Supporting Information

Near-Infrared Zn-Doped Cu_2S Quantum Dots: An Ultrasmall Theranostic Agent for Tumor Cell Imaging and Chemodynamic Therapy

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Effects of different reaction conditions on the PL intensity of Cu_2S and Zn:Cu_2S QDs

The effects of different reaction conditions on the fluorescence intensity were investigated to improve the luminescence properties of Cu_2S QDs. As shown in Figure S1a and 1b, the PL emission intensity of Cu_2S QDs significantly increased with the increased of Cu^{2+}/thiourea ratio, reaching a maximum when the ratio was 1:1. However, if the Cu^{2+}/thiourea ratio is further increased, the fluorescence intensity of Cu_2S QDs would gradually decreased. The PL spectra in the absence of thiourea showed no fluorescence, indicating that no emissive Cu_2S QDs was obtained without thiourea. The effect of reaction temperatures on the fluorescence spectra of Cu_2S QDs was also investigated (Figure S1c and 1d). The results showed that the maximum PL intensity was obtained at 120 °C. In our synthesis method, S^{2-} produced by the pyrolysis of thiourea was used as the precursor of sulfur (**Equation S1**). When the temperature was lower than decomposition temperature of thiourea, Cu_2S QDs could not be synthesized successfully. Howerver, if the temperature was too high, Cu_2S QDs would precipitated rapidly due to excessive growth and had no fluorescence. The PL spectra and PL intensity of Cu_2S QDs synthesized with different reaction time showed that the PL intensity increased with reaction time extended, reaching the maximum at 30 min, and then decreased with the further extension of reaction time (Figure S1e and 1f). The effect of the reaction pH on the PL intensity were also studied. As shown in Figure S1g and 1h, the PL intensity increased with the increase of pH values and reached the maximum at pH 5, then decreased with further increase of pH. These may be attributed to the different existence forms of GSH as ligand at different pH conditions.

$$(NH_2)_2CS \xrightarrow{\Delta} CO_2 + 2NH_3 + H_2S \qquad \textbf{(Equation S1)}$$

