Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

Evaluation of non-targeting, *C*- or *N*-pH (low) insertion peptide modified superparamagnetic iron oxide nanoclusters for selective MRI of liver tumor and their potential toxicity in cirrhosis

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Synthesis of hydroxyethyl starch coated SPIO

Iron (III) acetyl acetonate (17.7 g, 0.05 mol), oleylamine (40.1 g, 0.15 mol), oleic acid (42.3 g, 0.15 mol), 1,2-dodecanediol (50.6 g, 0.25 mol) and diphenyl ether (0.5 L) were mixed in a 2 L flask under nitrogen with a mechanic stirrer. The reaction solution was heated to 200 °C at a rate of 5 °C/min, then hold for 30 min and then to 250 °C for 30 min. The reaction was slowly cooled down to room temperature under nitrogen. The SPIO particles were precipitated with ethanol (2.5 L) and collected by centrifugation (5,000 g×20 min). The resulting solid was dissolved in hexanes and precipitated with ethanol. The obtained oil-based SPIO particles were dried under vacuum. The oil-based SPIO (5.0 g) and citric acid (2.5 g) were dissolved in dimethylformamide (DMF, 1.0 L) at 80 °C for 4 h under nitrogen. The resulting solution was diluted with DMF to a volume of 23 L and incubated at 80 °C. Aqueous hydroxyethyl starch solution (200/0.5, Wuhan HUST Life Science & Technology Co. Ltd., China, 10% w/w, 0.9 L) was then added, and the resulting solution was stirred at 80 °C for 5 h under nitrogen. The desired hydroxyethyl starch coated SPIO particles were precipitated with *t*-butyl methyl ether, collected by centrifugation and dried as a dark brown powder by lyophilization. The hydrodynamic diameter size of the synthesized SPIO was 40.4 ± 13.5 nm with the zeta potential of -l.63 mV in water. The iron content was determined to be 0.0365± 0.0012 mg Fe/mg solid by inductively coupled plasma (ICP) atomic absorbance analysis with a SpectrAA-40 spectrometer (Varian, USA) as reported (Wei et al. *J Biomed Nanotechnol.* 2015;11:854-864).

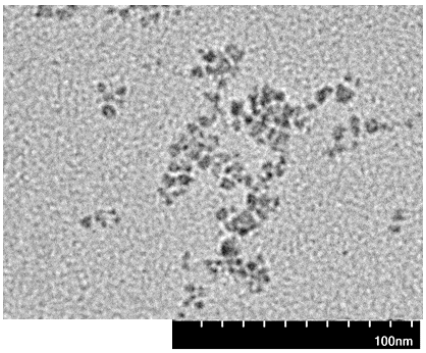

Figure S1. TEM image of the synthesized hydroxyethyl starch coated SPIO. The full-length of the bar shown in the image was 100 nm with an increment scale of 10 nm. The transmission electron microscopic images were obtained with a Hitachi HT-7700 transmission electron microscope (Tokyo, Japan) using uranyl acetate staining.

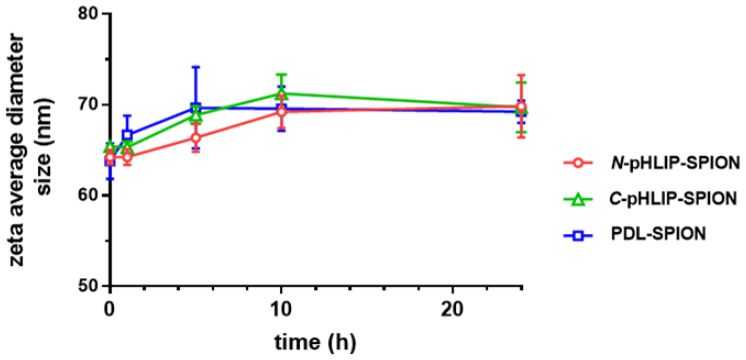

Figure S2. Stability of assembled SPION in 10% serum over time. The stability of SPION was assessed as the changes of nanoparticle zeta average diameter size in PBS (pH 7.4) containing 10% FBS over 24 h at 37 °C. The zeta average diameter size was determined with the Nano-ZS90 particle analyzer (Malvern, United Kingdom). Data presented were the average of triplicates with standard deviation.