

# **Cu-doped $\text{Co}_9\text{S}_{8-x}$ sonozymes for enhanced sonodynamic and chemodynamic therapy of gallbladder cancer through ion doping and vacancy engineering**

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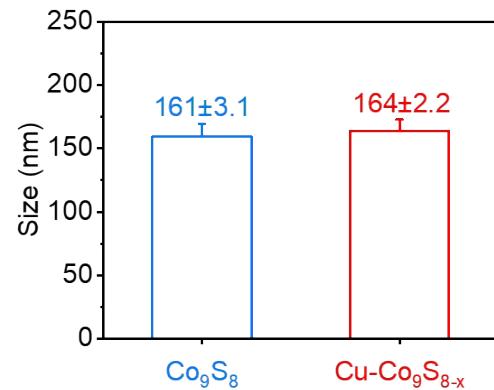
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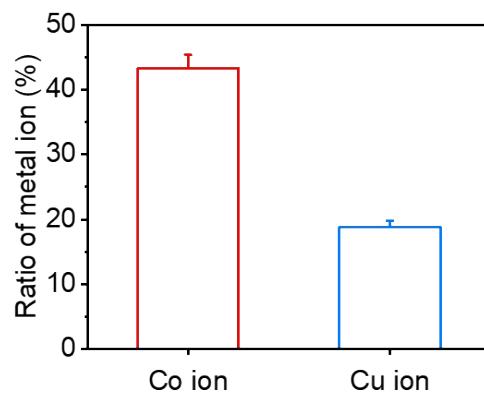
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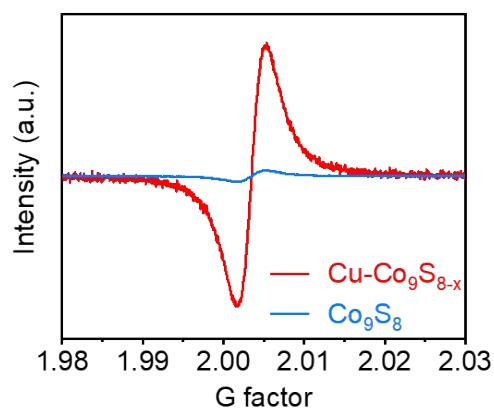
**Keywords:** Co<sub>9</sub>S<sub>8-x</sub>, ion doping engineering, vacancy engineering, sonodynamic therapy, chemodynamic therapy



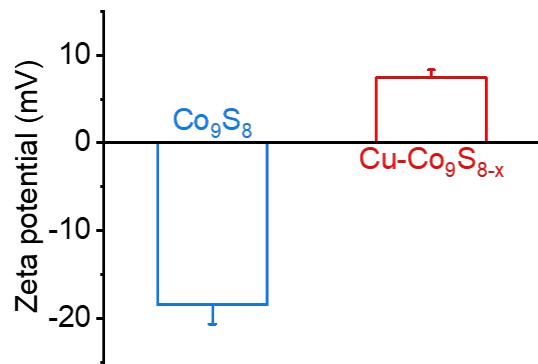
**Fig. S1.** DLS size of  $\text{Co}_9\text{S}_8$  and  $\text{Cu}-\text{Co}_9\text{S}_{8-x}$ . Data are presented as the mean  $\pm$  SD. (n = 3).



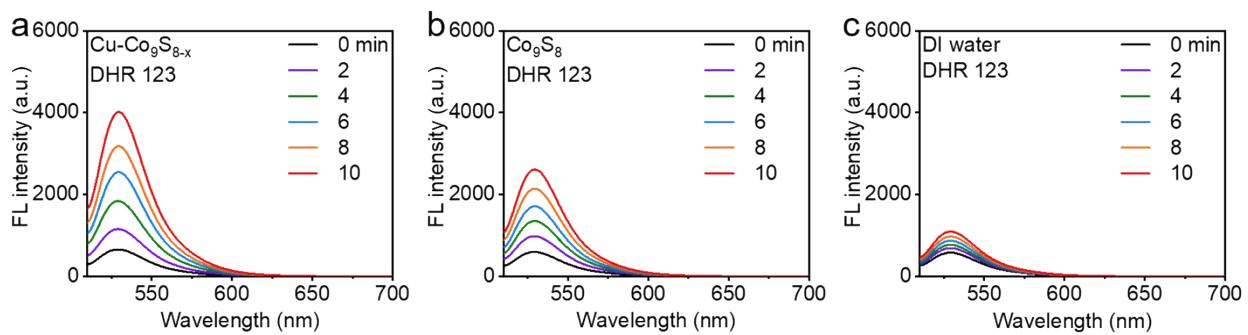
**Fig. S2.** The contents of Co and Cu ions in  $\text{Cu}-\text{Co}_9\text{S}_{8-x}$  determined by ICP-MS Data are presented as the mean  $\pm$  SD. (n = 3).



