Experiment section

Synthesis of Ferumoxytol by ordinary chemical co-precipitation method (sample A): Polyglucose sorbitol carboxymethyl ether (PSC, modified dextran) solution (50 mg/mL) was mixed with iron salt (ferrous chloride and ferric chloride) solution for 10 minutes at 25 ^{o}C. Then ammonia was slowly dropped into under nitrogen bubbled with mild stir. External heat source from oil bath was started for the solution temperature rising. When the solution achieved 80 ^{o}C about 20 minutes later, the temperature and nitrogen atmosphere is maintained for 40 minutes. Then continue to heat the solution for another 2 hours with air bubbling. Final sample was dialyzed and filtration, then lyophilized under vacuum to gain solid powder for comprehensive characterization.

Synthesis of Ferumoxytol by hydrocooling and magnetically internal heating coprecipitation method (sample C): Polyglucose sorbitol carboxymethyl ether (PSC, modified dextran) solution (50 mg/mL) was mixed with ferrous chloride (150 mg) and ferric chloride (300 mg) solution for 10 minutes at 25 ^{o}C. Then bathed the solution in ice water bath under nitrogen bubbling. The reaction vessel was transferred into the center of AMF coil, still bathed in ice water, the inner temperature presented a sustained gradually decrease and was kept at 0-2 ^{o}C. Aqueous ammonia (28% in weight, 1 mL) was slowly dropped wise into the solution with mild agitation. Immediately, the AMF production device of 790 kHz was ran, the output current was set at 15 A, also ice water was supplied for a sustained slow temperature around 0 ^{o}C for 60 minutes. In the following, another modulation of the output current was modulated from 15 A to 18A, to 20 A and to 22 A orderly in 120 minutes, ensuring a slow temperature rise from 0 ^{o}C to 80 ^{o}C. Lastly, high temperature was maintained for 2 hours by air bubbling, Ferumoxytol by HMIHC (sample C) was obtained finally. The whole AMF action span of sample C for growth and aging was 180 minutes, while that of sample B was 60 minutes and underwent without external hydrocooling. The two samples were purified by dialysis and filtration, then lyophilized under vacuum to gain solid powder for comprehensive characterization.

Characterization: Alternating magnetic field is produced by the moderate radio frequency

heating machine (Shuangping SPG-10-II, China). Hydrodynamic size and zeta potential was measured by particle size and potentiometric analyzer (Nano ZS90, Malvern). The morphological characterization was carried out by transmission electron microscopy (TEM, JEM-2100, Japan)/ (FEI, Tecnai G20) and NanoSight LM10-HSBF system (Malvern). The structure characterization was detected by X-ray diffractometer (X'TRA, ARL), Fourier transform infrared spectrometer (Nicolet is 50, Thermo) and thermogravimetric analyzer (Pyris 1 DSC, PerKinElmer). Magnetic properties characterization was measured using vibrating sample magnetometer (7407, Lakeshore), physical property measurement system (PPMS-9, Quantum Design), magnetic susceptibility balance (MK1, Sherwood), magnetic resonance scanner (Verio, 3T, Siemens) for sample solution test with True Fast Image with Steady-state Precession sequence and micro-magnetic resonance scanner (7T, PharmaScan, Brukers, Germany) for small animal. The iron concentration was measured by inductively coupled plasma mass spectrometry (Optima 5300DV, PE) and UV-Vis spectrophotometer (UV-3600, Shimadzu, Japan). Magnetocaloric characterization was measured using infrared thermal image instrument (Fluke, TI32) and optical fiber spectrometer (FISO UMI 8, Canada). Electromagnetic characterization was measured by electron paramagnetic resonance spectrometer (EMX-10/12, Bruker), soft X-ray spectroscopy microscopy (Synchrotron Radiation Facility, Shanghai, China), low frequency impedance analyzer (4294A, Agilent) and vector network analyzer (PNA N5224A, Agilent). Particle behavior simulation in AMF was calculated by the Object Oriented MicroMagnetic Framework (OOMMF) project.

