Support Information

Photolysis of methicillin-resistant *Staphylococcus aureus* using Cu-doped carbon spheres

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Experimental Section

Morphological observation and live/dead cell staining of MRSA

After the photo-induced antibacterial abilities were assessed, MRSA suspensions were divided into four groups: (1) MRSA (control, 0.9% NaCl), (2) MRSA + light, (3) MRSA + Cu-HCSs, (4) MRSA + Cu-HCSs + light. The final working concentration of Cu-HCSs was 200 μg mL^{-1}. For the groups of without light exposure, Cu-HCSs were incubated with MRSA for 60 min. For the groups with light exposure, the Cu-HCSs-treated MRSA were irradiated with a 450 nm light (0.25 W cm^{-2}) for 60 min. Then all MRSA suspensions were centrifuged and re-dispersed in glutaraldehyde (2.5%, Sigma-Aldrich, USA) for 4 h at 4 °C under dark conditions, and dehydrated with 30, 50, 70, 80, 90, and 100% of ethanol for 10 min, respectively. Finally, the dried MRSA were sputter-coated with gold for imaging using scanning electron microscopy (GeminiSEM 300, Germany). Moreover, MRSA suspensions treated by (1)-(4) were collected by centrifugation at 4000 rpm for 5 min. The MRSA were then stained with SYTO™ 9 and propidium iodide (PI) for 30 min and visualized via confocal fluorescence microscopy (Leica, TCS SP8 STED, Germany).

Determination of •OH, $^1O_2$, internal ROS, and malondialdehyde (MDA)

•OH *measurement*

Glass capillary tubes containing Cu-HCSs (200 μg mL^{-1}, 50 μL) and BMPO (10 mM) upon light exposure (450 nm, 0.25W cm^{-2}) for 0, 1 min, 3 min, 5 min, 10 min, 20 min , respectively, were inserted into the electron spin resonance (ESR) cavity to record •OH signals at selected times (A300-10ram 12 paramagnetic resonance spectrometer ESR, Germany Bruker).

$^1O_2$ detection

Singlet oxygen sensor green (SOSG) was applied to detect $^1O_2$ levels. Typically, experiments were divided into four groups: (1) MRSA (control, 0.9% NaCl), (2) MRSA + light, (3) MRSA + Cu-HCSs, (4) MRSA + Cu-HCSs + light. SOSG was dissolved in methanol to obtain a stock solution at 500 μM. SOSG (final concentration 50 μM) was added to above groups in 1.5-mL centrifuge tubes. The power density and time of light exposure were fixed at 0.25W cm^{-2} and 20 min, respectively. After reaction, $^1O_2$ levels were detected using a Tecon spectrophotometer (SPARK 10M, Switzerland) with excitation and emission wavelengths at 504 nm and 525 nm, respectively.

Internal ROS generation analysis

The oxidant-sensitive dye DCFH-DA was used to measure intracellular ROS levels. MRSA suspensions were divided

into four groups: (1) MRSA (control, 0.9% NaCl), (2) MRSA + light, (3) MRSA + Cu-HCSs, (4) MRSA + Cu-HCSs + light. The final working concentration of Cu-HCSs was 200 μg mL^{-1}. For the groups of without light exposure, Cu-HCSs were incubated with MRSA for 60 min. For the groups with light exposure, the Cu-HCSs-treated MRSA were irradiated with a 450-nm laser (0.25 W cm^{-2}) for 60 min. After treated by groups (1)-(4), MRSA were stained with 10 μM DCFH-DA for 30 min in the dark at room temperature and twice washed with 0.9% NaCl. The intracellular ROS levels were measured using Tecon spectrophotometer (SPARK 10M, Switzerland) with excitation and emission wavelengths at 488 nm and 525 nm, respectively.

Determination of internal malondialdehyde (MDA)

As a natural product of lipid oxidation in organisms, MDA can be used to determine the level of lipid oxidation. MRSA were treated with groups (1)-(4), and the level of lipid oxidation was determined by using a Micro-MDA Assay Reagent Kit (KeyGEN Biotech, China).

