

Electronic Supplementary Information

One-step approach to synthesize hollow mesoporous silica spheres co-templated by amphiphilic block copolymer and cationic surfactant

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Experimental

Synthesis of PS₂₁₅-*b*-PAA₁₂ and monodisperse magnetite nanoparticles:

Monodisperse 5 nm sized Fe₃O₄ nanoparticles were prepared following the method from the literature protocol by Sun et al¹. Amphiphilic block copolymer, polystyrene₂₁₅-*b*-poly (acrylic acid)₁₂ (PS₂₁₅-*b*-PAA₁₂) was synthesized *via* reversible addition-fragmentation chain-transfer polymerization (RAFT) as previously reported².

Synthesis of HMSSs: 0.05 g of PS₂₁₅-*b*-PAA₁₂ was dissolved in 10 ml THF, and then poured into a mixture solution containing 40 ml of H₂O, 0.05g of CTAB and 1.5 ml of ammonia. After stirring for 10 min, the mixture solution was diluted in 80 ml of ethanol. Then, 0.3g of TEOS dissolved in 5 ml of ethanol was added to the solution with continuous stirring in 30 minutes. After reaction for 18 h at room temperature, the product was collected by centrifugation (10,000 r/min, 10 min), dried in the air, and calcined at 550 °C for 6 h for surfactant removal. Finally, the HMSSs were produced.

Synthesis of Fe₃O₄@HMSSs: 0.05g of PS₂₁₅-*b*-PAA₁₂ was dissolved in 10 ml THF and 2 ml of Fe₃O₄ (10 mg/ml in THF) was added into the oil solution. Then it poured into a mixture solution containing 40 ml of H₂O, 0.05g of CTAB and 1.5 ml of ammonia. After stirring for 10 min, the mixture solution was diluted in 80 ml of ethanol. Then, 0.3g of TEOS dissolved in 5 ml of ethanol was added to the solution with continuous stirring in 30 minutes. After reaction for 18 h at room temperature,

the product was collected by centrifugation (10,000 r/min, 10 min), dried in the air and calcined at 550°C for 6 h for surfactant removal. Finally, the Fe₃O₄@HMSSs was obtained.

Doxorubicin hydrochloride (DOX) Adsorption and Release: A 2mg/ml of Doxorubicin hydrochloride (DOX)-phosphate buffer solution (PBS) solution was prepared at 40°C water baker. Then, 25 mg of Fe₃O₄@HMSSs was added into 25 ml of DOX-PBS. The mixture was stirred for one day. The solid materials were separated from the solution and dried at 60°C in vacuum for a night. For release study, respectively, 15 mg of the sample were re-suspended in two 4 ml PBS (pH 7.4 and pH 4.4) and transferred into a dialysis bag (Mw cut-off: 3500Da). The tubing was placed into 36ml PBS (pH 7.4 and pH 4.4), respectively. Release study was performed at 37 °C shaken at 100 rpm. At selected time intervals, buffered solution outside the dialysis bag was collected for UV-Vis analysis and return immediately after the measurement. The sample was analyzed for the DOX concentration by using UV-VIS spectrophotometer at a wavelength of 480nm. To evaluate the DOX-loading efficiency, the supernatant and washed solutions were collected and the residual DOX content (R_{DOX}) was obtained by UV measurements at a wavelength of 480 nm. The loading content (LC%) of DOX can be calculated as follows:

$$LC\% = [(O_{DOX} - R_{DOX}) / W_{HMSSs}] \times 100\%$$
, in which O_{DOX} is the original DOX content, W_{HMSSs} is the amount of HMSSs.

In vitro MR imaging: The *in vitro* MR imaging experiment was performed on a 3.0 T clinical MRI instrument (GE Signa HDx 3.0 T). For the T2-weighted Fast-recovery fast spin-echo (FR-FSE) sequence, the following parameters were adopted: TR (repetition time) = 2000 ms, TE (echotime) = 107.1 ms, Field of view (FOV) = 14 ms, slice thickness = 2 mm, echo length = 16, matrix = 256*192, number of acquisitions = 4. For MRI tests, the Fe content of the Fe₃O₄@HMSS in water was determined by inductively coupled plasma atomic emission spectrometry (ICP-AES) after dissolving the samples in a mixture of HNO₃/HClO₄ at 150 °C.

