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Supporting Information

Engineered Hollow Cu_2O@ZnO p-n Heterojunction Nanocomposites for Synergistic Photocatalytic Disinfection and Tissue Regeneration

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Experimental section

Calculation of band gap: The energy band gap of these samples was evaluated from the absorption spectra using Tauc's formula:

$$\alpha hv = A\,(Ep - Eg)^2$$

where α is the absorption coefficient, Ep is the incident photon energy, A is the proportionality constant, and Eg is the band gap energy. The corresponding band gap was determined by extrapolating the linear region of the plot of $(\alpha hv)^2$ *vs* Eg.

Photocatalytic activity: The photocatalytic activity of these samples was evaluated by the degradation of RhB at room temperature. These samples were put into a certain concentration of RhB solution and stirred in dark for 30 min to achieve the absorption-desorption equilibrium. Then these mixed solutions were exposed to light (black, blue, and yellow). The control group was pure RhB. The degradation efficiency of RhB was monitored through UV-Vis spectrophotometer.

Cell culture and cytotoxicity evaluation: Human umbilical vein endothelial cells (HUVECs) and NIH-3T3 cells were seeded at 2.0×10^3 cells per well in a 96-well plate and cultured with RPMI 1640 medium containing 10% FBS, 100 U/mL penicillin and 100 μg/mL streptomycin at 37°C under 5% CO_2 atmosphere. For cell treatments, various concentrations of the sample (25, 50, 100, 200 μg/mL) were added into the cell culture medium. The cells were further incubated at 37°C for 1, 3, and 7 days, respectively. Then, the cell viability after cocultivation was quantitatively analyzed by CCK-8 assay. These cells were incubated with 100 μL CCK-8 mixture (reagent: culture medium = 1: 10) for 2 h, and the absorbance at 450 nm was regarded as the indicator of viable cells. The hemolytic rate was calculated by the following formula:

$$\text{Cell viability}(\%) = A / A_0 \times 100\%$$

where A_0 was the absorbance of the Control group, and A was the absorbance of the experimental group.

Hemolysis analysis: Red blood cells (RBCs) were obtained by centrifuging (1500 rpm) Sprague-Dawley (SD) rat blood for 10 min. The RBCs were suspended in 10 mL normal saline to obtain RBCs dilution. Then 100 μL RBCs dilution was added into 1.1 mL normal saline, 1.1 mL Triton X-100 and 1.1 mL samples solution to construct the negative control, positive control, and experimental groups, respectively. After incubation at 37℃ for 2 h, the mixed solutions were centrifuged at 1500 rpm for another 10 min, and then each solution (100 μL) was diverted to a 96-well culture plate. The absorbance of the solution was recorded at 540 nm by a microplate reader. The hemolytic rate was calculated by the following formula:

$$\text{Hemolytic rate}(\%) = (A_s - A_p) / (A_t - A_p) \times 100\%$$

where A_s is the absorbance value of the samples solution, A_t is the absorbance value of Triton X-100, and A_p is the absorbance value of normal saline.

Cell scratch experiment: HUVECs were seeded in 6-well culture plates at a density of 5×10^5 cells/well for 48 h. Subsequently, the cell monolayer was scratched using a 10 μL pipette and

then washed three times with phosphate buffered saline (PBS). After that, the materials (200 μg/mL) were added to incubate with the cells. The control group was placed under dark condition, while the experimental group was given yellow light irradiation. Then, the changes of scratch spacing at 0 h, 6 h, 12 h, and 48 h were observed by inverted fluorescence microscope.

In vivo antibacterial test: Infected tissues were collected and placed in 2 mL of Luria-Bertani (LB) broth under aseptic condition on the third day. The uniform bacterial suspension was smeared onto LB agar plates and cultured at 37℃ for 12 h to form colony units that could be visualized. Finally, the number of colonies on the plate was counted, and the survival rate was calculated via the plate count method:

$$\text{Survival rate}\,(\%) = (N_0 - N) / N_0 \times 100\%$$

where N_0 presents the number of bacterial colonies in the control group, and N is the number of bacterial colonies in the experimental groups.

Histological analysis: Skin tissues were collected and fixed with 4% paraformaldehyde solution on days 3, 9 and 12. Tissues were embedded in paraffin and cross-sectioned to 5 μm thick slices. Hematoxylin and eosin (H&E) and immunofluorescence staining (day 12) were performed for histological evaluation, and histological images were taken by fluorescence microscope.

Statistical analysis: Data were represented as means ± standard deviation (SD). Statistical analyses were performed using GraphPad Prism 8.0 software (GraphPad Software, Inc., La Jolla, USA). Data were analyzed using one-way analysis of variance (ANOVA) and unpaired or paired Student's *t* test as appropriate. Statistical significance was set at $p < 0.05$ (n.s. represents no significant difference, * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$).