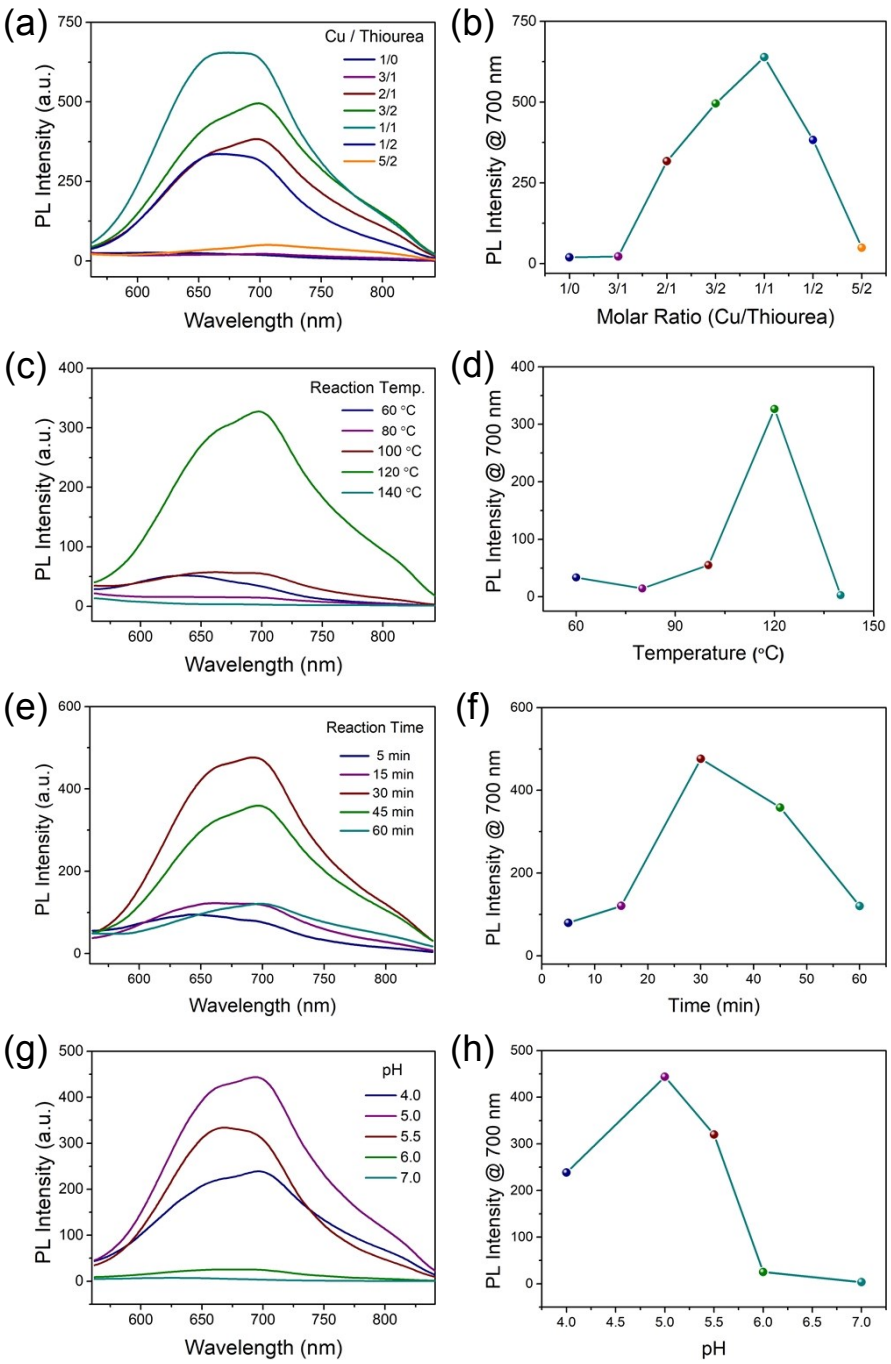

Figure S1. Effects of (a, b) Cu^{2+}/thiourea molar ratio, (c, d) reaction temperature, (e, f) time and (g, h) pH on the fluorescence spectra and intensity of Cu_2S QDs.

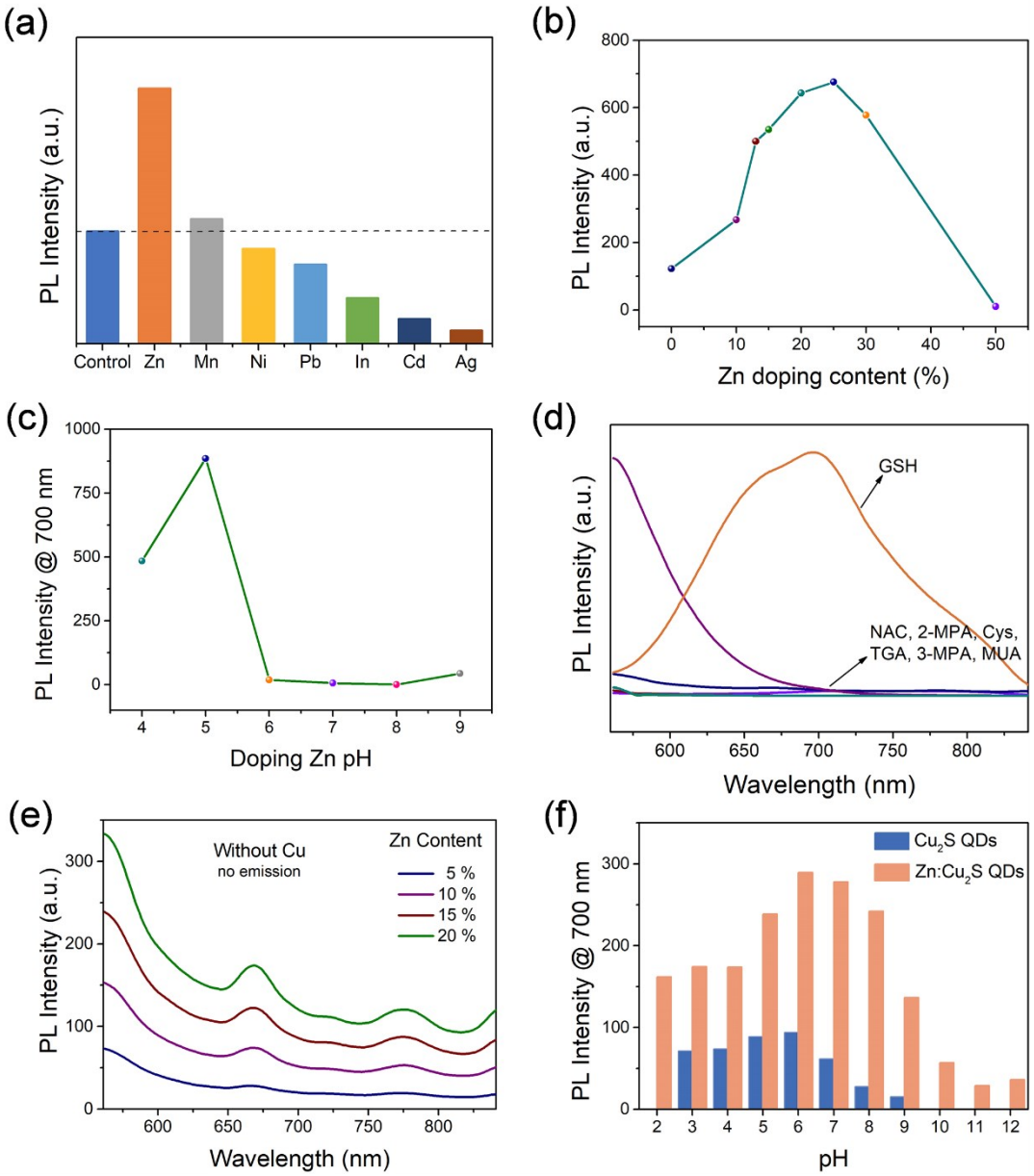

Figure S2. The effect of (a) different doping transition metal ion, (b) Zn content and (c) doping pH on fluorescence intensity of Zn:Cu_2S QDs. (d) The PL spectra of the products synthesized with different surface ligands. (e) The PL spectra of the products synthesized without Cu precursors. (f) The PL intensity of Cu_2S and Zn:Cu_2S QDs at different pH.