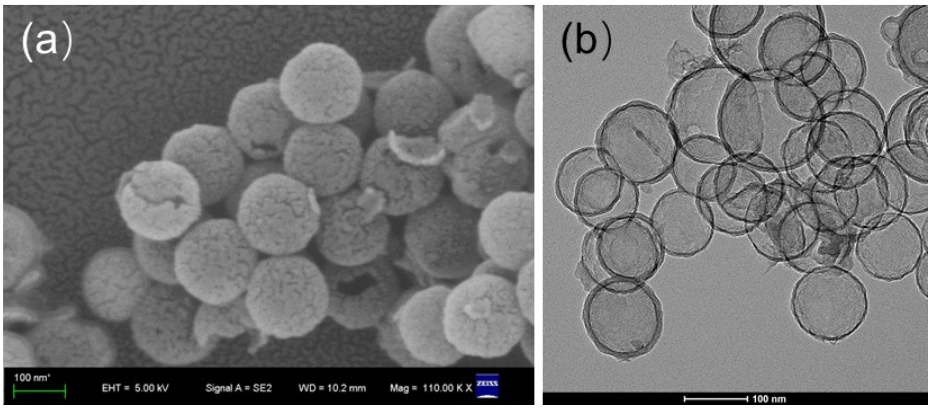

Fig. S1 SEM image (a) and TEM image (b) of Cu-HCSs.

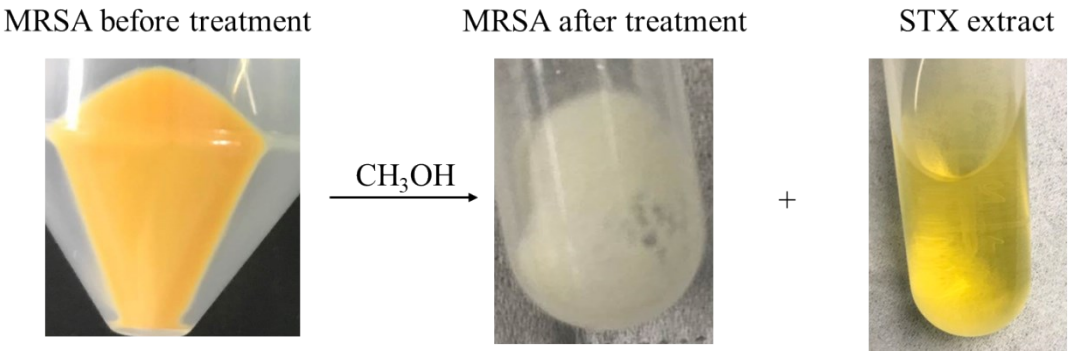

Fig. S2 Schematic diagram of STX extraction.

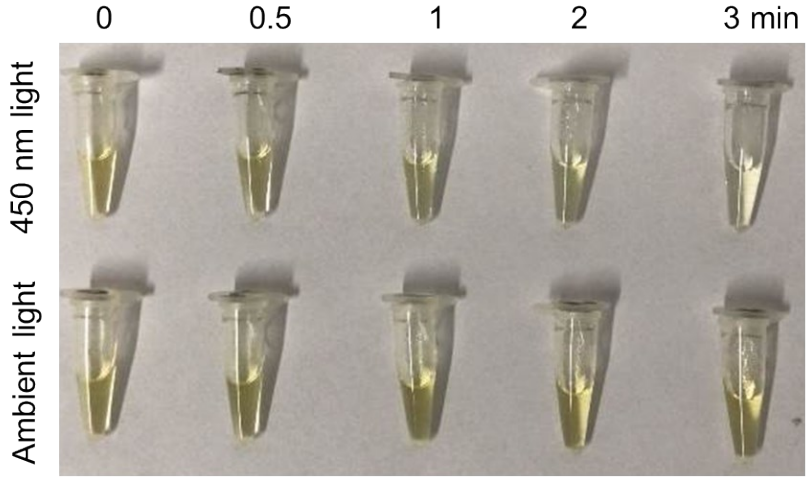

Fig. S3 Pictures of STX extract exposed to 450 nm light and ambient light at different time intervals. Light irradiation condition: 0.10 W cm^{-2}.

