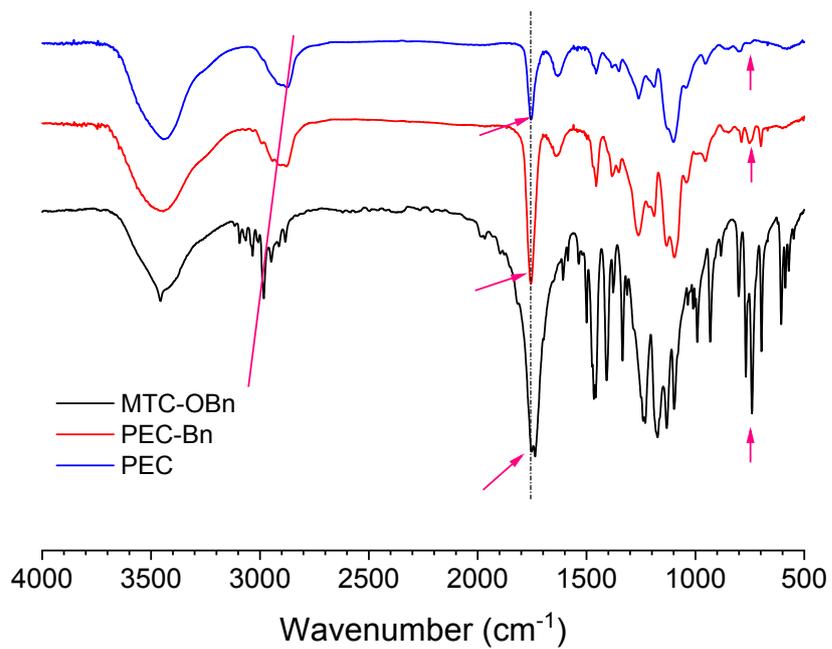


Figure S2. FT-IR spectra of MTC-OBn, PEC-Bn, and PEC.

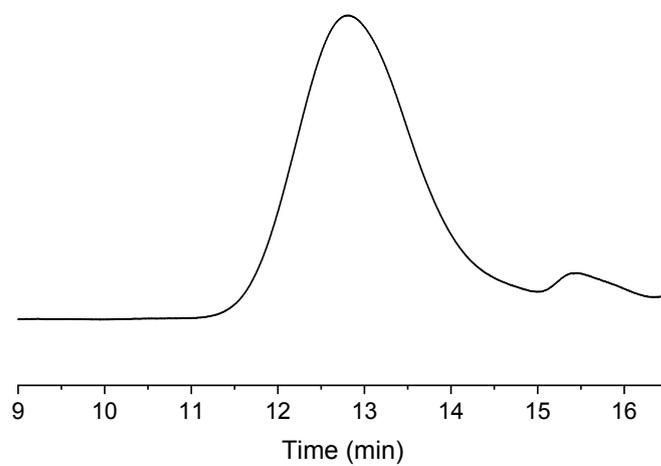


Figure S3. GPC trace of PEC-Bn.

Table S1 Molecular weights of PEC-Bn detected by GPC.

| | Feeding molar ratio of LA:C:PEG | LA:C:PEG in Polymers ^a | M_n (kDa) ^b | M_w (kDa) ^b | D_M |
|---------------|------------------------------------|--------------------------------------|--------------------------|--------------------------|-------|
| PEC-Bn | 26:13:1 | 22:11:1 | 4.71 | 12.7 | 2.70 |

a) Calculated by NMR; b) Determined by GPC. (LA: L-lactide; C: carbonate monomer)