For *r*₂ relaxivity measurement, the T₂ relaxation time was performed with the following parameters: TR = 4000 ms, TE = 13, 26, 39 and 52 ms. Relaxivity values of

r_2 were calculated through the curve fitting of $1/T_2$ relaxation time (s^{-1}) versus the Fe concentration (mM).

Characterization: The XRD pattern of prepared powder sample was collected using a BRUKER-AXS diffractometer (Bruker, Germany) with Cu target (40 KV, 40 mA). TEM (Transmission Electron Microscopy) analysis was conducted on a JEM 2100F electron microscope operated at 200 KV. N_2 adsorption and desorption isotherms were measured using Quantachrome NOVA 4200e. The specific surface area and pore size distribution were calculated by using the Brunauer-Emmett-Teller (BET) and Barrett-Joyner-Halenda (BJH) methods, respectively. An UV-Vis absorbance spectrophotometer (Shimadzu 2550) was used to determine the concentration of DOX in the supernatant solution at 480 nm.

1. S. Sun, H. Zeng, D. B. Robinson, S. Raoux, P. M. Rice, S. X. Wang and G. Li, *J Am Chem Soc.*, 2004, 126, 273-279.
2. Y. Kang and T. A. Taton, *Angew. Chem.*, 2005, 117, 413-416.

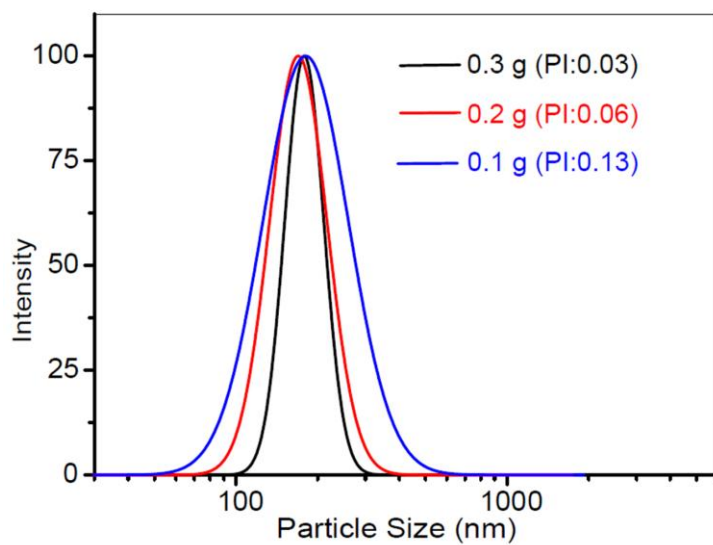


Figure S1. Diameter distribution curves of HMSSs with shell thickness of 25 nm in aqueous solution by dynamic light scattering technique.

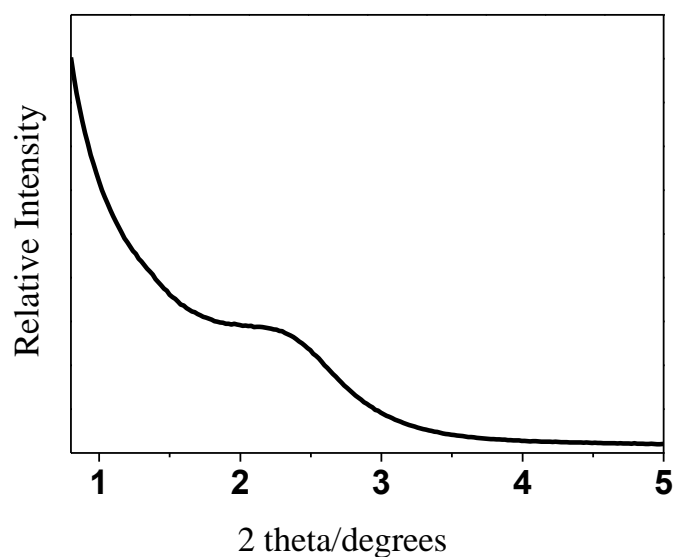


Figure S2. Low angle XRD pattern of HMSSs with shell thickness of 25 nm.

