Supporting Information

Oxygen-Sensitive Probe and Hydrogel for Optical Imaging and Photodynamic Antimicrobial Chemotherapy of Chronic Wounds

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1. Experimental Section

2. Complementary Results

1. Experimental Section

Synthesis of the irdium(III) complex Ir-fliq (10) and Ir-fliq-fliq-PVP (11)

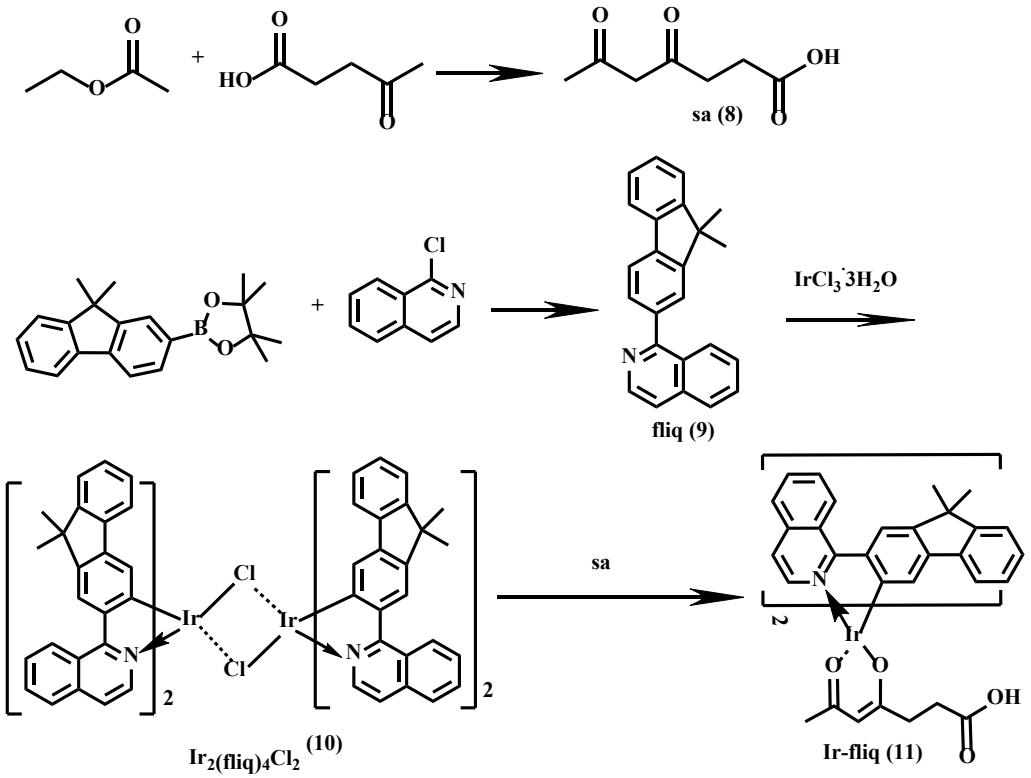
The probe Ir-fliq was synthesized as the **Scheme S1**. 1,3,2-dioxaborolane (2.5 g, 7.8 mmol) and (1.15 g,7.0 mmol) were dissolved in mixed solvent of K_2CO_3 solution (2 mol/L, 20 mL) and methylbenzene (60mL). Catalyst $Pd(PPh_3)_4$ (0.32 g, 0.28 mmol) and phase transfer catalyst 2-(9,9-Dimethyl-9H-fluoren-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.32 mL) were added to the mixture. The mixture was heated at 120 ℃ with Ar protection for 2 h and extracted by ethyl acetate for 3 times. The oranic layer was collected and washed with saturated brine and dried with anhydrous MgSO4. Remove the solvent under reduced pressure. The crude product was purified by silica-gel column chromatography using hexane:ethyl acetate (15:1 v/v) as eluent. The product was a white solid (1-(9,9-Dimethyl-9H-fluoren-2-yl)isoquinoline, fliq).

$IrCl_3•3H_2O$ (390mg, 1.1mmol) and fliq (687 mg, 2.2 mmol) were dissolved in mixed solvent of water (10mL) and 2-ethoxyethanol (30mL). Then the mixture was heated at reflux with Ar protection overnight. After the reaction, the precipitate was filtered and washed with water, methanol and n-hexane to give the chloride-bridged dimer, a dark red powder.

