

New Synthesis Method of Ultrasmall Iron Oxide Nanoparticles Using Polyvinylpyrrolidone

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Introduction

Biocompatible polymer coated iron oxide nanoparticles, which are superparamagnetic, have been used as a magnetic resonance(MR) T2 contrast agent[1]. In this study, we introduced the new synthesis method of polycaprolactone(PCL) coated iron oxide nanoparticles with use of polyvinylpyrrolidone(PVP). The major advantages of our method on the process of polycaprolactone and polyvinylpyrrolidone coated iron oxide nanoparticle(PCL-PVP-NP) is that it is not going through the polymerization of biocompatible polymer and so it can be more easy and inexpensive than existing method.

Material and Methods

Synthesis of Nanoparticles : Ferrous chloride tetrahydrate($\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$) and ferric chloride hexahydrate($\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$) solutions were mixed with a concentration ratio of 2:1. Ammonium hydroxide(NH_4OH) solution was added until a pH of 11 and a black suspension formed. Vigorous stirring was continued for 30 min, under nitrogen atmosphere. The black precipitate was washed several times with distilled water until the pH decreased from 11 to 7 by magnetic decantation. After washing, the particles were redispersed with ultrapure water. The PVP solution and PCL solution were then added and the suspension was stirred for 1hr. PCL-PVP-NP was separated into different size by centrifugation and an excessive polymer was removed.

Characterization : The particle size distribution and morphology were examined by high resolution transmission electron microscope(HRTEM, H-7600, Japan, HITACHI). The conjugation between iron oxide nanoparticles and PCL was confirmed by Fourier Transform infrared spectroscopy (FTIR, Mattson Instruments, Inc., Galaxy 7020A). The magnetic properties of nanoparticles were analyzed by vibrating sample magnetometer (VSM, Lake Shore model 955287). The magnetic resonance imaging(MRI) was performed at 1.5 MR scanner (GE Signa Advantage, GE Medical system, USA) to obtain T2 weighted MR imaging (FSE, TR/TE = 1500/40). The liver of rabbit was imaged before and after intra venous administration of PCL-PVP-NP (10 μ mol Fe/kg) through ear vein. For semi-quantitative analysis, the signal intensities of liver were measured before and after administration.

Results

HRTEM : Fig.1 shows that the PCL-PVP-NP has size of 30-70nm and has core-shell structure. Some of these particles form multiparticle aggregates.

FTIR : Fig.2a shows IR spectrum of iron oxide nanoparticles. Comparing PCL-PVP-NP (Fig.2c) with PVP coated iron oxide nanoparticles(PVP-NP : Fig.2b), the new band appeared at 2130-2260 cm^{-1} (-N=C=O), 1690-1700 cm^{-1} (-NH-CO), 1453 cm^{-1} (C-O), 1350-1465 cm^{-1} (-CH₃-CH₂). The carboxylic bands observed at 1730-1700 cm^{-1} (C=O) and 1453 cm^{-1} (C-O) indicate the presence of carboxylic groups on the surfaces of the PCL-PVP-NP.

VSM : PCL-PVP-NP exhibit superparamagnetic behavior with high magnetization values (Fig.3.).

MRI : After injection of PCL-PVP-NP(10 μ mol Fe/kg), the rabbit liver become darker due to high T2 relaxation effect of PCL-PVP-NP. Compared to the pre-injection image, the liver intensity decreased from (171.74 $\pm$ 12.08) to (111.01 $\pm$ 14.25) (Fig.4.).

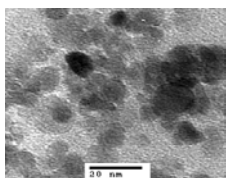


Fig. 1. HRTEM of PCL-PVP-NP

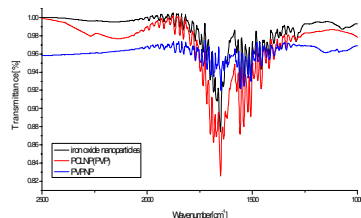


Fig. 2. FTIR spectra of iron oxide nanoparticles (a; black), PVPNP(b; blue), PCL- PVP-NP(c; red)

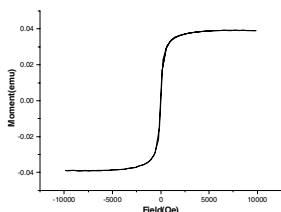


Fig. 3. VSM of PCL-PVP-NP

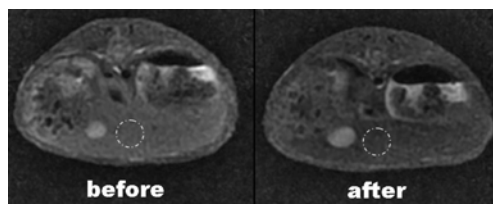


Fig. 4. Liver MRI before and after i.v. injection of PCL-PVP-NP 10 μ mol Fe/kg in rabbit. The white circle is ROI.

Discussion and Conclusion

Polycaprolactone and polyvinylpyrrolidone coated iron oxide nanoparticles (PCL-PVP-NP) was synthesized by a new simple-step method. Using the method, nanoparticle is bonded to PCL through the PVP. This process is different to conventional method and is easier than ring-opening polymerization method [2]. The PCL-PVP-NP has very small size and strong superparamagnetism. The strong T2-relaxation effect of the particles indicates that PCL-PVP-NP is suitable for T2 MR contrast agent. Moreover it has carboxylic groups on the surface of the PCL-PVP-NP. The carboxylic groups are advantageous in that they can be conjugated to other functional group or proteins. By its ability to make a conjugation with molecular markers such as antibody or small peptide, PCL-PVP-NP becomes a good model system for molecular imaging.

References

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