

Original Research

Synthesis and study of structural and magnetic properties of super paramagnetic $\text{Fe}_3\text{O}_4@\text{SiO}_2$ core/shell nanocomposite for biomedical applications

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Abstract

Objective(s): This paper describes coating of magnetite nanoparticles (MNPs) with amorphous silica shells.

Materials and Methods: First, magnetite (Fe_3O_4) NPs were synthesized by co-precipitation method and then treated with stabilizer molecule of trisodium citrate to enhance their dispersibility. Afterwards, coating with silica was carried out via a sol-gel approach in which the electrostatically stabilized MNPs were used as seeds. The samples were characterized by means of X-ray diffraction (XRD), transmission electron microscopy (TEM), Fourier transform infrared (FT-IR) spectroscopy and vibrating sample magnetometer (VSM).

Results: The results of XRD analysis implied that the prepared nanocomposite consists of two compounds of crystalline magnetite and amorphous silica that formation of their core/shell structure with the shell thickness of about 5 nm was confirmed by TEM images. The magnetic studies also indicated that produced $\text{Fe}_3\text{O}_4@\text{SiO}_2$ core/shell nanocomposite exhibits superparamagnetic properties at room temperature.

Conclusion: These core/shell structure due to having superparamagnetic property of Fe_3O_4 and unique properties of SiO_2 , offers a high potential for many biomedical applications.

Keywords: Biomedical applications, Core-shell structure, Magnetite, Silica, Super paramagnetism

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Introduction

In recent decade, the integration of nanotechnology with molecular biology and medicine has resulted in active developments of a new emerging research area, nanobiotechnology, which can significantly advances the current clinical diagnostic and therapeutic methods (1). In this field, core/shell nanostructures (the most common type of multifunctional nanoparticles) are new generation of nanostructures in nanomedicine that have combined components with different functionalities in one single entity and thus can achieve different tasks simultaneously.

Magnetite (Fe_3O_4) nanoparticles (MNPs) are one of the most used structures as a core to fabricate core/shell systems due to their strong superparamagnetic properties (2) in which nanoparticles would have zero magnetic remanence with a high magnetic susceptibility. Based on their unique properties, superparamagnetic nanoparticles offer a high potential for several biomedical applications, such as contrast agents in magnetic resonance imaging (MRI), carriers for targeted drug delivery, hyperthermia, magnetic separation in microbiology and detoxification of biological fluids (3,4).

In the past few years, many kinds of materials have been discovered for use as a shell coating around the MNPs, including noble metals, metal oxides and inorganic silica (5). Among these coating materials, silica due to having several unique advantages is one of the most ideal coating layers: (a) silica coating prevents magnetic nanoparticles from aggregation in wide pH ranges and improves their chemical stability, (b) silica surface is often terminated by a silanol group that can react with silane coupling agents for conjugation with a variety of biomolecules and specific ligands and (c) the SiO_2 layers possess a good biocompatibility and hydrophilicity, which are indispensable for biomedical applications (6,7). Up to date, several popular methods including co-precipitation, microemulsion, thermal decomposition, solvothermal and sonochemical have

been reported for synthesis of MNPs (8) among which, chemical co-precipitation is the preferred route due to its advantages such as simple and easy processing operation, high yield of products with superior crystallinity and magnetic behaviors, low temperature and time of reaction and utilization of inorganic reactant (9).

In spite of named benefits, there is a major shortcoming in using the prepared Fe_3O_4 NPs by co-precipitation method as a core to fabricate core/shell structures: as a result of large surface to volume ratio, high surface energy and magnetic dipole-dipole attractions between the particles, MNPs are highly prone to aggregation (10).

Therefore, in order to synthesize well-dispersed silica-coated MNPs, surface modification and stabilization of magnetite nanoparticles prior to fabrication of the core/shell nanostructures is necessary.

For example, Chang et al. (11) reported the formation of silica on the surface of magnetite NPs stabilized with a surfactant (oleic acid).

One has to consider that although surfactant stabilized MNPs could used to prepare of silica-coated MNPs via Stöber sol-gel approach (the most commonly used method for generate silica coatings on the surface of MNPs), the obtained composites are usually stained by surfactants and the coating process is difficult to control because surfactant molecules are easy to desorb from MNPs by alcohol dissolution (12).

To solve this problem, in this paper, we report a facile approach which is based on using electro-statically stabilized MNPs as seeds. For this purpose, the prepared Fe_3O_4 nanoparticles by co-precipitation method were firstly coated with stabilizer molecules of trisodium citrate to enhance their dispersion in reaction media during the coating process and then, magnetite-silica nanocomposite were synthe-sized by using these electrostatically stabilized NPs as seeds (12) through the Stöber method.