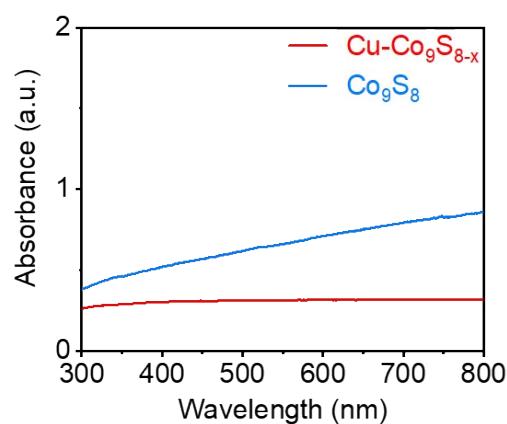
**Fig. S3.** EPR spectrum of  $\text{Co}_9\text{S}_8$  and  $\text{Cu}-\text{Co}_9\text{S}_{8-x}$ .



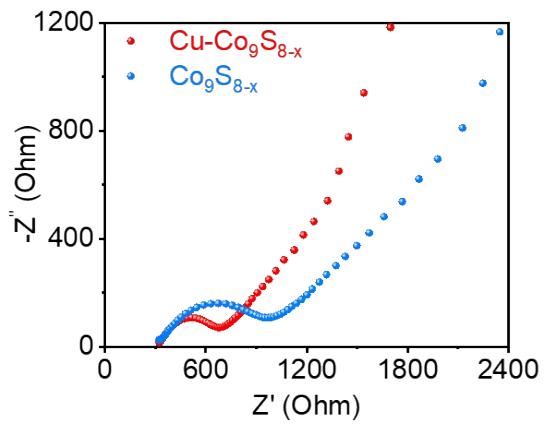
**Fig. S4.** Zeta potential of  $\text{Co}_9\text{S}_8$  and  $\text{Cu}-\text{Co}_9\text{S}_{8-x}$ . Data are presented as the mean  $\pm$  SD. ( $n = 3$ ).



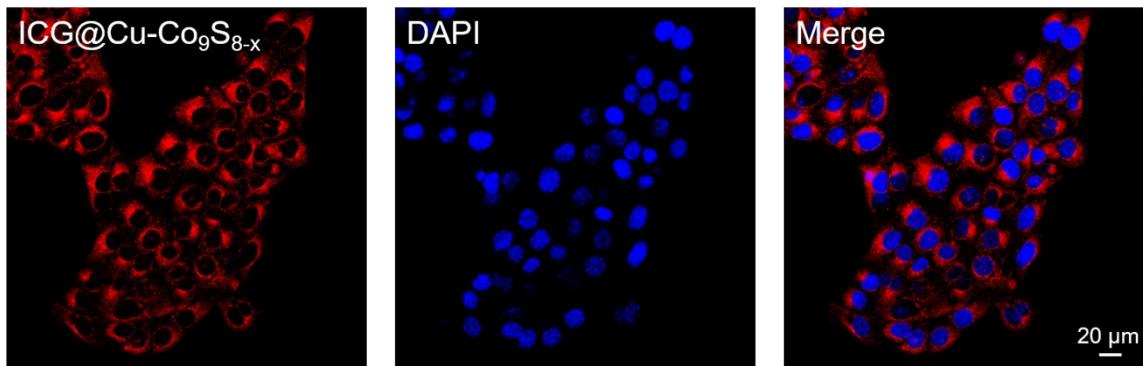
**Fig. S5.** Measurement of the  $\text{O}_2^-$  generation of  $\text{Cu}-\text{Co}_9\text{S}_{8-x}$  and  $\text{Co}_9\text{S}_{8-x}$  under US irradiation (50 kHz, 1.0  $\text{W}/\text{cm}^2$ ).



