Electronic Supplementary Material (ESI) for Biomaterials Science.

Ultrasound-Enhanced Cascade Chemodynamic Tumor Nanotherapy with Lactic Acid-Enabled Hydrogen Peroxide Self-Production

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Supplementary figures

Figure S1 The color changes after USPION@PEG-LOD solution reacted with LA in TMB solution.

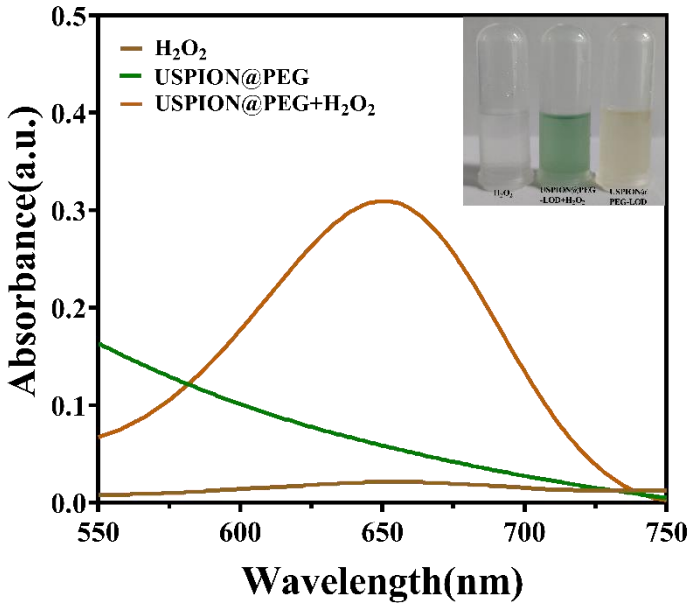

Figure S2 The TMB UV-vis absorption curves of USPION@PEG (100 ppm) with or without H_2O_2.

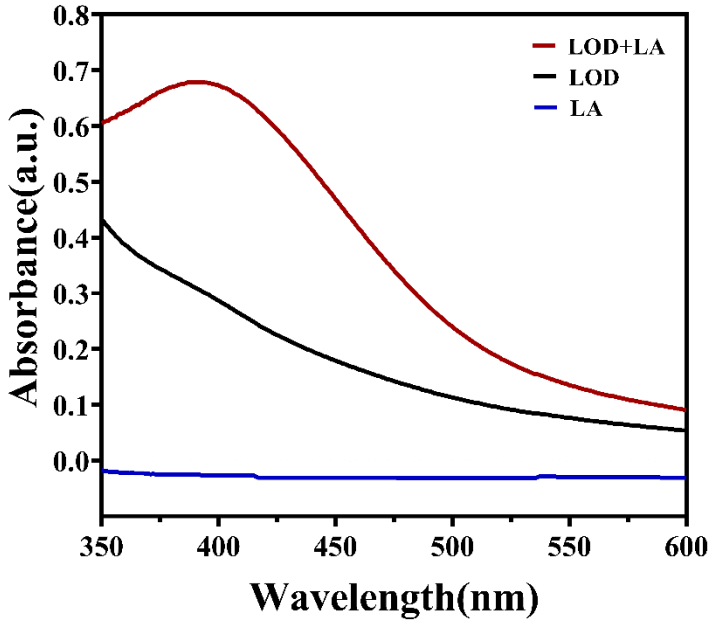

Figure S3 By the H_2O_2 assay kit, the UV-vis spectra detected after the LOD (1000 ppm) aqueous solution interacted with LA (50 mM) at 37 ℃, separately reacted LOD or LA solution as the control group.