Figures

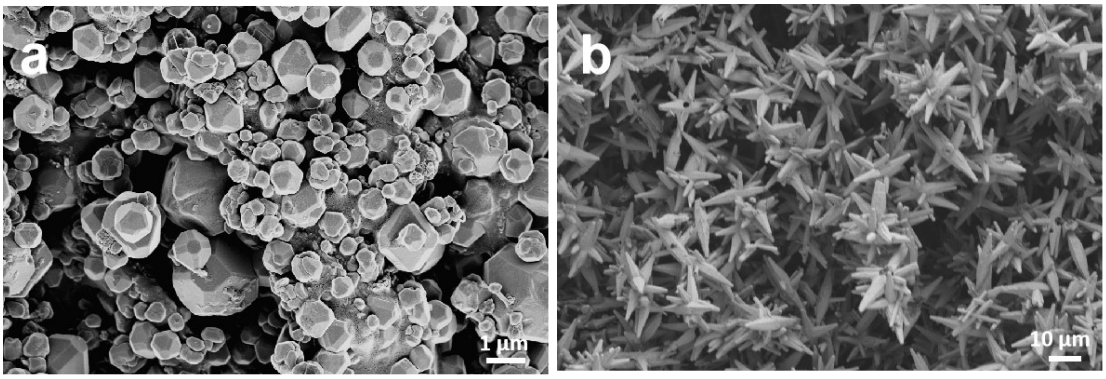

Fig. S1. SEM images of Cu_2O (a) and ZnO (b).

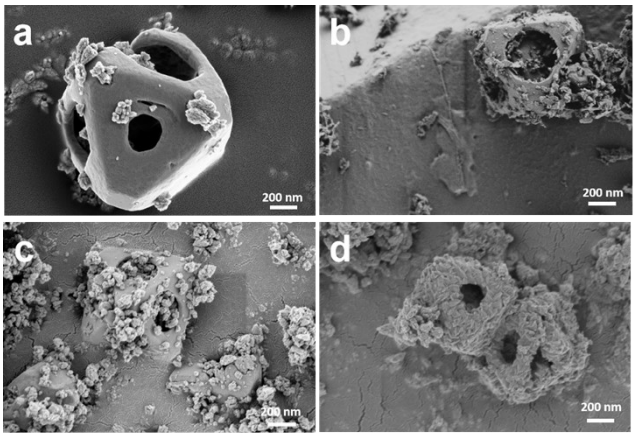

Fig. S2. SEM images of Cu_2O@ZnO after microwave treatment for 0 min (a), 5 min (b), 15 min (c), and 30 min (d).

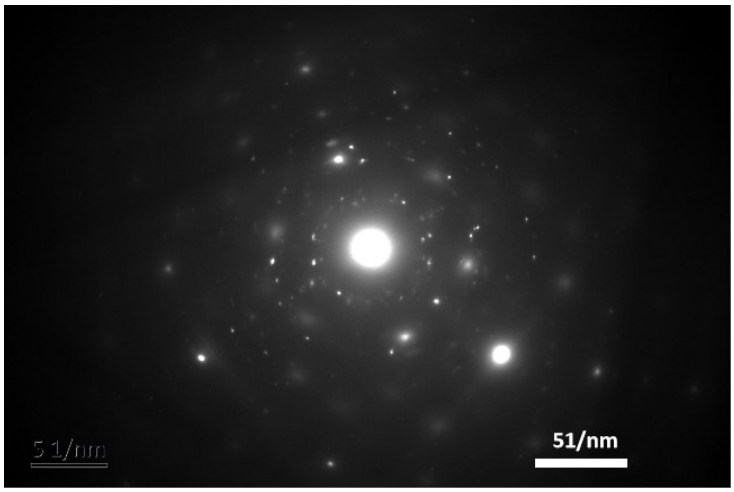

Fig. S3. The SAED pattern of Cu_2O@ZnO.