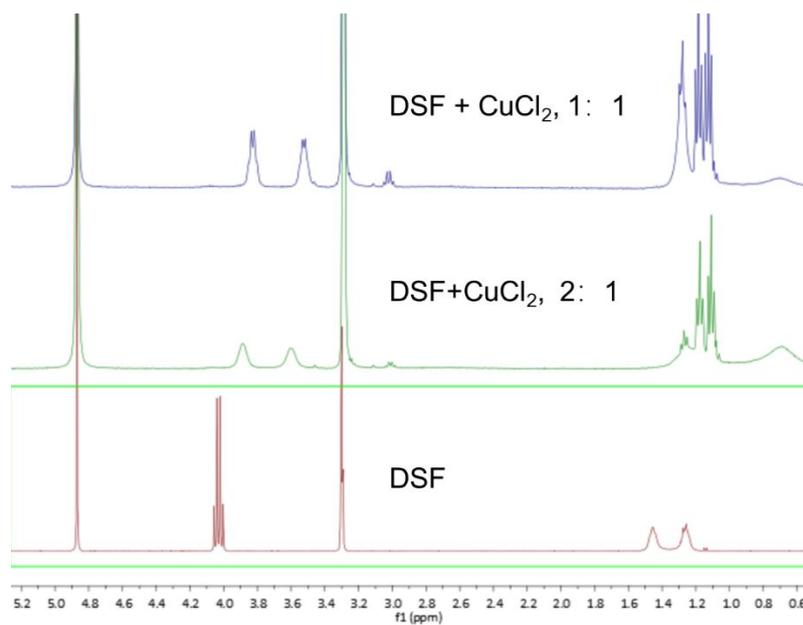


Figure S4. ^1H NMR spectra of DSF and the mixtures of DSF and CuCl_2 with different molar ratios in CD_3OD .

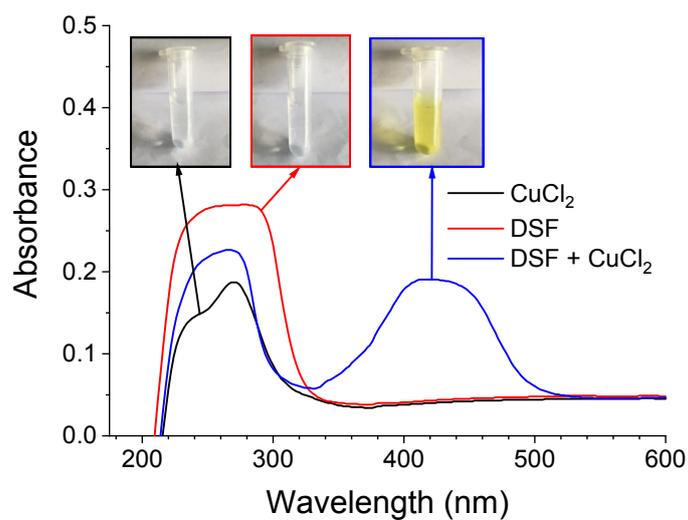


Figure S5. The UV-Vis spectra of the DSF, CuCl_2 , and their mixture in CH_3OH .

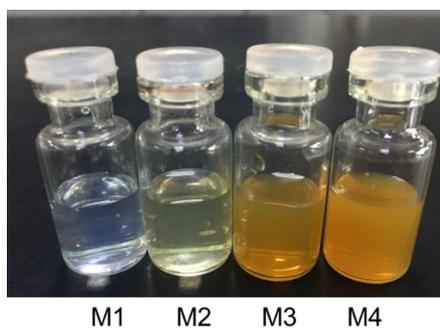


Figure S6. Photographs of M1–M4.