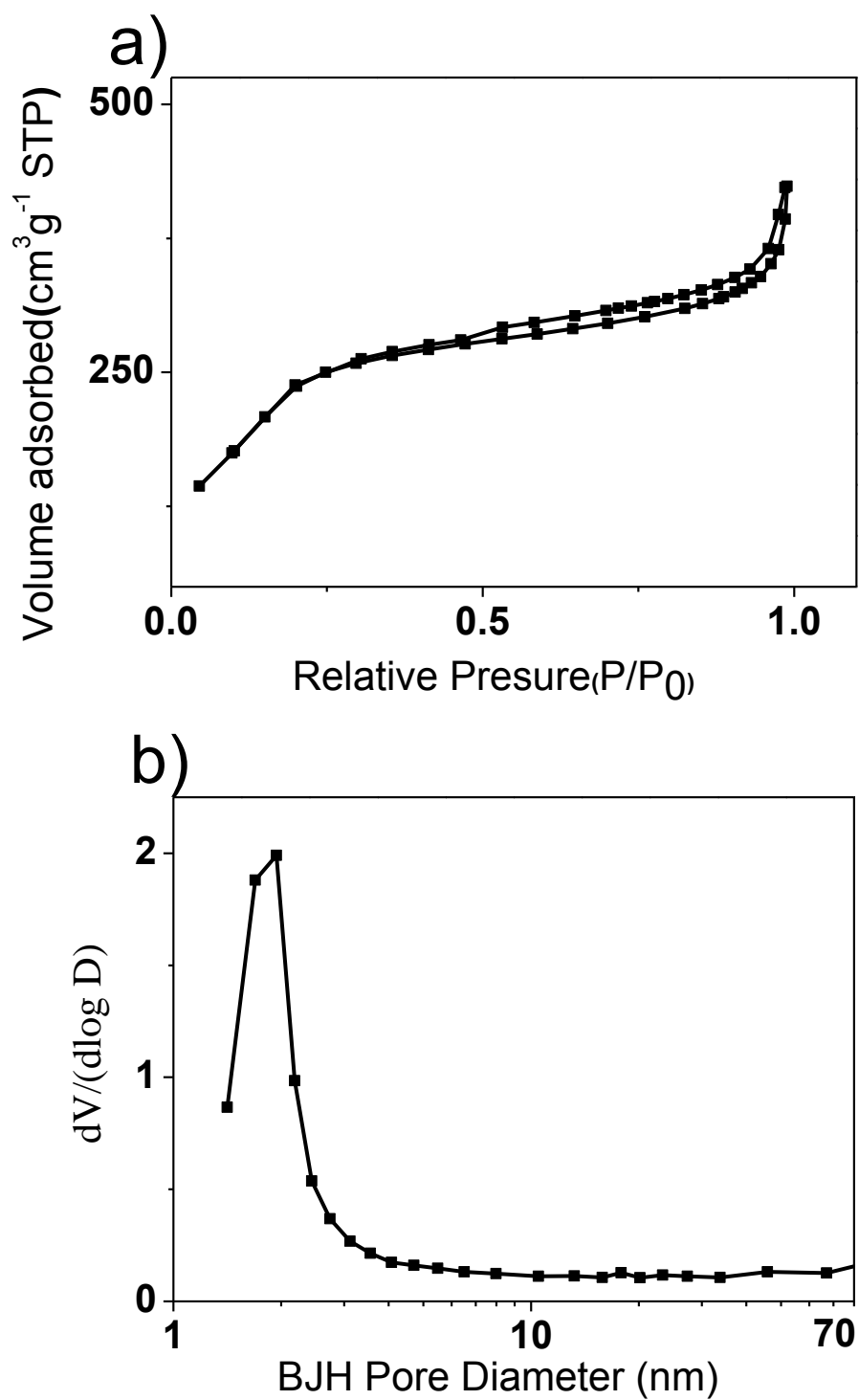


Figure S3 Nitrogen adsorption- isotherm (a) and the pore size distribution curve (b) of HMSSs with shell thickness of 25 nm.