Sodium hydride (7.2g, 300 mmol) was added to ethyl acetate (100 mL) and stirred until no bubbles. Levulinic acid (11.6g, 100 mmol) was dissolved in ethyl acetate (30 mL) and then added into the flask drop by drop. The mixture was reacted at room temperature with Ar protection for 12 hours. After the reaction, 100 mL water was added into the mixture slowly. The water layer was adjusted to pH=2 by sulfuric acid and extracted by ethyl acetate for 3 times. The oranic layer was collected, washed 3 times with saturated brine and dried with anhydrous $MgSO_4$. Remove the solvent under reduced pressure and the crude product was recrystallized from petroleum. Wash by diethyl ethe for 3 times to give the succinyl acetone (sa), a white crystal.

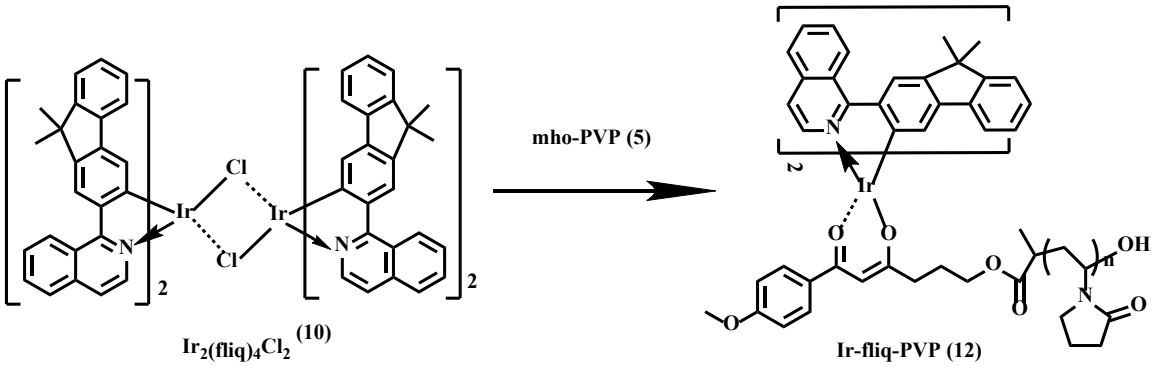
$Ir_2(fliq)_4$-Cl_2 (136 mg, 0.08 mmol), sa (50 mg, 0.2 mmol) and Na_2CO_3 (85 mg, 0.8 mmol) were dissolved in 2-ethoxyethanol (10mL). Then the mixture was heated at reflux with

Ar protection for 18 h. After the reaction, the solvent was distilled off under reduced pressure. The crude product was washed with diethyl ether and the purified by silica-gel column chromatography using chloroform as eluent. The product was a dark-red podwer.



Scheme S1. Synthesis of Ir-fliq

The probe Ir-fliq-PVP was synthesized as the **Scheme S2**. The mho-fliq-PVP (0.767 g, 0.08 mmol), $Ir_2(fliq)_4Cl_2$ (136 mg, 0.08 mmol) and Na_2CO_3 (85 mg, 0.8 mmol) were dissolved in 2-ethoxyethanol (15mL). Then the mixture was heated at reflux with Ar protection for 48 hours. After cooling to room temperature, the precipitate was filtered off and the filtrate was concentrated under reduced pressure. Then the mixture was precipitated into diethyl ether. The precipitate was washed with diethyl ether and dried in vacuo to give an orange powder.



Scheme S2. Synthesis of Ir-fliq-PVP

Structure Characterization

^{1}H NMR spectra were collected on a Bruker DRX-400 spectrometer. ESI-MS spectrometric data were determined with a LCQ ESI-MS Therso Finnigan mass spectrometer.

fliq: ^{1}H NMR (400 MHz, DMSO): δ 8.65 (m, 1H), 8.20 (m, 1H), 7.90 (m, 2H), 7.82 (m, 2H), 7.71 (m, 2H), 7.48 (t, 1H), 7.38 (d, 2H), 1.57 (s, 6H); ESI-MS (m/z): $[M]^+$ calcd. for $C_{24}H_{19}N$, 321.42; found, 321.

sa: ^{1}H NMR (400 MHz, DMSO): δ 3.61 (s, 2H), 2.73 (m, 2H), 2.60 (m, 2H), 2.23 (s, 3H); ESI-MS (m/z): $[M]^+$ calcd. for $C_7H_{10}O_4$, 158.15; found, 158.