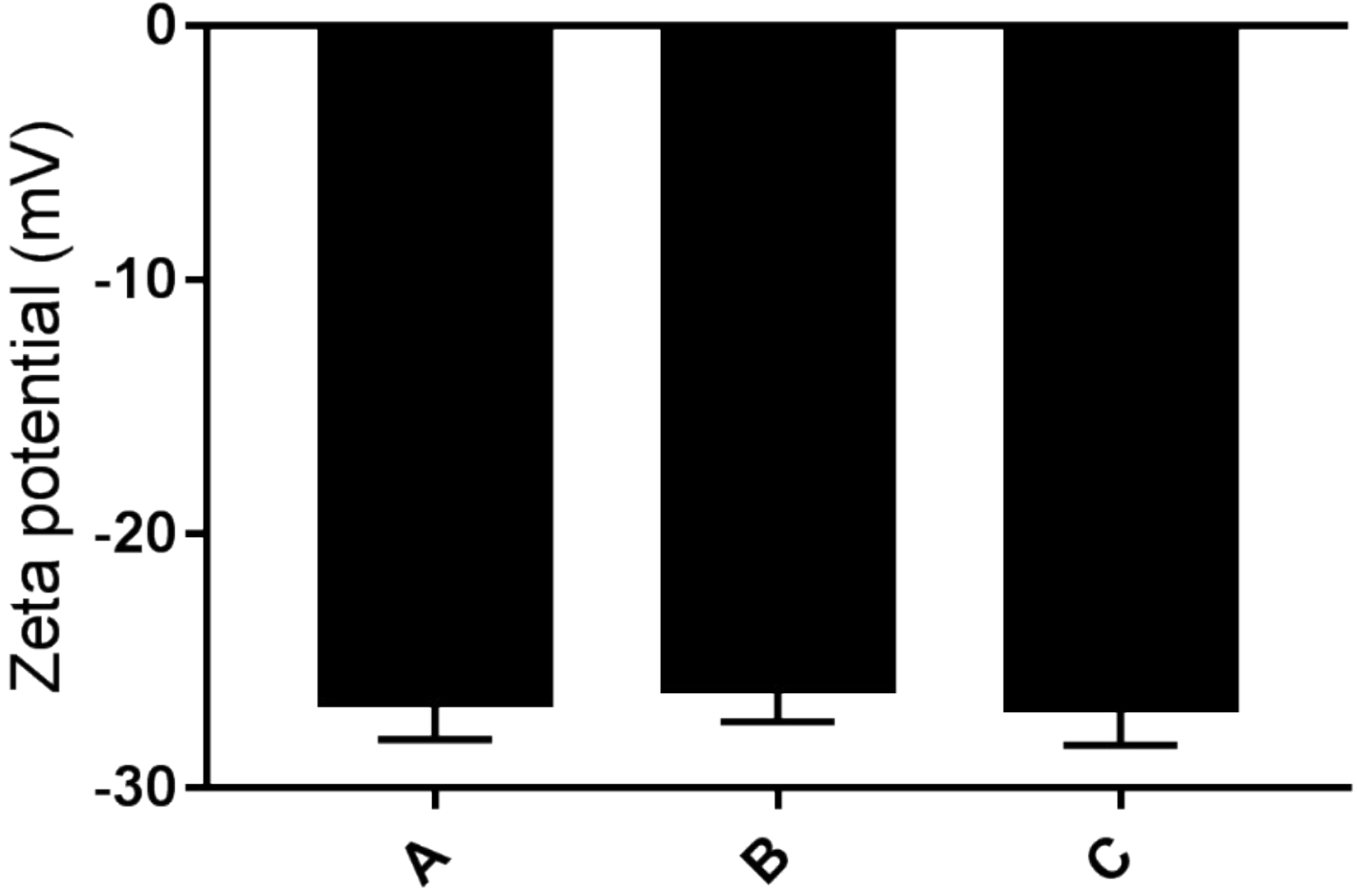

Figure S1. ξ potential measurement for Sample A-C (N=3).