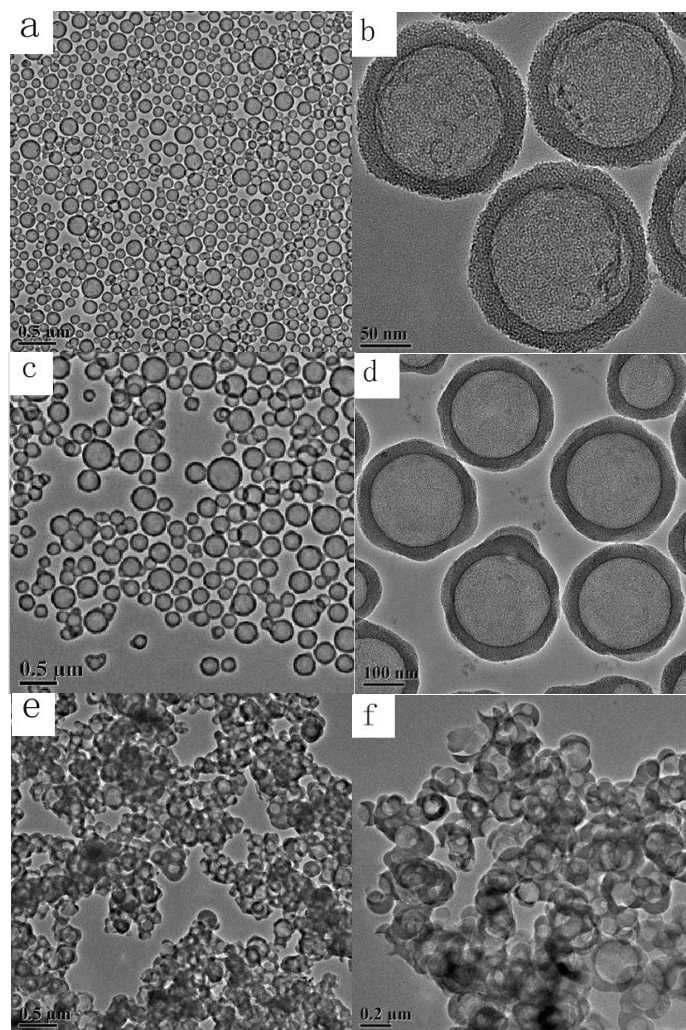


Figure S4 TEM images of HMSSs prepared with different amounts of CTAB: a, b) 50 mg; c, d) 100 mg; e, f) 200 mg, respectively.

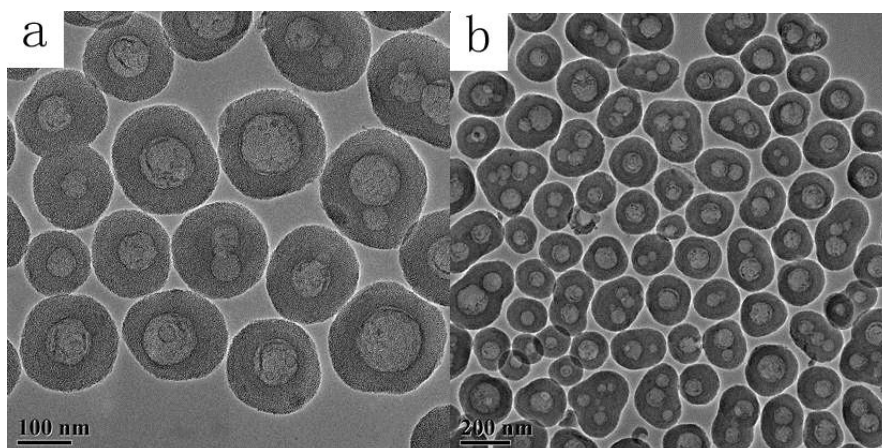


Figure S5 TEM images of HMSSs prepared with 10 mg of PS₂₁₅-*b*-PAA₁₂, while keep other experimental parameters unchanged.