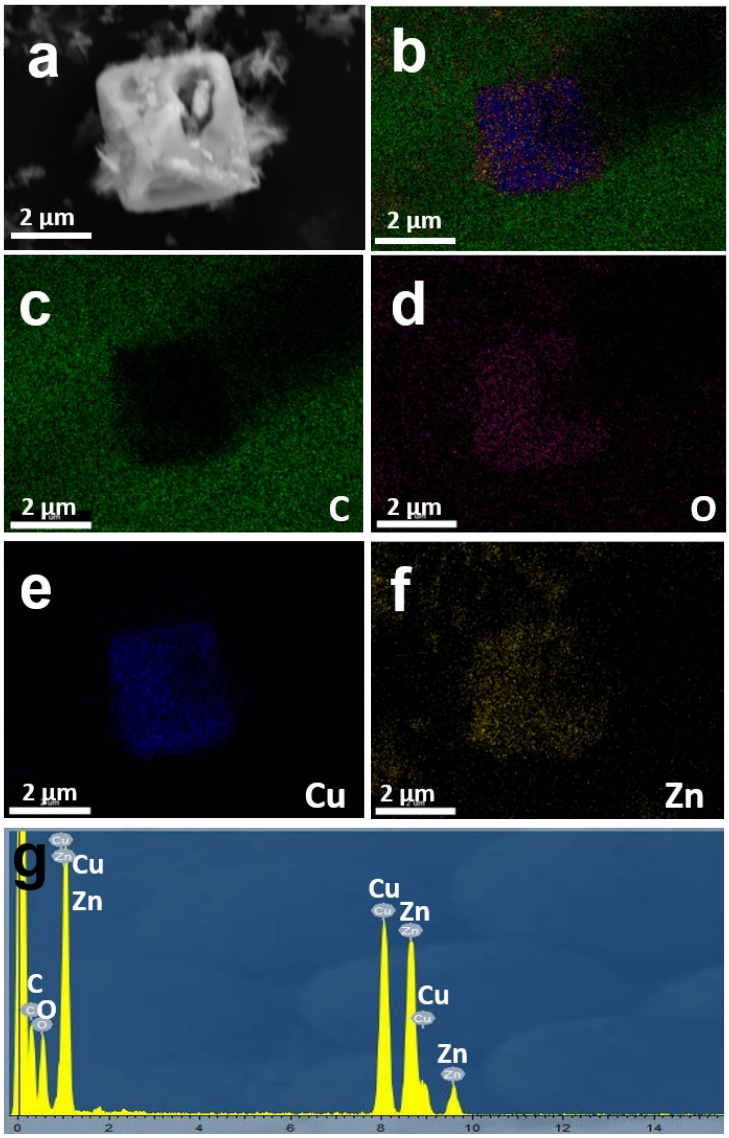

Fig. S4. (a) The SEM image of Cu_2O@ZnO. (b-f) Corresponding EDS elemental mappings of C, O, Cu, and Zn. (g) The corresponding EDS spectrum of Cu_2O@ZnO.

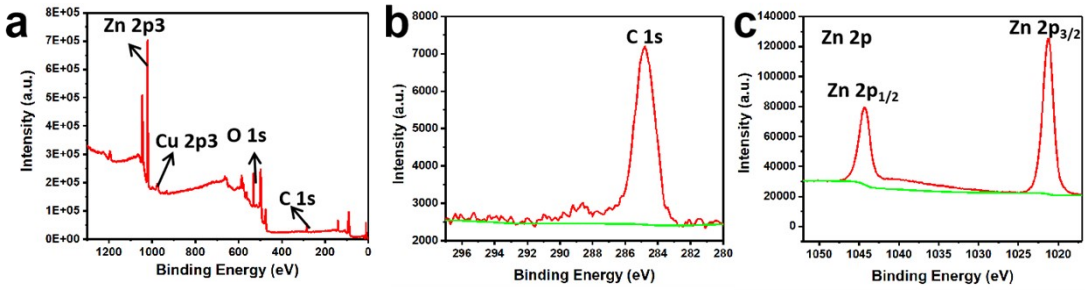

Fig. S5. XPS spectra of Cu_2O@ZnO. (a) Survey spectrum. (b) C 1s spectrum. (c) Zn 2p spectrum.

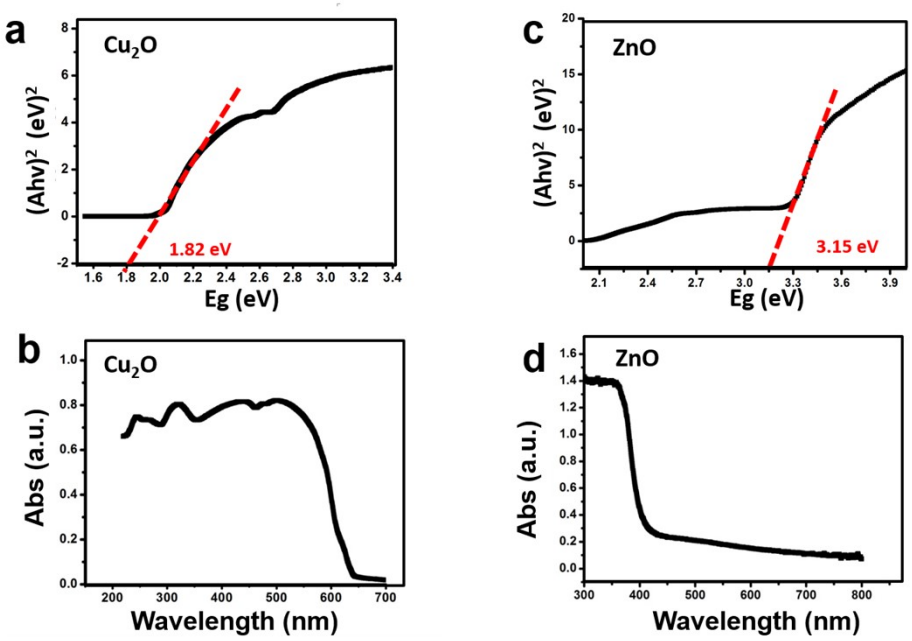

Fig. S6. (a) The $(Ahv)^2$ *vs* photon energy plot of Cu_2O. (b) The corresponding UV-Vis absorption spectrum of Cu_2O. (c) The $(Ahv)^2$ *vs* photon energy plot of ZnO. (d) The corresponding UV-Vis absorption spectrum of ZnO.