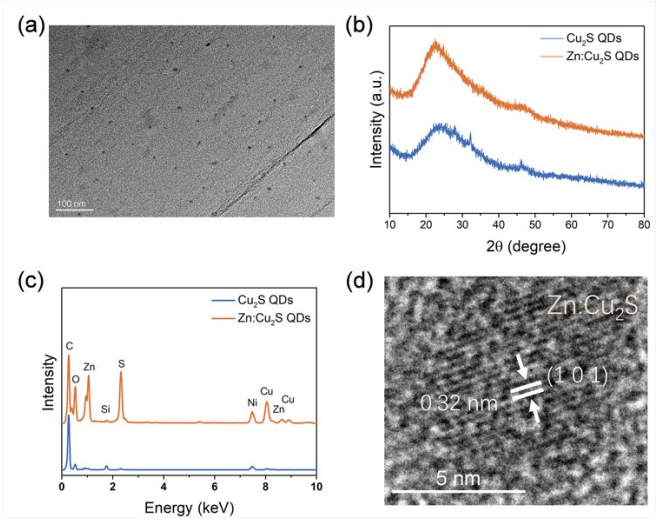

Figure S3. (a) The representative TEM images of Cu_2S QDs and (b) XRD patterns and (c) EDX of the Cu_2S QDs and Zn:Cu_2S QDs. (d) HRTEM image of Zn:Cu_2S QDs.

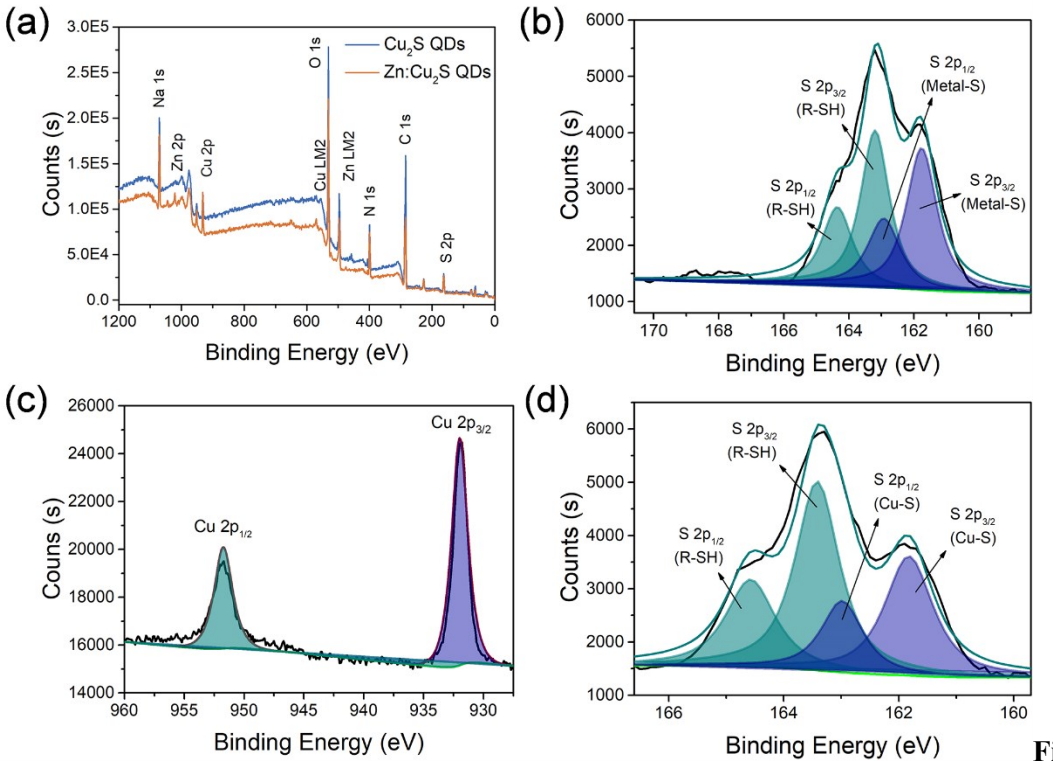

Figure S4. High-resolution XPS spectra of (a) summary, (b) S 2p in Zn:Cu_2S QDs, (c) Cu 2p and (d) S 2p in Cu_2S QDs.

First-order reaction integral rate equation function

$$I_{Z,n} = I_{Z,0}e^{-k_1 n} \quad \textbf{(Equation S2)}$$

Where $I_{Z,0}$, $I_{Z,n}$ are defined as PL intensity of Zn:Cu_2S QDs before and after n times excitation, and k_1 is photoactivation rate constant.