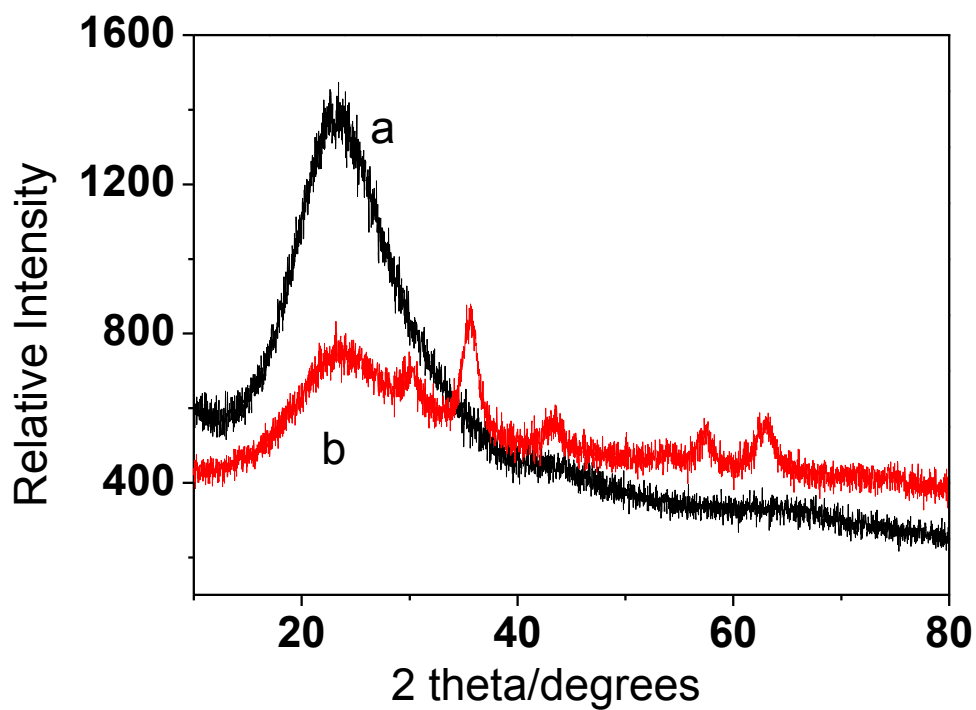


Figure S6 Wide angle XRD patterns of a) HMSSs and b) Fe₃O₄@HMSSs.

