Electronic Supplementary Information (ESI)

Iron Oxide – Loaded Hollow Mesoporous Silica Nanocapsules for Controlled Drug Release and Hyperthermia

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Experimental Procedures:

Synthesis of iron oxide – loaded hollow mesoporous silica nanocapsules:

Iron oxide nanoparticles (IONPs) with an average diameter of 12 nm were prepared according to a previously reported method with some modifications.[1] In a typical synthesis, 8.00 g of $FeCl_3 \cdot 6H_2O$ and 3.27 g of $FeCl_2 \cdot 4H_2O$ were dissolved in 33.3 mL deionized water under nitrogen gas protection. The reaction mixture was heated to 80 ^oC, afterwards, 16.7 ml of concentrated ammonium hydroxide was added rapidly into the reaction mixture. The reaction mixture was kept at 80 ^oC for an additional 30 min. The resulting iron oxide nanoparticles were separated from the solvent using an external magnet, and were subsequently washed two times with deionized water. The isolated magnetic nanoparticles were then redispersed in 370.0 mL deionized water, and 4.70 g oleic acid and 0.74 g sodium dodecyl benzene sulfonate (SDBS) were added to the nanoparticle suspension. The mixture was sonicated for 1 h to get obtain a homogeneous nanoparticle suspension. The polymer coated iron oxide nanoparticles were prepared by an emulsion polymerization process. A 20-mL portion of the iron oxide nanoparticle suspension was added to 80 mL of deionized water under nitrogen flow. Styrene (7.50 mL), 0.75 mL α-methacrylic acid (0.75 mL), and sodium styrene sulfonate (0.1 g) were added into the nanoparticle suspension in sequence order indicated. The mixture was then heated in an oil bath set at 70^oC. Subsequently, 0.5 g ammonium persulfate was added to trigger the polymerization process and the reaction mixture was stirred for 5 h. The fabricated polymer-encapsulated iron oxide nanoparticles were harvested by centrifugation and washed with ethanol and water. Finally, the nanoparticles were dispersed in 10 mL deionized water to form a homogeneous suspension. For the silica coating process, 0.50 mL of polymer-encapsulated iron oxide nanoparticle suspension was mixed with 3.0 mL water, 20.0 mL isopropanol, and 1.0 mL concentrated ammonium hydroxide under vigorous stirring. Afterwards, 140 uL of a mixture of tetraethyl orthosilicate (TEOS) and octadecyltrimethoxysilane (C_{18}TMS) with a fixed TEOS:C_{18}TMS molar ratio of 4.7:1 was added dropwise to the nanoparticles under vigorous stirring. The silica coating process was continued for 6 h before isolating the resulting nanoparticles. The silica-coated, polymer-encapsulated iron oxide nanoparticles were isolated using an external magnet and subsequently washed with isopropanol/ ethanol and then air-dried at room temperature. Finally, the hybrid nanoparticles were calcined in air at 550℃ for 6 h to obtain the iron oxide-loaded hollow mesoporous silica nanocapsules.

Drug loading:

The nanocapsules (2 mg) were mixed with various concentrations of aqueous Dox solution, and shaken for 3 days in a revolving tube rotator. The resulting Dox-loaded nanocapsules were centrifuged at 8000 rpm for 10 min and washed with deionized water two times in order to remove free Dox molecules. The loading capacity and efficiency were evaluated by measuring the relative intensity of the UV-vis absorption of Dox at 480 nm.

Drug release studies:

Dox-loaded nanocapsules (2.0 mg) were dispersed in 1.5 mL pH 7.4 or pH 5 tris buffer with 150 mM NaCl. A salt concentration of 150 mM NaCl was used in the drug release studies to mimic the ionic strength under physiological saline conditions. Solutions that were and were not exposed to an alternating magnetic field were centrifuged every hour at 8000 rpm for 8 min, after which 1 mL of the supernatant was removed and evaluated by UV-vis absorption spectroscopy to determine the concentration of Dox released in solution. Fresh buffer (1 mL) replaced the removed supernatant and the solutions were either subjected to hyperthermia again or allowed to sit at room temperature for 40 min.

Hyperthermia: Sample excitation with an alternating magnetic field was performed using a Hyperthermia System (MSI Automation, Inc.). The frequency and magnetic field strength were 380 kHz and 75 kA/m, respectively. A total amount of 2.0 mg Dox loaded nanocapsules in 1.5 mL tris buffer was placed in a sample holder equipped with an optical fiber temperature probe (Neoptix T1™), which was used for temperature monitoring. The temperature was recorded every minute.