Ir-fliq: ^{1}H NMR (400 MHz, DMSO): δ 8.67 (m, 2H), 8.25 (m, 2H), 7.87 (m, 4H), 7.78 (m, 4H), 7.67 (m, 4H), 7.43 (t, 2H), 7.33 (d, 4H), 5.88 (s, 1H), 2.58 (m, 2H), 2.36 (m, 2H), 1.99(s, 3H), 1.67 (s, 12H); ESI-MS (m/z): $[M]^+$ calcd. for $C_{55}H_{46}O_4N_2Ir$, 991.18; found, 991.

2. Complementary Results

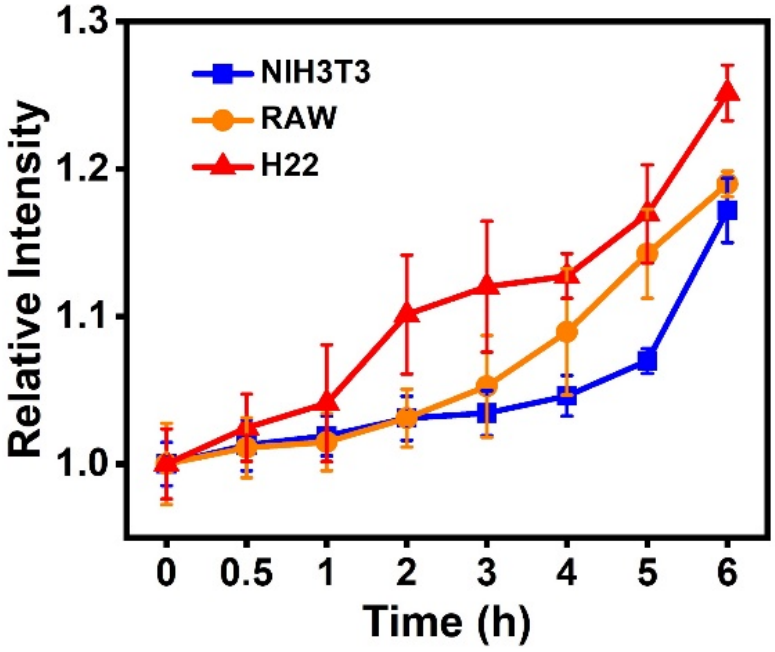


Fig. S1 The signal intensity of the probe in NIH3T3, RAW264.7 and H22 cells was observed over time.

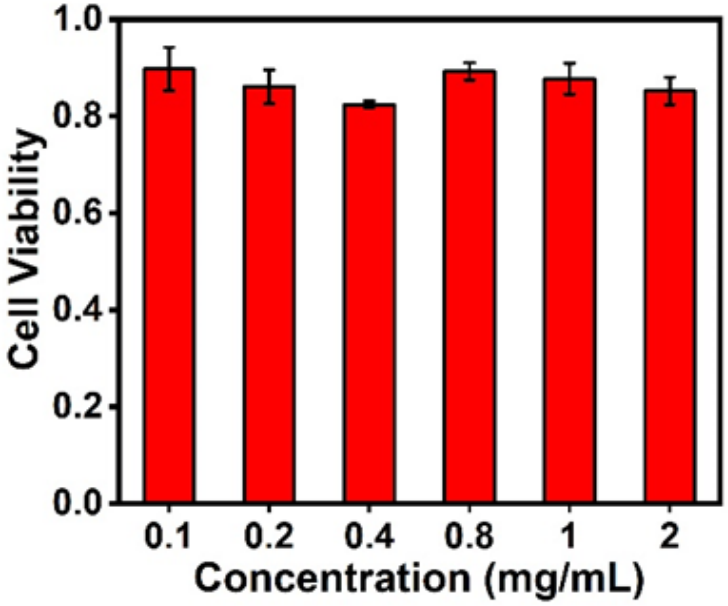


Fig. S2 *In vitro* cytotoxicity of Ir-fliq-PVP against RAW264.7 cells with different concentrations.