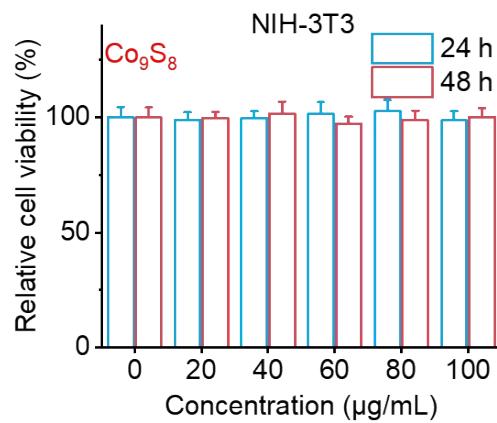
**Fig. S6.** UV-vis absorption of  $\text{Co}_9\text{S}_8$  and  $\text{Cu}-\text{Co}_9\text{S}_{8-x}$ .



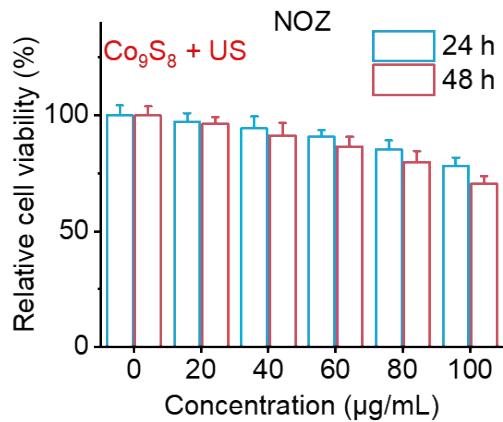
**Fig. S7.** The impedance spectra of  $\text{Co}_9\text{S}_{8-x}$  and  $\text{Cu}-\text{Co}_9\text{S}_{8-x}$  electrodes.



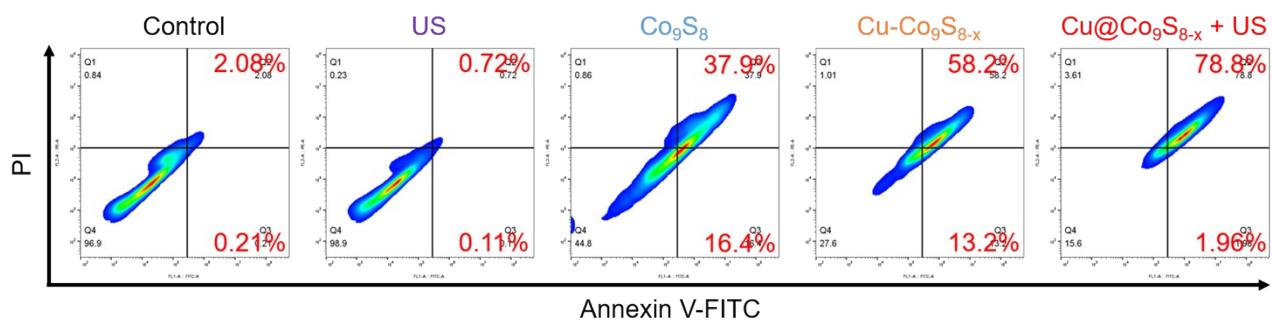
**Fig. S8.** Confocal images of NOZ cells after being treated with ICG-labeled  $\text{Cu}-\text{Co}_9\text{S}_{8-x}$  and DAPI.



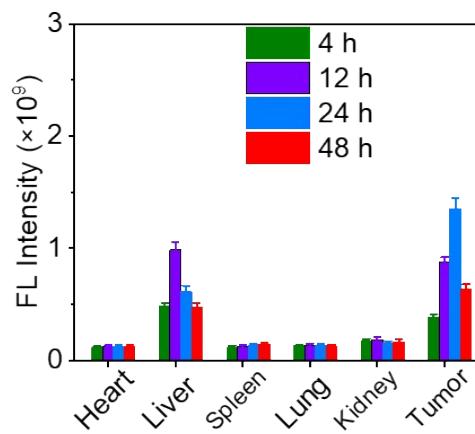
**Fig. S9.** Relative cell viabilities of NIH-3T3 cells incubated with  $\text{Co}_9\text{S}_8$  with varied concentrations for 24 or 48 h. Data are presented as the mean  $\pm$  SD. ( $n = 6$ ).