Table S2 Drug loading contents and efficiencies of Cu(II)- and Cu(II)/DDC-loaded micelles.

| Cu(II)/COOH ^a | DSF/Cu(II) ^a | [DDC] (mM) ^b | [Cu(II)] (mM) ^c | DLCs/DLEs of DDC | DLCs/DLEs of Cu(II) | DLCs of Cu(DDC) ₂ |
|--------------------------|-------------------------|----------------------------|-------------------------------|---------------------|------------------------|---------------------------------|
| 1:3 | 0 | 0 | 0.20 | - / - | 2.66% / 71.8% | - |
| | 0.5 | 0.01 | 0.22 | 0.46% / 5.38% | 3.09% / 84.4% | 0.56% |
| | 1 | 0.20 | 0.24 | 6.39% / 40.1% | 3.17% / 92.4% | 7.76% |
| | 1.5 | 0.24 | 0.18 | 7.66% / 31.8% | 2.54% / 74.5% | 9.30% |
| 2:3 | 0 (M1) | 0 | 0.22 | - / - | 3.04% / 40.9% | - |
| | 0.5 (M2) | 0.05 | 0.29 | 1.41% / 8.27% | 3.84% / 51.8% | 1.71% |
| | 1 (M3) | 0.22 | 0.36 | 6.40% / 20.4% | 4.55% / 66.6% | 7.77% |
| | 1.5 (M4) | 0.27 | 0.17 | 8.28% / 17.3% | 2.11% / 30.7% | 10.0% |
| 1:1 | 0 | 0 | 0.24 | - / - | 3.10% / 27.7% | - |
| | 0.5 | 0.21 | 0.35 | 6.06% / 25.2% | 4.28% / 41.4% | 7.36% |
| | 1 | 0.28 | 0.26 | 8.04% / 16.9% | 3.13% / 30.5% | 9.77% |
| | 1.5 | 0.24 | 0.21 | 7.07% / 9.74% | 2.65% / 25.4% | 8.58% |
| 4:3 | 0 | 0 | 0.20 | - / - | 2.68% / 17.9% | - |
| | 0.5 | 0.16 | 0.30 | 4.25% / 12.9% | 3.37% / 23.8% | 5.17% |
| | 1 | 0.29 | 0.27 | 8.13% / 12.8% | 3.18% / 23.4% | 9.87% |
| | 1.5 | 0.09 | 0.04 | 2.79% / 2.69% | 0.56% / 3.80% | 3.39% |

a) Feeding molar ratios. b) Determined by HPLC. c) Measured by ICP-AES.

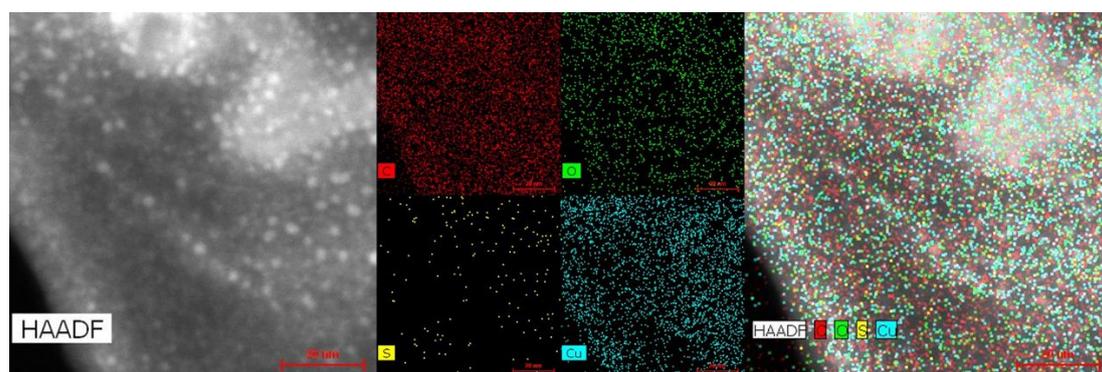


Figure S7. The STEM images of M3 micelle.