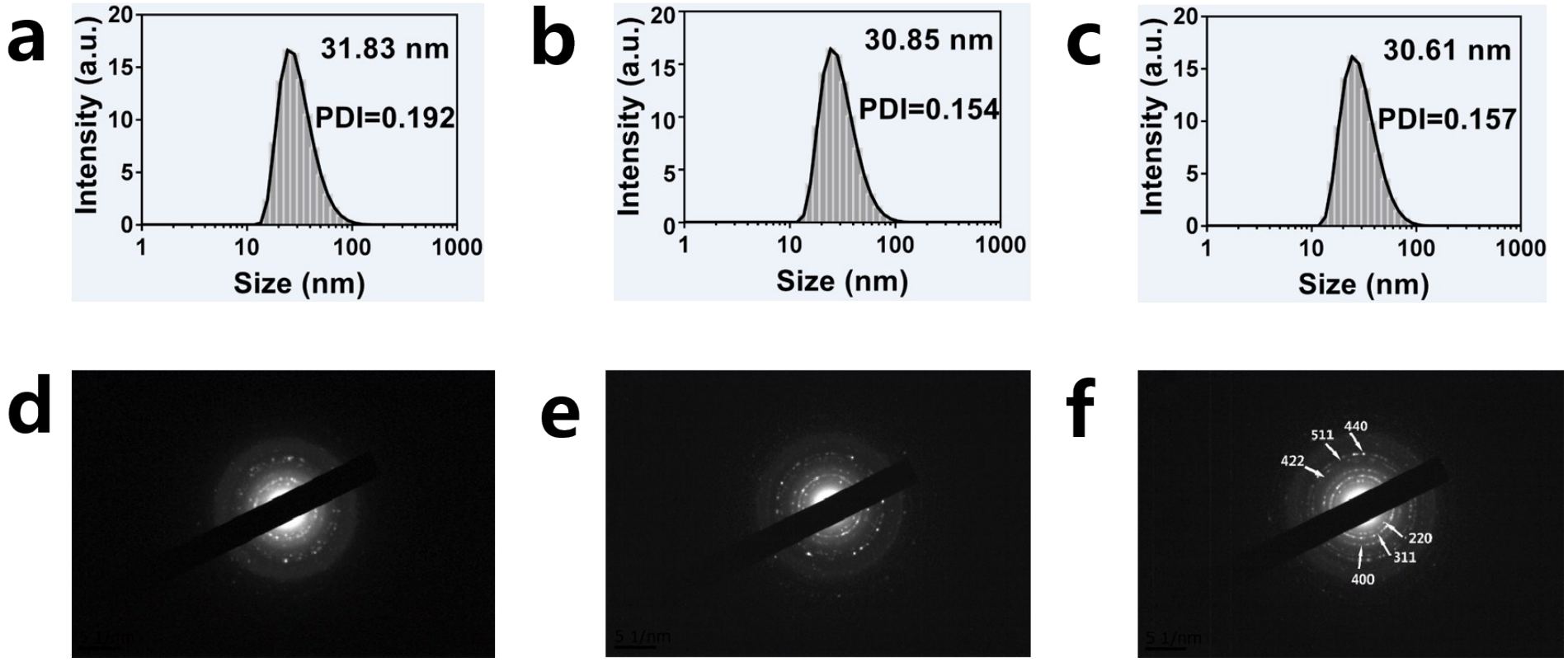

Figure S2. Hydrodynamic size of a) Sample A, b) Sample B and c) Sample C; SAED pattern of d) Sample A, e) Sample B and f) Sample C.

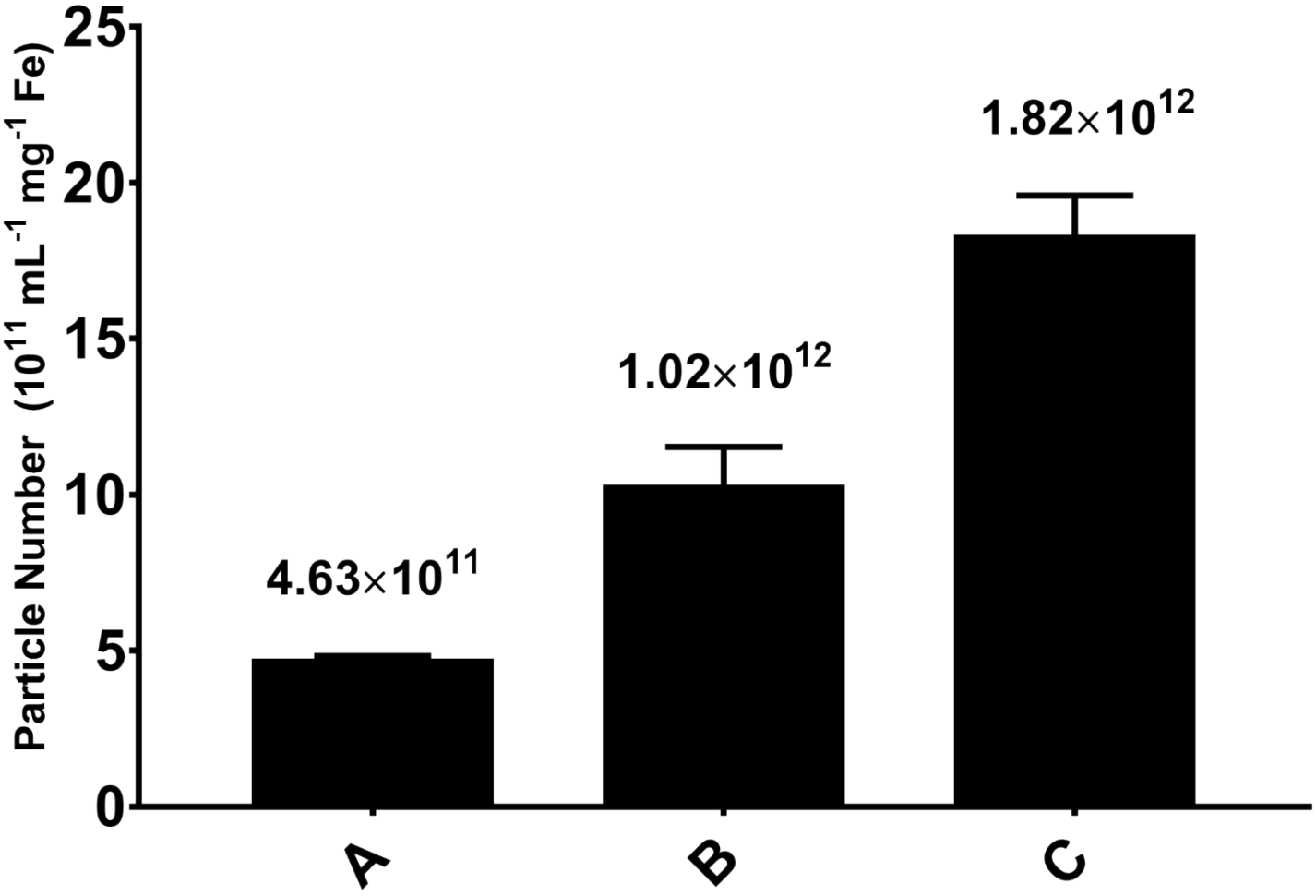

Figure S3. Particle number measurement for Sample A-C (N=3).