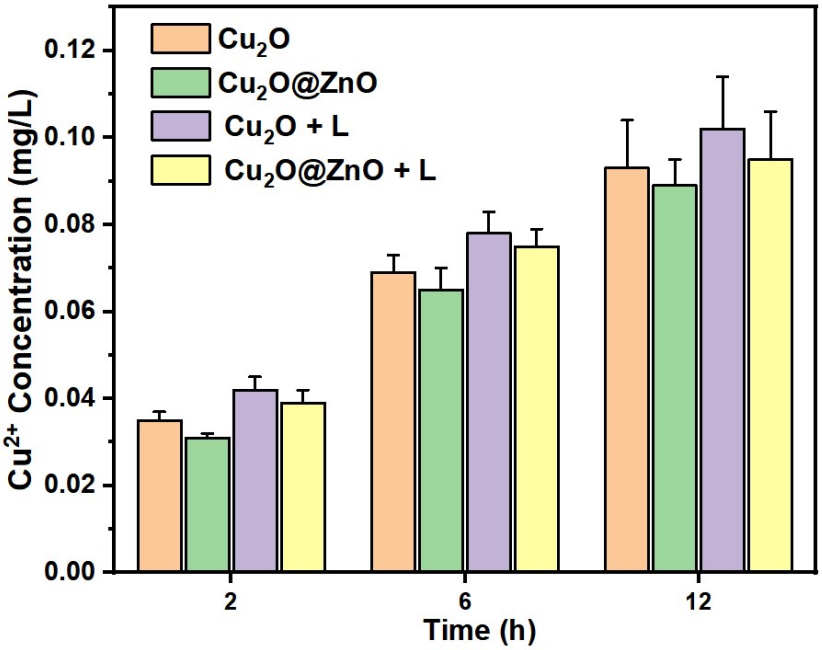

Fig. S7. The concentration of copper ions released by Cu_2O and Cu_2O@ZnO after being exposed to darkness and yellow light for 2, 6, and 12 hours respectively. Date are means ± SD (n = 3).

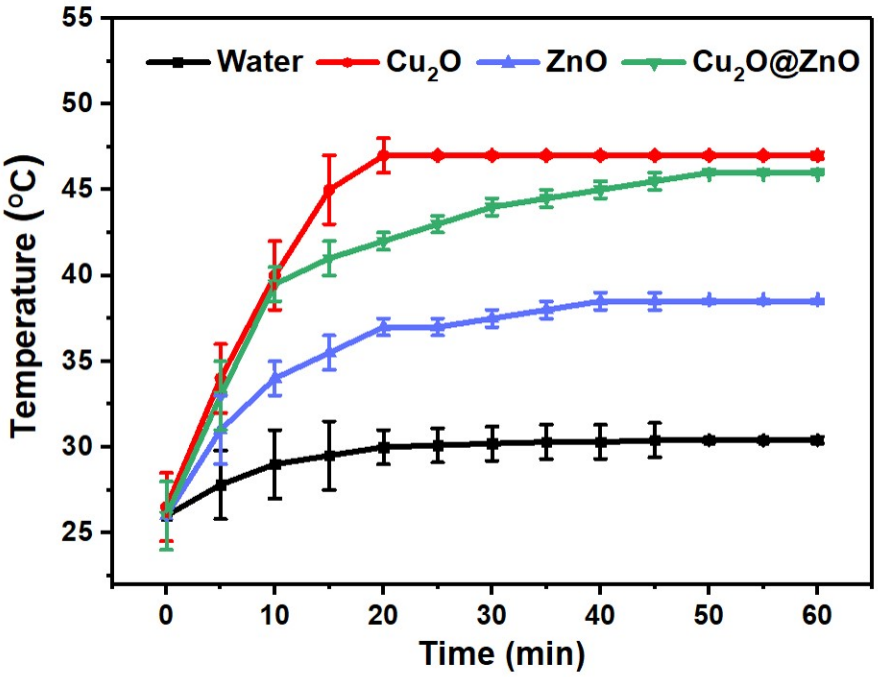

Fig. S8. Photothermal heating curves of water, Cu_2O, ZnO, and Cu_2O@ZnO. Date are means ± SD (n = 3).