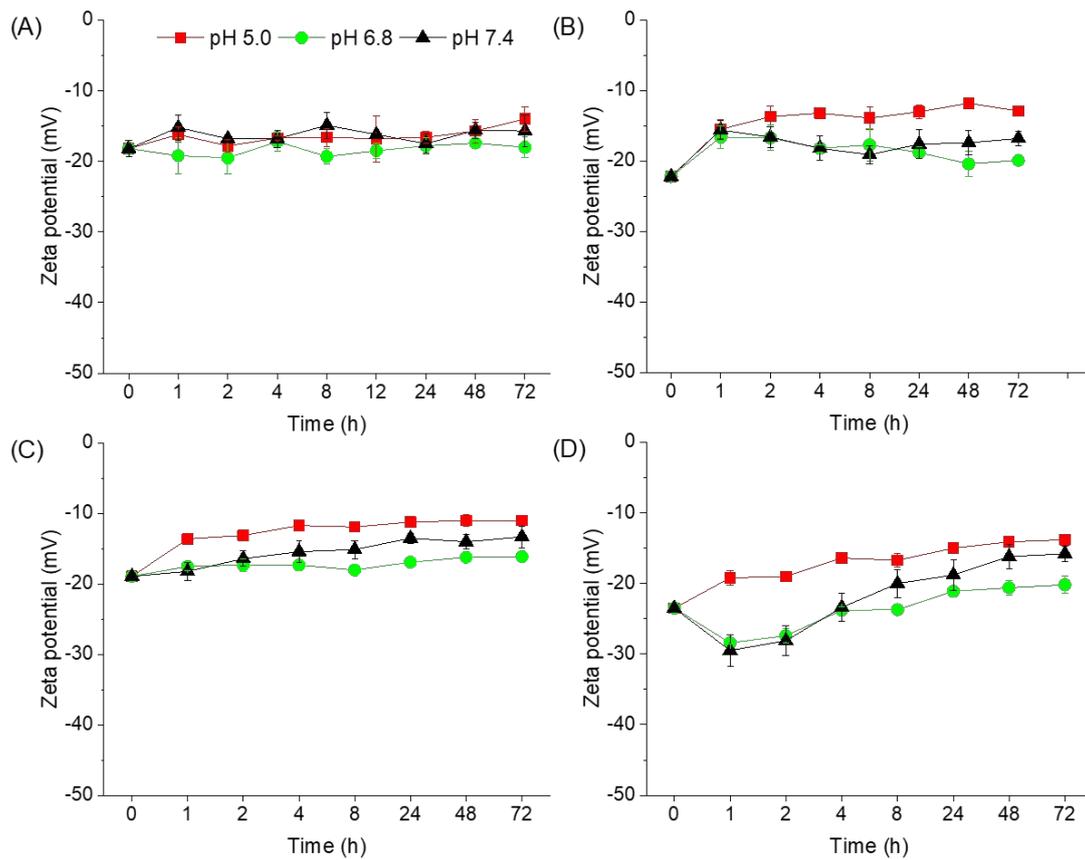


Figure S8. The zeta potential changes of M1–M4 micelles in different pH conditions.