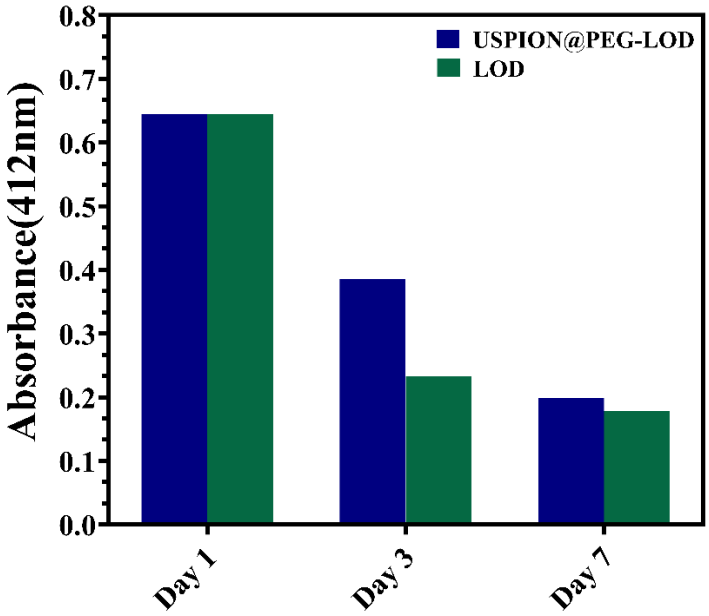

Figure S4 After being placed at 4 ℃ for 0, 3, and 7 days, the USPION@PEG-LOD solution and the uncombined LOD aqueous solution reacted with LA (50 mM) at 37 ℃ for 5 minutes, and then a hydrogen peroxide kit was used to detect the 412 nm UV absorption peak. The concentration of LOD is 1000 ppm.

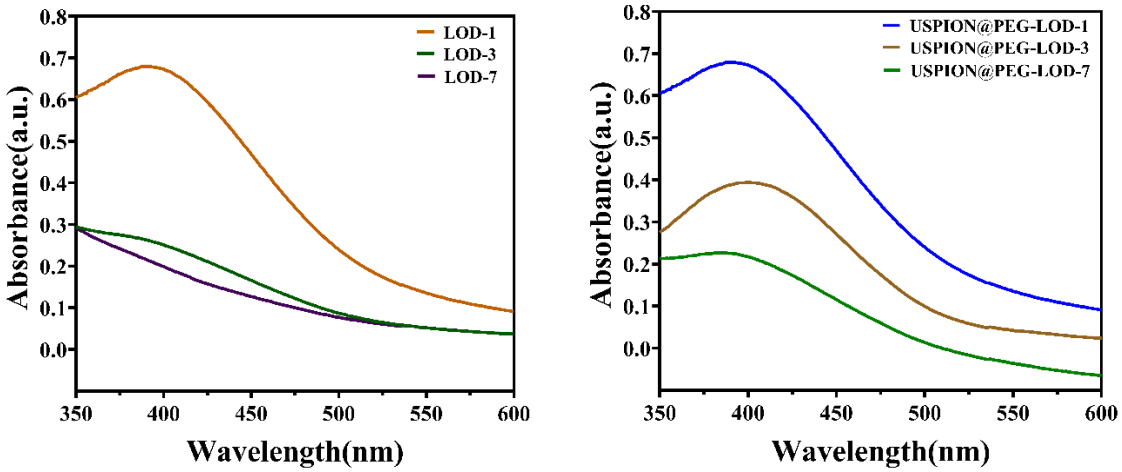

Figure S5 By the H_2O_2 assay kit, the ultraviolet absorption curves of LOD and USPION@PEG-LOD solution were recorded after reaction with LA (50 mM) at 37 ℃ for 5 minutes, which were placed for 0, 3, and 7 days, respectively. The concentration of LOD is 1000 ppm.