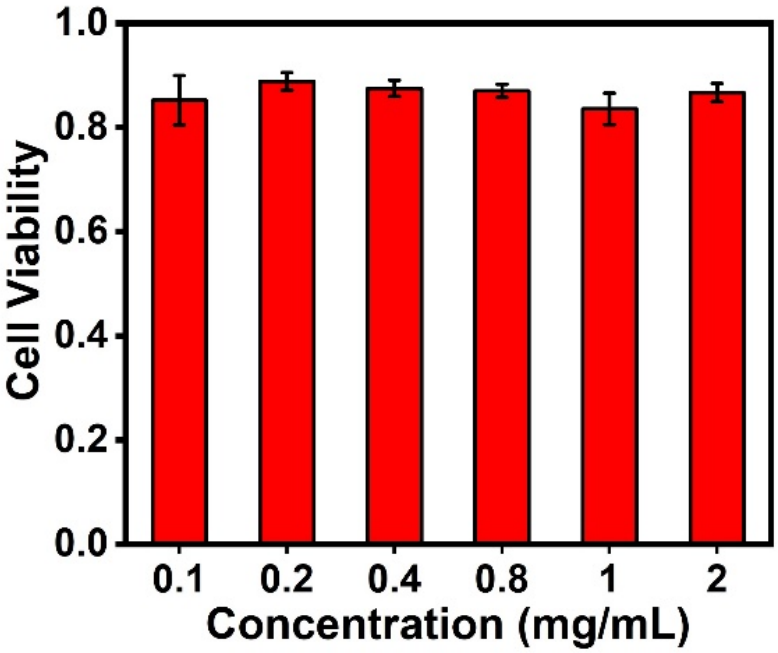


Fig. S3 *In vitro* cytotoxicity of Ir-fliq-PVP against NIH3T3 cells with different concentrations.

Table S1 The forming time of composite hydrogels prepared by different mass ratios of CMCS/SA under the catalysis of different molar ratios of EDC/NHS.

	CMCS/SA		
EDC/SA	**2:1**	**1:1**	**1:2**
1:1	5 h, **CS121**	Semigel	Solution
2:1	2 h, **CS221**	＜1 h, **CS211**	Solution
5:1	＜1 h, **CS521**	＜1 h, **CS511**	Semigel

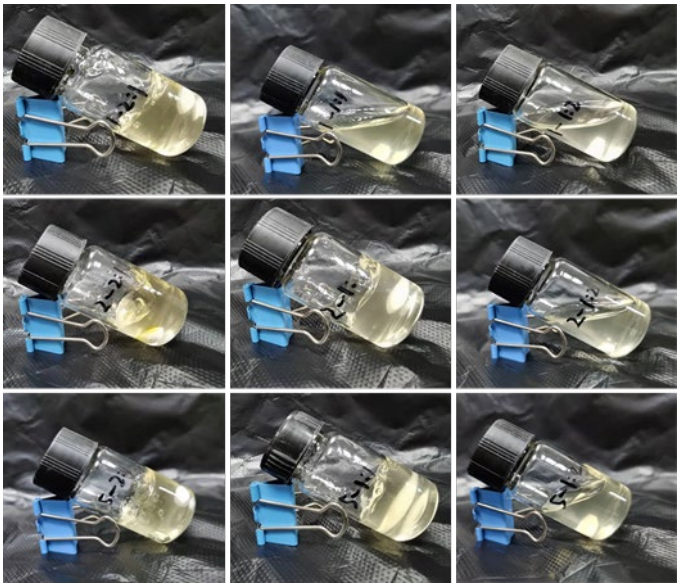


Fig. S4 The digital images of the product after mixing CMCS/SA with EDC/NHS for 12 hours.