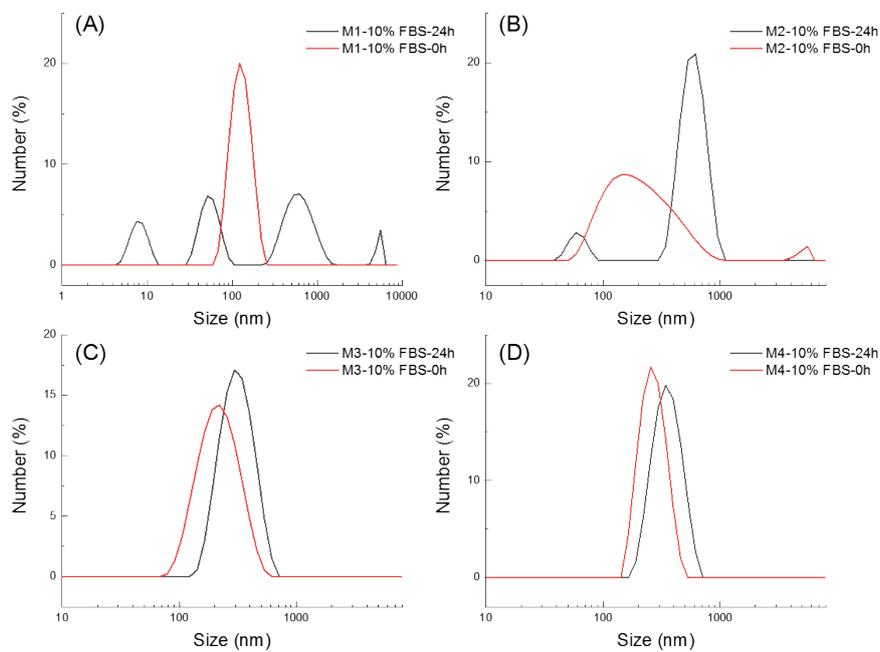


Figure S9. The sizes of M1 (A), M2 (B), M3 (C), and M4 (D) before and after an incubation with 10% FBS PBS for 24 h.

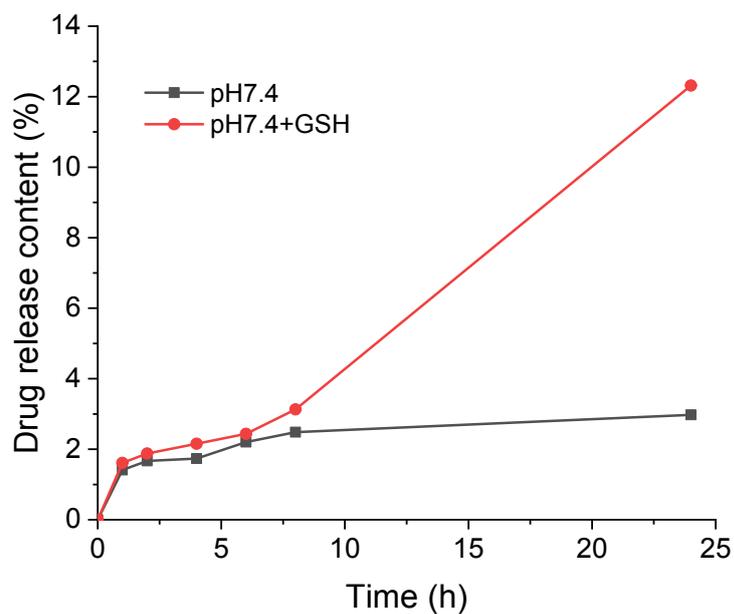


Figure S10. The release behavior of Cu(II)-loaded nanoparticles in the presence and absence of 5 mM GSH.

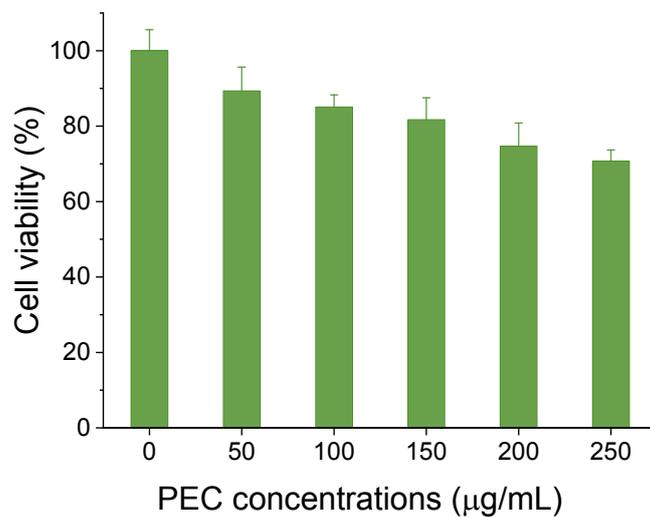


Figure S11. The cell viability of NIH 3T3 cells after incubation with PEC at various concentrations for 48 h.