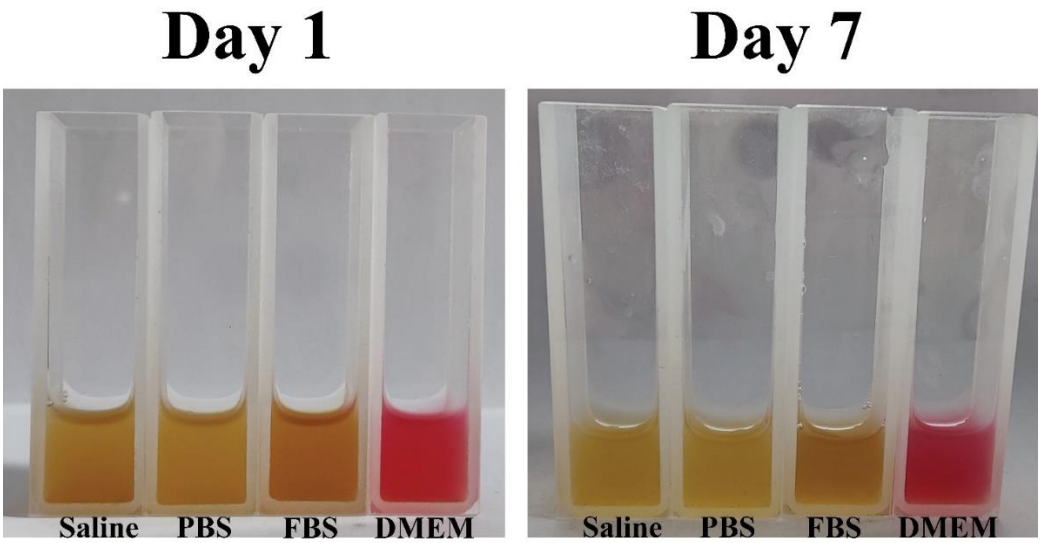

Figure S6 After being placed at 4 ℃ for 0, 7 days, the USPION@PEG-LOD solution was taken pictures respectively, which was dispersed in several representative solvents including saline, PBS, fetal calf serum (FBS), and DMEM.

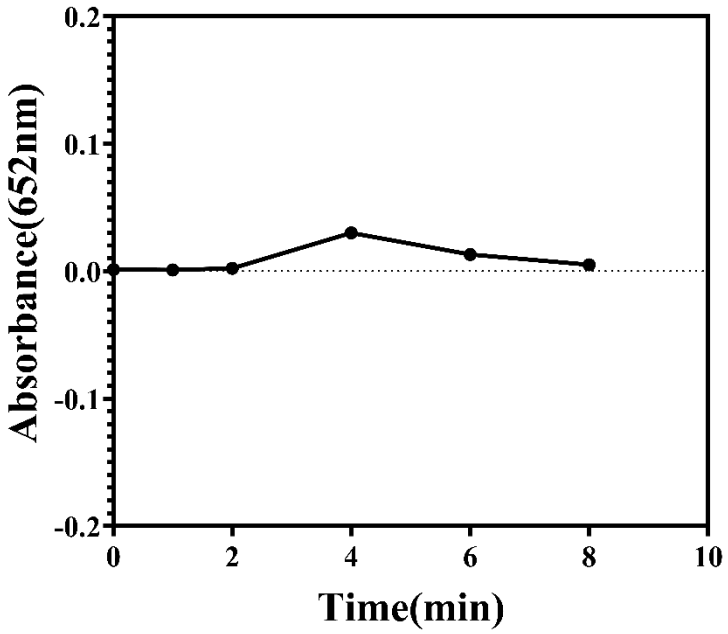

Figure S7 The TMB aqueous solution was irradiated by ultrasound (frequency of 1.0 MHz, power density of 1.5 W/cm^2, time of 1 minute) and then detected by ultraviolet spectrophotometer. The values of the UV-vis spectra at 652 nm were recorded every measurement.

