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### Capping-ligands-induced synthesis of non-spherical magnetite nanoparticles for hyperthermia and their biocompatibility study.

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Magnetic property of nanoparticles is intimately related with their structure, size, morphology, and magnetic anisotropy. In recent years, some non-spherical iron oxide nanoparticles are found to have superior performance in biomedical applications compared to their spherical counterparts. For example, iron oxide nanocubes was reported to have higher magnetic heating efficiency in hyperthermia, and octapod iron oxide nanoparticles was demonstrated to be more effective T2 contrast agents for magnetic resonance imaging. [1, 2] However, controlling the morphology of iron oxide nanoparticles for hyperthermia still remains a challenge, and there are few published studies on their biocompatibility and potential cytotoxicity. In this work, we aim to use different kinds of capping ligands (including oleic acid, oleylamine, 1,2-tetradecanediol, decanoic acid, and lauric acid) in thermal decomposition to adjust the morphology of magnetite nanoparticles into non-spherical shape for hyperthermia application, and perform comparative cytotoxicity study of as-synthesized nanoparticles on human hepatoma cell lines and immortalized normal human liver cell lines. The nanoparticle products were characterized by using TEM, EDX, electron diffraction pattern, SEM, and VSM. As shown in the SEM images, we successfully obtained magnetite nanoparticles with different morphologies, including nanocuboctahedrons (Fig. 1a), nanooctahedrons (Fig. 1b), and nanocubes with different sizes (Fig. 1c and 1d). The insets in the SEM images of Fig. 1 are the corresponding TEM images of nanoparticles. In magnetic properties study (Fig. 2a), spherical magnetite nanoparticles of 10 nm were synthesized for comparison, and they displayed typical superparamagnetic behavior with a saturation magnetization ( $M_s$ ) value of 54 emu/g. In comparison, all the non-spherical magnetite nanoparticles showed higher  $M_s$  values, and non-zero coercivities. Particularly, the  $M_s$  value of 65-nm nanooctahedrons was 91 emu/g, which is close to the value of bulk magnetite (92 emu/g). The 20-nm nanocubes and 22-nm nanocuboctahedrons displayed a  $M_s$  value of 82 emu/g and 76 emu/g, respectively. As shown in the inset in Fig. 2a, the coercivities of nanooctahedrons, nanocubes, and nanocuboctahedrons are 80 Oe, 25 Oe, and 15 Oe, respectively. The *in vitro* cytotoxicity study of those non-spherical magnetite nanoparticles were carried out on BEL-7402 cells (Fig. 2b) and MIHA cells (Fig. 2c). After 24-hour incubation with the nanoparticles, cell viability, cell morphology, and cellular uptake of nanoparticles were examined and analyzed. These results will be reported in the full paper.

[1] Zhao Z, Zhou Z, Bao J, Wang Z, Hu J, Chi X, et al. Octapod iron oxide nanoparticles as high-performance T2 contrast agents for magnetic resonance imaging. Nat Commun. 2013;4.

[2] Martinez-Boubeta C, Simeonidis K, Makridis A, Angelakeris M, Iglesias O, Guardia P, et al. Learning from Nature to Improve the Heat Generation of Iron-Oxide Nanoparticles for Magnetic Hyperthermia Applications. Sci Rep. 2013;3.

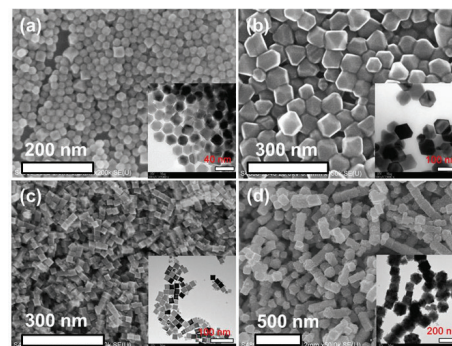


Figure 1. SEM images of magnetite nanoparticles with shape controlled by using different capping ligands during synthesis process. (a) nanocuboctahedrons, using oleic acid, oleylamine, and 1,2-tetradecanediol; (b) nanooctahedrons, using oleic acid and oleylamine; (c) 20-nm nanocubes, using decanoic acid; (d) 80-nm nanocubes, using lauric acid. Insets are the TEM images of corresponding nanoparticles.

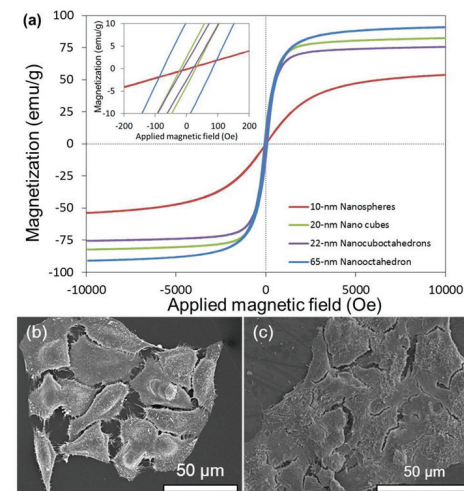


Figure 2. (a) Magnetization curves of magnetic iron oxide nanospheres, nanocubes, nanocuboctahedrons, and nanooctahedrons. Inset is the magnified view of the magnetization curves in the low magnetic field. (b, c) SEM images of (b) BEL-7402, human hepatoma cells and (c) MIHA, immortalized normal human liver cells.