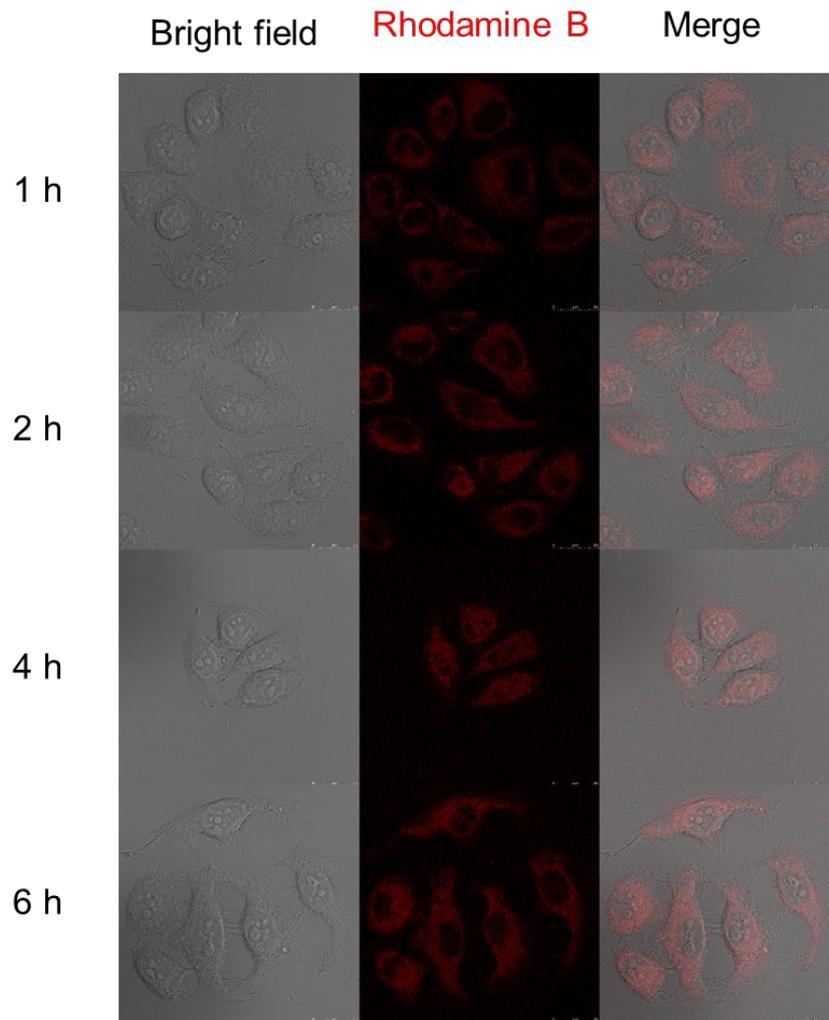


Figure S12. The CLSM images of A549 cells treated with Rhodamine B-loaded PEC micelle for different times.

