Supporting Information

S1.1 Materials

Doxorubicin (DOX) was provided by Beijing Hua Feng United Technology Co., Ltd. PBS solution (10mmol/L, pH 7.2-7.4) was purchased from Beijing Zoman Biotechnology Co., Ltd. All aqueous solutions were prepared in deionized water. The pH value of PBS solution could be adjusted by adding HCl solution. Isopentyl acetate (PEA), 3-(trimethoxysilyl) propyl methacrylate (TPM), Ludox TM-40 sol (30nm colloidal silica; 40wt% in water) and potassium persulfate (KPS) were purchased from Sigma-Adlrich. Balb/c nude mice were purchased from the Experimental Animal Center of Shanghai (Shanghai, China).

S1.2 Characterizations

Transmission electron microscopy (TEM) image was acquired on a JEM-2100F electron microscopy. Scanning electron microscope (SEM) image was obtained on HITACHI S-4800 microscopy. Hydrodynamic particle size was obtained by Zetasizer (Malvern, Nano-ZS90). The thermo-gravimetric analysis (TGA) profile was obtained by NETZSCH STA 449C. UV-vis spectrum was recorded on a UV-3101PC shimadzu spectroscope. The nitrogen adsorption-desorption curve was obtained on a Micrometitics Tristar 3000 system. The Brunauer- Emmett-Teller (BET) method was used to calculate the specific surface area. The ^{29}Si one pulse experiments were performed on a Bruker AVANCE III 400WB spectrometer operating at 79.49MHz for ^{29}Si. A recycle delay of 100s was used to ensure the complete relaxation. A 4mm double resonance MAS probe was used for the experiments. The spinning rate was set to 8kHz. The ^{29}Si chemical shifts were calibrated using SiO_2 (δ =-90 ppm).

S1.3 Cellular uptake

Cellular uptake of HMONs was investigated by Bio-TEM imaging. The PC3 cells were incubated in a 6-well plate at a density of 1×10^5/well for 4h, followed by the addition of 100μg/mL of HMONs in each well. Then, after being cultured for another 24h and collected by centrifugation at 1000rpm for 5min, the cells were fixed by 2.5% glutaraldehyde solution, and dehydrated with ethanol and propylene oxide. Samples were embedded in EPSM812 and polymerized in the oven at 37°C for 12h. After being cut by a diatome diamond knife, the images were observed.

S1.4 In vitro evaluation of chemo-therapeutic efficacy

The apoptotic effects of DOX and DOX-HMONs against PC3 cells were further confirmed by Annexin V-FITC detection kit. After co-incubation of PC3 cells and drugs for 48h, the sequential addition of annexin V-FITC and propidium iodide were conducted. The stained cells were incubated for 15min at room temperature and then were resuspended in 400μL of binding buffer. Finally, flow cytometer (Fac-santo; Beckton Dickinson, San Jose, CA, USA) analysis was carried out for each cell sample.

S1.5 In vivo long-term toxicity studies of HMONs

The blood parameters consisting of white blood cells (WBC), red blood cells (RBC), lymphocytes (LYM), hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), alkline phosphatase (AKP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN) and creatinine (CREA) were measured in JRDUN Biotechnology Co., Ltd.

