Supporting Information for:

# Efficacy-shaping nanomedicine by loading Calcium Peroxide into Tumor Microenvironment-responsive Nanoparticles for the Antitumor Therapy of Prostate Cancer

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Supplementary Figures (Figures S1-S19):

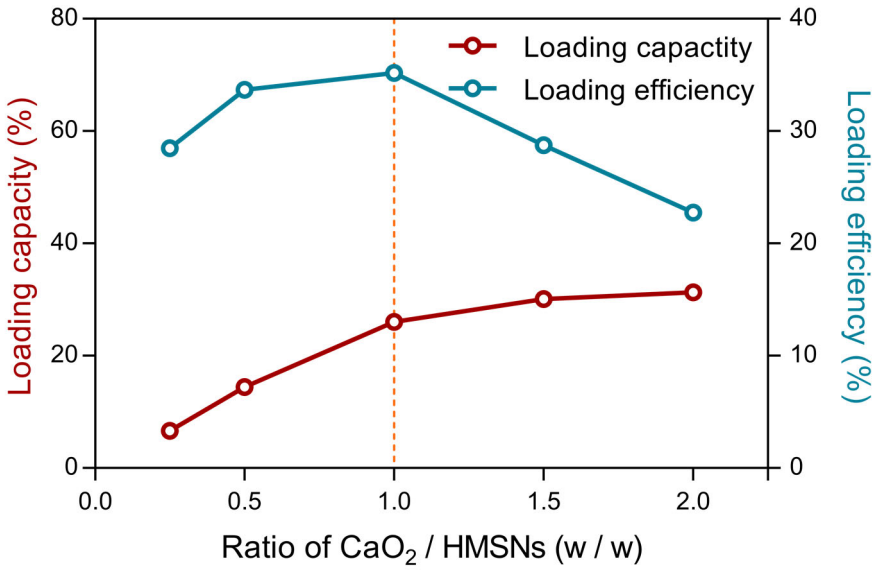


**Figure S1. The influence of the mass ratio of $CaO_2$ to HMSNs on the loading capacity and the loading efficiency of $CaO_2$@HMSNs.**

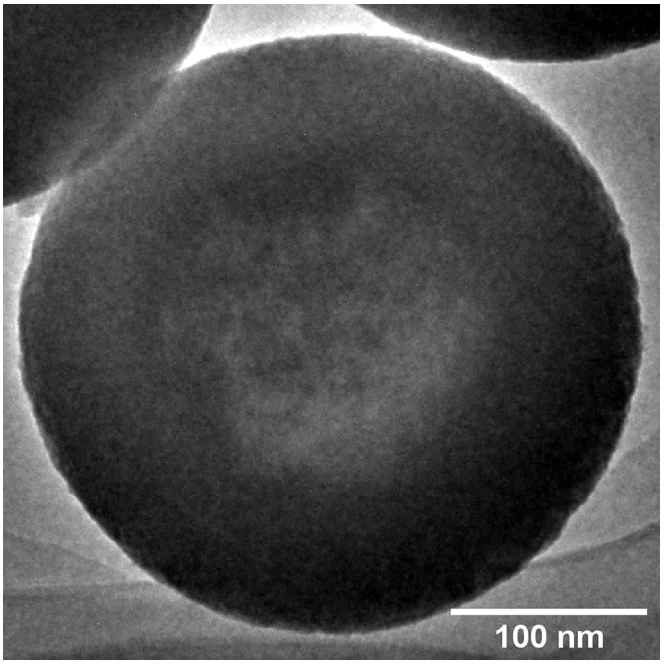


**Figure S2. Transmission electron microscopy (TEM) image of $CaO_2$@HMSNs.** Scale bar, 100 nm.

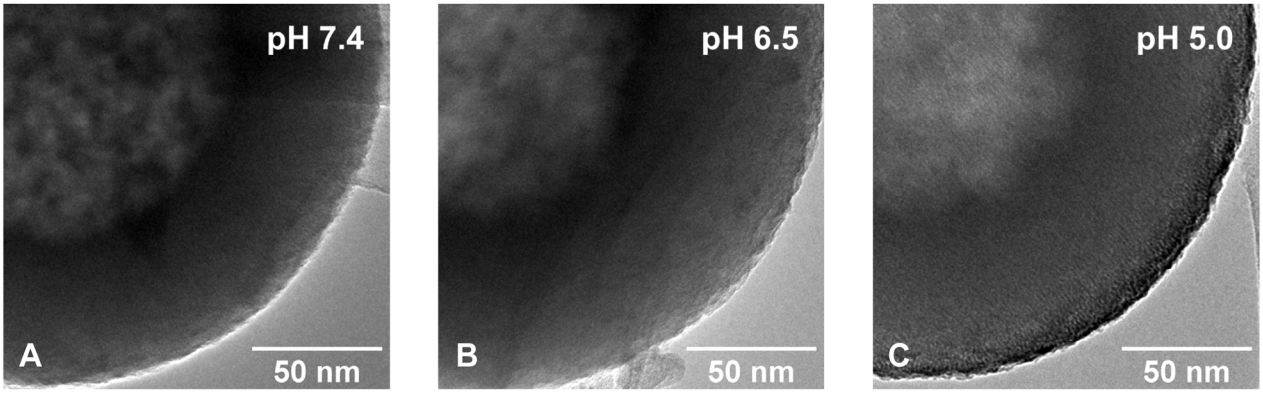


**Figure S3. Transmission electron microscopy (TEM) images of $CaO_2$@HMSNs-PAA at different pH values.** TEM images of $CaO_2$@HMSNs-PAA at pH values of 7.4 (**A**), 6.5 (**B**) and 5.0 (**C**). Scale bars, 50 nm.

