Supplementary Information

Cytochrome C capped mesoporous silica nanocarriers for pH-sensitive and sustained drug release

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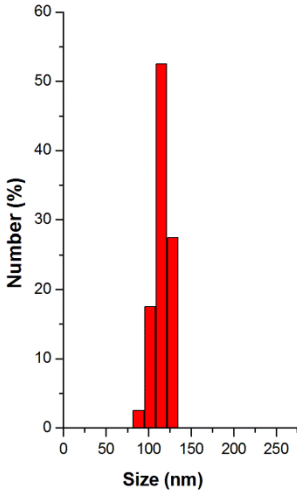

Figure S1. The size distribution of mesoporous silica nanoparticles (MSNs) by measuring about 100 particles.

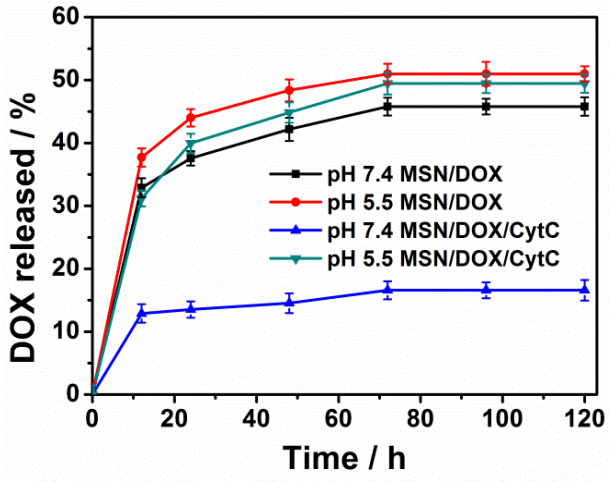

Figure S2. DOX release profiles from MSN/DOX and MSN/DOX/CytC at pH 7.4 and pH 5.5 within 120 h.

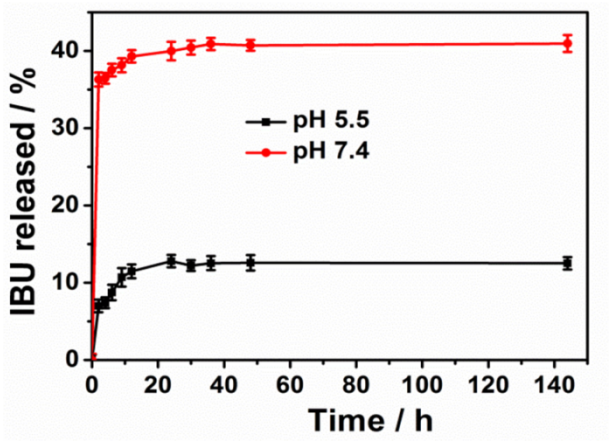

Figure S3. Ibuprofen (IBU) release profiles from MSN/IBU/CytC at pH 7.4 and pH 5.5 within 144 h. Experiments of IBU loading and release: 10 mg of MSNs and 5 mg of IBU were mixed within 10 mL n-hexane solution. The mixture was sealed to prevent evaporation of solvent and allowed to mix for 24 h at room temperature under stirring. Then, the obtained composites (MSN/IBU) were centrifuged at 10,000 g for 15 min and the n-hexane supernatant was removed. To remove surface adsorbed IBU, the MSN/IBU was further washed with 10 mL n-hexane and dried. Then, 5 mg of above-prepared MSN/IBU was mixed with 3 mL PBS containing 2 mg of CytC. The mixture was allowed to stand at room temperature for 24 h under dark conditions to construct cytochrome C capped nanocarriers. Then the suspension was centrifuged for 10 min at 12000 rpm and rinsed three times using PBS to remove the free CytC, resulting in MSN/IBU/CytC. The in vitro release of IBU was executed by soaking the obtained MSN/IBU/CytC in pH 5.5 and 7.4 buffer solutions. Typically, 2.5 mg MSN/IBU/CytC was immersed into 5 mL PBS buffer solution with slow stirring at 37 ^{o}C. Then, 0.2 mL of release medium was removed for analysis at given time intervals. The content of IBU was measured by UV/Vis spectroscopy at a wavelength of 222 nm.