Supplementary figure

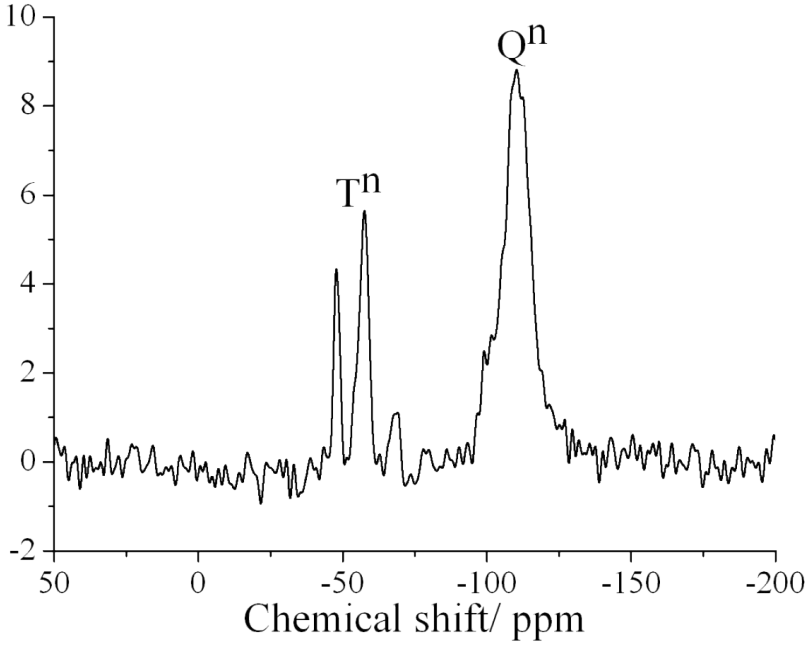

Fig.S1. Solid state ^{29}Si MAS NMR spectra of HMONs. The presence of T^n (T^n=$RSi(OH)_{3-n}(OSi)_n$, n=1, 2, 3; R represents the organic group bonded to Si atom) signal between -45~ -70 ppm confirms the formation of organosilica. Meanwhile, the presence of Q^n (Q^n=$SiO(OH)_{3-n}(SiO)_n$, n=1, 2, 3) signal between -95~-120 ppm confirms the existence of inorganic silica component, which is originated from the 30nm colloidal silica NPs in the precursor solution.

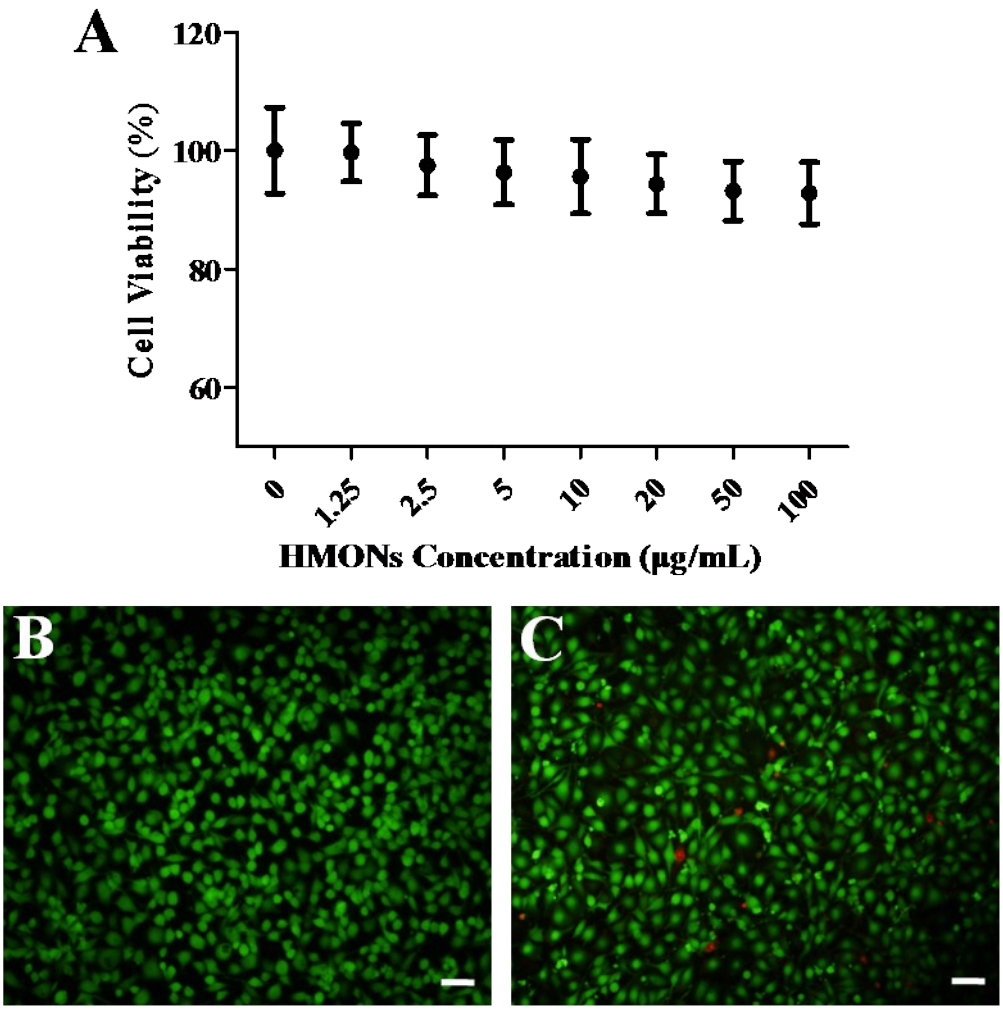

Fig.S2 Cell viabilities of PC3 cells after incubation for 24h with various concentrations of HMONs. (A) WST-8 assay result (*$p < 0.05$). (B, C) The fluorescence images of Calcein-AM/propidium iodide stained PC3 cells after co-incubation with (B) 0μg/mL HMONs and (C) 100μg/mL HMONs. Scale bars are 50μm for B and C.