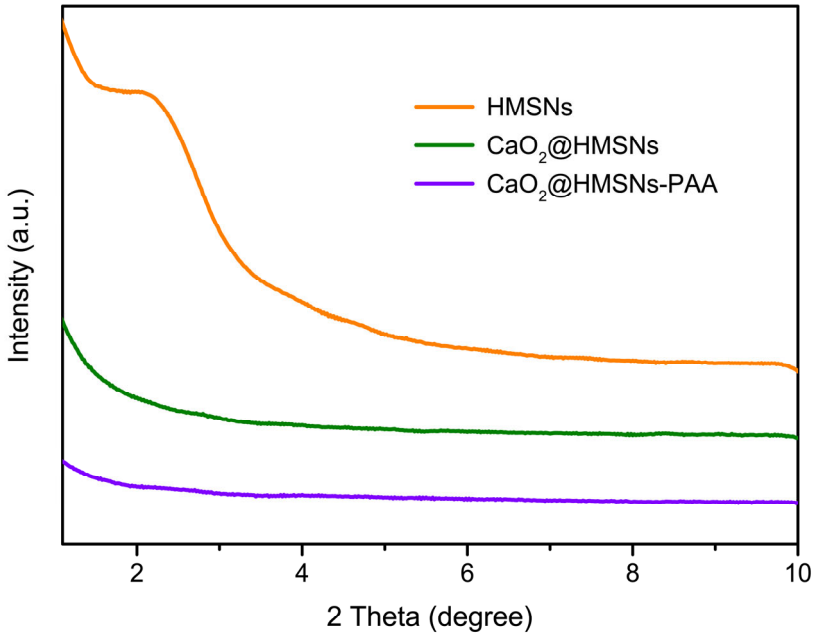


**Figure S4. Low-angle X-ray diffraction (XRD) patterns of HMSNs, $CaO_2$@HMSNs and $CaO_2$@HMSNs-PAA.**

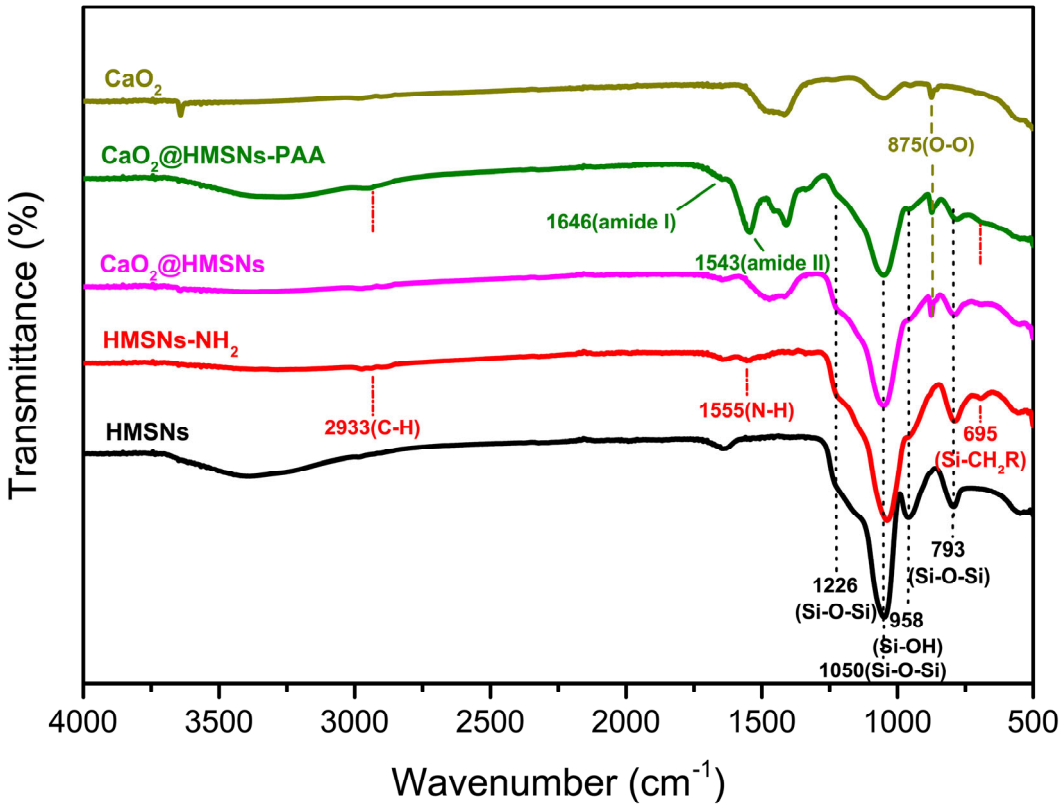


**Figure S5. Fourier transform infrared (FT-IR) spectra of HMSNs, HMSNs-$NH_2$, $CaO_2$, $CaO_2$@HMSNs and $CaO_2$@HMSNs-PAA.**

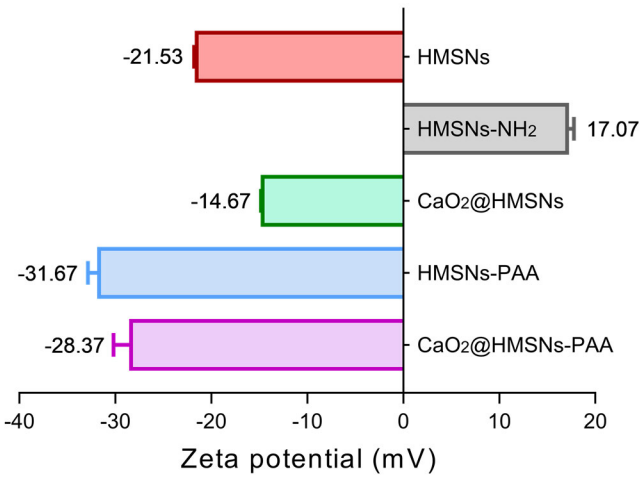


**Figure S6. Zeta potentials of HMSNs, HMSNs-$NH_2$, $CaO_2$@HMSNs, HMSNs-PAA and $CaO_2$@HMSNs-PAA dispersed in ethanol.**

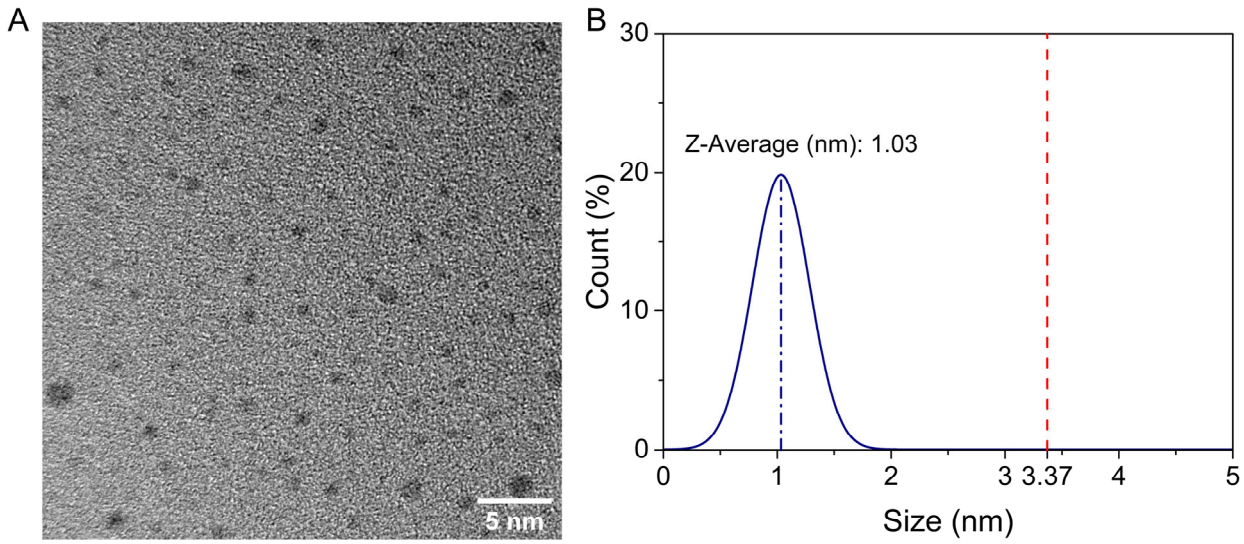


**Figure S7. Transmission electron microscopy (TEM) image and particle size distribution of $CaO_2$ particles.** (**A**) TEM image of $CaO_2$ particles. Scale bar, 5 nm. (**B**) Particle size distribution of $CaO_2$ particles. The red dash line indicates the average pore size of HMSNs (about 3.37 nm).

