Functional magnetic nanoparticles for use in a drug delivery system

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Abstract. γ-Fe₂O₃ nanoparticles encapsulated in amorphous SiO₂ were prepared by the wet chemical method and carboxyl-modified functionalized nanoparticles were produced. The prepared samples were examined by X-ray diffraction measurements and TEM images. Particles sizes in the range 4–20 nm were determined from the Scherrer formula. Magnetization was measured by a SQUID magnetometer under a ±50-kOe magnetic field. The magnetization curves showed ferromagnetic or superparamagnetic behaviour depending on particle size. Functionalized nanoparticles were confirmed by Fourier transform infrared spectroscopy (FT-IR) measurements. The typical C=O peak was detected in the spectrum of functionalized nanoparticles. These magnetic nanoparticles are expected to be used as carriers in drug delivery systems (DDS), hyperthermia treatment, and other biomedical applications.

1. Introduction
Magnetic nanoparticles have attracted considerable attention in recent years, given their tremendous potential for use not only in magnetic recording media but also in biomedical applications. One of the authors has developed a unique method for the preparation of magnetic nanoparticles and has reported on the magnetic properties of these nanoparticles [1–5]. In recent years, we proposed a biomedical application that involved modifying amino groups on the surface of the magnetic nanoparticles and introducing them into the cells [6–9]. The amino groups were successfully modified by using an amino-silane coupling procedure. The functionalized magnetic nanoparticles were introduced into the cells and were then localized in the tissues by an external magnetic field. Cell selective magnetic particles were also obtained by modification of the amino acid. It is possible that after introduction into the cells, magnetic particles yield thermal energy when an external field is applied. These particles are also expected to act as carriers in drug delivery systems. In this study, γ-Fe₂O₃ nanoparticles were prepared and the carboxyl group was then modified in order to realize conjugation with drugs or other chemical molecules. Furthermore, the properties of the functional magnetic nanoparticles were investigated.
2. Experiment

2.1. Preparation of precursor particles

\( \gamma \)-Fe\(_2\)O\(_3\) nanoparticles were produced by mixing aqueous solutions of FeCl\(_2\) \( 4\)H\(_2\)O and Na\(_2\)SiO\(_3\) \( 9\)H\(_2\)O. The mole ratio of the prepared reagent was Fe:Si = 1:1. The precipitates obtained were washed several times with distilled water and dried at about 350 K in a thermostat. The as-prepared samples were subjected to heat treatment in a furnace; heating was carried out in air at an annealing temperature of 973 K.

2.2. Functionalization

Nanoparticles with sizes of 3 nm were used for modification of the carboxyl groups. Fe\(_2\)O\(_3\) particles were wetted in distilled water and then mixed with triethoxysilylpropyl succinic anhydride (TESPSA). The mixtures were stirred for 24 h on a heating plate at a temperature of 403 K. The particles were washed several times in distilled water and were dried at 350 K. Fourier transform infrared (FT-IR) spectra were observed to confirm the modification of the carboxyl groups. Zeta potential was also measured using a Zetasizer Nano ZS (Malvern, UK) for recognition. Before and after modification, each sample was examined by CuK\(\alpha\) X-ray powder diffraction (\(\lambda = 0.154\) nm). DC magnetization was measured using a superconducting quantum interference device (SQUID) magnetometer (Quantum Design, MPMS) under a ±50-kOe magnetic field; the magnetization measurements were performed at temperatures ranging from 5 to 300 K.

3. Results and Discussion

3.1. X-ray diffraction and magnetization curves

The X-ray powder diffraction patterns confirmed the presence of the spinel phase of \( \gamma \)-Fe\(_2\)O\(_3\). No structural differences appeared before or after the modification of the carboxyl groups. The magnetization curves of \( \gamma \)-Fe\(_2\)O\(_3\) before and after modification are shown in figure 1. After modification, the magnetization seems to decrease because the longitude exhibits magnetization value per weight. The difference between the values before and after modification can be ascribed to the modified carboxyl groups; the weight of the carboxyl groups is estimated to be approximately 0.04 g for a sample of 1 g. As shown in figure 1, superparamagnetic behaviour at room temperature was observed.
3.2. FT-IR and zeta-potential

After modification, the presence of carboxyl groups in the functionalized magnetic nanoparticles was confirmed by FT-IR. In figure 2, the dotted line shows the absorbance before modification and the solid line shows absorbance after modification. Typical C–H peaks [labeled 1] and C=O peaks [labeled 2] were detected for the first time in the spectrum of the functionalized particles at around 2800 cm$^{-1}$ and 1600–700 cm$^{-1}$, respectively. Si-O peak [labeled 3] was also indicated. We can conclude that the carboxyl groups are successfully modified with magnetic nanoparticles.
Figure 2. FT-IR spectra of unmodified nanoparticles (dotted line) and carboxyl-modified nanoparticles (solid line) as a function of the pH of the buffer solution.

![FT-IR spectra](image)

Figure 3. Plot of the zeta potential, $\zeta$, of the functionalized magnetic nanoparticles (filled squares) and unmodified nanoparticles (empty squares).

The zeta-potentials of the nanoparticles were measured by a Zetasizer using the laser Doppler velocimetry technique. Figure 3 shows a plot of the zeta potential as a function of the pH of both before and after the modification of the carboxyl groups. The modified particles tend to show a negative potential as the pH value increases. It appears that carboxyl groups maintain the equilibrium position between COOH and COO$^- + H^+$ in solution, and the equilibrium shifts to the right at higher pH values. From this measurement negative charges on the surface were confirmed. Thus we have successfully modified carboxyl groups with magnetic nanoparticles. Though we have already established the way of functionalization by amino groups [6, 7], modification of carboxyl groups achieves great advantages. The carboxyl-modified functionalized nanoparticles can be easy to conjugate other molecules or drugs, and they improve hydrophilic properties of the particles, as the result prior biocompatibility is expected. These novel functionalized magnetic particles are more practical for use in drug delivery systems.

4. Conclusion

$\gamma$-Fe$_2$O$_3$ nanoparticles encapsulated in amorphous SiO$_2$ were prepared by the wet chemical method, and carboxyl-modified functionalized nanoparticles were successfully produced. Magnetization curves confirmed the presence of ferromagnetic or superparamagnetic behaviour, depending on particle size. These magnetic nanoparticles are expected to be used as carriers in drug delivery systems (DDSs), and they could also be employed in hyperthermia treatment and other biomedical applications.

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