Lifetime bi-exponential function

$$I(t) = A_1 e^{\left(-t/\tau_1\right)} + A_2 e^{\left(-t/\tau_2\right)} \quad \textbf{(Equation S3)}$$

$$\tau_{av} = \left(A_1\tau_1^2 + A_2\tau_2^2\right)/\left(A_1\tau_1 + A_2\tau_2\right) \quad \textbf{(Equation S4)}$$

Where τ_1, τ_2 are defined as lifetimes, A_1, A_2 are corresponding pro-exponential factors, respectively and τ_{av} calculates by **Equation S4** represents the average lifetime of Cu_2S QDs.

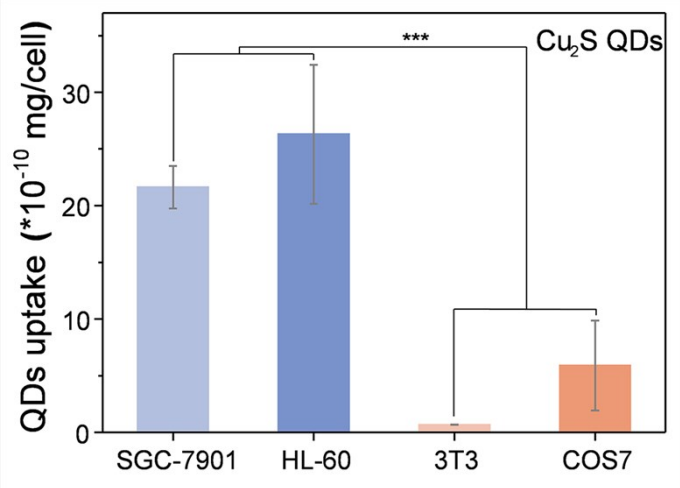

Figure S5. Intracellular Cu contents of SGC-7901, HL-60 and 3T3, COS7 cells treated with Cu2S QDs for 24 h (n = 3) (Statistical analysis was based on Student's t test: ***$P < 0.001$).

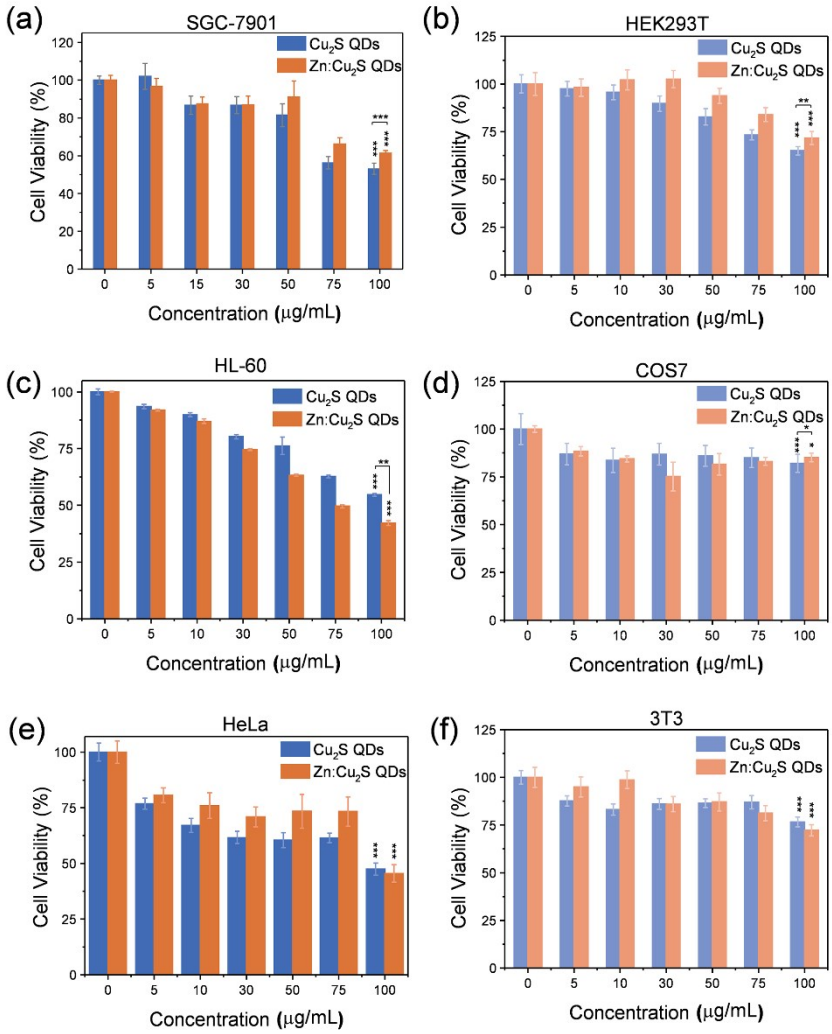

Figure S6. MTT results of normal cells (a, c and e) and tumor cells (b, d and f) incubated with Cu_2S and Zn:Cu_2S QDs for 24 h at different concentrations. (*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$)