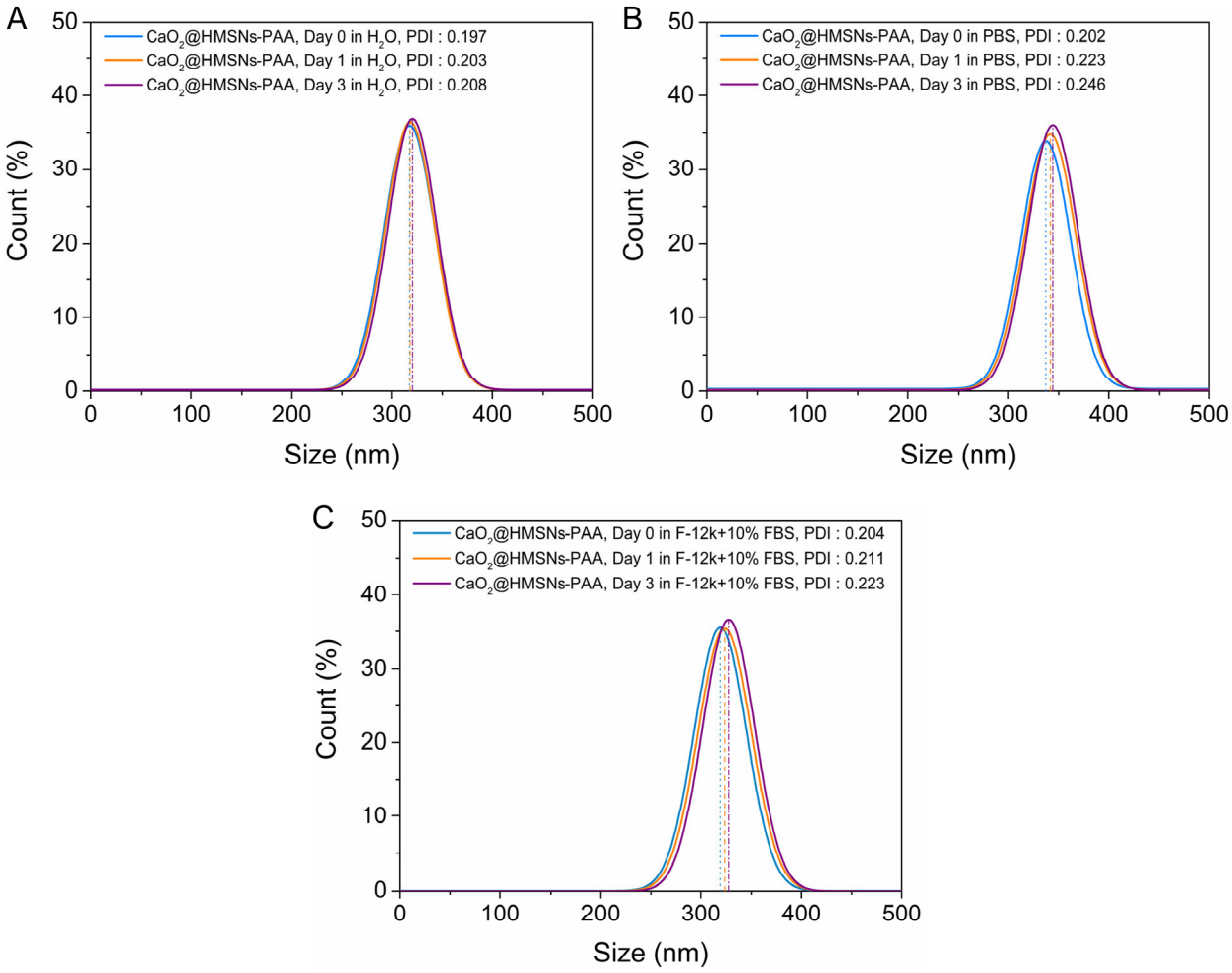


**Figure S8. Dispersibility and stability of $CaO_2$@HMSNs-PAA in various buffers.** Dynamic light scattering (DLS) particle size distributions and polydispersity indexes (PDI) of $CaO_2$@HMSNs-PAA in $H_2O$ (**A**), phosphate-buffered saline (PBS) (**B**) and F-12K medium + 10% fetal bovine serum (FBS) (**C**) on day 0, day 1 and day 3.