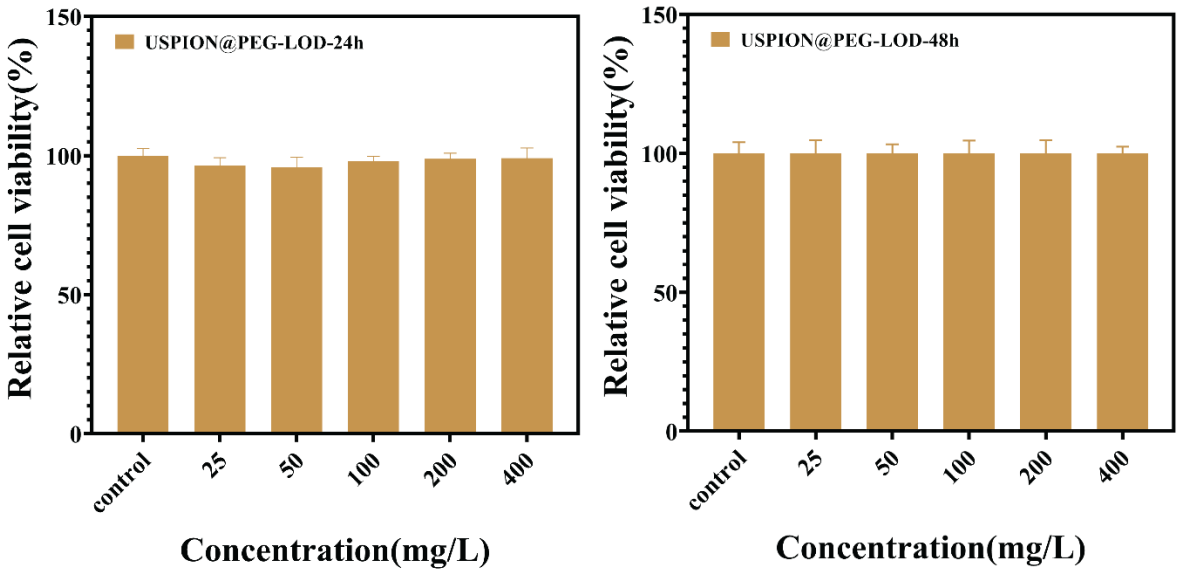

Figure S8 The relative cell viability of 4T1 cells co-cultured with USPION@PEG-LOD solution in various concentrations for 24 hours and 48 hours, respectively.

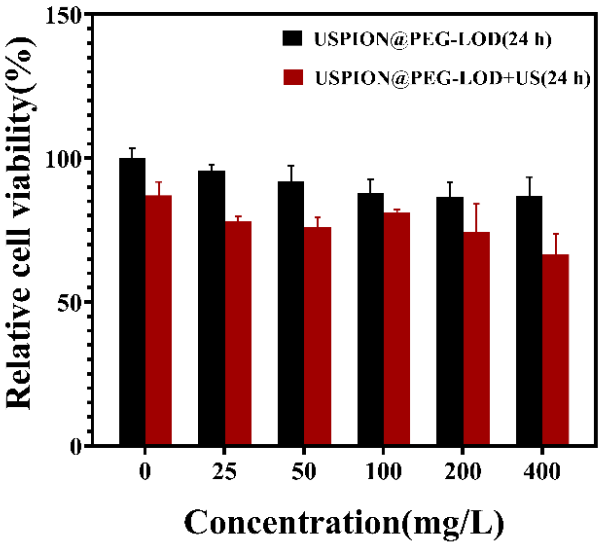

Figure S9 The relative cell viability of 4T1 cells co-cultured with USPION@PEG-LOD and LA solution in various concentrations for 24 hours in corporation of ultrasound treatment or not.