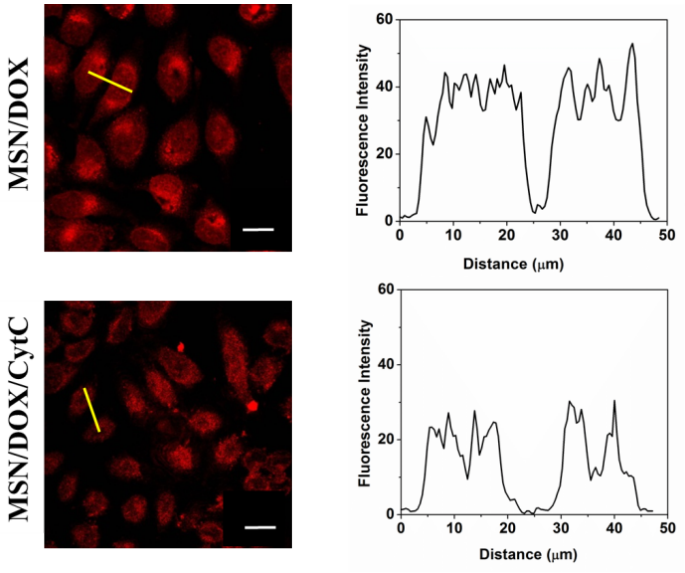

Figure S4. Fluorescence images and intensity profiles of MCF-7 cells incubated with MSN/DOX and MSN/DOX/CytC (DOX = 5 mg mL^{-1}) for 12 h (the red fluorescence is expressed by DOX). Yellow lines are located in cell nuclei, Scale bar: 20 μm.

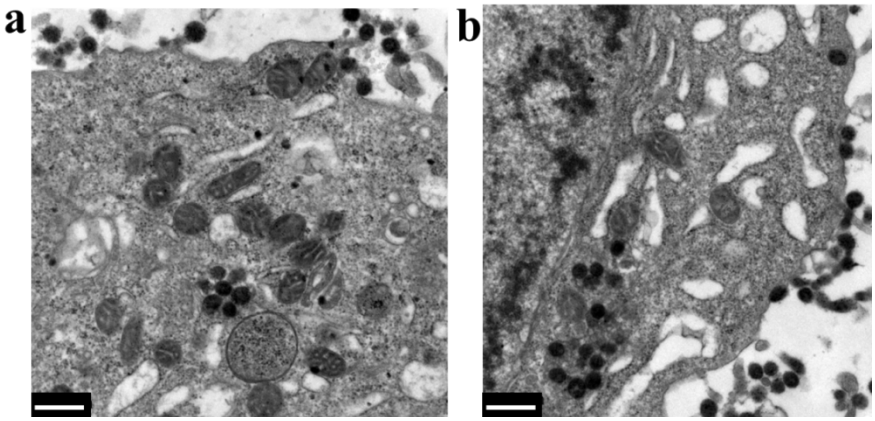

Figure S5. TEM images of MCF-7 cells incubated with (a) MSN/DOX and (b) MSN/DOX/CytC (MSN = 100 μg mL^{-1}) for 12 h. Scale bar: 0.5 μm.

Table S1. Statistical analyses of viabilities of cells treated with DOX/MSN/CytC and DOX/MSN for different time under various DOX concentrations.

Incubate time	DOX concentration (μg mL^{-1})	*P-values*
12 h	0.5	0.043
12 h	1.0	0.005
12 h	2.0	0.035
12 h	4.0	0.002
12 h	8.0	0.000
24 h	0.5	0.006
24 h	1.0	0.000
24h	2.0	0.006
24 h	4.0	0.000
24 h	8.0	0.000