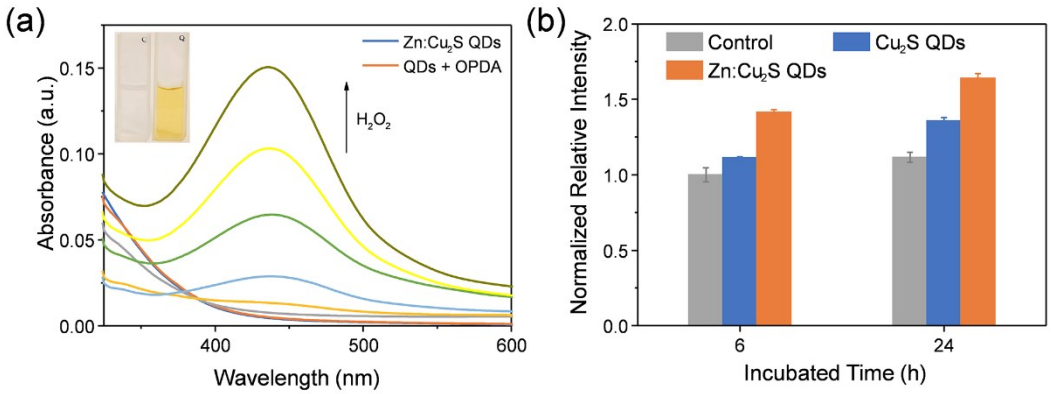

Figure S7. (a) UV-vis spectra and photographs (inset) of Zn:Cu_2S QDs solution treated with OPDA and OPDA plus H_2O_2, (b) The relative ROS intensity of SGC-7901 cells after incubated with Zn:Cu_2S QDs for different time.

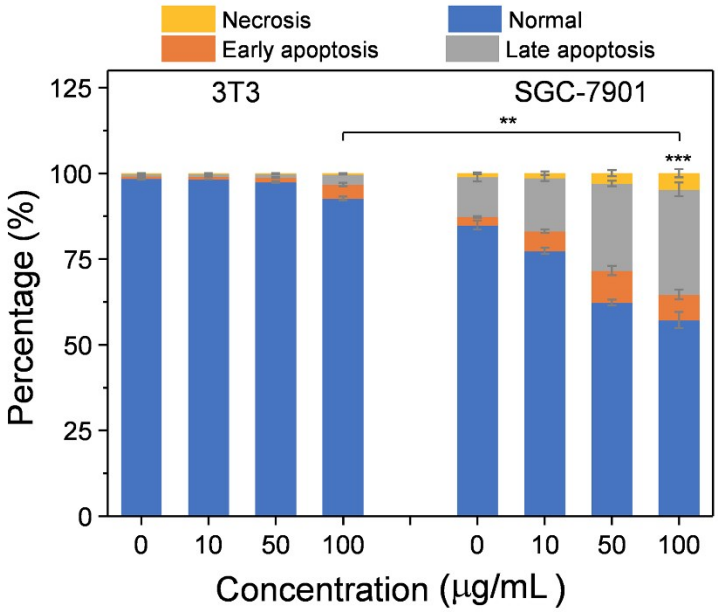

Figure S8. Histogram of apoptosis after incubated with Zn:Cu_2S QDs for 24 h (**$P < 0.01$, ***$P < 0.001$).

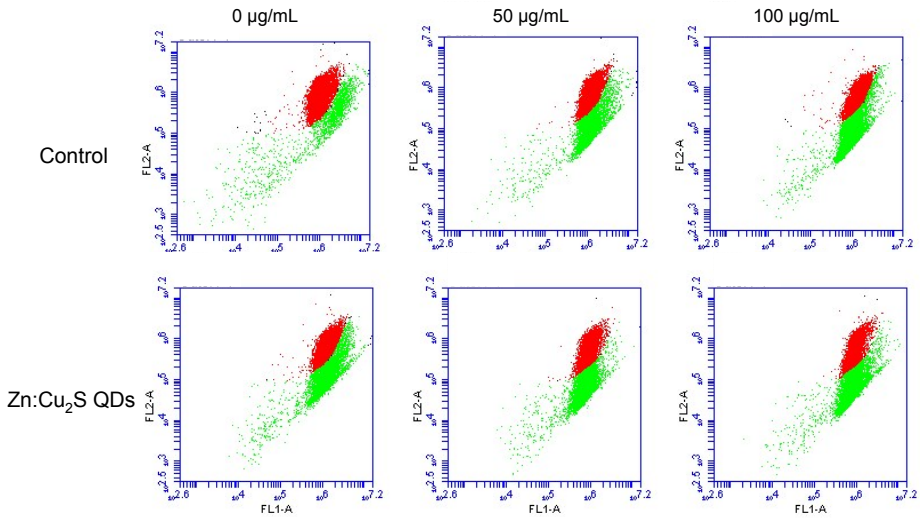

Figure S9. Flow cytometry analysis of mitochondrial membrane potential of SGC-7901 cells after treated with or without Zn:Cu_2S QDs at different concentration for 24 h.

