Supporting information

pH-Triggered hydrogel degradation for the smart release of antibiotic aiming at bacterial infection

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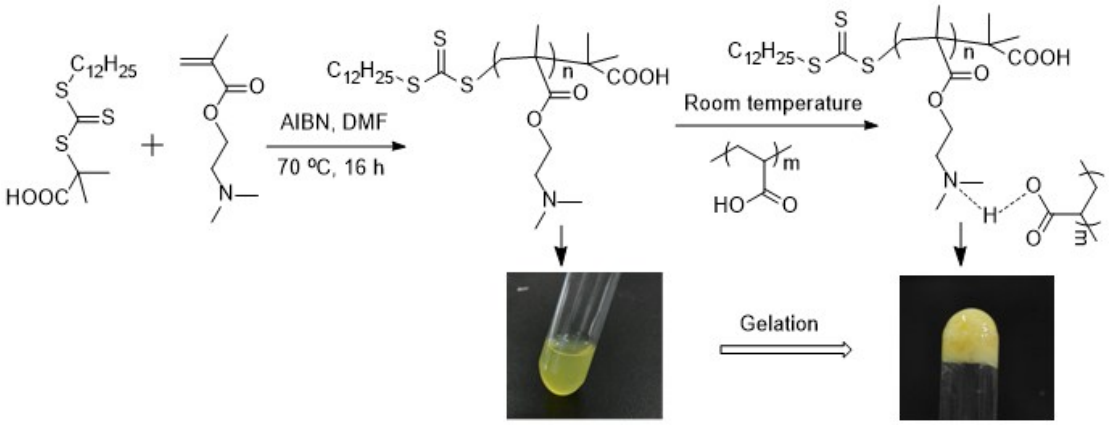
Materials and equipment

2-Dodecylsulfanylthiocarbonylsulfanyl-methylpropionic acid (DMP), DMAEMA (98%), PAA (M_n=4000 Da, 0.5 mg/mL) and 2,2'-azobis(isobutyronitrile) (AIBN, 99%) were purchased from Sigma-Aldrich (Saint Louis, MO, US), and AIBN was purified by recrystallization from ethanol and dried at room temperature in a vacuum oven. DMAEMA was filtered through an activated basic alumina column before use. *S. aureus* ATCC 6538 strains were purchased from NanjingBianzhen biological technology Co., Ltd.The molecular weight and polydispersity of polymers were measured with Gel Permeation Chromatography(GPC, Waters 1525). The UV-vis absorption spectrum was recorded on a UV-vis spectrophotometer (Shimadzu, UV-2550).The FT-IR was recorded using infrared spectrometer (Bruker, vertex70). The surface morphology of hydrogel was observed by scanning electron microscope (SEM, JSM-5510LV).

Synthesis of PDMAEMA

PDMAEMA was synthesized by RAFT polymerization using DMP as a chain transfer agent and AIBN as an initiator. DMAEMA was mixed with DMP and AIBN in N,N-dimethylformamide (DMF)(50 wt%) in a tube, the concentration ratio was DMAEMA:DMP:AIBN=100:1:0.4. The tube was sealed, put through three cycles of vacuum purging and backfilling with nitrogen for 30 min in an ice-water bath, and then transferred to a 70 °C water bath for predetermined time. After 16 h, the reaction was stopped by cooling the tube in an ice-water bath. The obtained polymers were dissolved in tetrahydrofuran, precipitated into a large excess (more than 10 times) of cold n-hexane and the obtained solid polymer was dried in a vacuum oven.



Scheme S1.Preparation of the pH-sensitivehydrogel.