**Fig. S10.** Relative cell viabilities of NOZ cells incubated with  $\text{Co}_9\text{S}_8$  with varied concentrations for 24 or 48 h under US irradiation. Data are presented as the mean  $\pm$  SD. (n = 6)

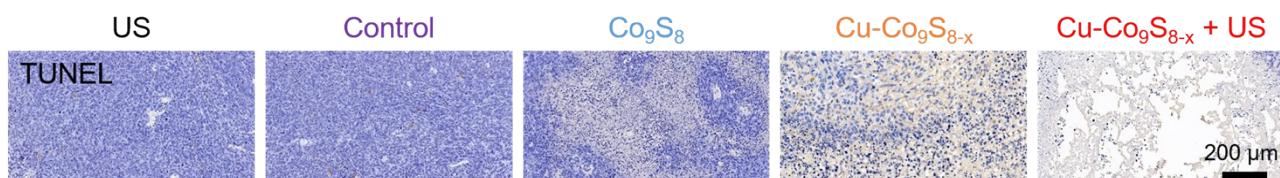


**Fig. S11.** Apoptosis assay of NOZ cells after different treatments through flow cytometry.

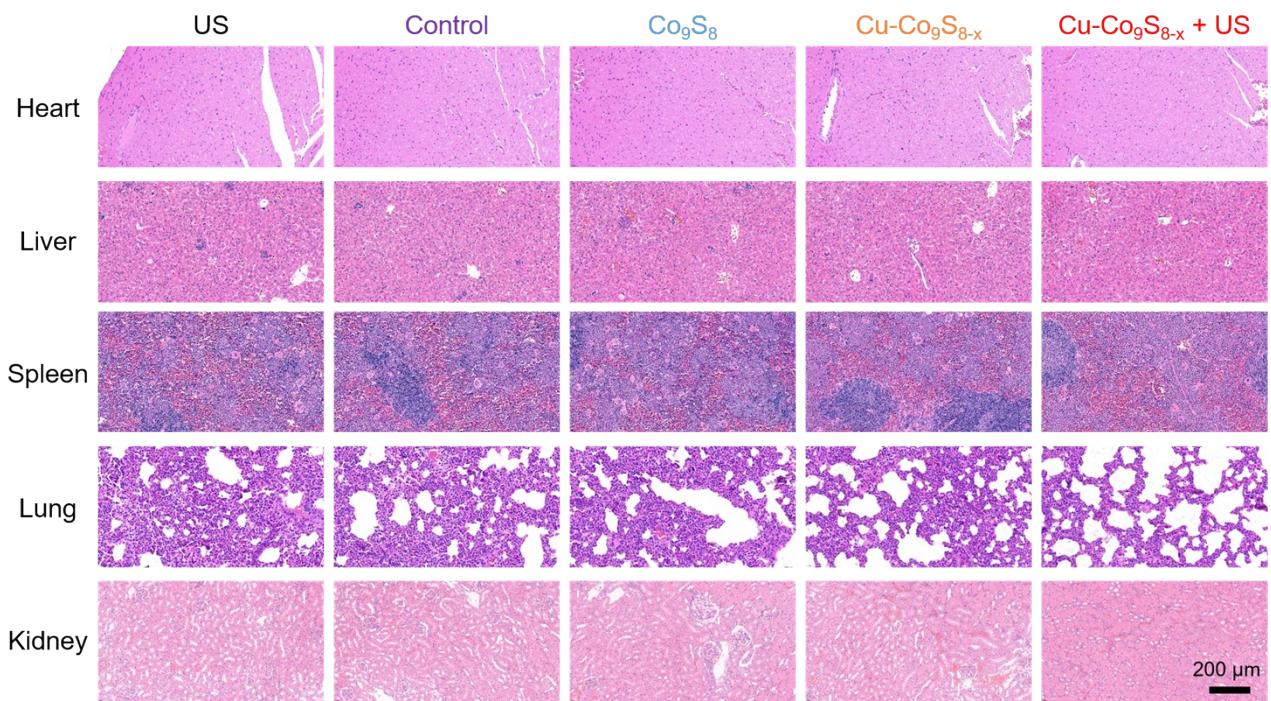


**Fig. S12.** Time-dependent fluorescence intensity of  $\text{Cu}-\text{Co}_9\text{S}_{8-x}$  in the major organs and tumor tissues.