Figure 1 shows schematic presentation of this process.

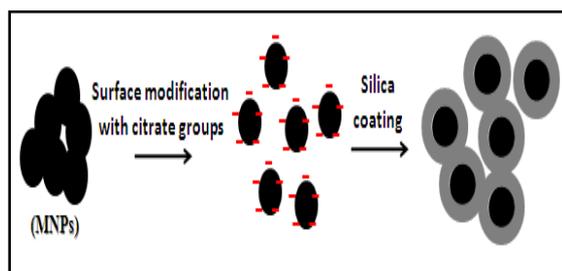


Figure 1. Schematic presentation of the synthesis process of magnetite-silica nanocomposite.

Materials and Methods

Materials

Ferrous chloride tetrahydrate ($\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$), ferric chloride hexahydrate ($\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$), hydrochloric acid (HCl), ammonia solution (NH_3 , 32%), ethanol, trisodium citrate dehydrate ($\text{C}_6\text{H}_5\text{Na}_3\text{O}_7 \cdot 2\text{H}_2\text{O}$) and tetraethyl orthosilicate (TEOS) were purchased from Merck Co. All the chemicals were analytical grade and were used without further purification. Deionized water was also used throughout the experiment.

Synthesis and stabilization of Fe_3O_4 nanoparticles

Fe_3O_4 NPs were synthesized by coprecipitation method. The typical procedure is as follow:

First, a 2M solution of NH_4OH (alkali source) was added dropwise into a solution containing 4.54 g $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 1.9 g $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ and 0.18 ml HCl dissolved in 15 ml deoxygenated deionized water under vigorous magnetic stirring and N_2 gas protection at a temperature of 70°C .

The color of solution turned from orange to black immediately, due to the formation of magnetite NPs. Then, after stirring for 30 min, heating of precipitate was allowed to crystallize completely for another 90 min. Finally, MNPs were isolated from solution by applying an external magnetic field and washed several times with deionized water and ethanol.

To stabilize Fe_3O_4 nanoparticles, the obtained magnetic mud was re-dispersed in 150 ml trisodium citrate solution (0.5 M) via

ultrasonic irradiation and the reaction mixture was then stirred for 1h at 80°C .

Thereafter, the magnetic precipitate was washed with acetone to remove the excessive citrate groups and dried under vacuum.

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In this step, first, a 2.0 wt% magnetic fluid (MF) was made by dispersing the citrate-modified MNPs (MNPs-C) in deionized water via ultrasonic irradiation and then, the coating process were carried out by using obtained MF as seed through the Stöber method.

2 g of the MF was well-dispersed in the solution containing 40 ml water, 120 ml ethanol and 2.35 ml ammonia by ultrasonic vibration for 1 h. TEOS solution was prepared by addition of 0.1ml TEOS to 20ml ethanol and subsequently was dropwise added to the reaction mixture.

Finally, after stirring for 12 h at ambient temperature, the obtained product was washed with ethanol and dried under vacuum for 12 h.

Characterizations

The phase purity and crystal structure of the samples were investigated using Philips PW1800 X-ray diffractometer with $\text{Cu K}\alpha$ radiation ($\lambda = 0.154 \text{ nm}$) in the 2θ range of $20\text{-}70^\circ$ and 0.04 degree step size. Transmission electron microscope (TEM, LEO 912 AB) and Fourier transform infrared (FT-IR) spectrophotometer (Avatar-370-FTIR Thermo Nicolet) were also employed for the characterization of the samples. Magnetic measurements were carried out at room temperature (300 K) by means of vibrating sample magnetometer (VSM).

Result and Discussion

Morphology and structure study of the synthesized samples

The crystallinity and phase purity of the synthesized MNPs were determined by X-ray diffraction (XRD) (Figure. 2).

Synthesis of superparamagnetic core/shell nanocomposite

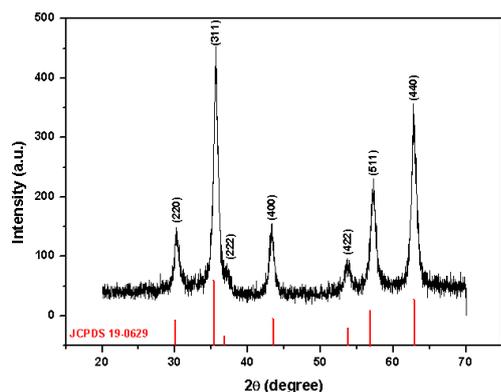


Figure 2. X-ray diffraction pattern of Fe_3O_4 nanoparticles.