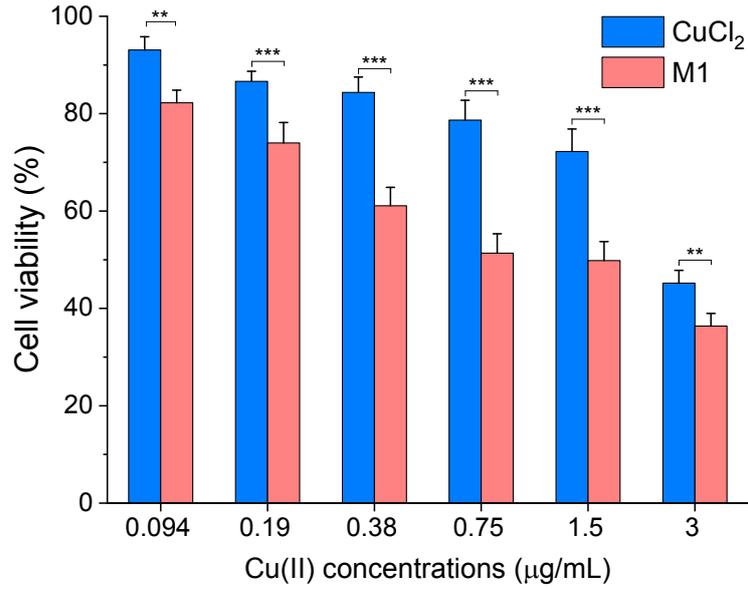


Figure S13. The cell viability of A549 cells after incubation with CuCl₂ and M1 at various Cu(II) concentrations for 48 h ($n = 5$. ** indicates $P < 0.01$ and *** indicates $P < 0.001$).

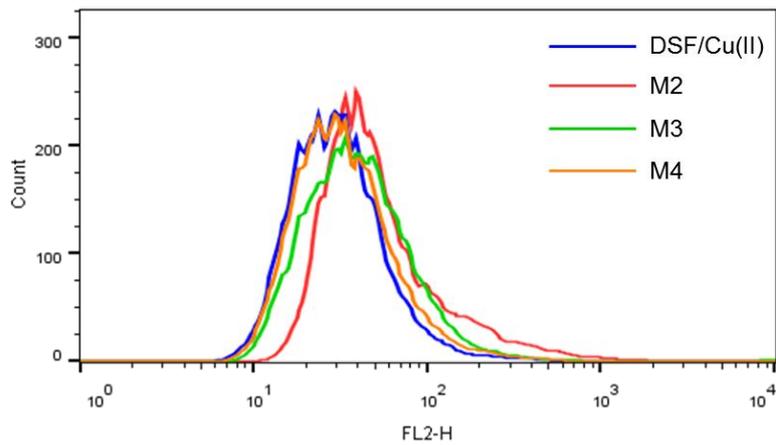


Figure S14. The intracellular ROS level of cells treated by DSF/Cu(II), M2, M3 and M4 detected by flow cytometry.