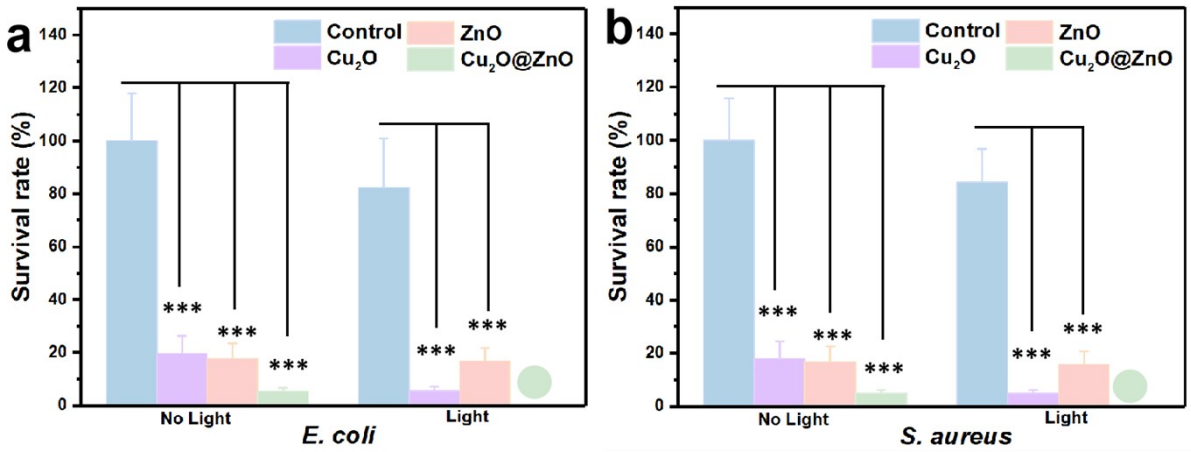

Fig. S9. Survival rates of *E. coli* (a) and *S. aureus* (b) under the action of Cu_2O, ZnO and Cu_2O@ZnO at the concentration of 2 mg/mL. Green circle means no bacteria survive. Date are means ± SD (n = 3).

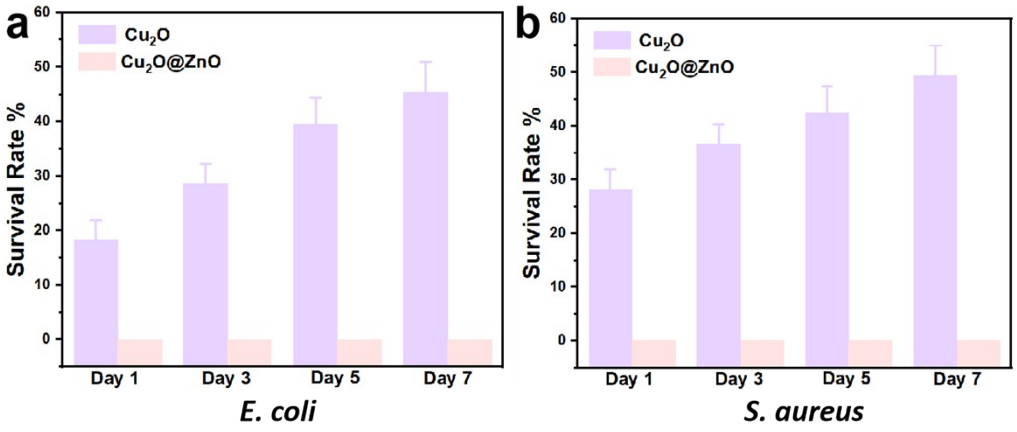

Fig. S10. Survival rates of *E. coli* (a) and *S. aureus* (b) under the action of Cu_2O and Cu_2O@ZnO at the concentration of 200 μg/mL. Date are means ± SD (n = 3).

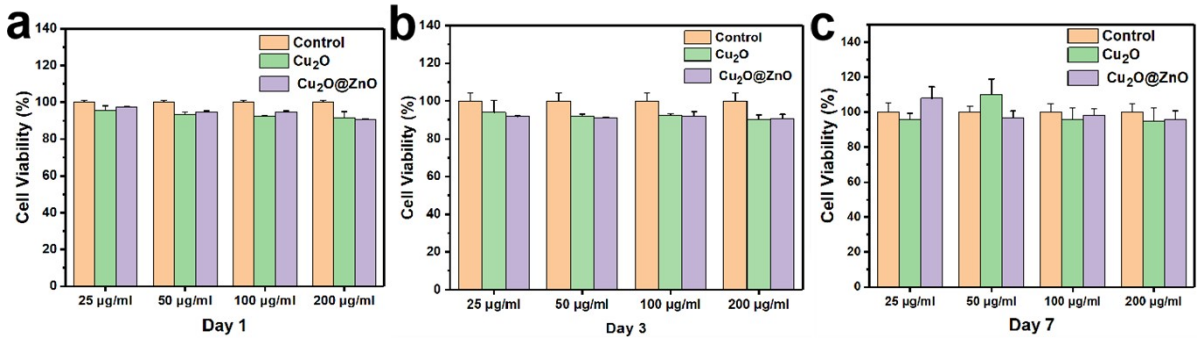

Fig. S11. Cell viabilities of NIH-3T3 cells with different concentrations of Cu_2O and Cu_2O@ZnO on day 1 (a), day 3 (b), and day 7 (c). Data are means ± SD (n = 3).