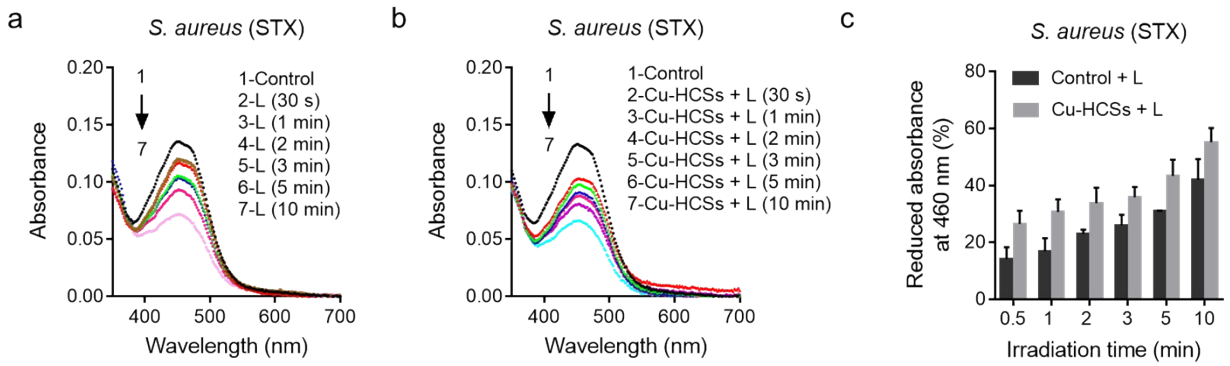

Fig. S4 (a) UV-Vis spectra of STX extract from *S. aureus* upon light exposure. (b) UV-Vis spectra of STX extract from *S. aureus* with Cu-HCSs plus blue light exposure treatment. (c) Reduced absorbance of STX after exposure to blue light for 3 min with/without Cu-HCSs. Light condition: 0.10 w cm^{-2}. [Cu-HCSs] = 10 μg mL^{-1}.

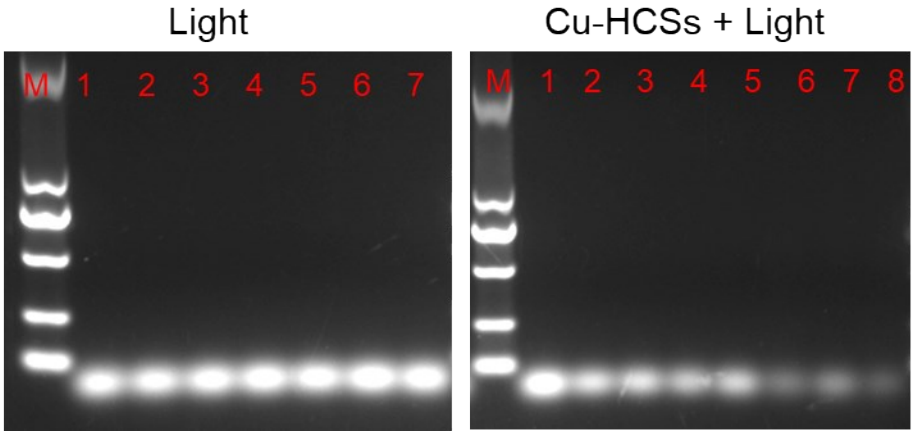

Fig. S5 Small single-strand DNA photocleavage with/without Cu-HCSs at different power density of light. For the light-treated group only, M: molecular marker; 1: DNA, 2-7: L (0.01, 0.10, 0.25, 0.40, 0.55, 0.70 W cm^{-2}, respectively). For Cu-HCSs/light-treated group, M: molecular marker; 1: DNA; 2-7: Cu-HCSs + L (0, 0.01, 0.10, 0.25, 0.40, 0.55, 0.70 W cm^{-2}, respectively). [Cu-HCSs] = 200 μg mL^{-1}, Irradiation time of light (450 nm) = 10 min.