Table S1. Mitochondrial transmembrane potential assay of Cu_2S QDs.

	Cells	Control	Cu_2S (μg/mL)		
			25	50	100
P_{Red}/P_{Green}	SGC-7901	1.00 ± 0.35	0.91 ± 0.06	0.50 ± 0.02	0.39 ± 0.02
	3T3	1.00 ± 0.36	0.84 ± 0.09	0.78 ± 0.10	0.87 ± 0.04

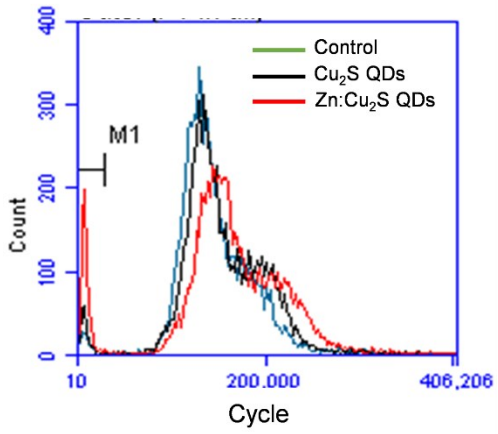

Figure S10. Flow cytometry analysis of cycle of SGC-7901 cells after treated with Cu_2S and Zn:Cu_2S QDs for 24 h.

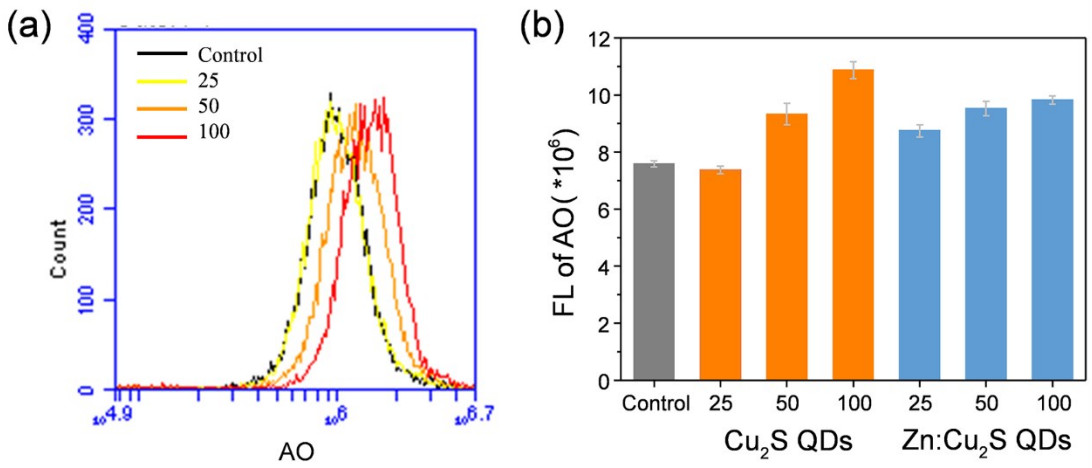

Figure S11. (a) The Cu_2S QDs treated 24 h and (b) summary analyse of AO staining SGC-7901 cells by flow cytometry.

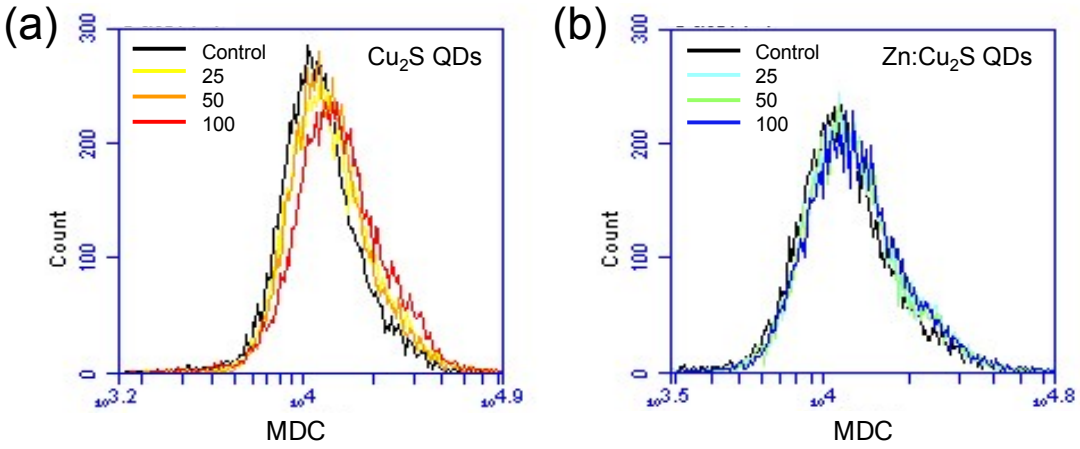

Figure S12. Flow cytometry analysis of MDC staining SGC-7901 cells after treated with (a) Cu_2S and (b) Zn:Cu_2S QDs for 24 h.