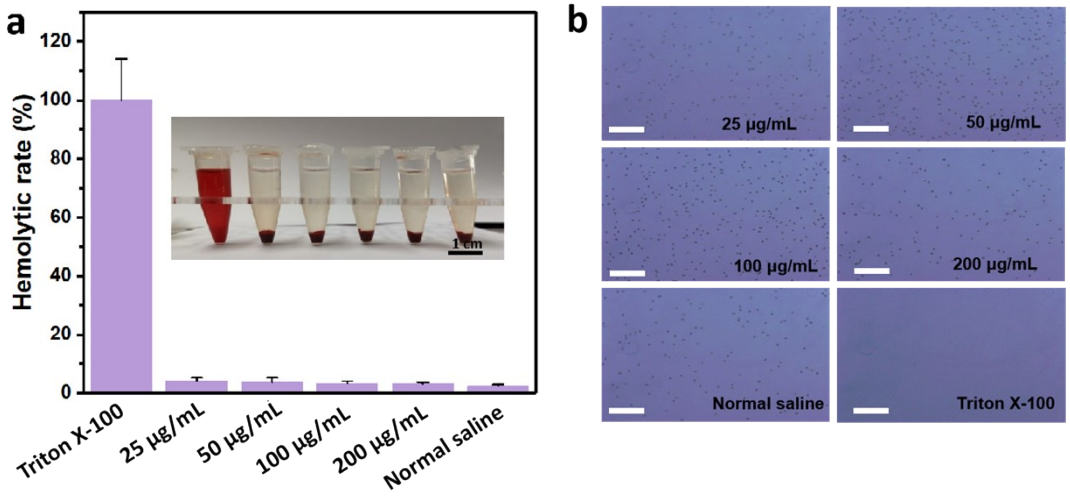

Fig. S12. (a) The hemolytic rate of Cu_2O@ZnO with varied concentrations (25, 50, 100 and 200 μg/mL). The inset is the optical image of the hemolytic effect. (b) Microscopic images of red blood cells treated with different concentrations of Cu_2O@ZnO. Scale bar: 70 μm. Data are means ± SD (n = 3). Scale bars: 1 cm.

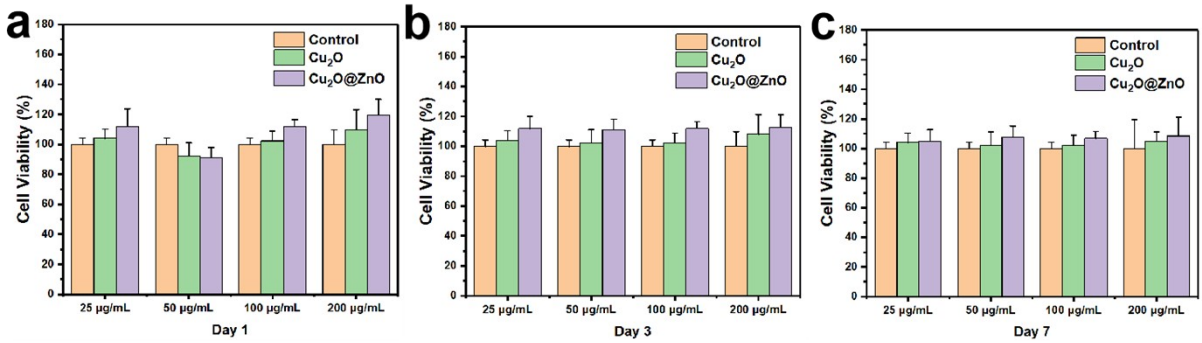

Fig. S13. Cell viabilities of HUVEC cells with different concentrations of Cu_2O and Cu_2O@ZnO on day 1 (a), day 3 (b), and day 7 (c). Data are means ± SD (n = 3).

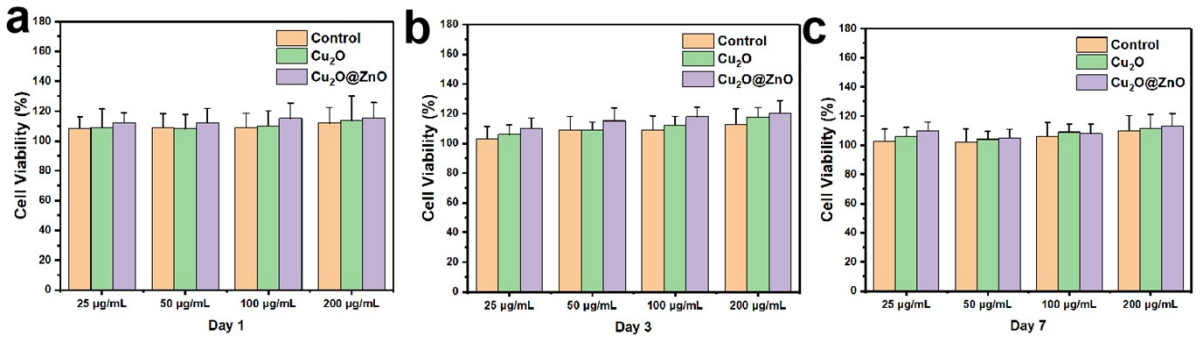

Fig. S14. Cell viabilities of HUVEC cells with different concentrations of Cu_2O and Cu_2O@ZnO under the yellow light irradiation on day 1 (a), day 3 (b), and day 7 (c). Data are means ± SD (n = 3).