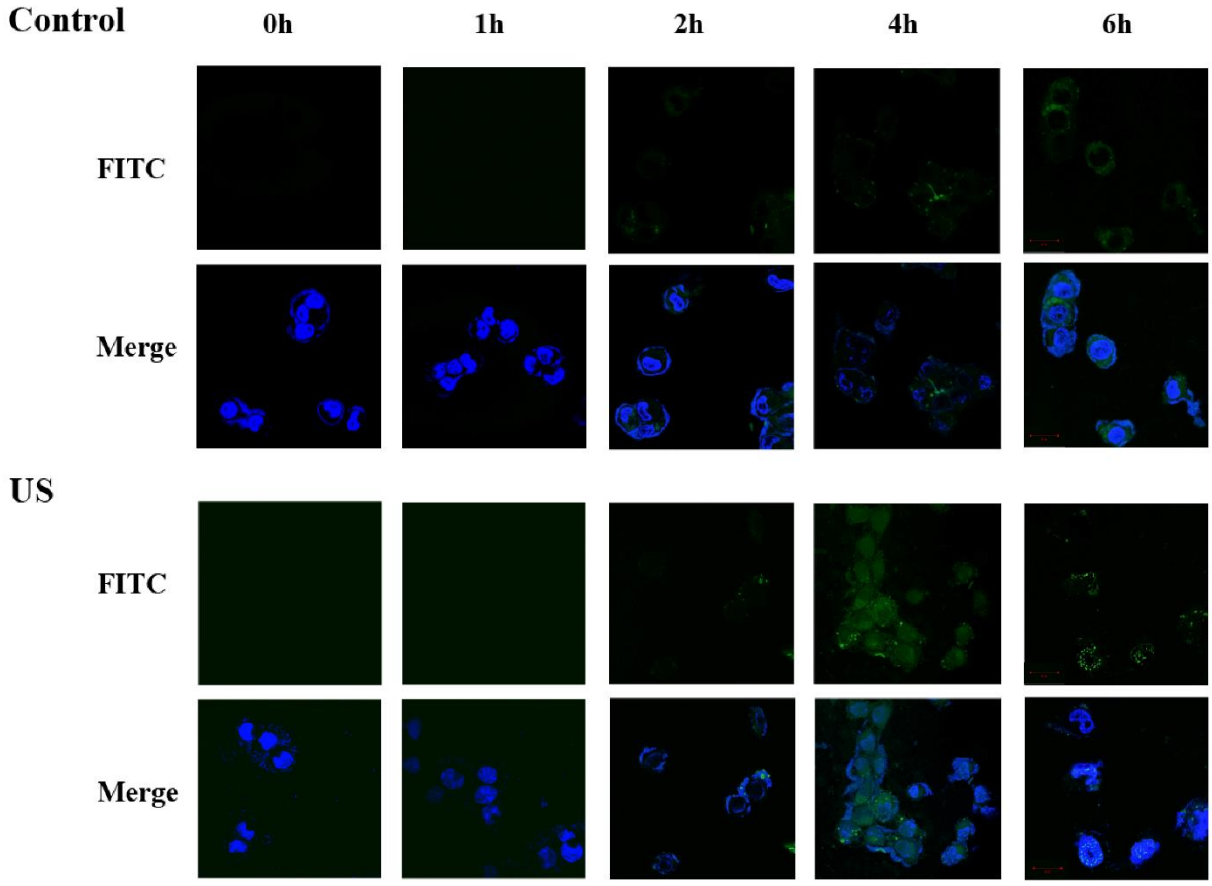

Figure S10 The uptake evaluation of USPION@PEG-LOD (100 ppm) at various times with ultrasound or not. The FITC-labeled USPION@PEG-LOD nanoparticles were cultured with 4T1 cell for different times, and the sonic group was subjected to ultrasound stimulation for 1 minute (frequency of 1.0 MHz, power density of 1.0 W/cm^2). The CLSM pictures were taken at 1, 2, 4,

6 hours of cultivation, scale bar, 20 μm.