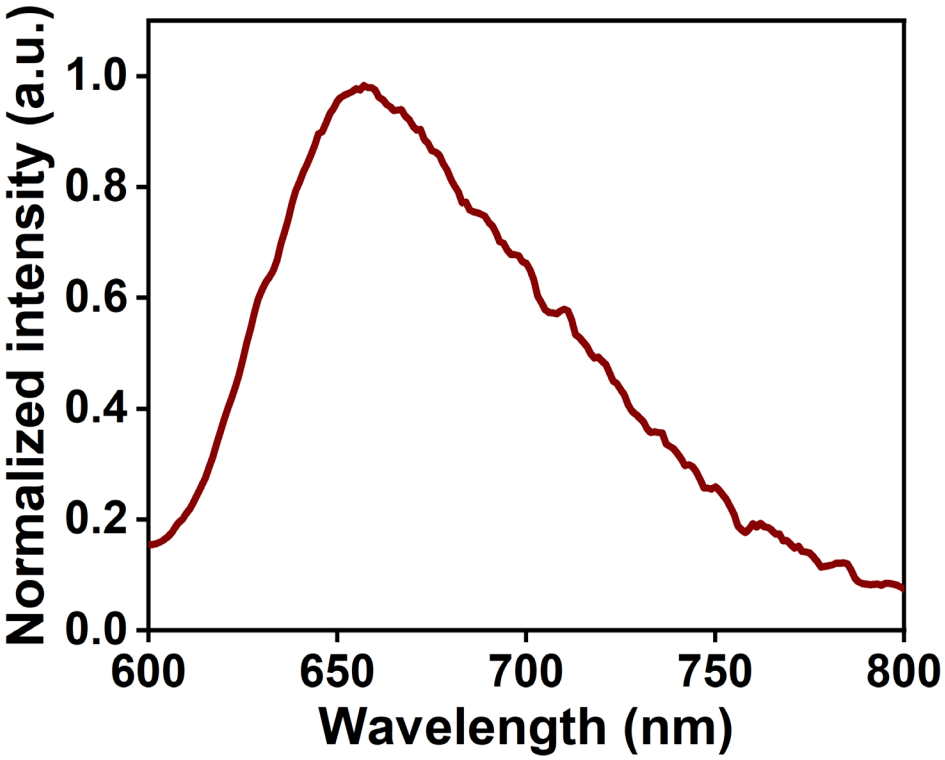


Fig. S5 Emission spectra of CSGI hydrogel.

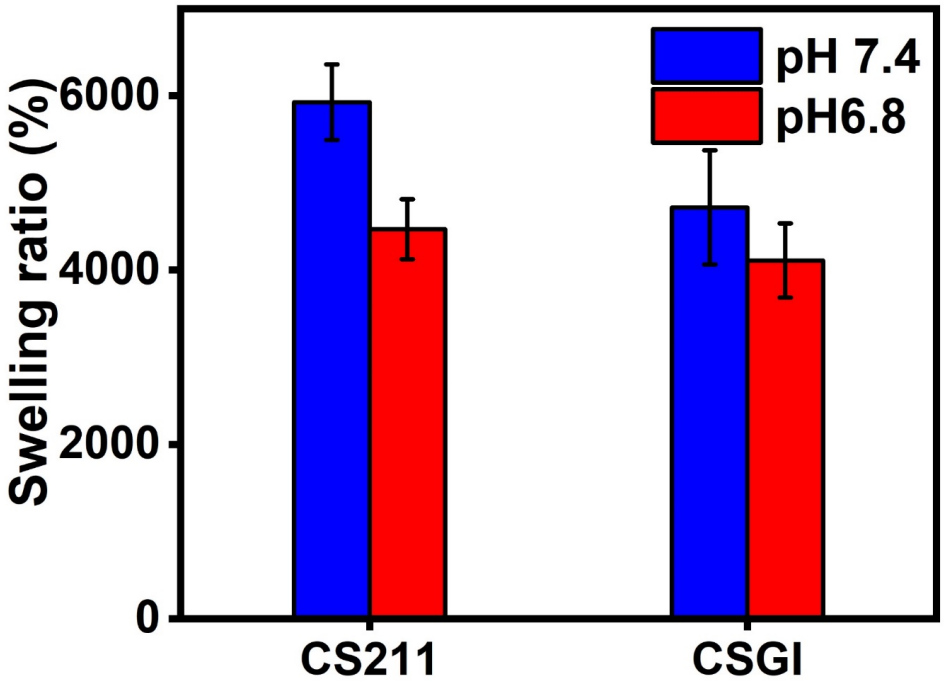


Fig. S6 Swelling quality of CMSA hydrogels.