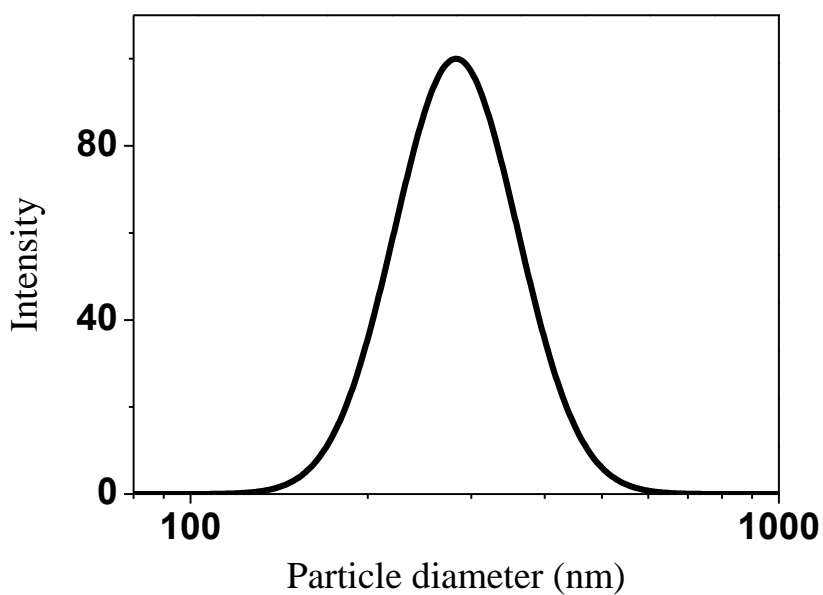


Figure S7 Diameter distribution curves of Fe₃O₄@HMSSs nanocomposite in aqueous solution by dynamic light scattering technique.

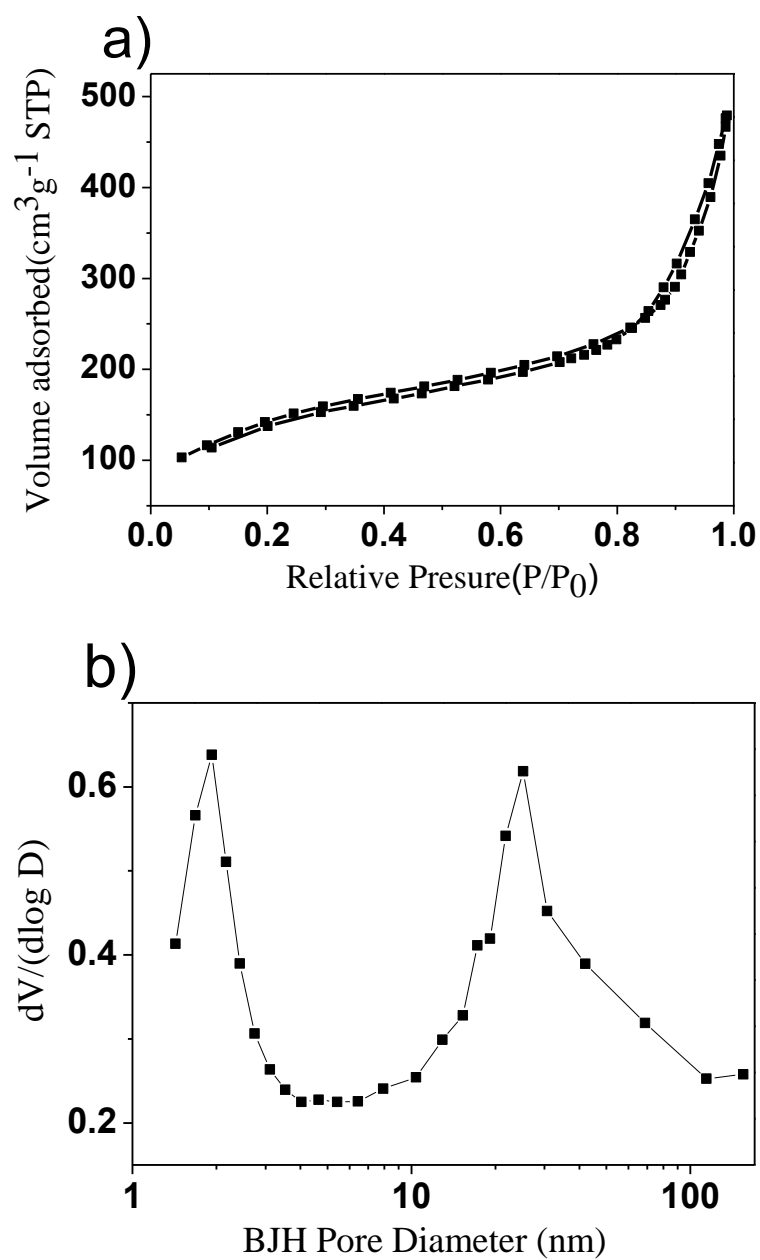


Figure S8 Nitrogen adsorption-isotherm (a) and the BJH pore size distribution curve (b) of Fe₃O₄@HMSSs.