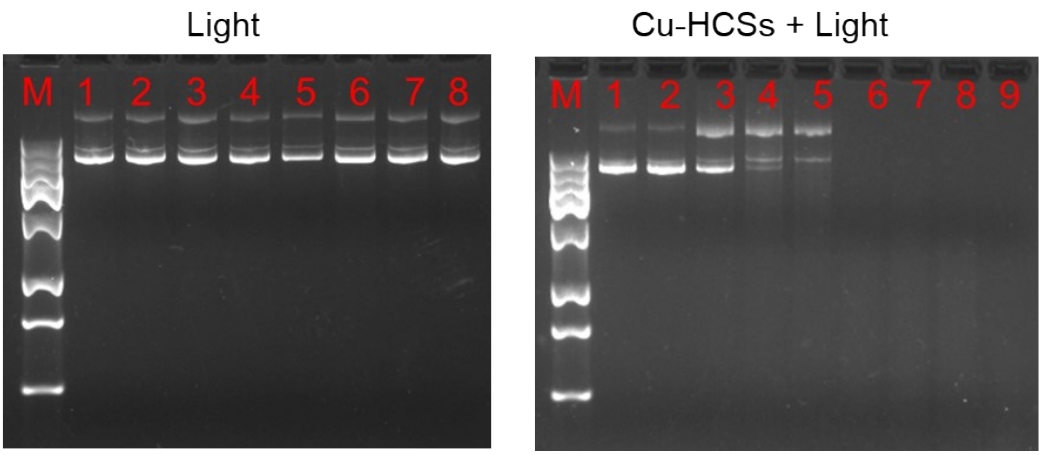

Fig. S6 Plasmid DNA photocleavage with/without Cu-HCSs at different irradiation time of light. For light-treated group only, M: molecular marker; 1: DNA, 2-8: L (1, 3, 6, 9, 12, 15, 30 min, respectively). For Cu-HCSs/light-treated group, M: molecular marker; 1: DNA; 2-7: Cu-HCSs + L (0, 1, 3, 6, 9, 12, 15, 30 min, respectively). [Cu-HCSs] = 200 μg mL^{-1}, power density of light (450 nm) = 0.55 W cm^{-2}.

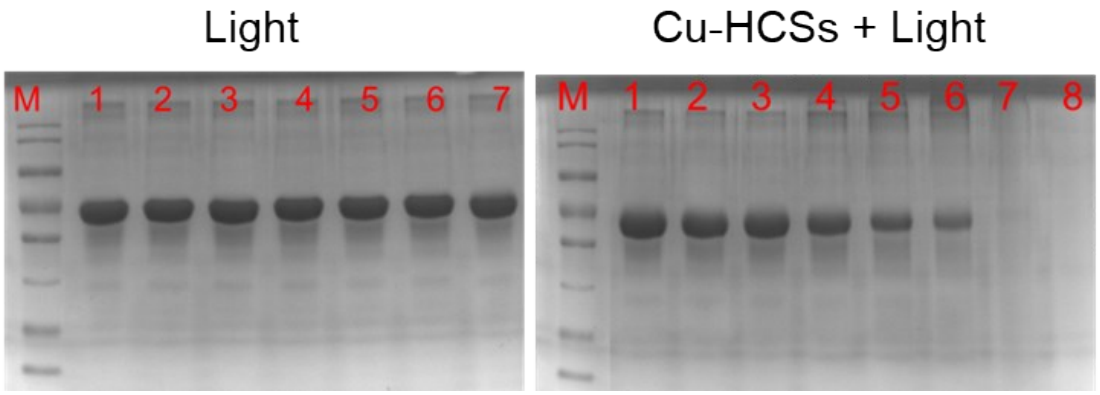

Fig. S7 BSA photocleavage with/without Cu-HCSs. For light-treated group only, M: molecular marker; 1-BSA; 2-7: L (0.01, 0.10, 0.25, 0.40, 0.55, 0.70 W cm^{-2}, respectively). For Cu-HCSs/light-treated group, M-molecular marker; 1-BSA; 2-8: Cu-HCSs + L (0, 0.01, 0.10, 0.25, 0.40, 0.55, 0.70 W cm^{-2}, respectively). [Cu-HCSs] = 200 μg mL^{-1}, Irradiation time of light (450 nm) = 20 min.

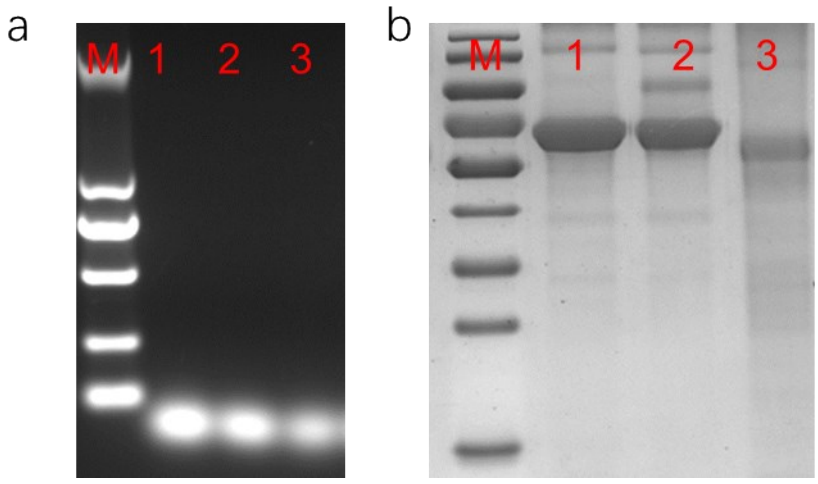

Fig. S8 (a) Small single-strand DNA photocleavage in the presence of canbon spheres with and without Cu-doping. M: molecular marker; 1: DNA, 2: HCSs + L, 3- Cu-HCSs + L. Light irradiation condition: 450 nm, 0.55 W cm^{-2} for 10 min. (b) BSA photocleavage in the presence of carbon spheres with and without Cu-doping. M: molecular marker; 1: DNA, 2: HCSs + L, 3- Cu-HCSs + L. Light irradiation condition: 450 nm, 0.25 W cm^{-2} for 30 min. [Cu-HCSs] = 200 μg mL^{-1}, [HCSs] = 200 μg mL^{-1}.