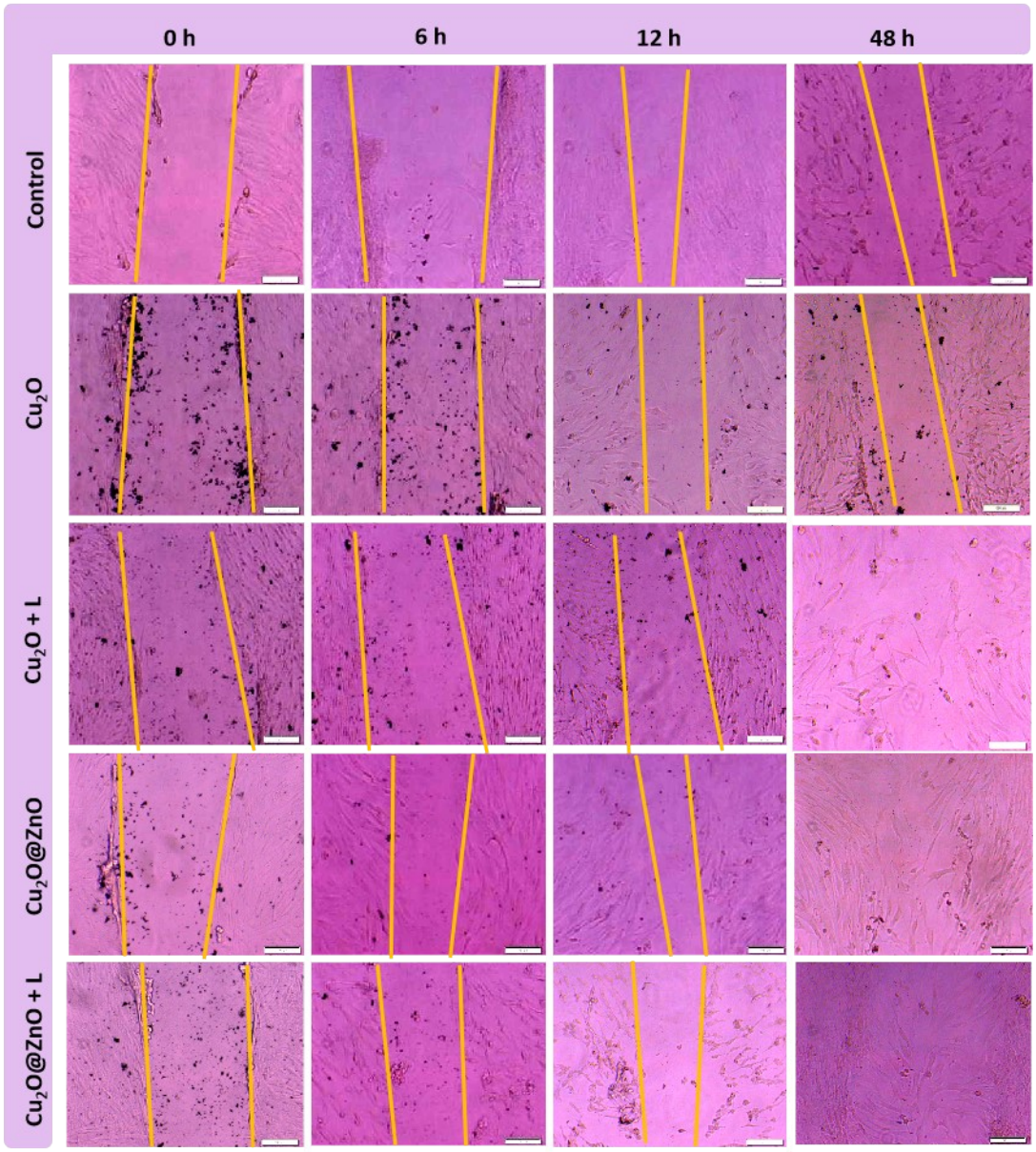

Fig. S15. Microscopic images of HUVECs scratch tests in different experimental groups. After scratching, different materials were added and cultured with HUVECs for 0 h, 6 h, 12 h, and 48 h. Scale bars: 100 μm (0 h); Scale bars: 600 μm (6 h, 12 h and 48 h).

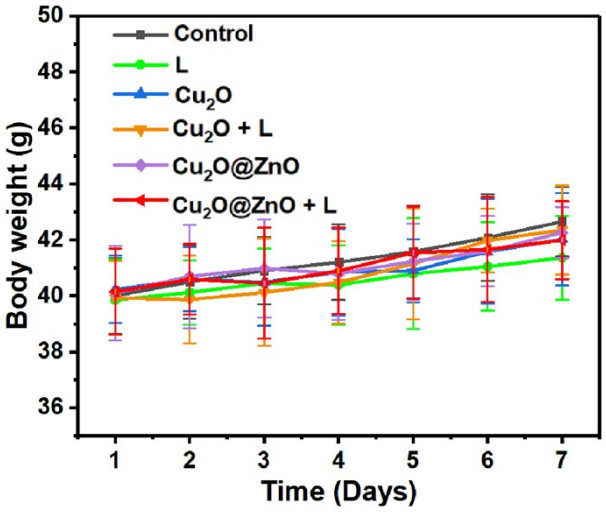

Fig. S16. Short term changes in body weight of mice. The control was given the same amount of normal saline. Data are means ± SD (n = 3).