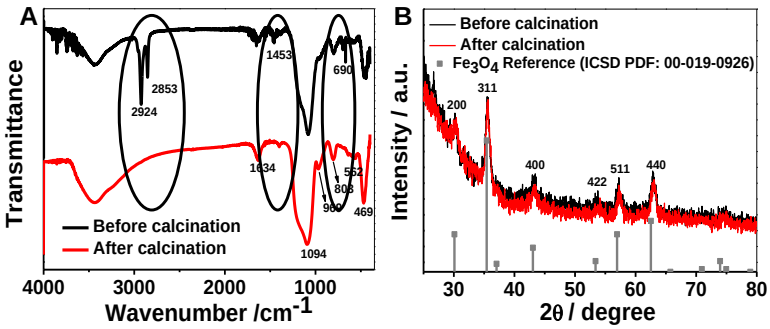

Fig. S1. A) FT-IR spectra of the nanocapsules before and after calcination at 550 °C showing the disappearance of polystyrene (major component of the polymer template) absorption bands[2,3] at 690, 1453, 2853 and 2924 cm^{-1}, indicating the effective removal of the polymer upon heat treatment. B) Powder XRD patterns of the nanocapsules before and after calcination at 550°C showing no obvious change in crystal phase of the iron oxide nanoparticles upon annealing and removal of the polymer template.

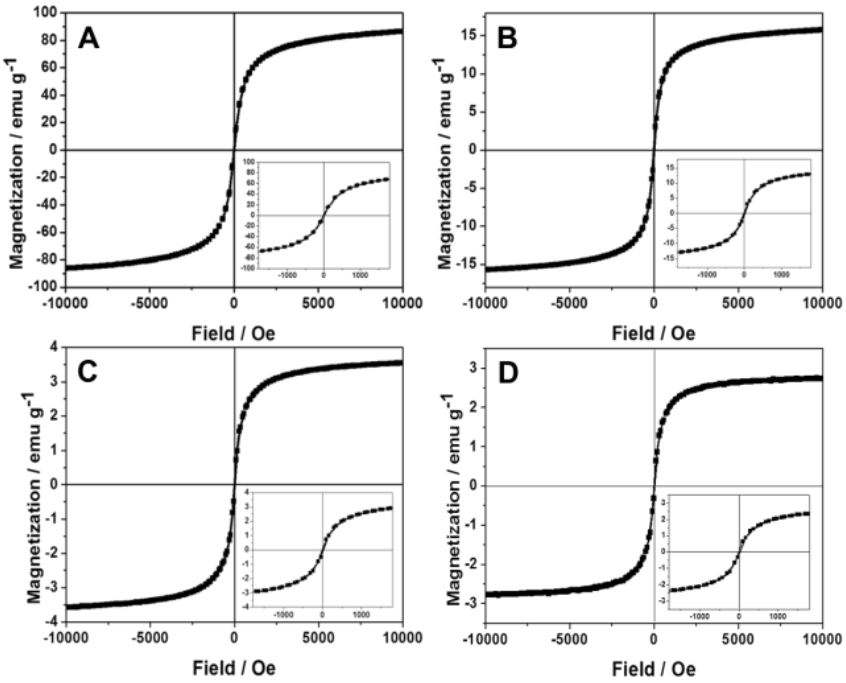

Fig. S2. Room-temperature magnetization curves of A) iron oxide nanoparticles with a 12 nm average diameter, B) polymer-encapsulated iron oxide nanoparticles, C) silica-coated, polymer-encapsulated iron oxide nanoparticles, and D) iron oxide-loaded hollow mesoporous silica nanocapsules; insets: corresponding close-up magnetization curves around zero field showing superparamagnetic behavior.

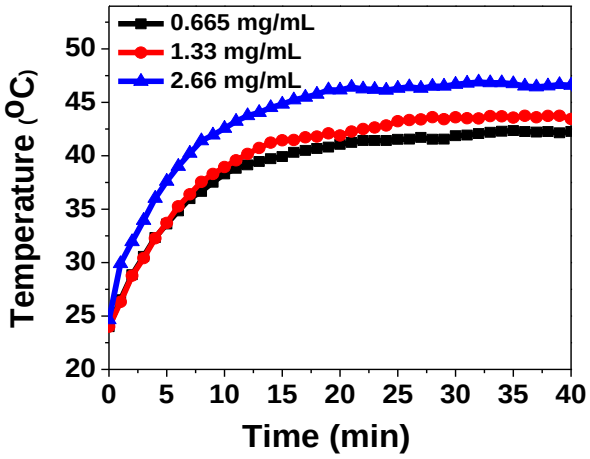

Fig. S3. Concentration effect on the heating curves obtained from the nanocapsule samples exposed to alternating magnetic field.

References:

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