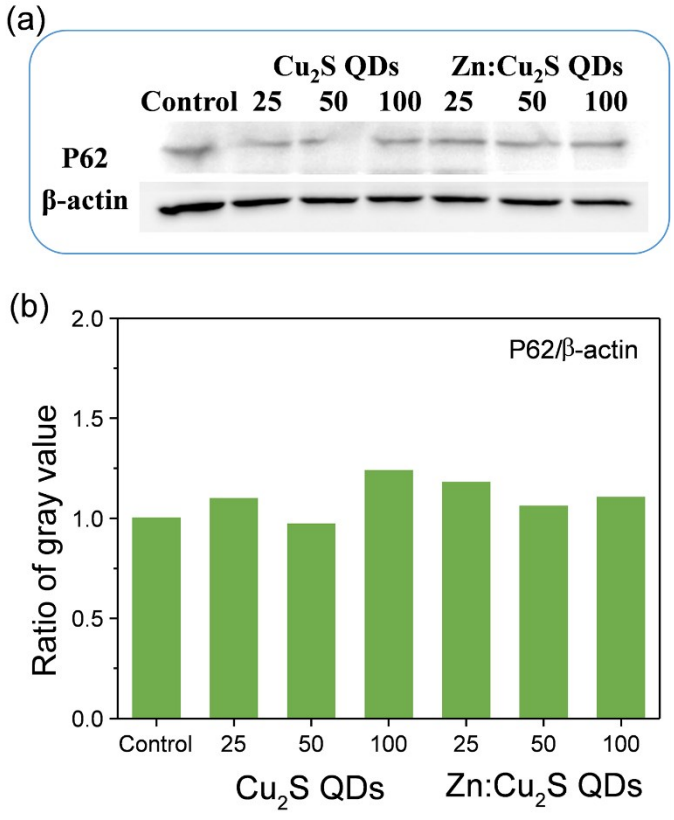

Figure S13. Western blot analysis of P62 protein in SGC-7901 cells after different treatments taking β-actin as a reference.

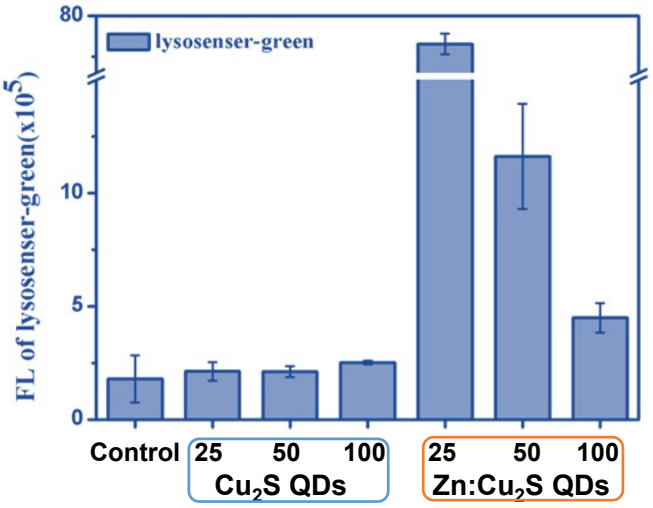

Figure S14. Lysosersor-Green staining of SGC-7901 cells after treatment with Cu_2S and Zn:Cu_2S QDs for 24 h.