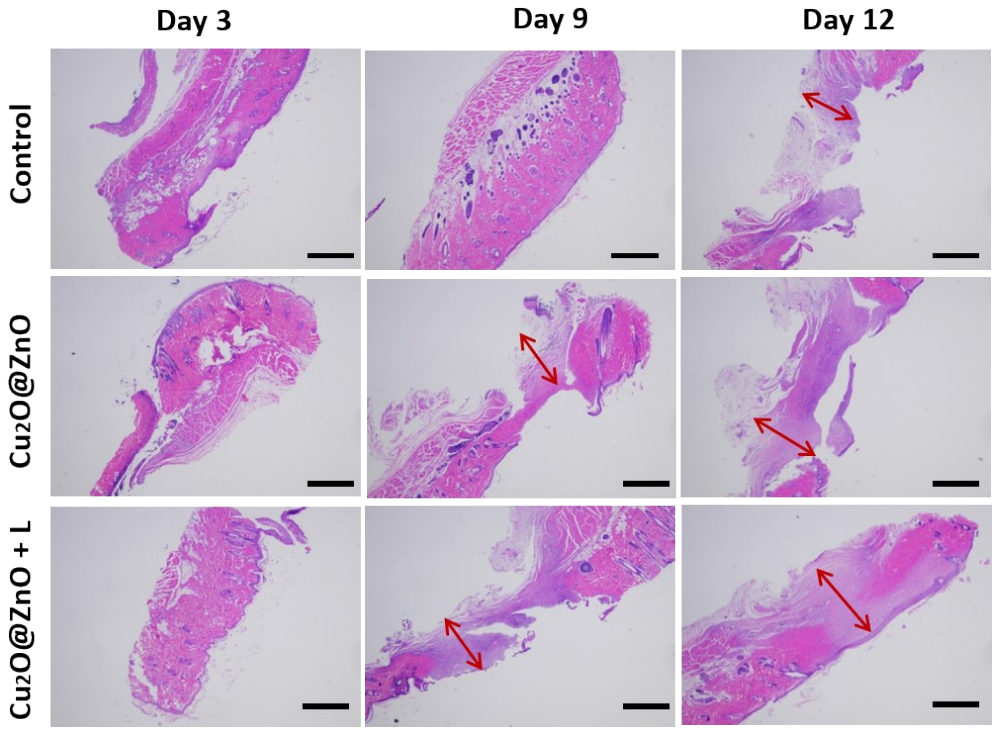

Fig. S17. H&E staining images of wound tissues in the Control, Cu_2O@ZnO, and Cu_2O@ZnO + L groups. Red double-headed arrows represent the range of granulation tissue. Scale bars: 500 μm.

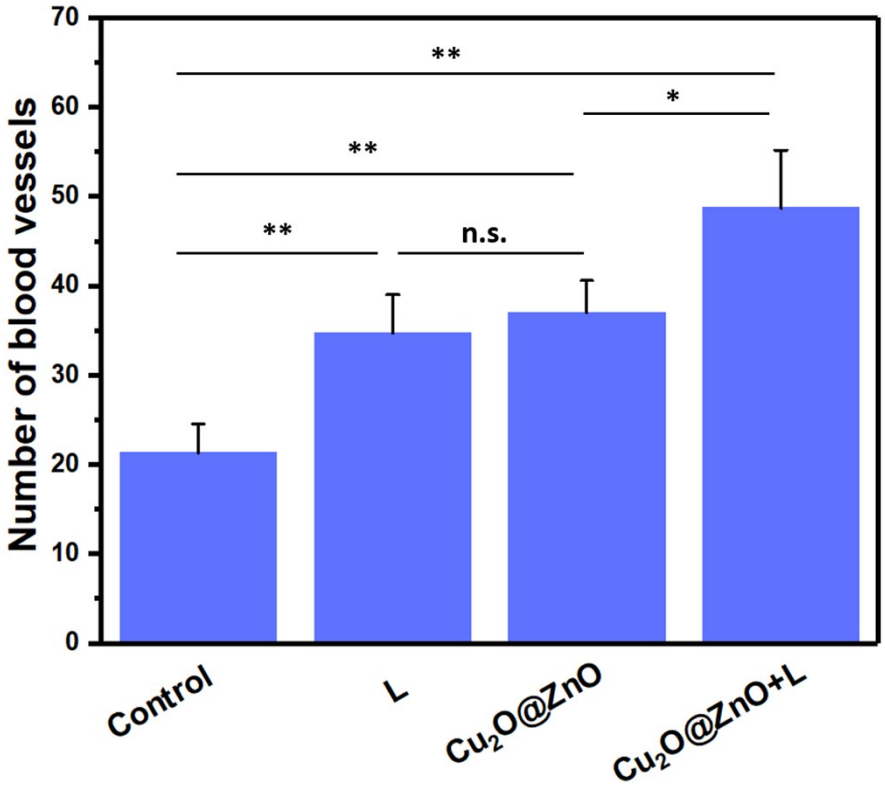

Fig. S18. Statistical analysis of the number of blood vessels per wound field. Data are means ± SD (n = 3). * $P < 0.05$, ** $P < 0.01$, n.s. represents no significance.