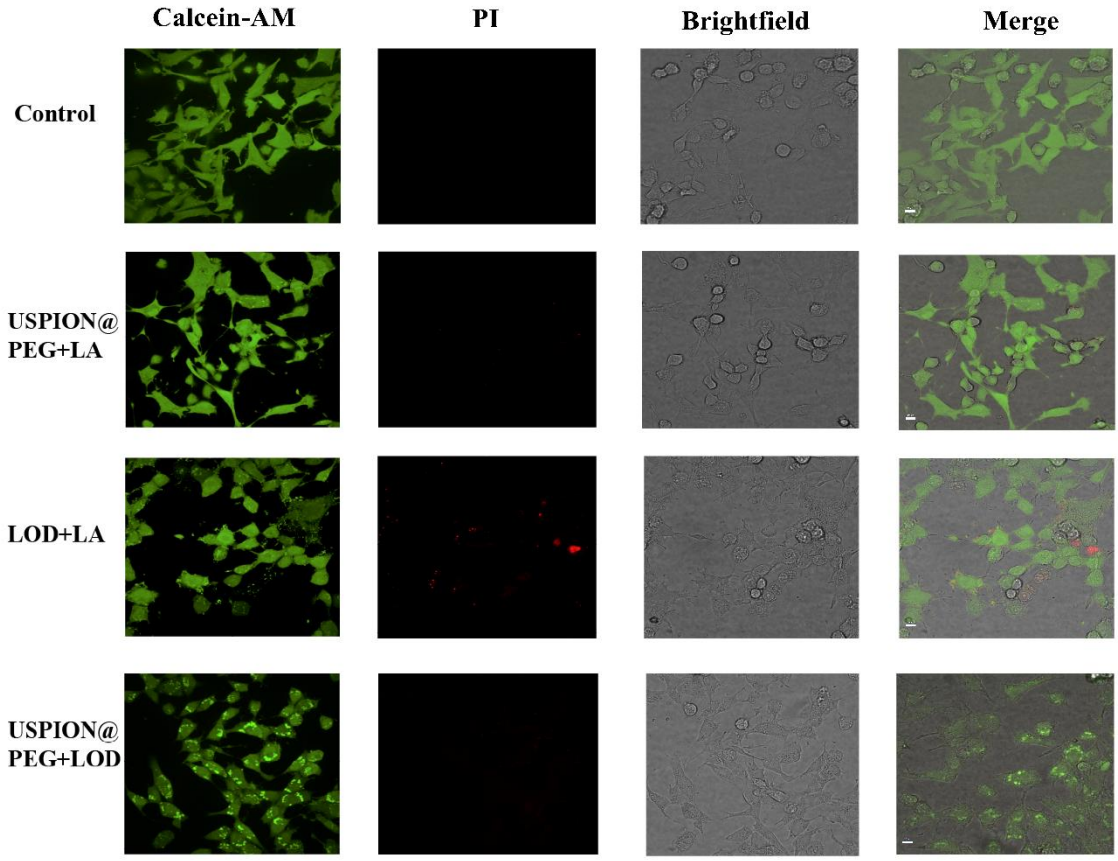

Figure S11 The CLSM images of live or dead cell distributions after co-incubation for 4 hours under various conditions, followed by staining with calcein-AM/PI reagents for 15 minutes at 37 ℃, scale bar, 10 μm.

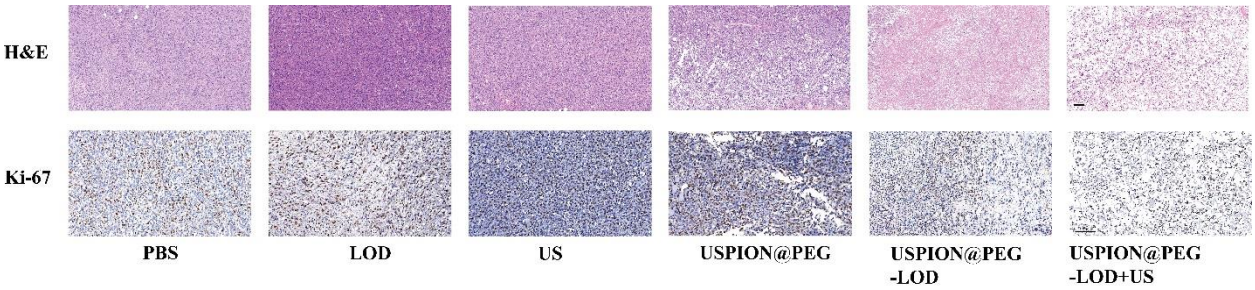

Figure S12 The images of H&E and Ki-67 staining of tumor sections from different groups, scale bar, 100 μm.