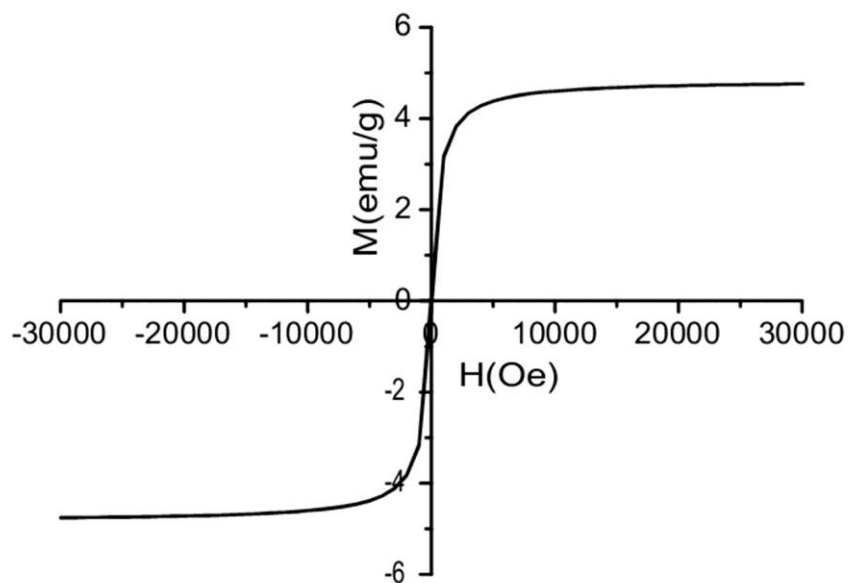


Figure S9 Field-dependent hysteresis loop at 300K of $\text{Fe}_3\text{O}_4@$ HMSSs.

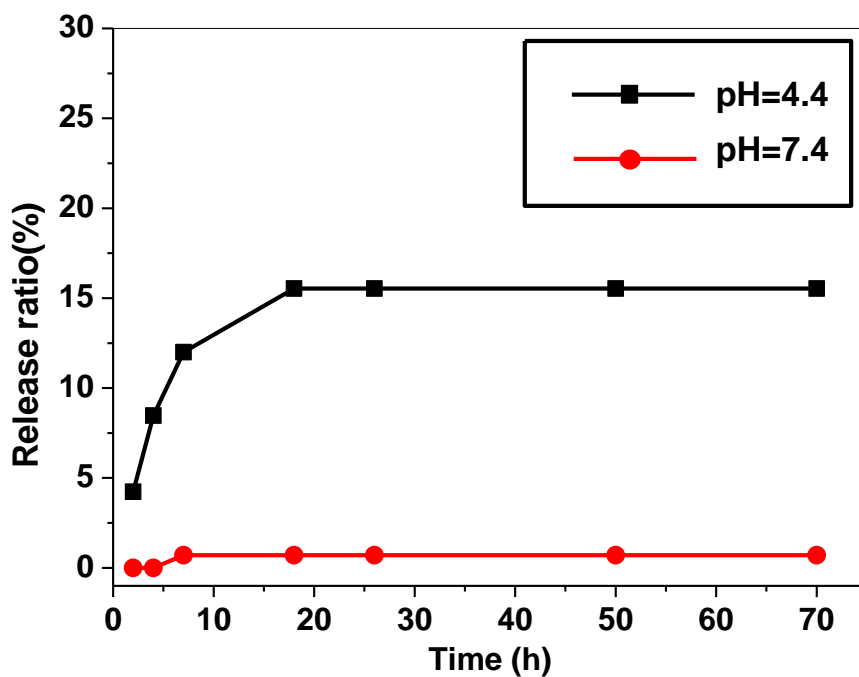


Figure S10 Release profile of DOX from DOX-loaded $\text{Fe}_3\text{O}_4@$ HMSS in PBS (pH 7.4 and pH 4.4) at 37°C.