Data are presented as the mean  $\pm$  SD. (n = 5).

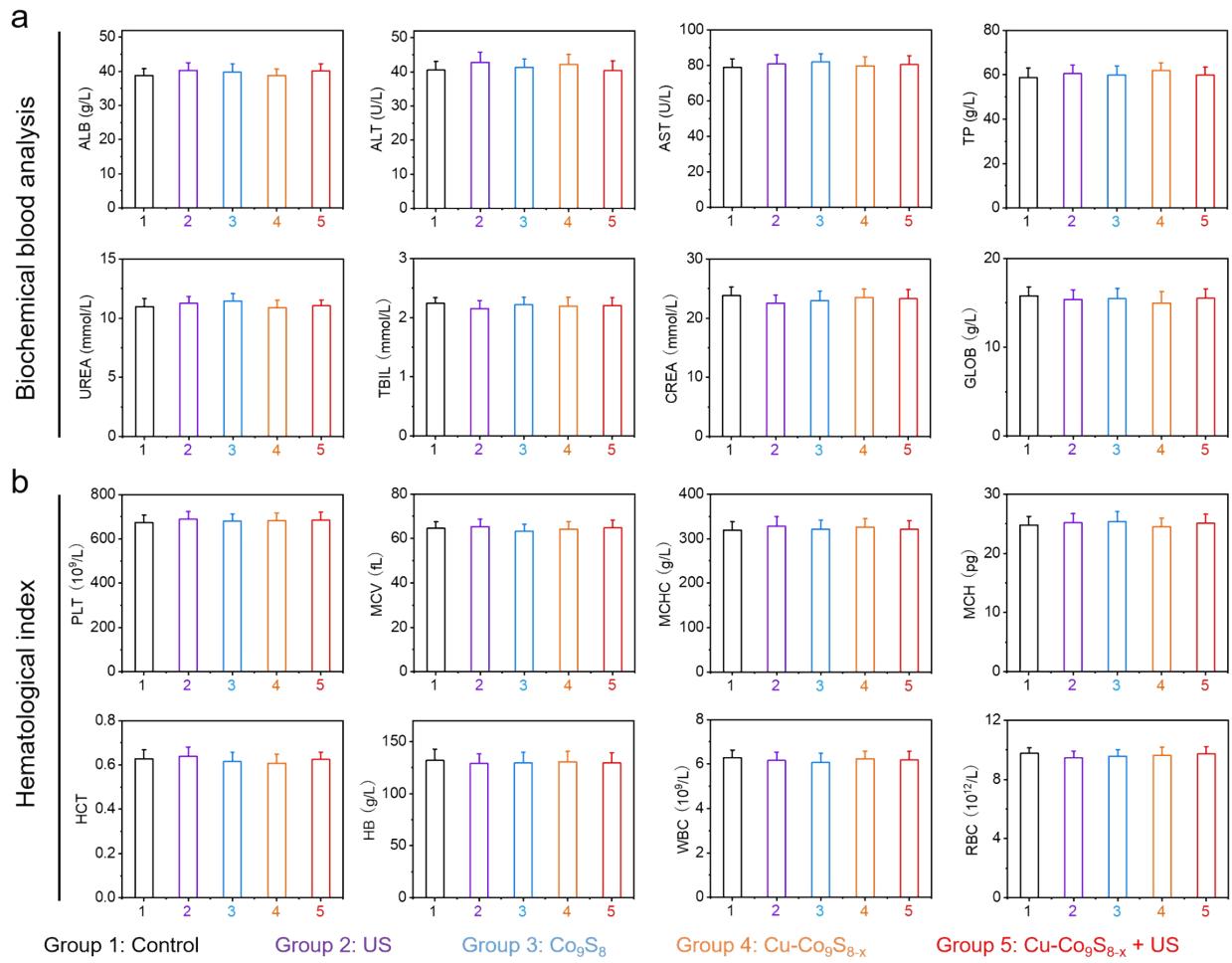


**Fig. S13.** TUNEL staining of tumors in mice after different treatments.



**Fig. S14.** H&E-stained images obtained from the major organs (heart, liver, spleen, lung, and kidney) of mice in different treatment groups.

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**Fig. S15.** (a-b) Biochemical blood analysis (a) and hematological index (b) of the mice that were sacrificed 18 days after different treatments.