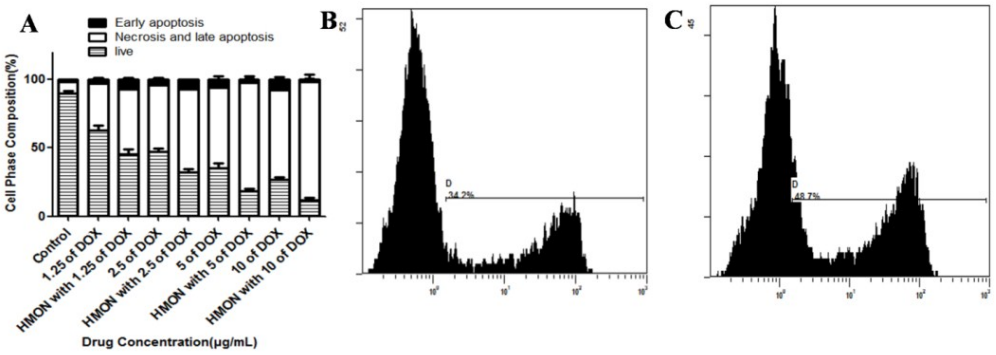

Fig.S3 (A) The phase composition percentage of PC3 cells after incubation with different concentrations of DOX and DOX-HMONs. Necrosis and late apoptosis of PC3 cells after incubation with (B) 2.5μg/mL DOX and (C) DOX-HMONs containing 1.25μg/mL DOX.

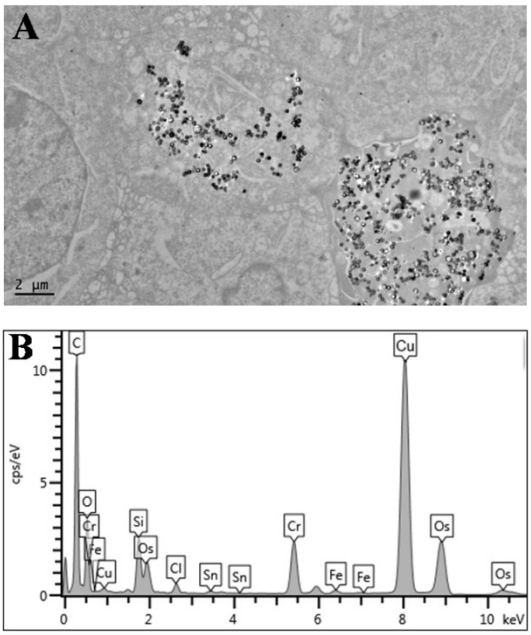

Fig.S4 (A) TEM images of PC3 cells treated with HMONs. (B) Energy-dispersive spectroscopy of the representative HMONs-contained region in PC3 cell. The scale bar is 2μm.