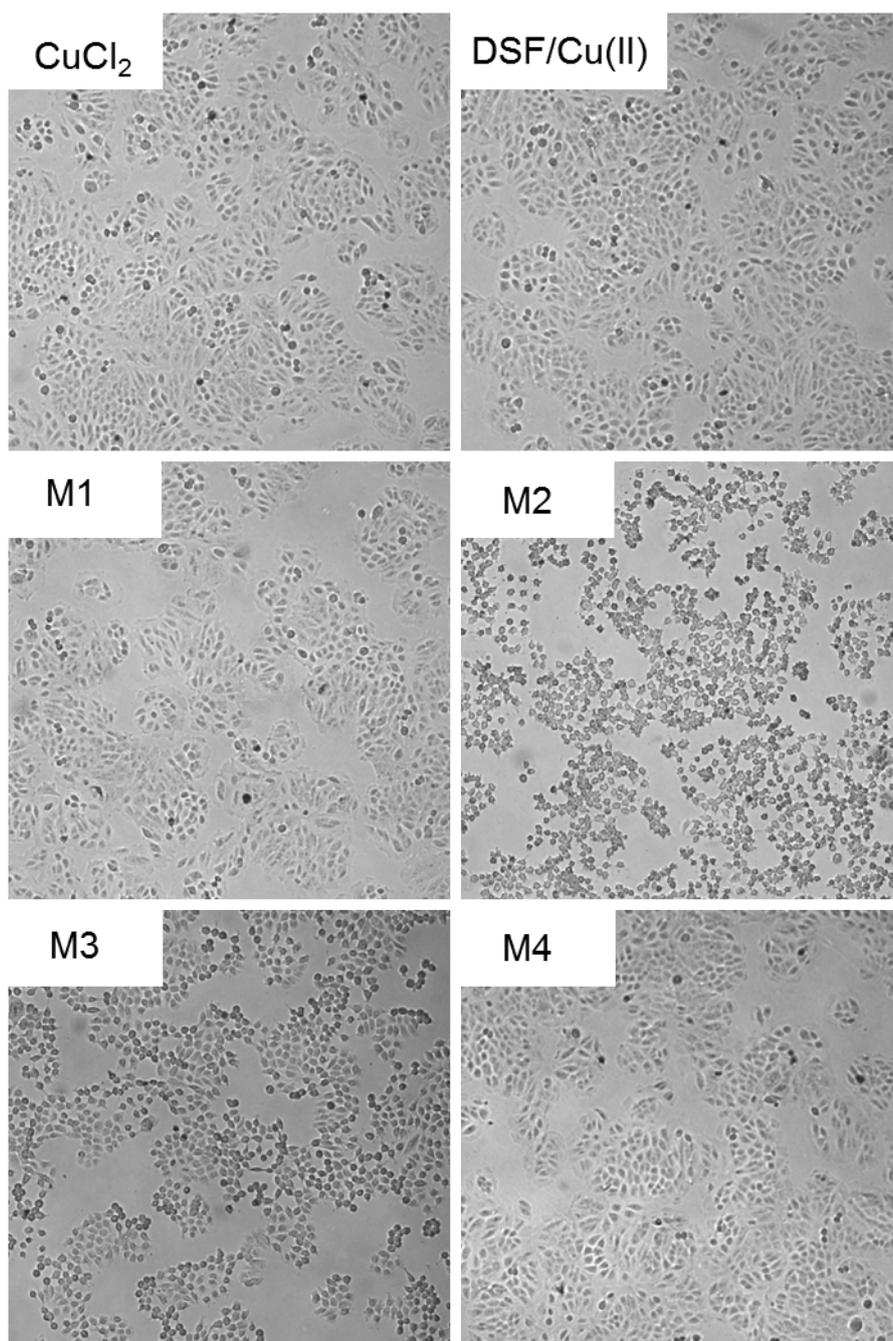


Figure S15. The microphotographs of A549 cells treated with CuCl₂, DSF/Cu(II), and M1–M4 at a Cu(II) concentration of 2 µg/mL for 4 h.

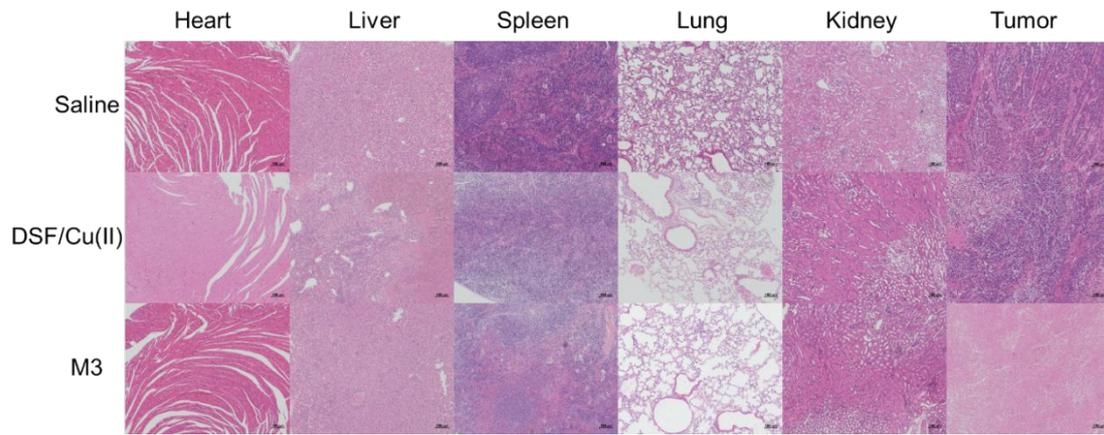


Figure S16. The H&E histological analysis (100×) of heart, liver, spleen, lung, kidney, and tumor in different groups (saline, DSF/Cu(II) and M3).