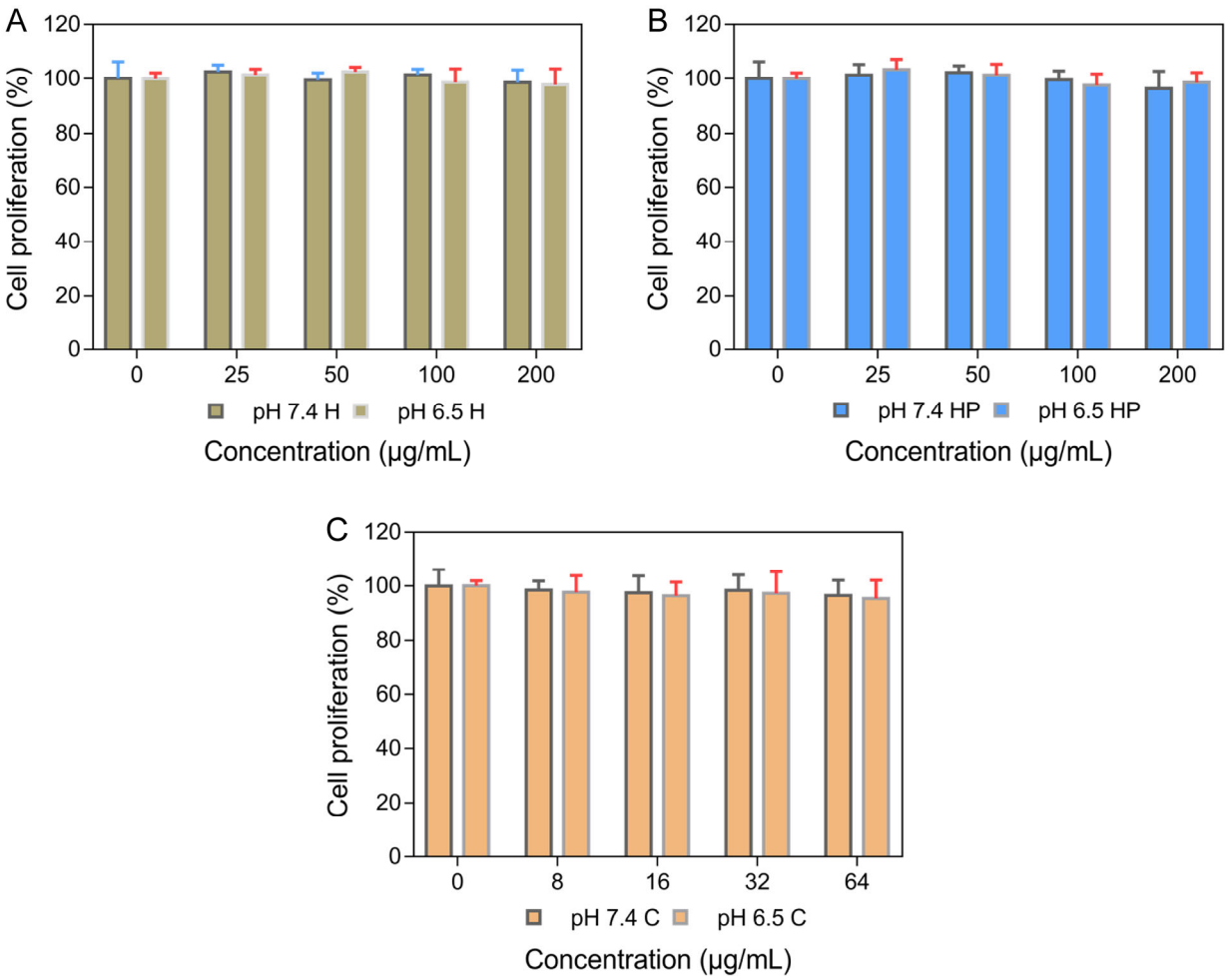


**Figure S9. *In vitro* cytotoxicities of HMSNs, HMSNs-PAA and $CaO_2$ against PC-3 cells.** Cell proliferation rates after incubation with HMSNs (**A**), HMSNs-PAA (**B**) and $CaO_2$ (**C**). Data are presented as the mean ± SD ($n = 5$, $p > 0.05$).

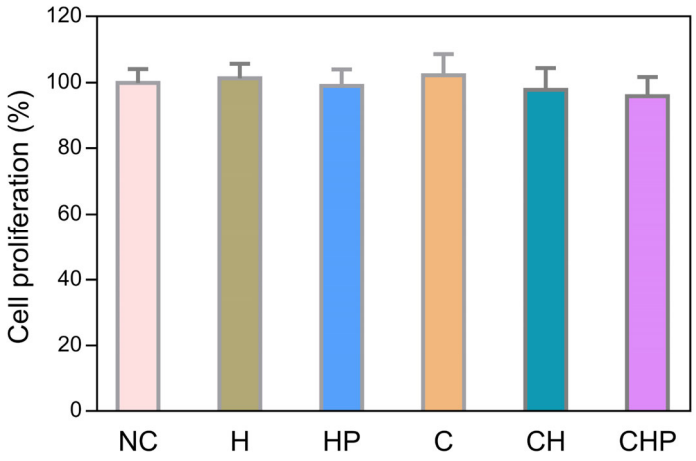


**Figure S10. *In vitro* cytotoxicities of HMSNs, HMSNs-PAA, $CaO_2$, $CaO_2$@HMSNs and $CaO_2$@HMSNs-PAA against RWPE-1 cells under the simulated physiological condition.** NC, negative control; H, HMSNs; HP, HMSNs-PAA; C, $CaO_2$; CH, $CaO_2$@HMSNs; CHP, $CaO_2$@HMSNs-PAA. Data are presented as the mean ± SD (n = 5, $p > 0.05$).

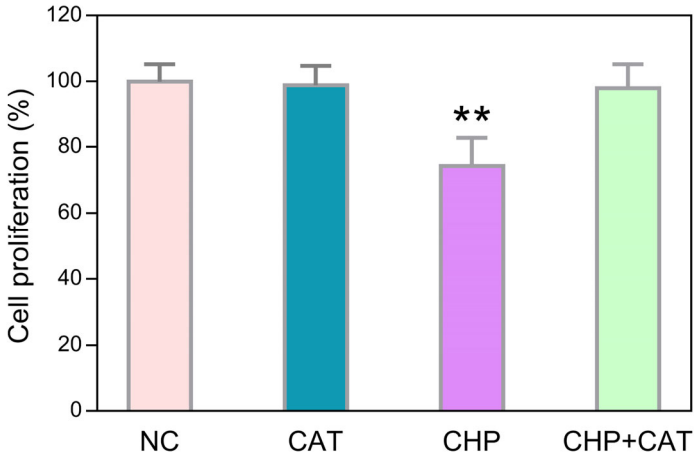


**Figure S11. *In vitro* cytotoxicity of $CaO_2$@HMSNs-PAA plus with catalase against PC-3 cells.** NC, negative control; CAT, catalase; CHP, $CaO_2$@HMSNs-PAA. Data are presented as the mean ± SD (n = 5; **, $p < 0.01$, *vs.* the NC group, the CAT group and the CHP+CAT group).

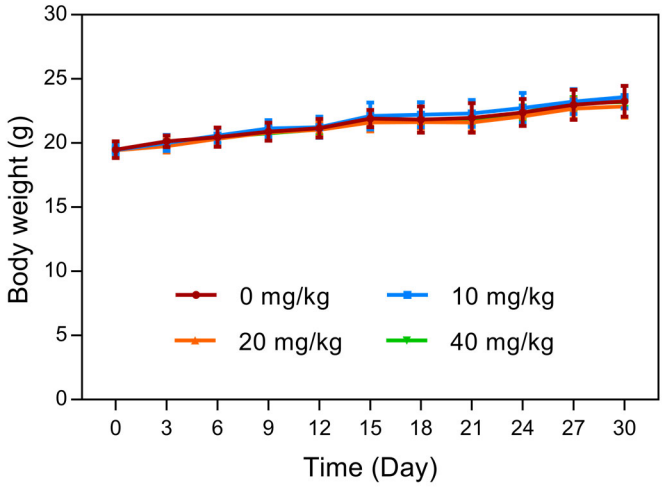


**Figure S12. Body weights of BALB/c mice recorded during the measurement period of 30 days after intravenous administration of $CaO_2$@HMSNs-PAA with doses of 0 mg/kg, 10 mg/kg, 20 mg/kg and 40 mg/kg.** Data are presented as the mean ± SD (n = 5, $p > 0.05$).