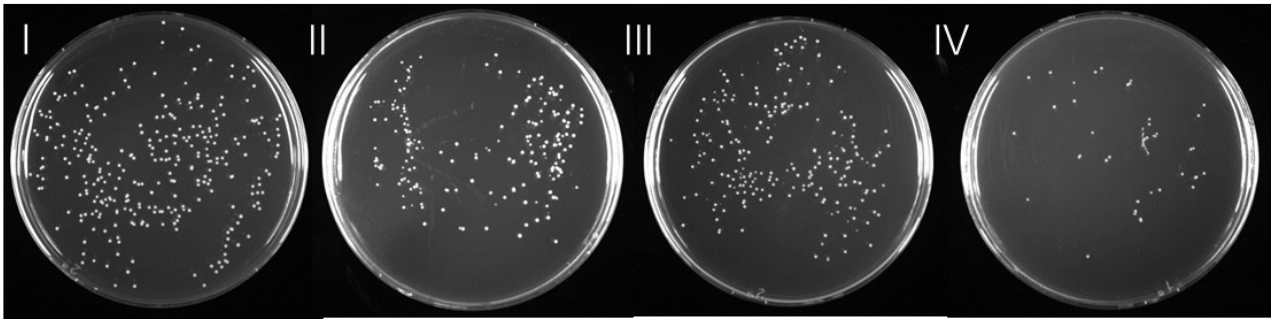

Fig. S9 Photographs of agar plates onto MRSA bacterial cells after different treatments. I- Control; II-Control + L; III-Cu-HCSs; IV-Cu-HCSs + L. [Cu-HCSs] = 200 μg mL^{-1}. Light irradiation condition: 450 nm, 0.25 W cm^{-2} for 60 min.

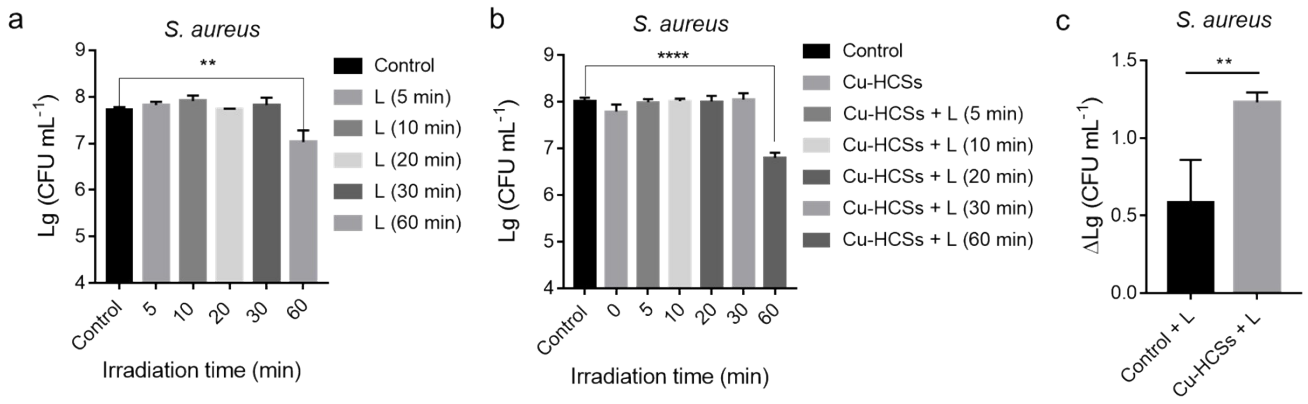

Fig. S10 (a) Log change in *S. aureus* CFUs after exposure to blue light at different times. (b) Log change in *S. aureus* CFUs after exposure to blue light in the presence of Cu-HCSs at different times. (c) The comparative study of log change in *S. aureus* CFUs after exposure to blue light for 60 min with and without Cu-HCSs. [Cu-HCSs] = 200 μg mL^{-1}. Light irradiation condition: 450 nm, 0.25 W cm^{-2}.