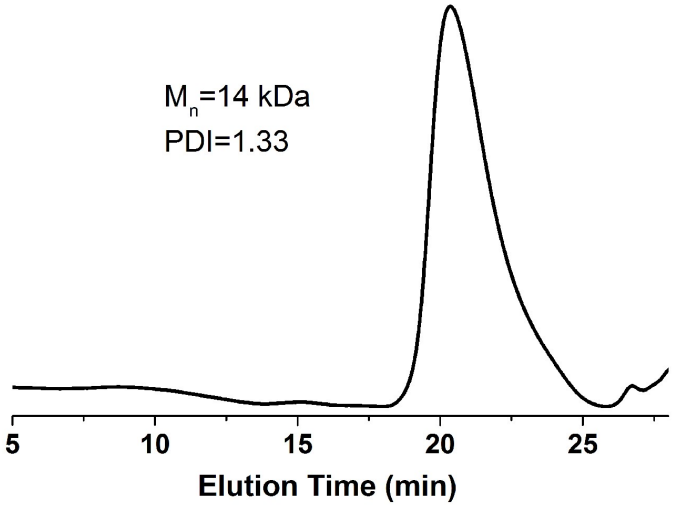


Fig. S1. TheGPC profile of PDMAEMA

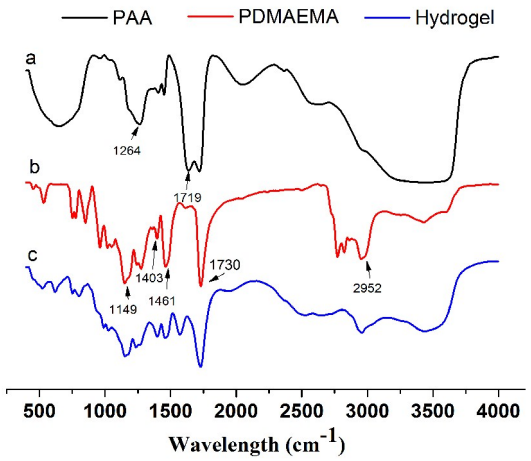


Fig. S2 The FT-IR spectraof PAA, PDMAEMA and the hydrogel.

The wide peak at 3400 cm^{-1} belonged to the -OH of PAA, and 1719 cm^{-1} and 1264 cm^{-1} was stretching vibration of C=O and C-O, respectively. In Fig. S2 b, 2952 cm-1 was belongs to the stretching vibration of C-H of $-CH_3$, 1730 cm^{-1} was attributed to the stretching vibration of -C=O, 1461 $cm^{-1}$was the bending vibration of $-CH_2-$, 1403 cm^{-1} represented the absorption of C-N, 1149 cm^{-1} was the stretching vibration of C-O. The spectrum of hydrogel contains the characteristic absorption peak of both PAA and PDMAEMA.

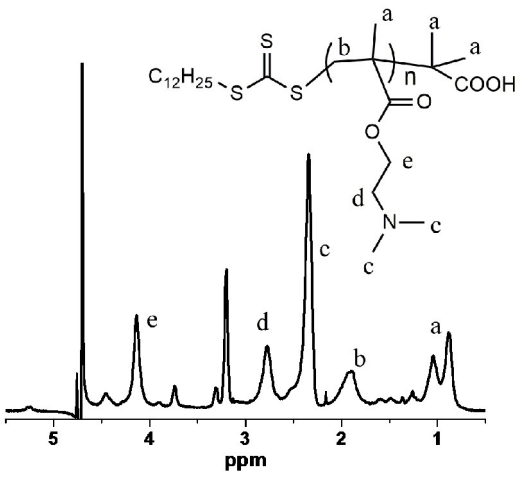


Fig. S3. The ^1H NMR of PDMAEMA

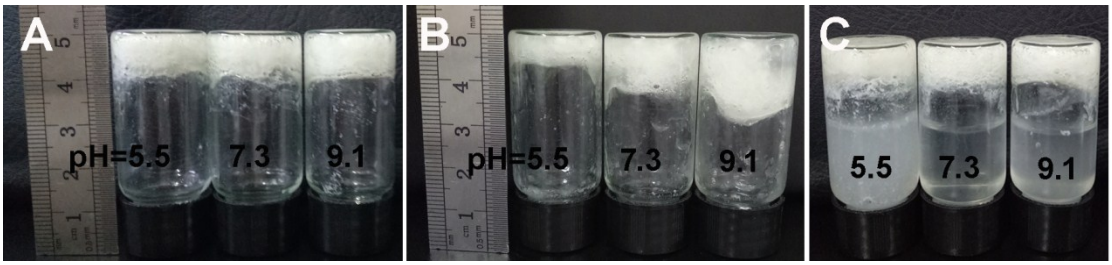


Fig. S4. The photograph of hydrogel when hydrogels were soaked in the solution with pH=5.5, 7.3 or 9.1 for 6 h. respectively.