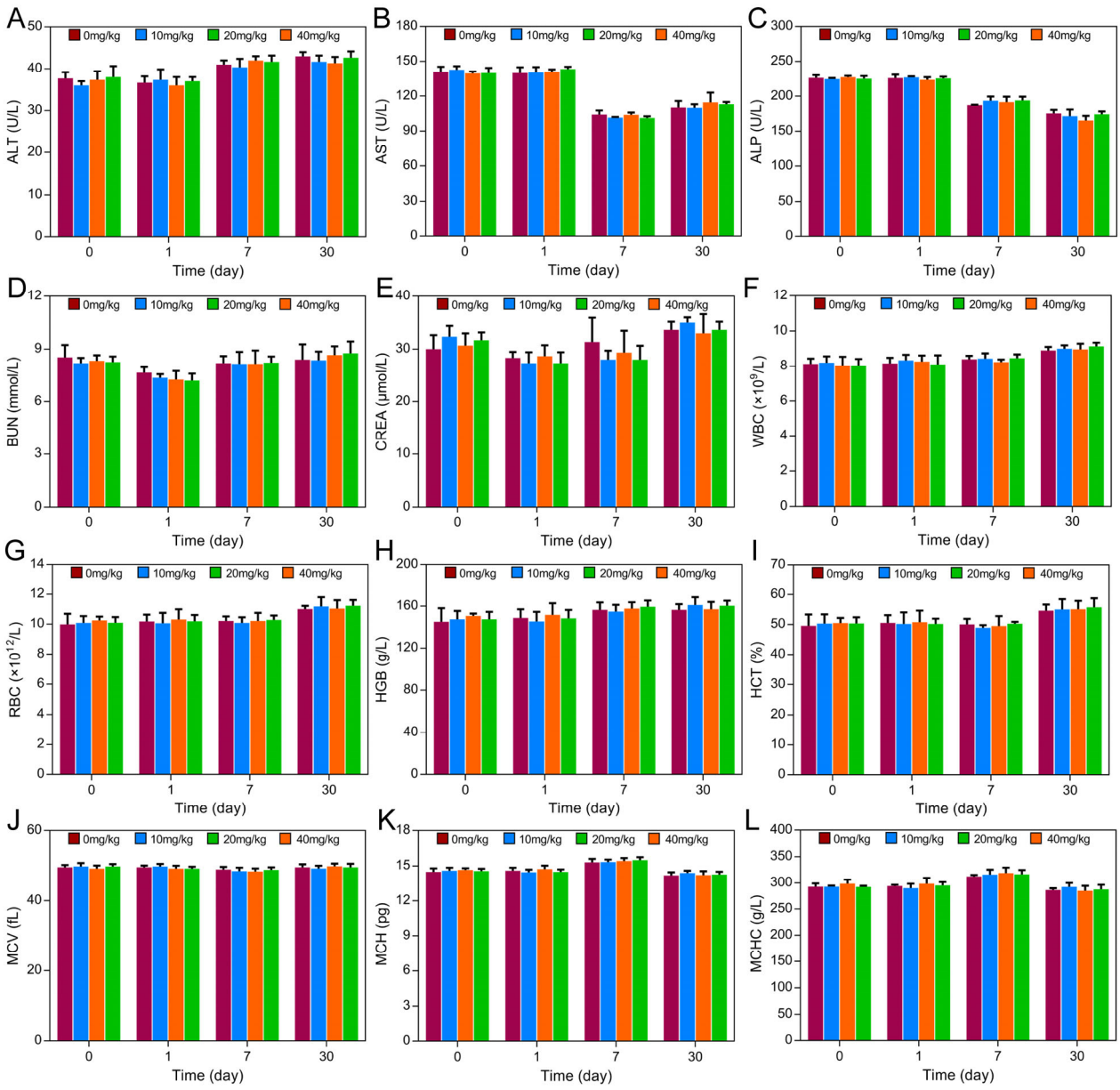


**Figure S13. Liver function, renal function and blood panel parameters of BALB/c mice recorded on day 0, day 1, day 7 and day 30 after intravenous administration of $CaO_2$@HMSNs-PAA with doses of 0 mg/kg, 10 mg/kg, 20 mg/kg and 40 mg/kg.** ALT (**A**), alanine aminotransferase; AST (**B**), aspartate aminotransferase; ALP (**C**), alkaline phosphatase; BUN (**D**), blood urea nitrogen; CREA (**E**), creatinine; WBC (**F**), white blood cells; RBC (**G**), red blood cells; HGB (**H**), hemoglobin; HCT (**I**), hematocrit; MCV (**J**), mean corpuscular volume; MCH (**K**), mean corpuscular hemoglobin; MCHC (**L**), mean corpuscular hemoglobin concentration. Data are presented as the mean ± SD (n = 3, $p > 0.05$).