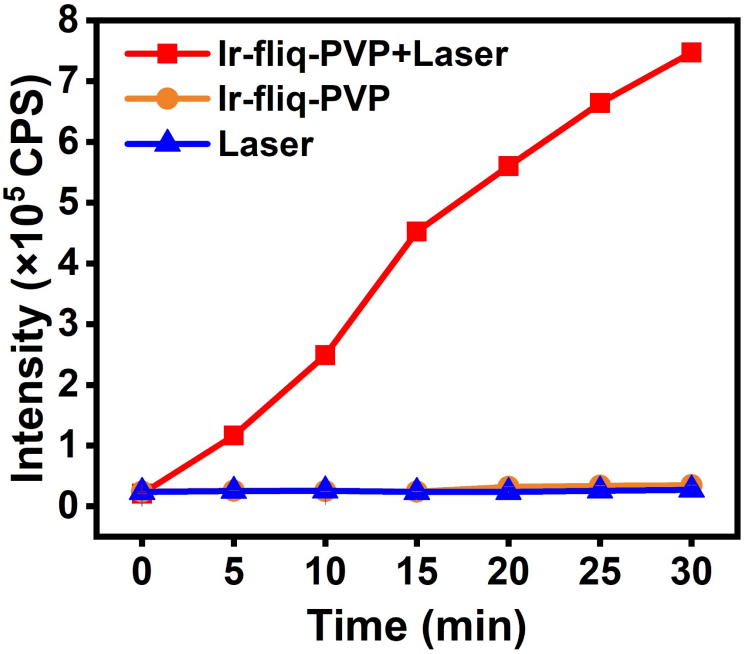


Fig. S7 Fluorescence intensity of SOSG over time in the aqueous solution with the absence or presence of Ir-fliq-PVP and laser irradiation.

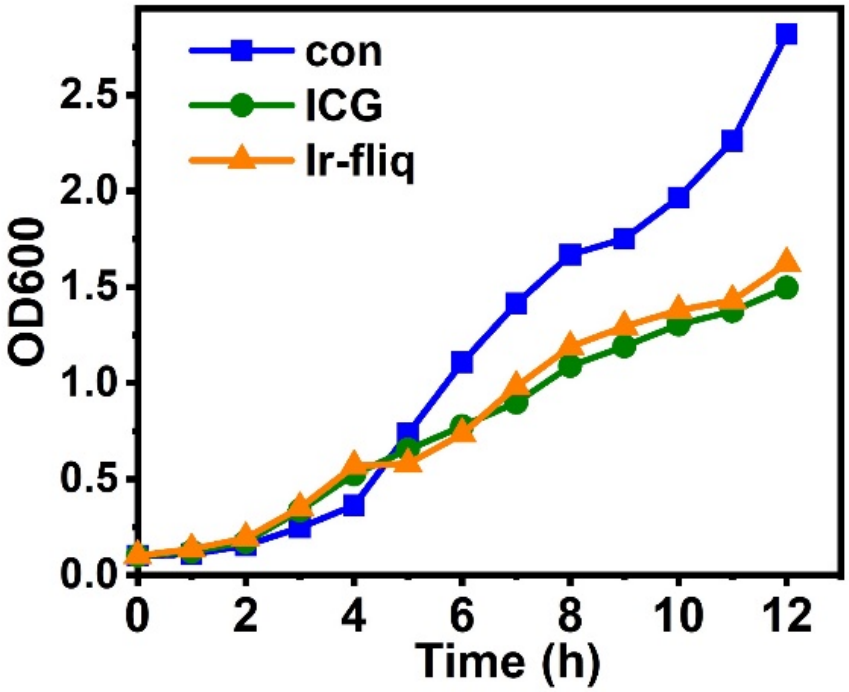


Fig. S8 Growth curve of *S. aureus* in different conditions.