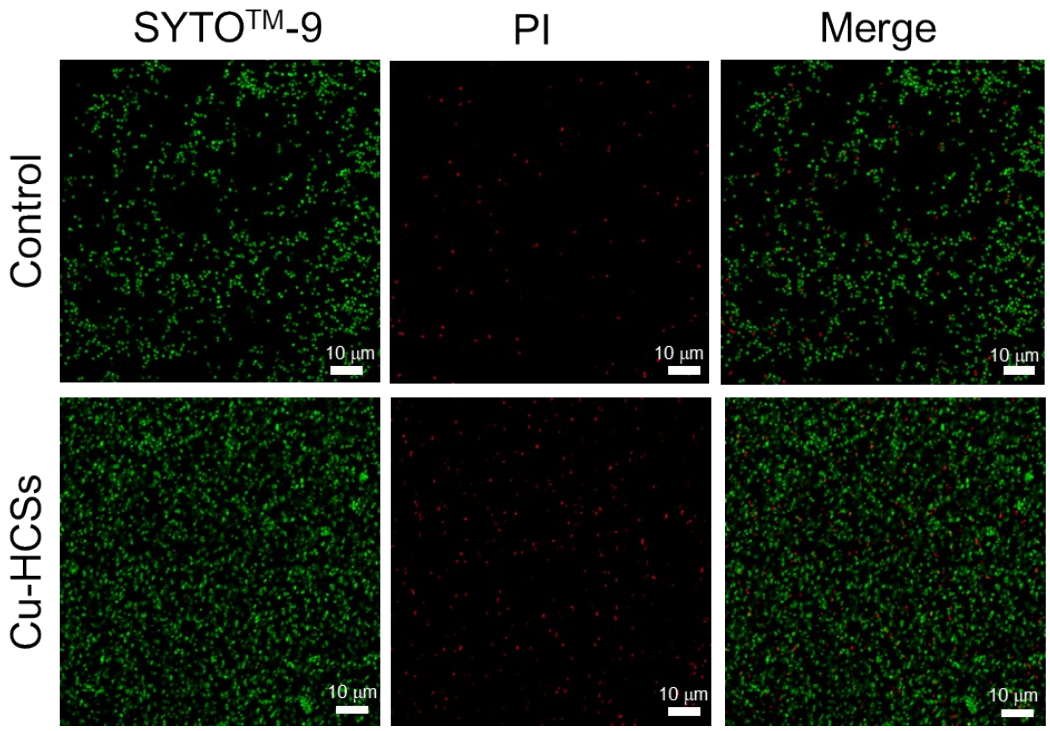

Fig. S11 Confocal microscopy images of MRSA after treatment with PBS (control) and Cu-HCSs (200 μg mL^{-1}).

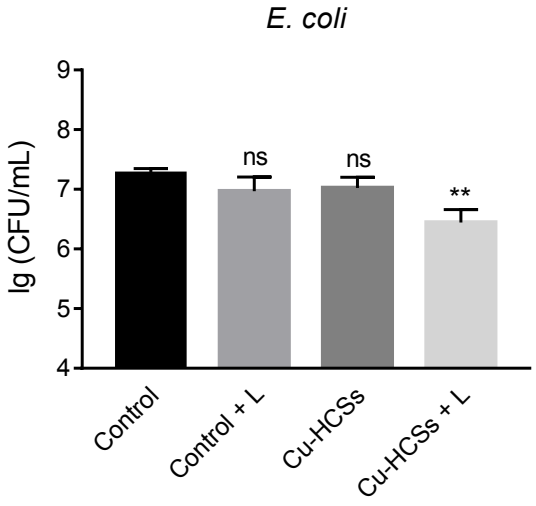

Fig. S12 Log change in *E. coli* CFUs after exposure to blue light in the presence of Cu-HCSs (200 μg mL^{-1}). Light irradiation conditions: 450 nm, 0.25 W cm^{-2}, 60 min.