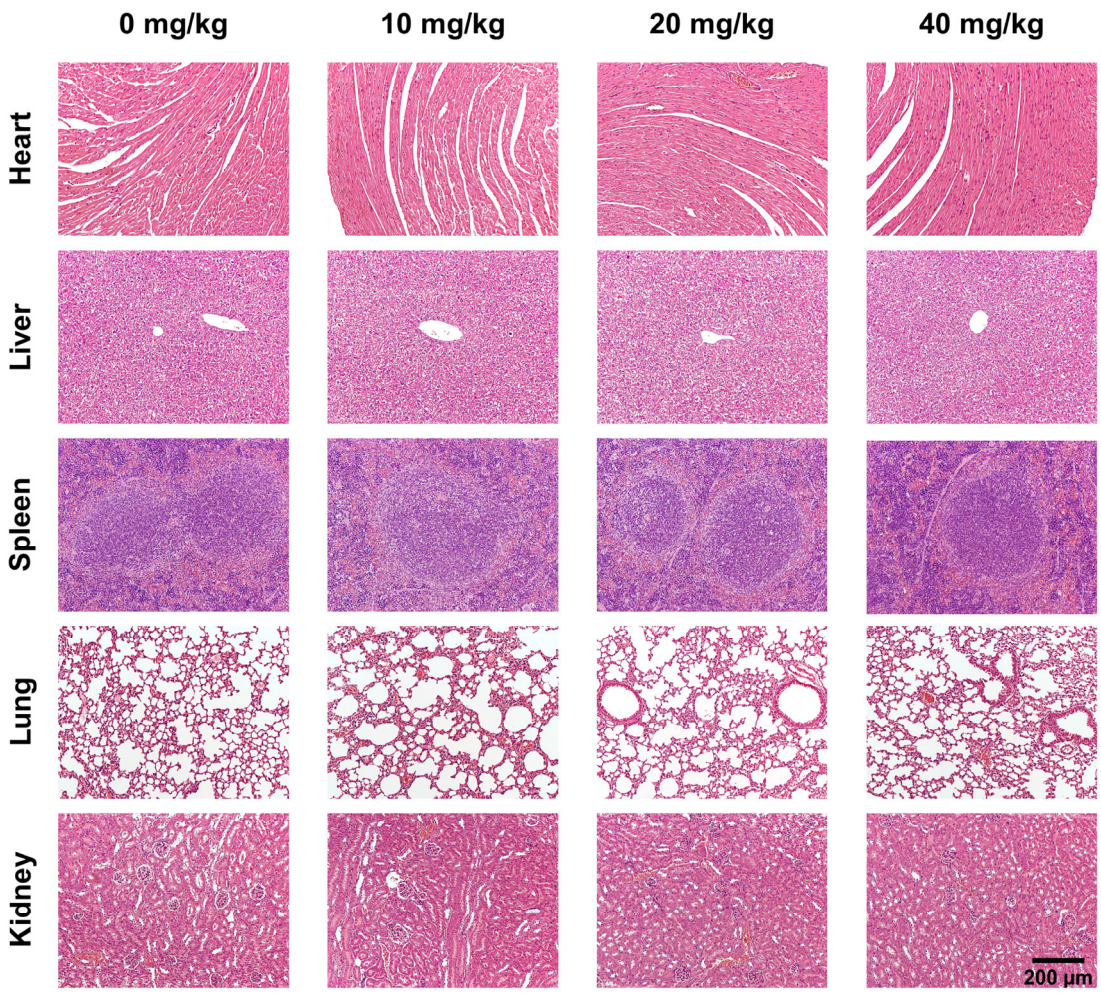


**Figure S14. Hematoxylin and eosin (H&E) stained sections of major organs (the heart, liver, spleen, lung and kidney) from BALB/c mice before intravenous administration of $CaO_2$@HMSNs-PAA (n = 3).** Scale bar, 200 μm.

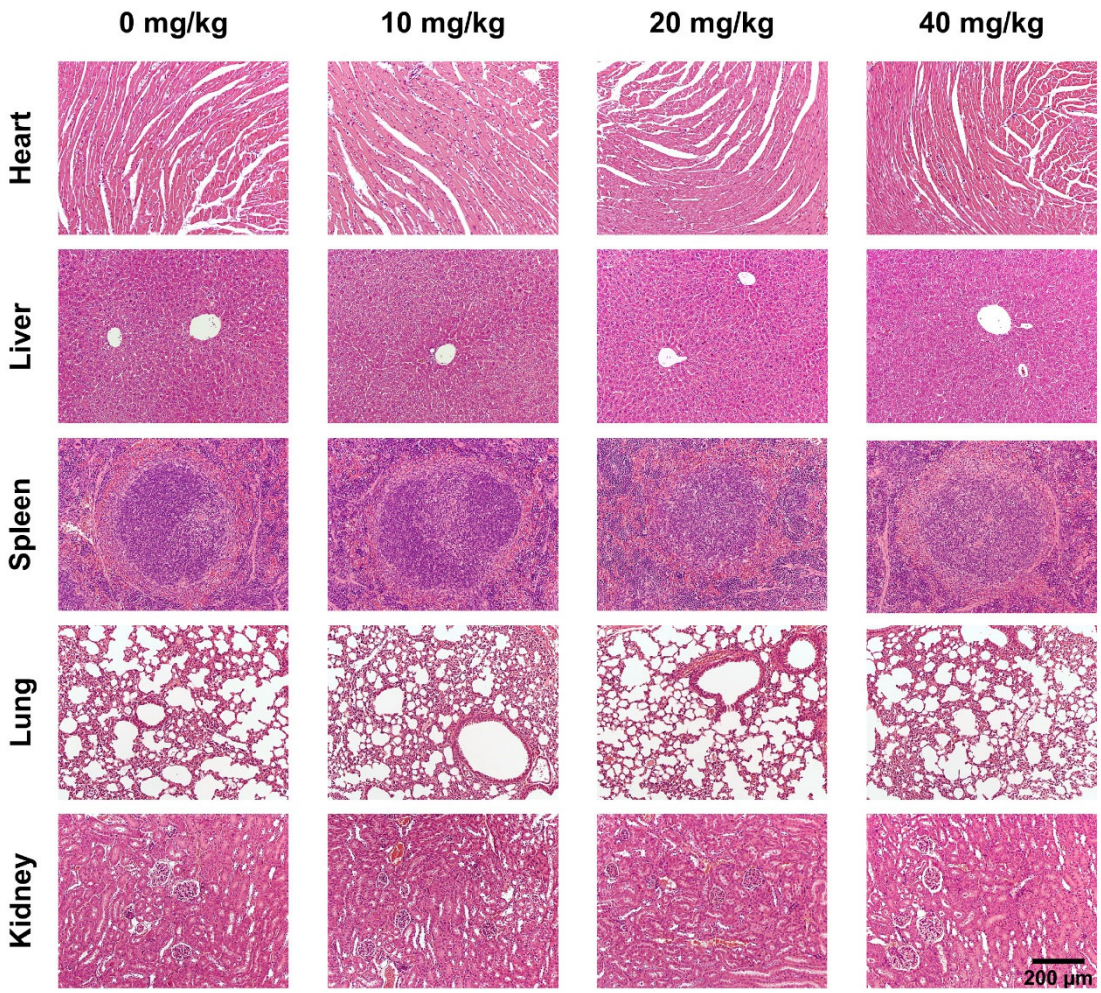


**Figure S15. Hematoxylin and eosin (H&E) stained sections of major organs (the heart, liver, spleen, lung and kidney) from BALB/c mice on day 1 after intravenous administration of $CaO_2$@HMSNs-PAA with doses of 0 mg/kg, 10 mg/kg, 20 mg/kg and 40 m/kg (n = 3).** Scale bar, 200 μm.