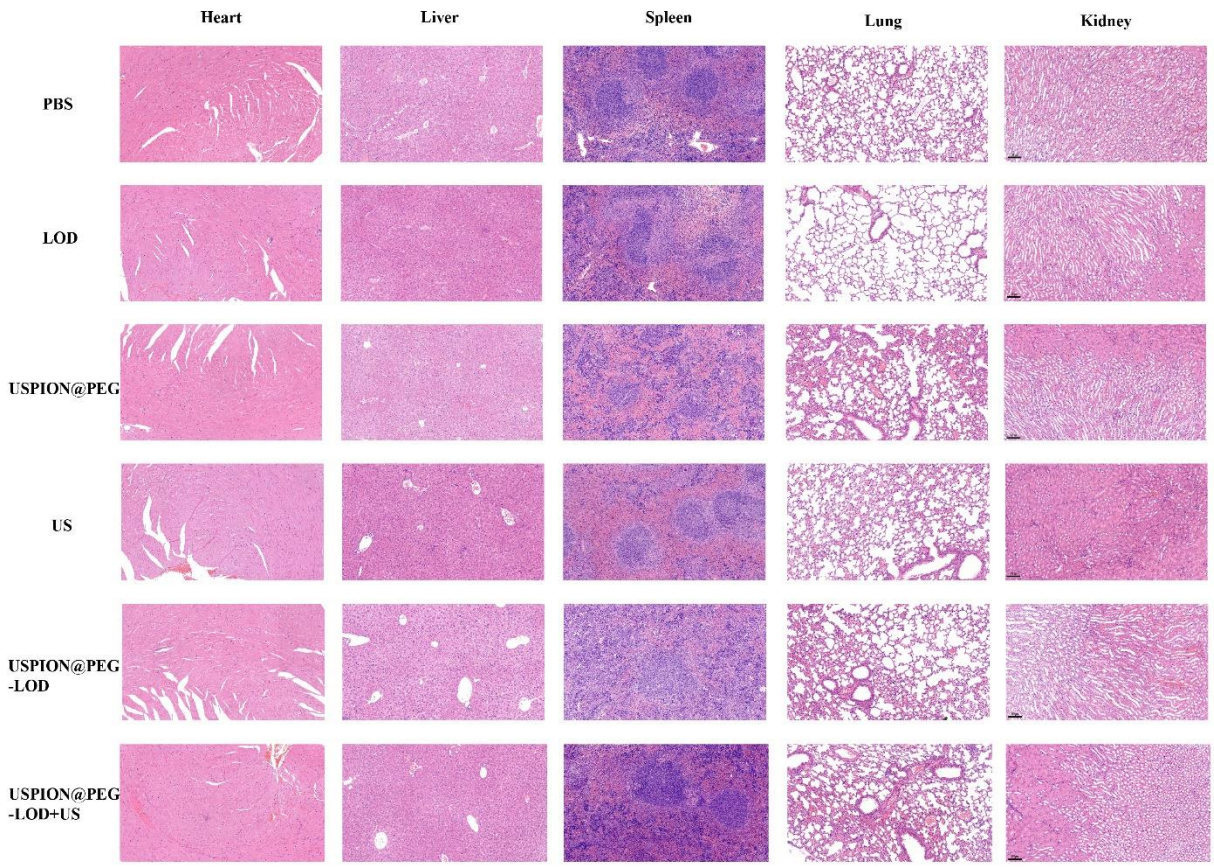

Figure S13 The images of H&E staining of major organs sections from different groups after 14 days treatment, scale bar, 100 μm.