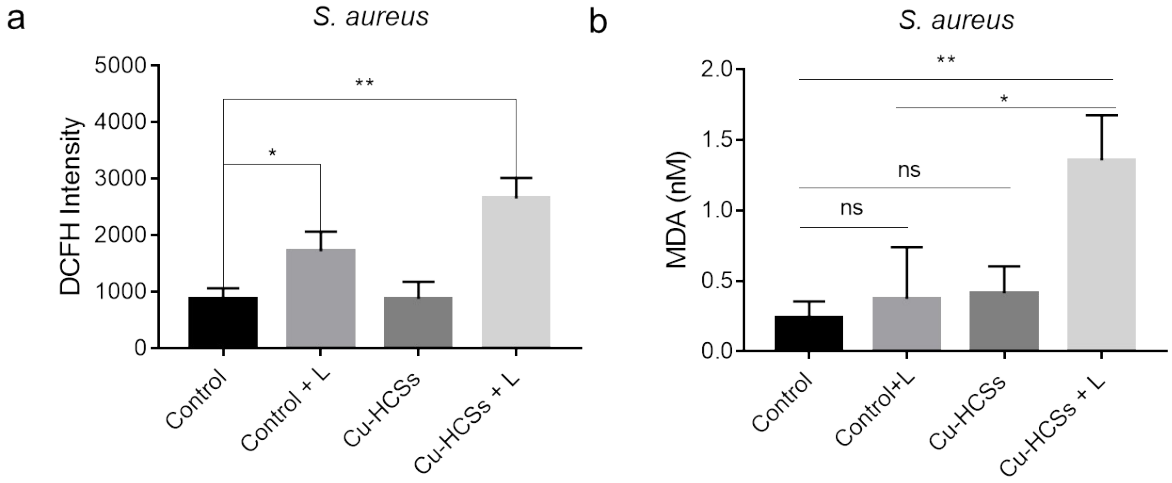

Fig. S13 ROS level (a) and lipid peroxidation (b) of *S. aureus* treated by Cu-HCSs and blue light illumination. [Cu-HCSs] = 200 μg mL^{-1}. Light irradiation condition: 450 nm, 0.25 W cm^{-2}.

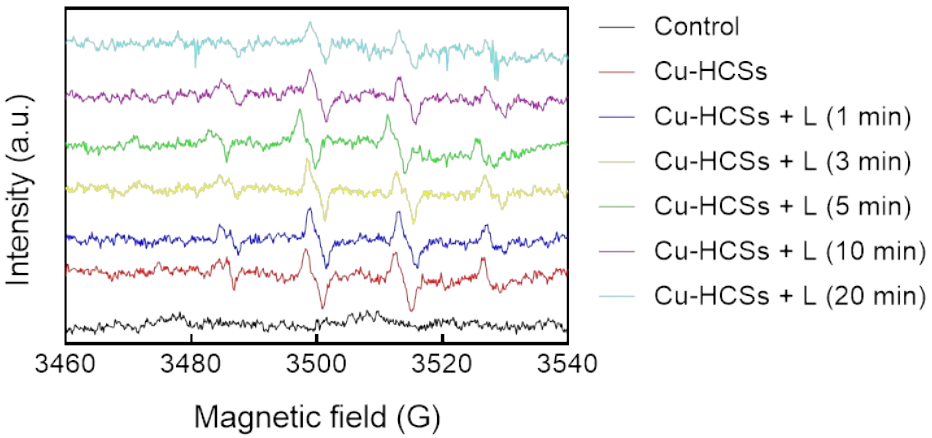

Fig. S14 Electron spin resonance (ESR) spectra of hydroxyl radicals generated by Cu-HCSs at different irradiation time of light. [Cu-HCSs] = 200 μg mL^{-1}. [BMPO] = 10 mM. Light irradiation condition: 450 nm, 0.25 W $cm^{-2.}$