Table S1. Pharmaceutical quality criteria for Ferumoxytol.

Pharmaceutical quality testing items	Commercial product FMT	FMT obtained by AMF
Hydrodynamic diameter	29-51 nm	31-40 nm
Iron oxide core size	7.4 ± 0.4 nm	7.1 ± 0.3 nm
Total organic carbon content	11.3-13.9 mg/g	12.1-12.9 mg/g
Molecular weight	750-790 kDa	760-770 kDa
Ferric content	96%-98.5%	96%-97.5%
Iron ion content	< 0.1%	< 0.05%
Magnetic susceptibility	26400-42600 $\times 10^{-6}$ c.g.s. /g Fe	27000-42500 $\times 10^{-6}$ c.g.s. /g Fe

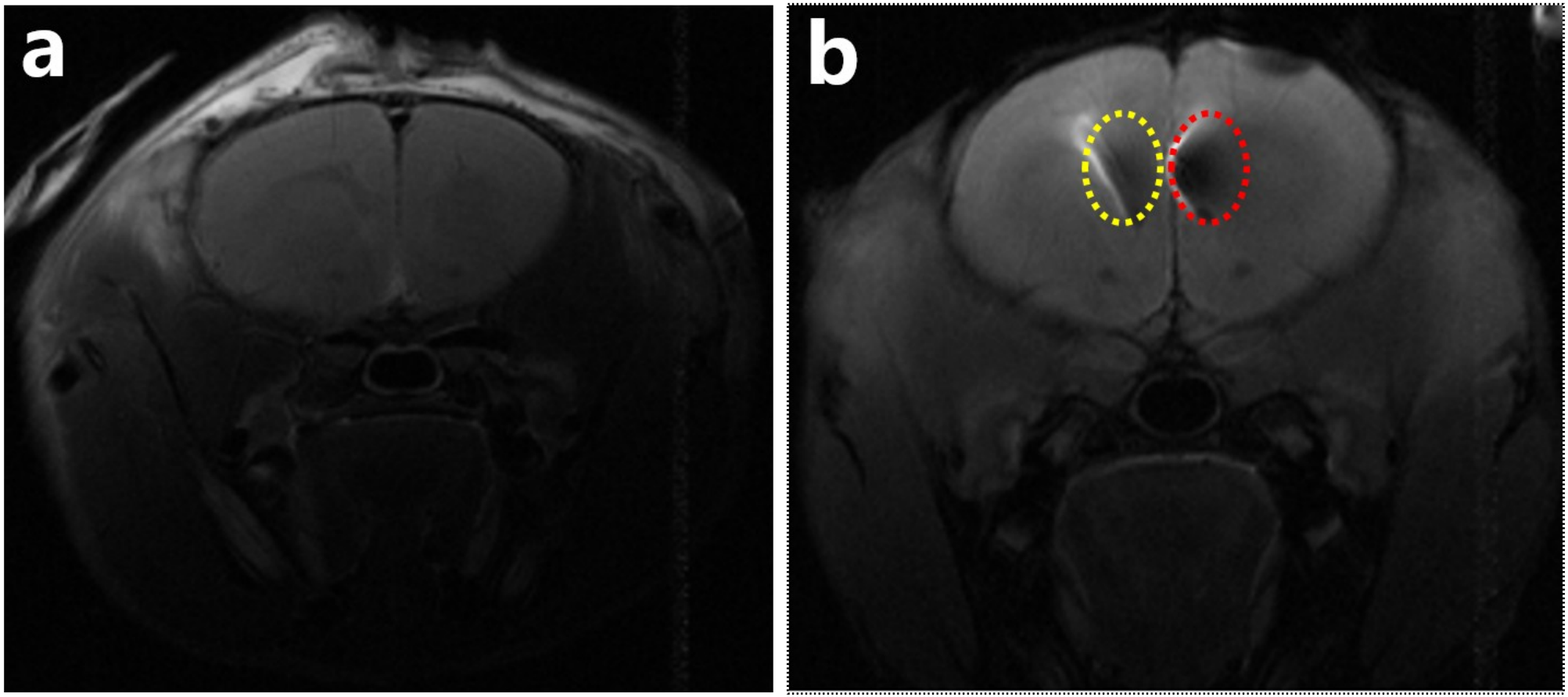

Figure S4. Healthy rat brain T_2-weighted MR images: a) before injection and b) 8 hours after injecting Sample A (left brain, yellow dashed circle region) and Sample C (right brain, red dashed circle region) respectively（8 μL, 1 mg/mL Fe）.