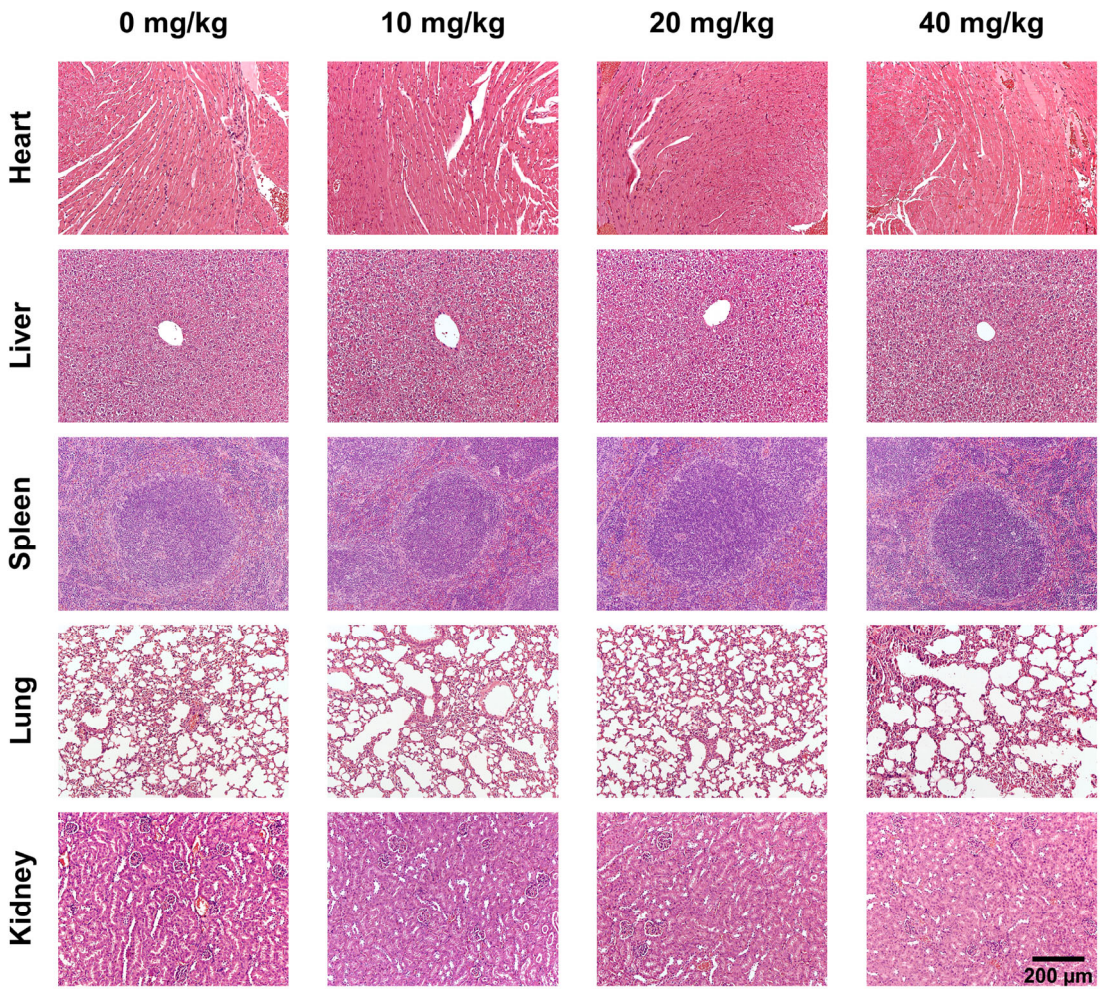


**Figure S16. Hematoxylin and eosin (H&E) stained sections of major organs (the heart, liver, spleen, lung and kidney) from BALB/c mice on day 7 after intravenous administration of $CaO_2$@HMSNs-PAA with doses of 0 mg/kg, 10 mg/kg, 20 mg/kg and 40 m/kg (n = 3).** Scale bar, 200 μm.

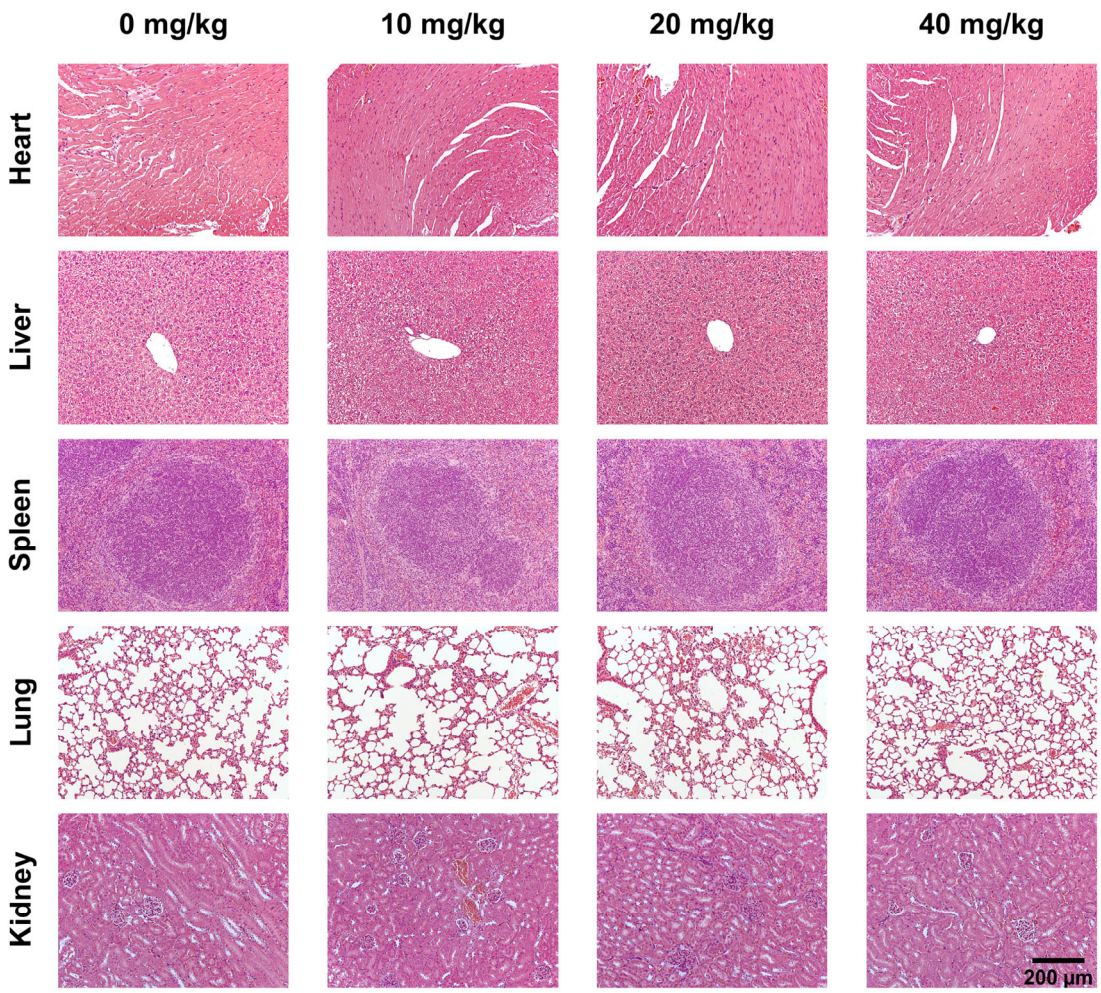


**Figure S17. Hematoxylin and eosin (H&E) stained sections of major organs (the heart, liver, spleen, lung and kidney) from BALB/c mice on day 30 after intravenous administration of $CaO_2$@HMSNs-PAA with doses of 0 mg/kg, 10 mg/kg, 20 mg/kg and 40 m/kg (n = 3).** Scale bar, 200 μm.