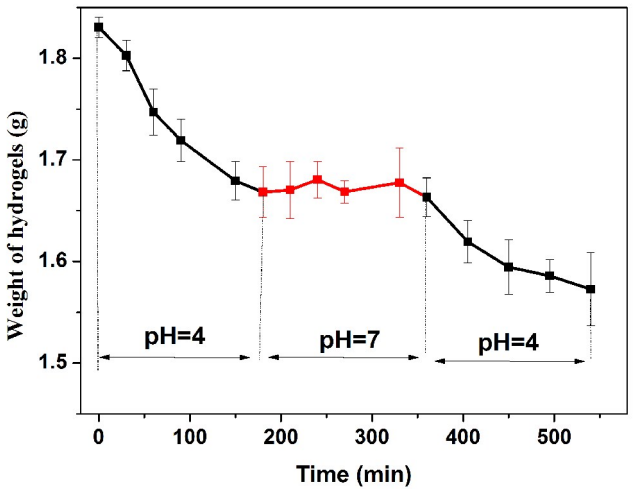


Fig. S5. The degradation process of hydrogel in changing pH solutions.

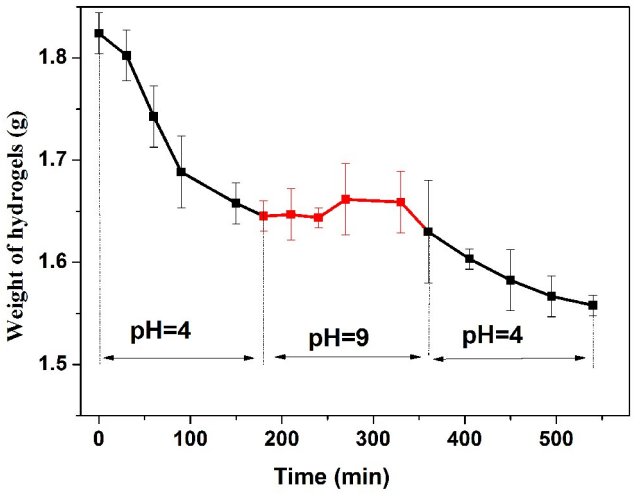


Fig. S6. The degradation process of hydrogel in changing pH solutions.

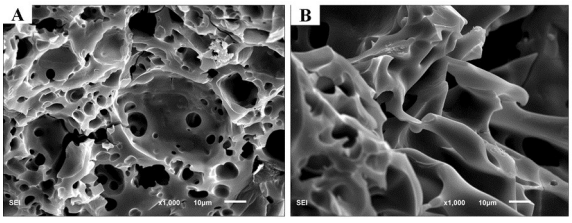


Fig. S7. The SEM of hydrogel before (A) and after (B) soak in PBS of pH=5.5 for 60 min.

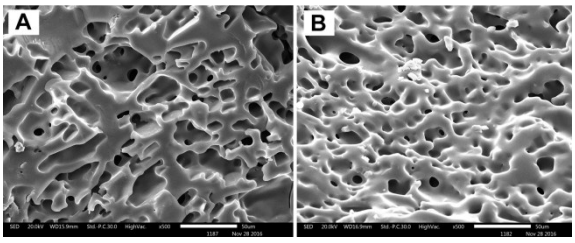


Fig. S8. The SEM of hydrogel before (A) and after (B) soak in PBS of pH=9.1 for 60 min.

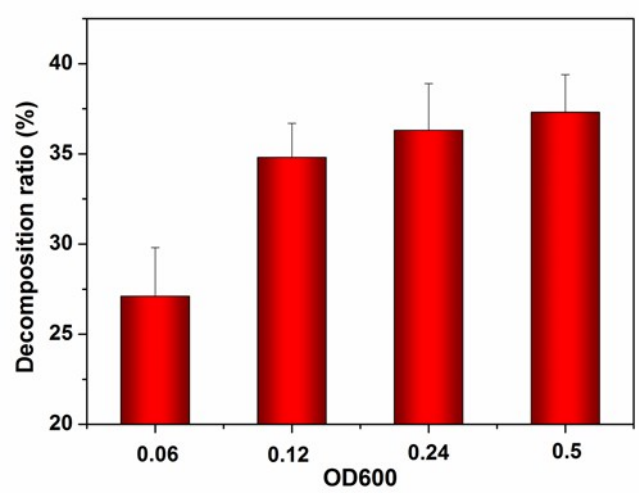


Fig. S9. The degradation rate of the hydrogel under different bacterial concentration.

