Enhanced permeability and retention effect of novel magnetic resonance imaging contrast agents using fatty acid

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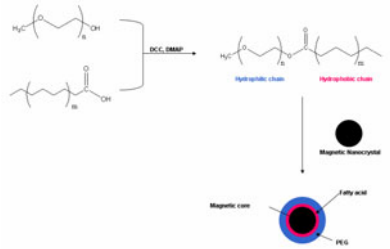
Statement of Purpose: The magnetic nanocrystals can be utilized as magnetic probes and carrier due to magnetic sensitivity, which can apply the biomedical applications; such as targeted drug delivery[1], cell labeling and separation[2-3], immunoassay[4], magnetic resonance imaging (MRI)[5] and magnetic hyperthermia[6]. In this research, surface modification of magnetic nanocrystals was performed with amphiphilic ligand that composed of monometoxy polyethylene glycol and fatty acid (dodecanoic acid). The monodisperse ultra sensitivity magnetic nanocrystals were synthesized by thermal decomposition method. The magnetic and physico-chemical properties of nanoparticles were analyzed. In addition, the applicapablity of magnetic resonance imaging contrast agents was evaluated with in vitro cell test and animals models.

Methods: A synthetic scheme of dodecanoic acid (DA, Sigma, USA) conjugated monometoxy polyethylene glycol (mPEG, Fluka, USA) block copolymer is shown Scheme 1. These amphiphilic ligands were synthesized with DCC method and purified ethyl ether. The magnetic nanocrystals were thermally synthesized and keep in organic solvent[7]. The novel mPEG coated contrast agents were prepared by solvent evaporation methods and the products were dispersed in aqueous medium.



Scheme 1. Synthetic scheme of fatty acid conjugate with mPEG and novel magnetic resonance imaging contrast agents.

Results/Discussion: The chemical structure and molecular weight of prepared mPEG-DA block copolymer is confirmed by ^{1}H-NMR and gel permeation chromatography, respectively (data not shown). The hydroxyl group of mPEG and the carboxyl group of DA were conjugated by DCC method. The size of magnetic nanocrystals was around 10 nm and the aqueous novel magnetic resonance imaging contrast agent was similar with MNC. The spherical shape of both nanoparticles was confirmed with TEM.

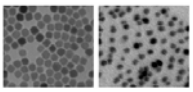


Figure 1. TEM images of magnetic nanocrystals (left) and novel imaging contrast agents using mPEG-DA (right).

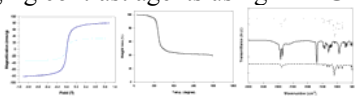


Figure 2. The hysteresis loop of magnetic nano crystals and novel contrast agents (left). The superparamagnetic behavior was presented and high saturation of magnetization values was shown. The weight loss of novel contrast agents by thermogravity analyzer (medium). Approximately, 40 % of magnetic materials presented and the organic compounds were eliminated at 200 □. FT-IR spectra of mPEG, DA and mPEG-DA (right). We could evaluate these results by FT-IR spectra; the shifting of C=O band and Fe-O: 570 cm^{-1}.

The MR images were captured for in vitro cell model and in vivo mouse model. The non-treated cells with novel contrast agents were shown with white and treated cells were black. In addition, we could verify same results at in vivo mouse model. The tumor site was changed with black and we could detect there.

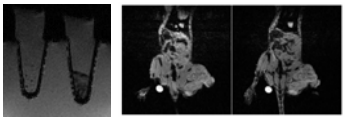


Figure. 3. The MR imaging of target cells and in vivo model.

Conclusions: The amphiphilic ligands were synthesized with monometoxy polyethylene glycol and dodecanoic acid. The ligands were used to modify the organic magnetic nanocrystals for MRI contrast agents. These PEGylated novel magnetic resonance imaging contrast agents had high physico-chemical stability and magnetic sensitivity and the surface modification step could increase the blood circulation time and EPR effects.

References:

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