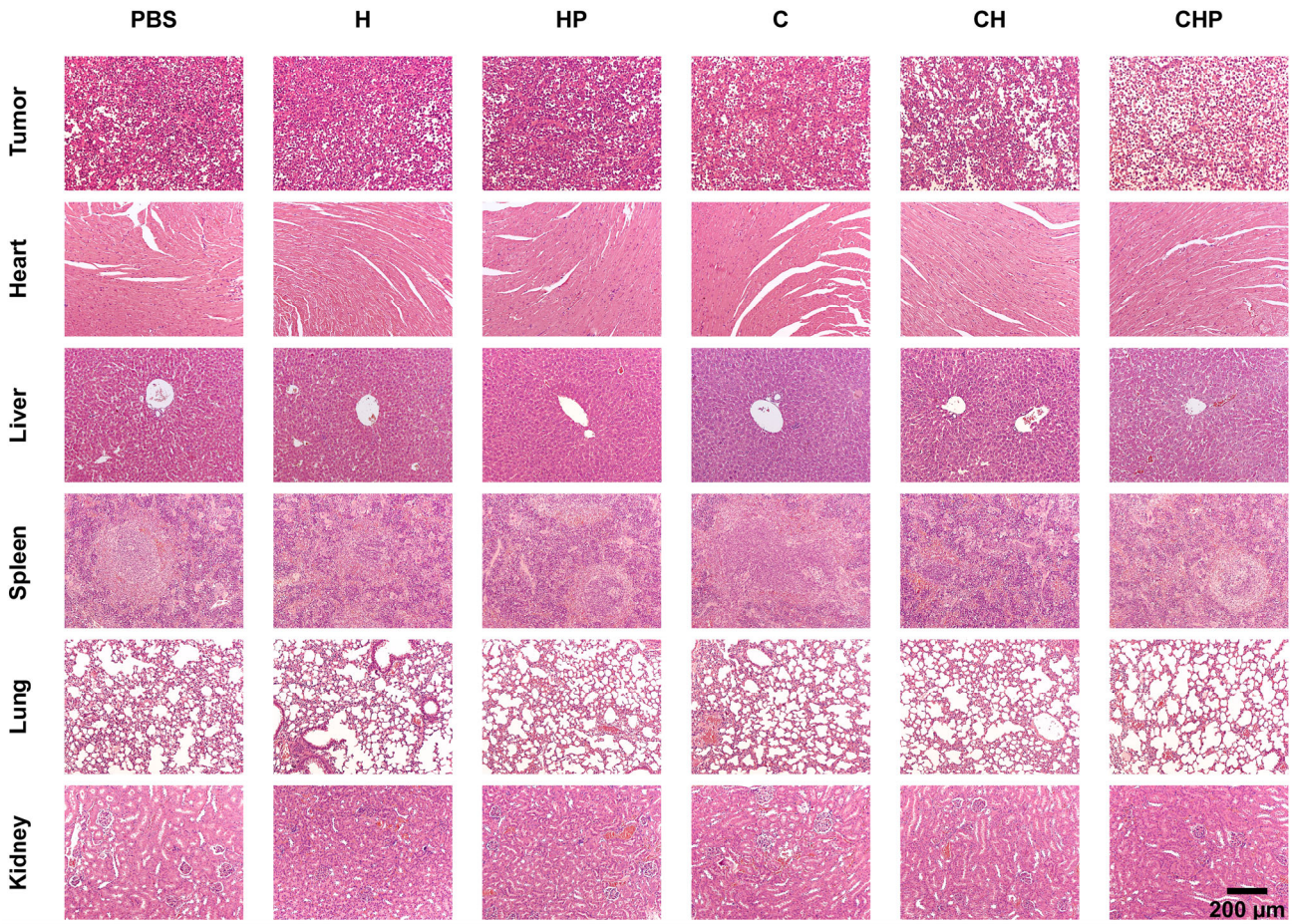


**Figure S18. Histological changes of the PC-3 xenografted tumors and major organs after intravenous administration of $CaO_2$@HMSNs-PAA.** Hematoxylin and eosin (H&E) stained sections of the tumors and major organs (the heart, liver, spleen, lung and kidney) from subcutaneous PC-3 xenografted tumor-bearing BALB/c nude mice on day 14 after intravenous administration of phosphate-buffered saline (PBS), HMSNs (H), HMSNs-PAA (HP), $CaO_2$ (C), $CaO_2$@HMSNs (CH) and $CaO_2$@HMSNs-PAA (CHP) (n = 5). Scale bar, 200 μm.

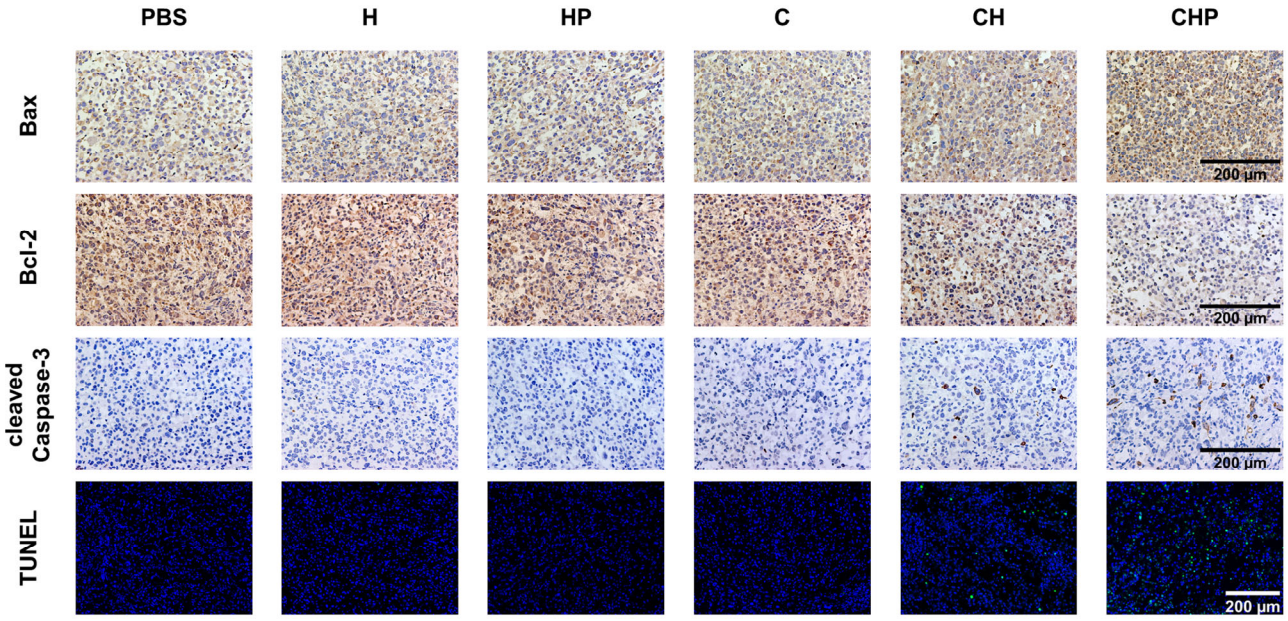


**Figure S19. Immunohistochemical and TUNEL analysis of the PC-3 xenografted tumors after intravenous administration of $CaO_2$@HMSNs-PAA.** Immunohistochemically stained images of the antigens (Bax, Bcl-2 and cleaved Caspase-3) and TUNEL analysis in the tumors from subcutaneous PC-3 xenografted tumor-bearing BALB/c nude mice on day 2 after intravenous administration of phosphate-buffered saline (PBS), HMSNs (H), HMSNs-PAA (HP), $CaO_2$ (C), $CaO_2$@HMSNs (CH) and $CaO_2$@HMSNs-PAA (CHP) (n = 3). Scale bars, 200 μm.