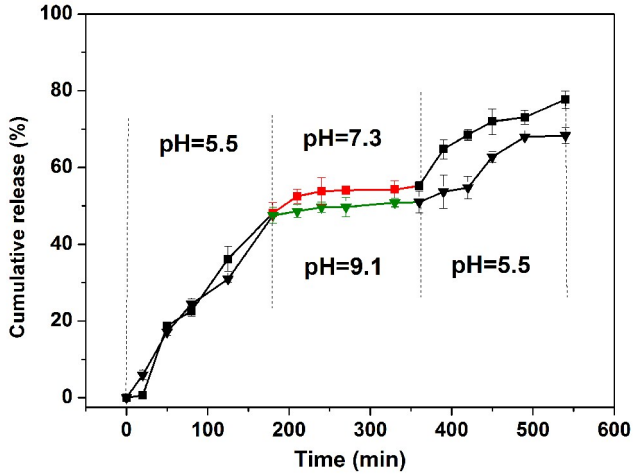


Fig. S10. The drug release process of hydrogel upon pH variation.

Cytotoxicity of the hydrogel

MTT assay was used to evaluate cytotoxicity of the hydrogels, HepG2 and NIH3T3 as model cells. First, 20 mg hydrogels was incubated in 5 mL of pH 7.4 PBS for 72 h, and then filtrated and diluted to give a leaching solution concentration range from 0.25 to 2 mg/mL with Dulbecco's modified Eagle's medium (DMEM), and the diluted leaching solutions were sterilized and sealed in bottles. The cells were seeded in a 96-well plate at a density of 1.0×10^4 cells per well in DMEM with 10% fetal bovine serum. After incubated for 24 h at 37 oC in 5% CO_2, the media in the wells were replaced with the diluted leaching solution (0.2 mL). Then, the plates were again placed in the incubator and

maintained in 5% CO_2 at 37°C for 24 and 48 h, respectively. Then, 20μL of MTT solution was added in each well and incubated for a further 4 h. After the medium was completely removed, 150 μL of dimethylsulfoxide (DMSO) was added to dissolve the formazan crystals. The plate was placed at 37 °C for 10 min, and then the optical density was read on a microplate reader at 490 nm. The cells without the treatment of leaching solution were used as the control and their cell viability was set at 100%.

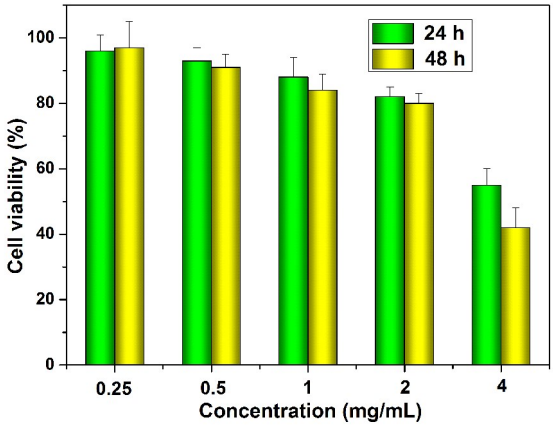


Fig.S11. Viability of HepG2 cellcultured with the hydrogel under different concentration.

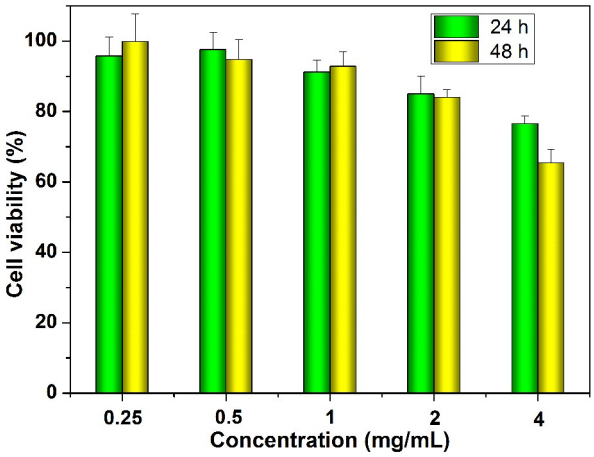


Fig. S12. Viability of NIH3T3 cellcultured with the hydrogel under different concentration.