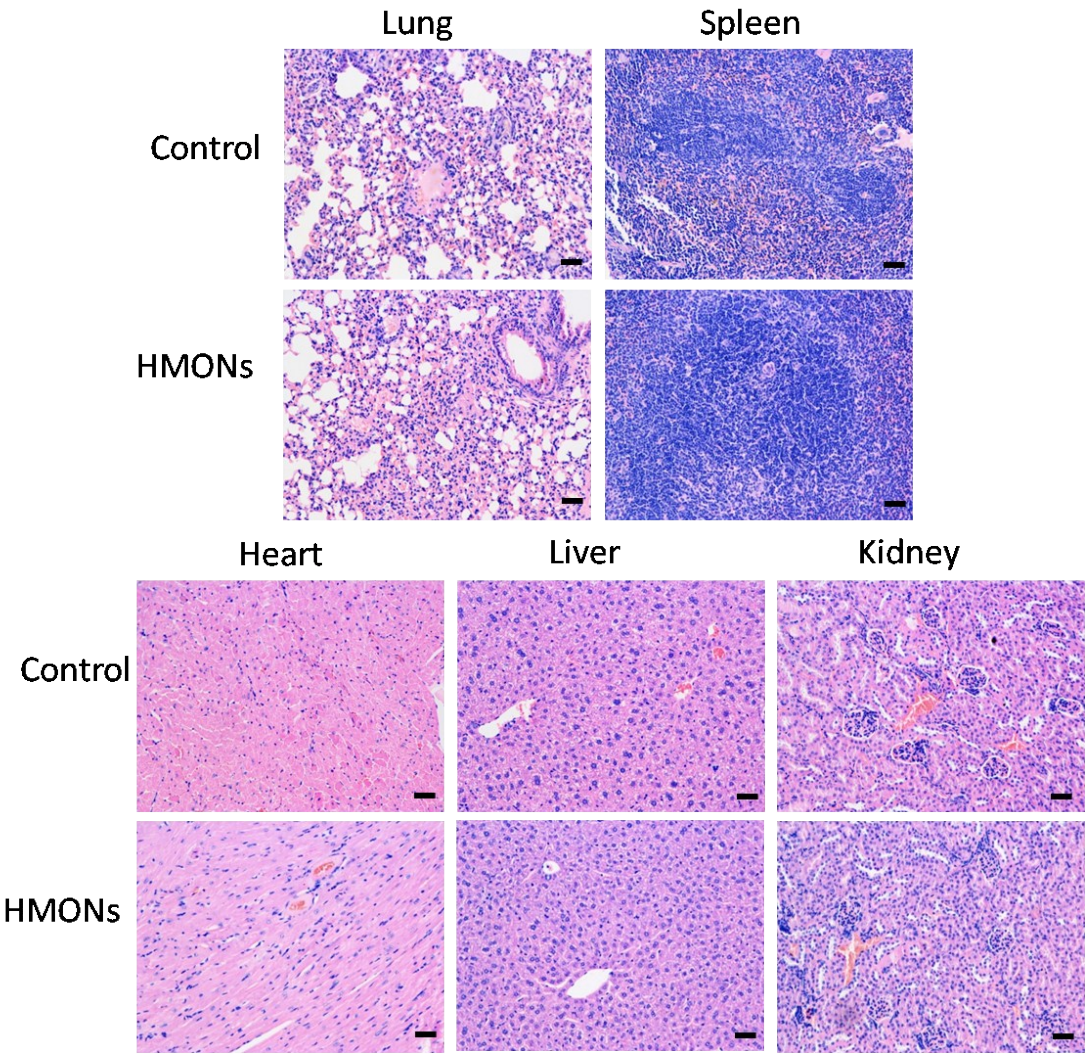

Fig.S5 H&E-stained tissue sections from tumor-bearing nude mice after injection of HMONs, and PBS. No obvious tissue damage and adverse effects were observed in the lung, spleen, heart, liver and kidneys of these groups. Magnification is 20×, Scale bar is 50μm.

Parameter	Saline	HMONs	Parameter	Saline	HMONs	Parameter	Saline	HMONs
AKP(IU/L)	219±11.02	227±4.72	WBC(10^9/L)	8.60±0.53	8.40±1.82	MCH(pg)	16.54±0.19	15.82±0.39
ALT(IU/L)	34.50±4.95	30.17±3.13	LYM(%)	54±0.42	54±3.85	MCV(fL)	55.44±0.62	53.34±1.02
AST(IU/L)	140±1.41	146±7.81	RBC(10^{12}/L)	8.95±0.35	8.86±0.67	RDW(%)	29.54±1.13	29.05±0.85
BUN(mmol/L)	9.40±0.31	8.77±0.24	HGB(g/L)	148±4.74	140±7.68	MCHC(g/L)	298±3.7	297±3.11
CERA(mmol/L)	9.78±0.92	9.53±1.16	HCT(%)	0.50±0.02	0.47±0.03			

Table S1 The blood biochemistry and complete blood panel profiles of HMONs, containing alkline phosphatase (AKP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), creatinine (CREA), white blood cells (WBC), lymphocytes (LYM), red blood cells (RBC), hemoglobin (HGB), hematocrit (HCT), mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV), red cell distribution width (RDW), and mean corpuscular hemoglobin concentration (MCHC).