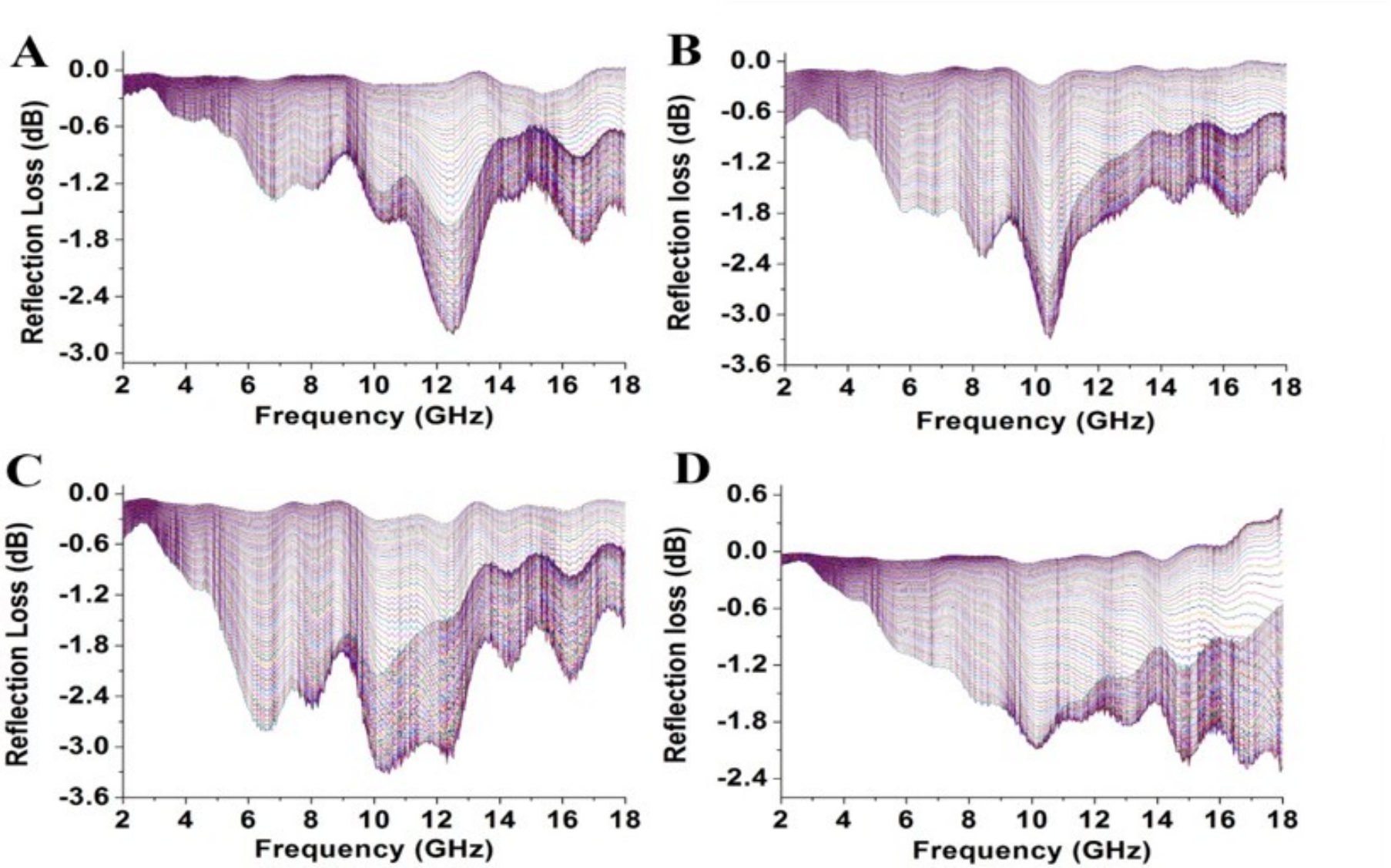

Figure S5. Frequency and thickness dependence of the reflection loss (RL) curves of Sample A-C and Sample D (PSC) in vector network analyzer.