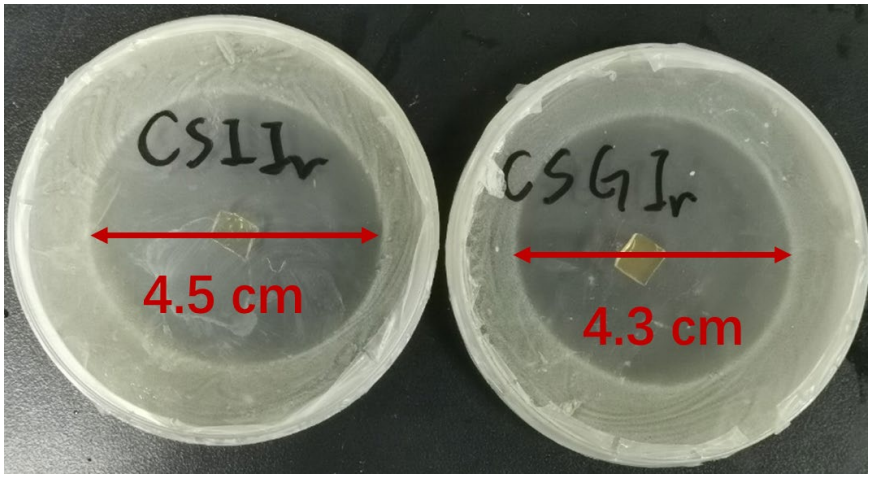


Fig. S9 The zone of inhibition of hydrogels against *S. aureus*.

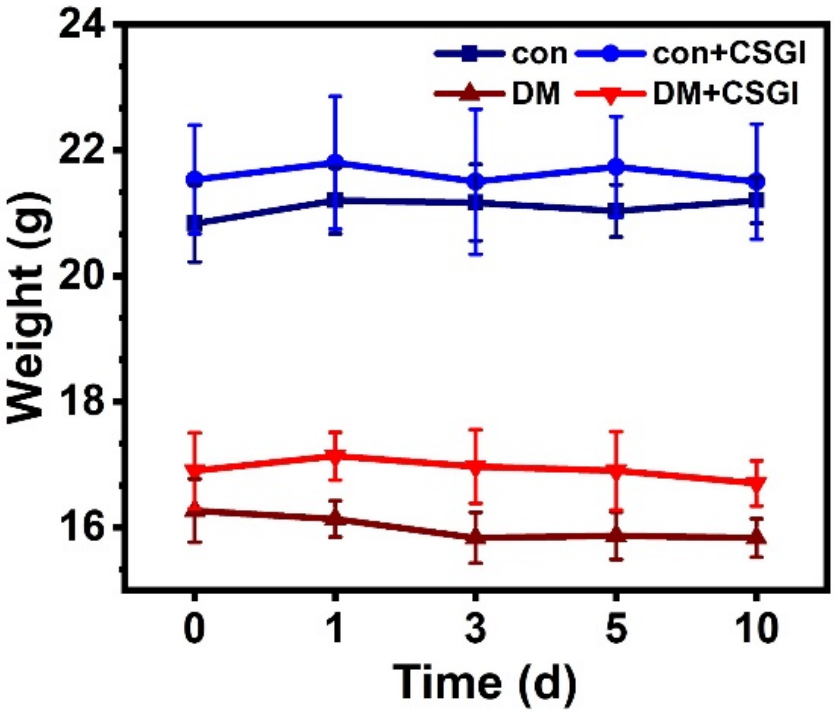


Fig. S10 Body weights of healthy/diabetic mice with/without treated by PACT.

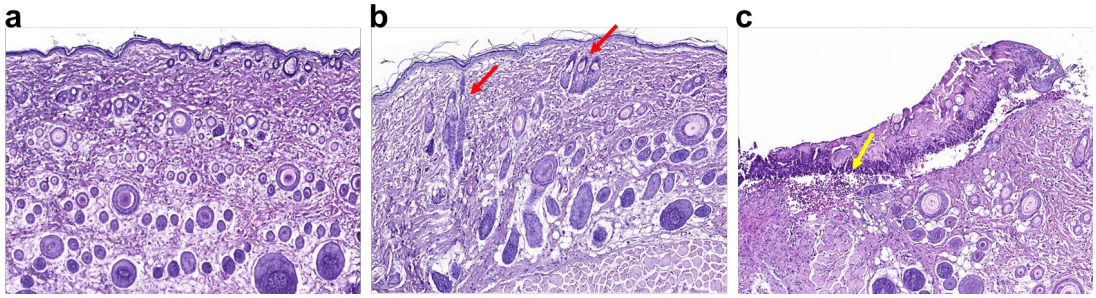


Fig. S11 The H&E stained slices of normal skin (a) and hurt skin in day 1(b) and day 3(c) respectively. Arrows pointing to inflammatory infiltrate and tissue damage.