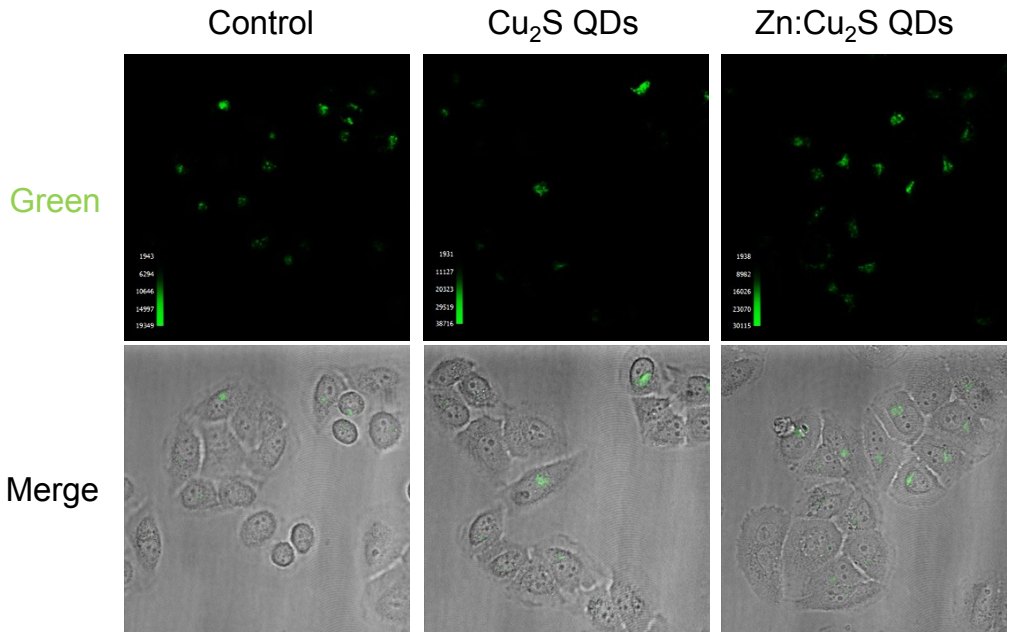

Figure S15. Confocal microscopy analysis of LysoSensor-Green stained SGC-7901 cells after treatment with 100 μg/mL Cu_2S and Zn:Cu_2S QDs for 24 h.

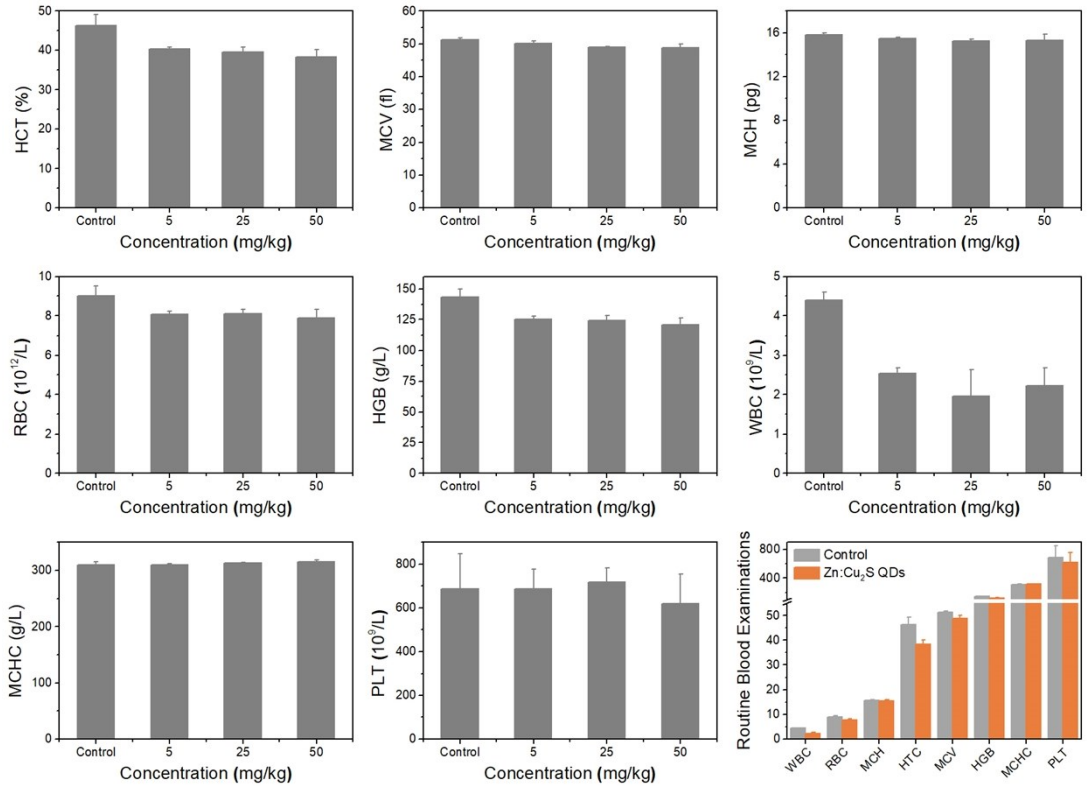

Figure S16. Hematological assay. The related indexes of mice from each group at different Zn:Cu_2S QDs doses of 0 mg kg^{-1}, 5 mg·kg^{-1}, 25 mg·kg^{-1} and 50 mg·kg^{-1} after axillary subcutaneous administration and further 15 days feeding.

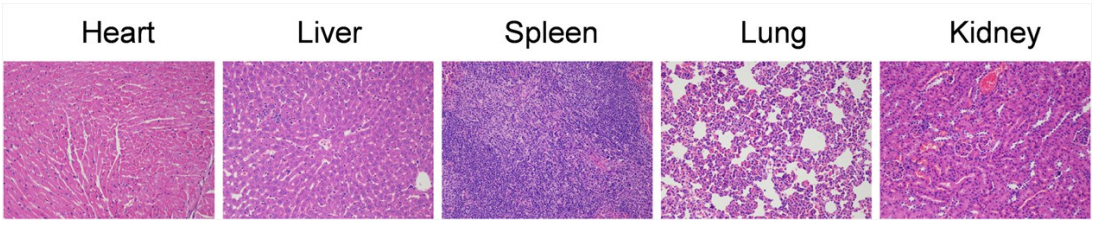

Figure S17. Histological analyses of the major tissues for systemic toxicity analysis at Zn:Cu_2S QDs doses of 50 mg·kg^{-1}.