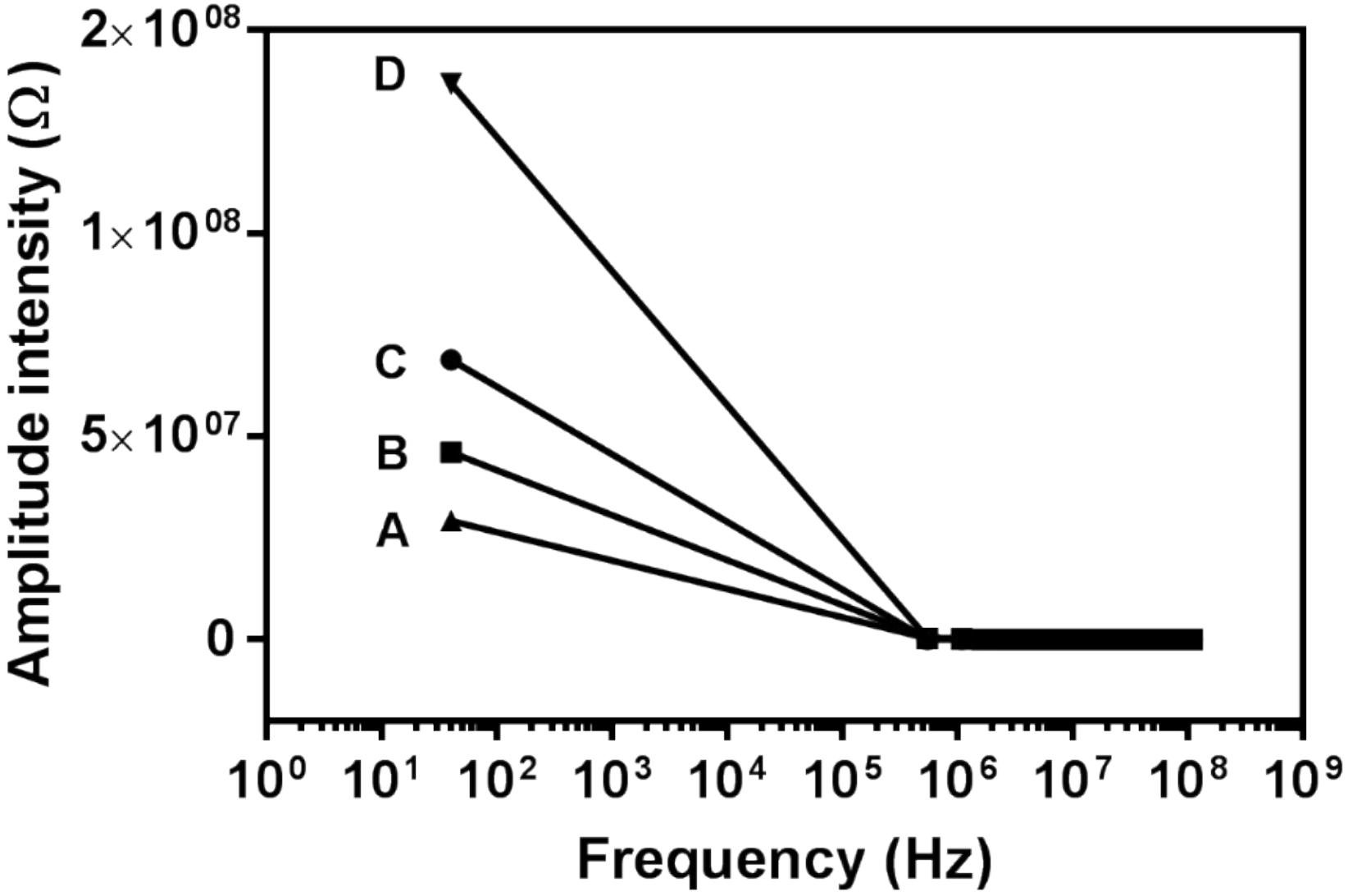

Figure S6. Frequency dependent impedance amplitude intensity plot of Sample A-C and Sample D (PSC).