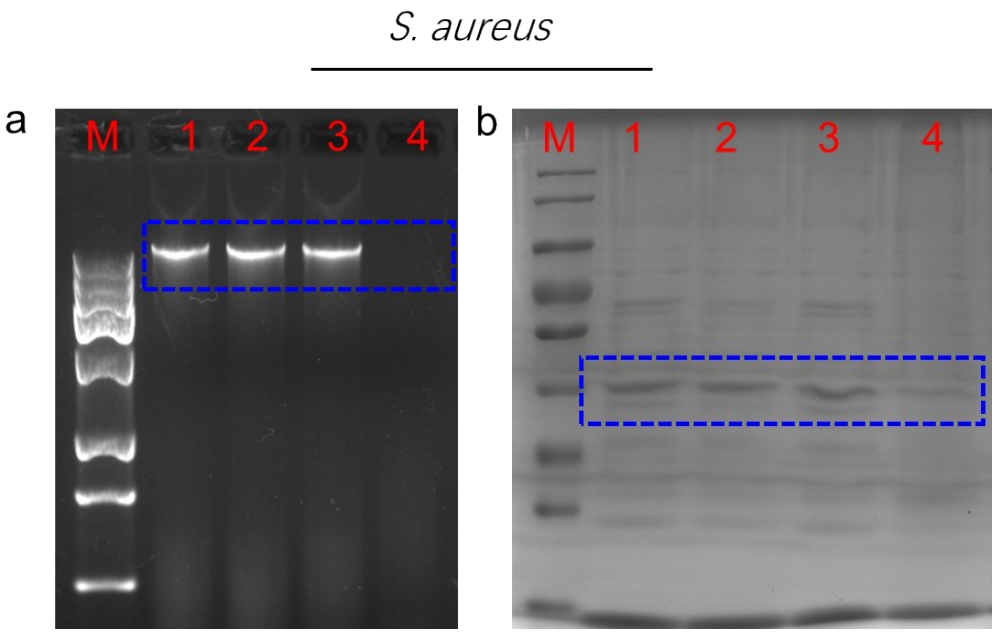

Fig. S15 Genomic DNA degradation and of *S. aureus* treated by Cu-HCSs and light exposure. (a) M-molecular marker; 1-DNA; 2-DNA+ Light; 3-DNA + Cu-HCSs; 4-DNA + Cu-HCSs + Light. (b) Protein degradation of *S. aureus* treated by Cu-HCSs and light exposure. M-molecular marker; 1- protein; 2- protein + Light; 3-protein + Cu-HCSs; 4-protein + Cu-HCSs + Light. [Cu-HCSs] = 200 μg mL^{-1}. Light irradiation condition: 450 nm, 0.25 W cm^{-2} for 60 min.

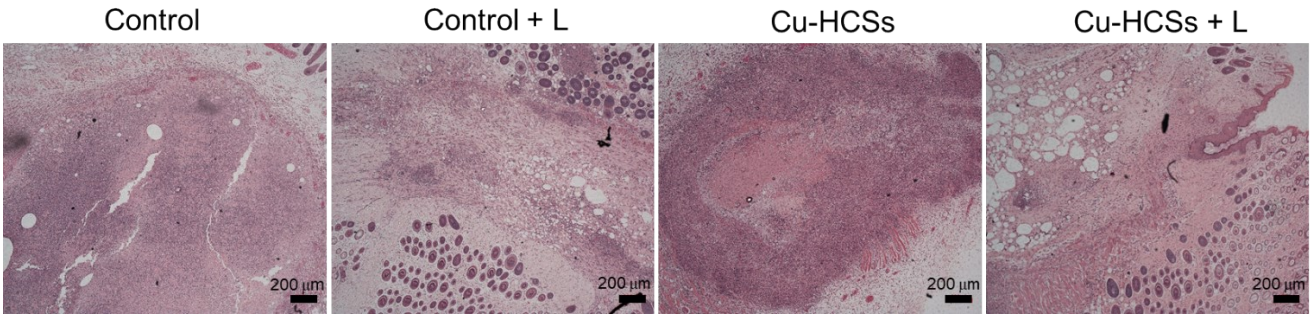

Fig. S16 Representative H&E staining images of infected skins in different groups, showing in in low magnification.

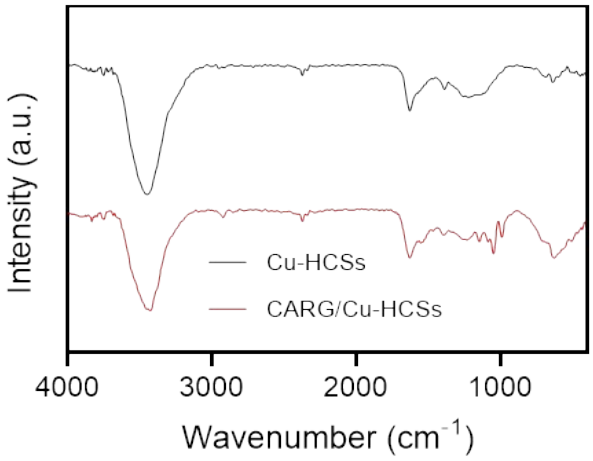

Fig. S17 FTIR spectra of Cu-HCSs and CARG/Cu-HCSs.

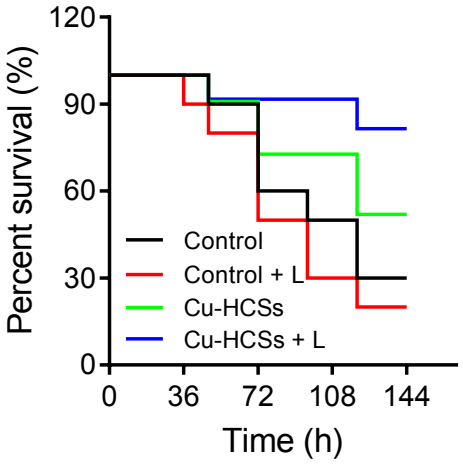

Fig. S18 The percent survival of the mice bearing bacteremia after different treatments.