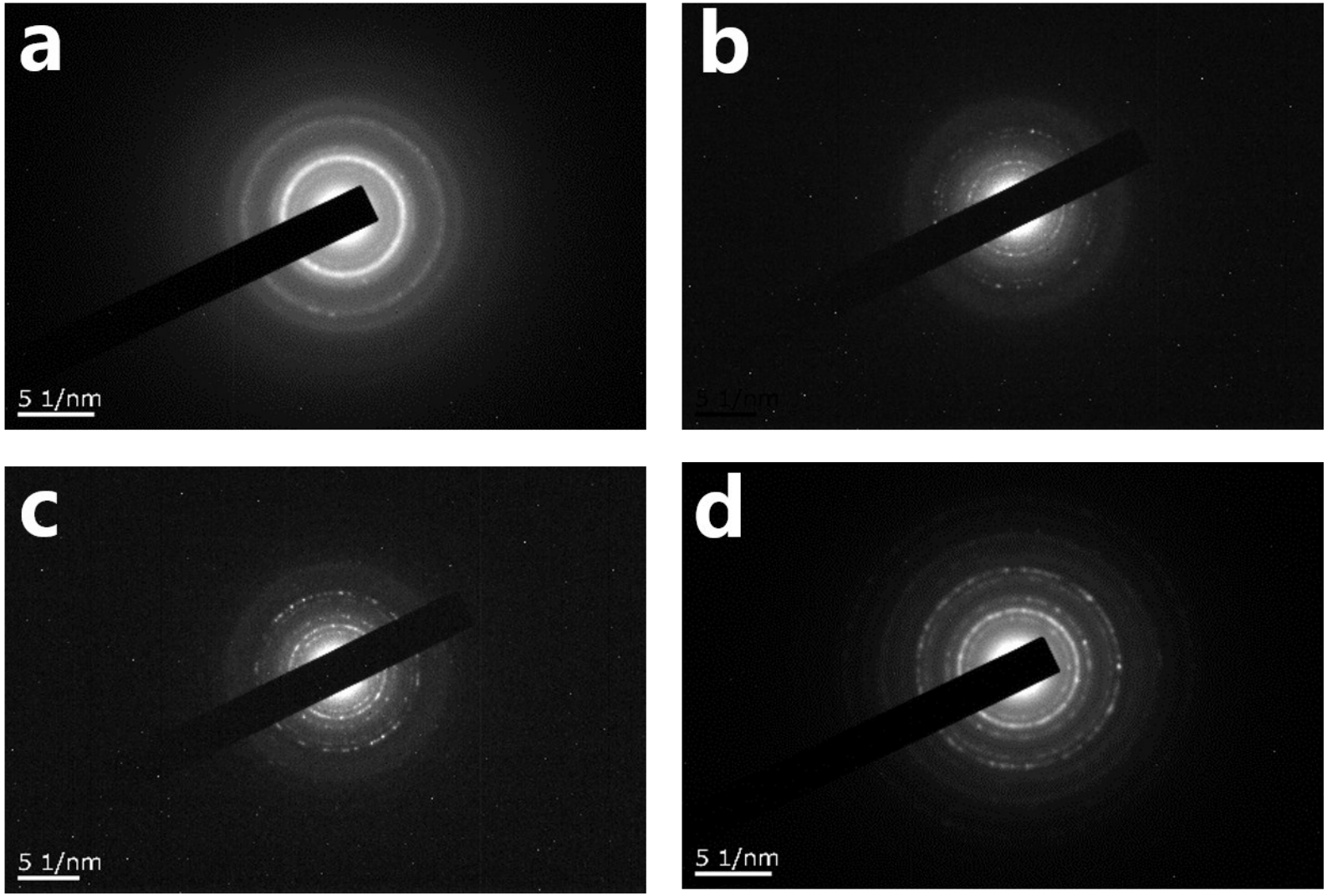

Figure S7. SAED pattern of samples extracted at a) 10 min, b) 60 min, c) 120 min and d) end stage in the Sample C synthesis process.

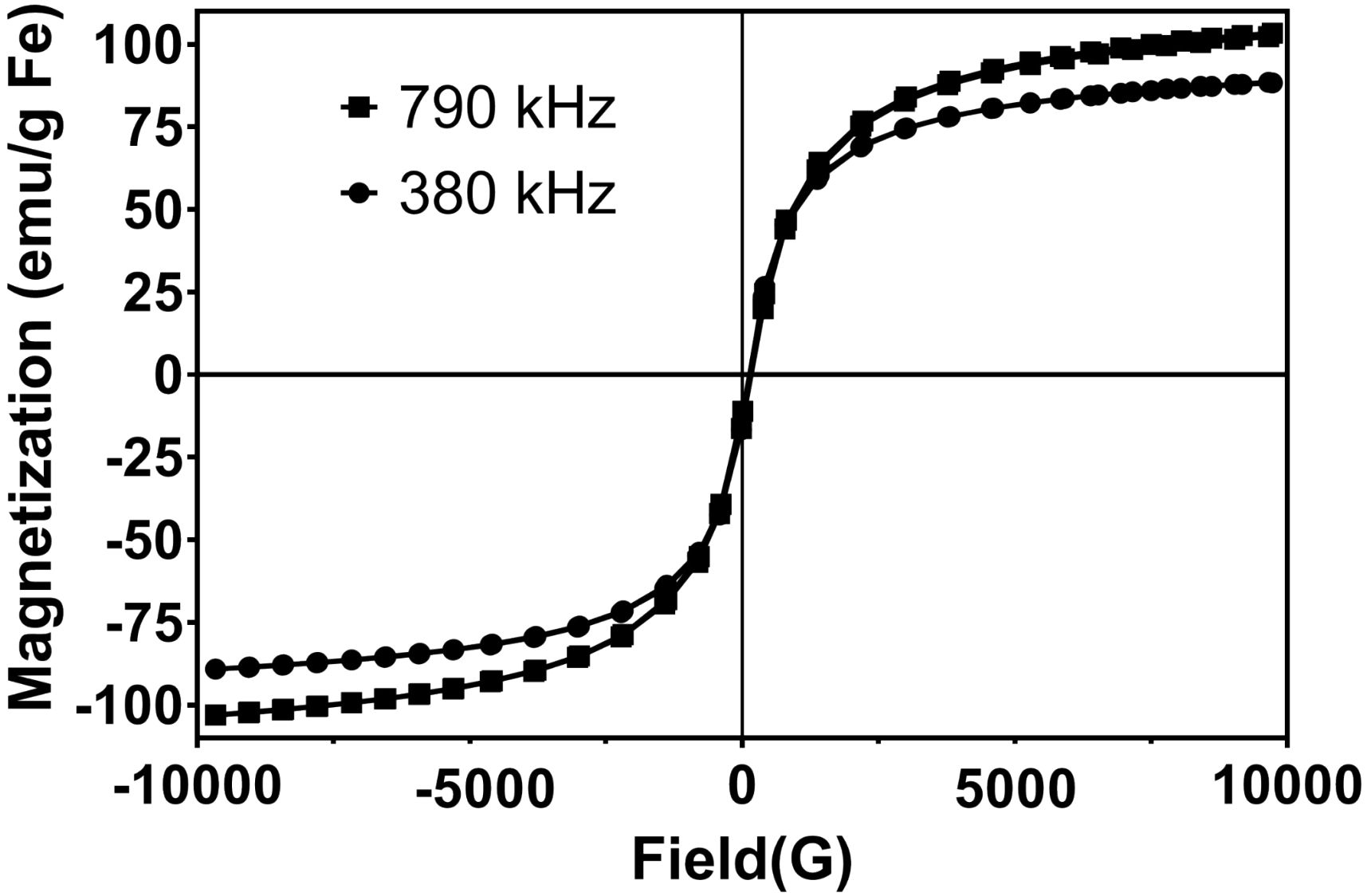

Figure S8. Magnetization comparison for Ferumoxytol produced by AMF production device at frequency of 380 kHz and 790 kHz.

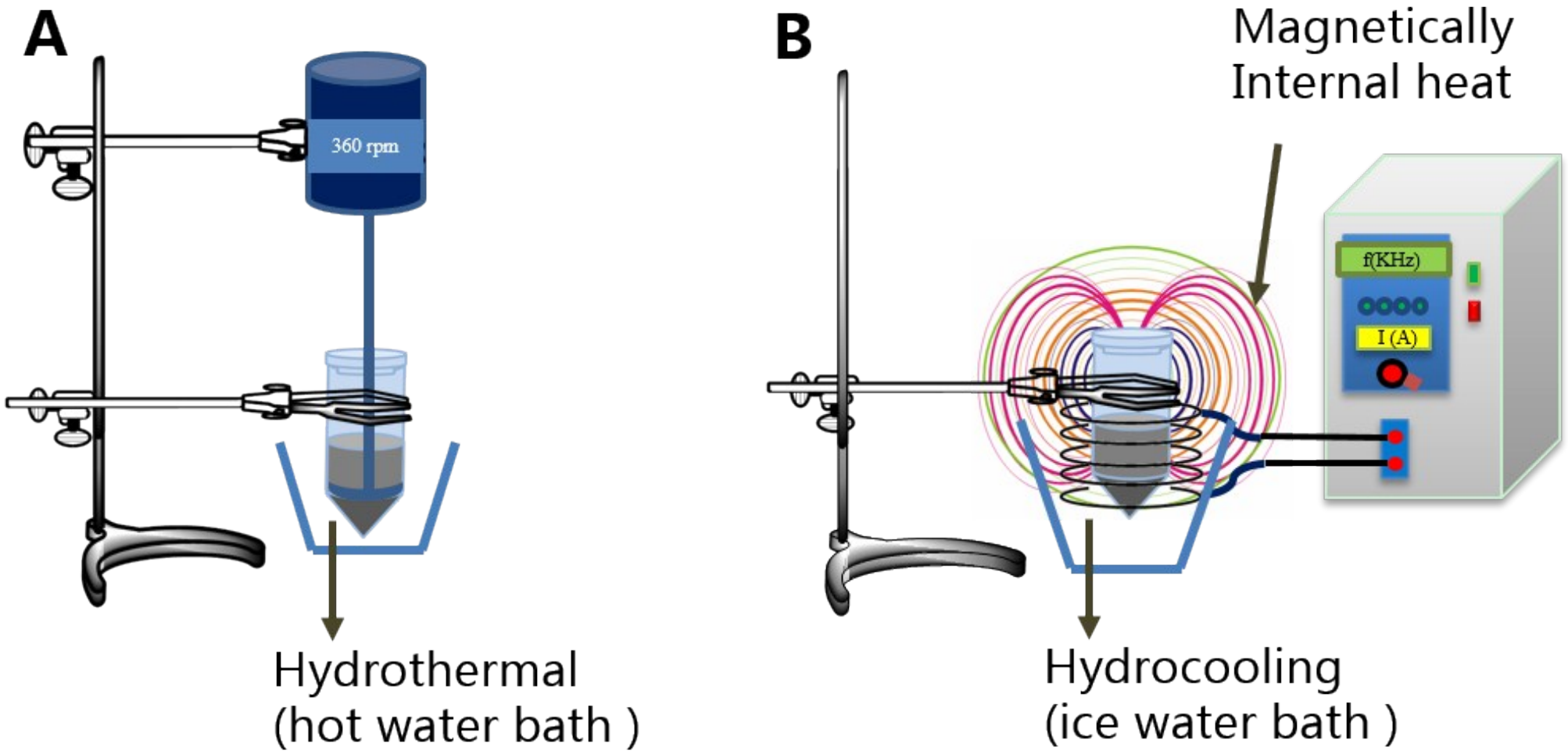

Figure S9. Reaction device diagrammatic sketch of A) common external heating co-precipitation and B) magnetically internal heating co-precipitation.