As seen, all the characteristic peaks corresponding to Bragg diffractions of the crystal planes (220), (311), (222), (400), (422), (511) and (440) agree with standard JCPDS (joint committee on powder diffraction standards) pattern characteristic peaks of the magnetite cubic inverse spinel structure (19-0629) which indicates high phase purity of synthesized nanoparticles. Moreover, the sharp peaks observed in Figure. 2 indicate a high degree of crystallinity for the MNPs. Based on XRD data, Fe_3O_4 NPs structural parameters such as position and width of peaks, crystalline size, lattice constant and distance between crystal planes, were calculated by analyzing (311) and (440) major peaks whose results are summarized in Table 1. The average crystalline size was calculated using the Debye-Scherrer formula (13):

$$D_{\text{XRD}} = k \lambda / \beta \cos \theta \quad (1)$$

where k is the grain shape factor (0.94), λ is the incident X-ray wavelength (1.54 \AA), β is the full width at half-maximum (FWHM) and θ is the diffraction angle.

Also, the average value of the lattice constant was obtained from the following formula:

$$a = d_{\text{hkl}} [h^2 + k^2 + l^2]^{1/2} \quad (2)$$

where h , k and l are the Miller indexes, and d_{hkl} is the interplanar spacing ($d_{\text{hkl}} = \lambda / 2\sin\theta$) (2). The average values of crystalline size and lattice constant were calculated to be 12.75 nm and 8.315 \AA by application of (1) and (2) formulas to the (311) and (440) major

reflection peaks at $2\theta = 35.61^\circ$ and $2\theta = 62.84^\circ$, respectively.

Figure 3 shows TEM images together with size distribution histograms of both the unmodified MNPs and citrate-modified MNPs. The average size for MNPs is about $14.29 \pm 4.05 \text{ nm}$ whilst for MNPs-C is about $15.41 \pm 4.11 \text{ nm}$ and both of them have approximately spherical shape. One can see that there was no significant change in the size or the morphology alterations of the MNPs and citrate-modified MNPs.

As observed in Figure. 3(a), despite of their hydrophilicity, Fe_3O_4 NPs are extremely aggregate which is attributed to their large specific surface area, high surface energy and magnetization (10).

Therefore, in this work, for the purpose of well-dispersed silica-coated MNPs synthesis, stabilizer molecules of trisodium citrate were used to modify the surface and to stabilize prepared Fe_3O_4 NPs prior to coating with silica.

The citrate molecules, by creating electrostatic repulsion between nanoparticles (due to the presence of di-carboxyl ($-\text{COO}$) groups with negative charge on the surface of NPs), prevent their aggregation and promote their dispersion (Figure. 3(b)).

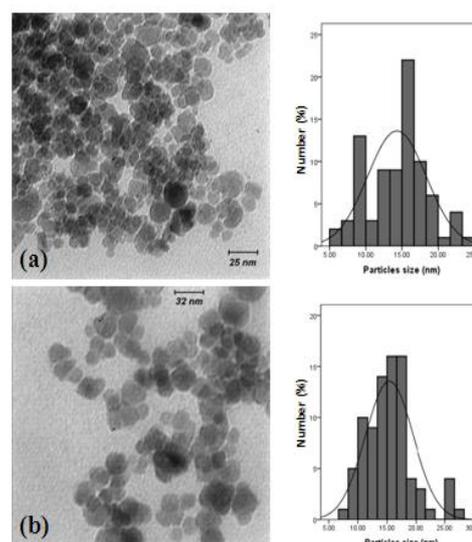


Figure 3. TEM images of MNPs (a) before and (b) after surface modification with 0.5M trisodium citrate solution.

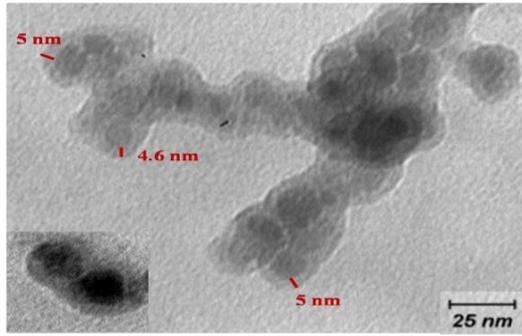


Figure 4. TEM image of the magnetite-silica core/shell nanocomposite.

The TEM image of silica-coated MNPs is shown in Figure. 4. In this figure, two regions with different electron densities can be distinguished that confirms formation of core/shell structure: an electron dense region which corresponds to magnetic cores and a less dense and more translucent region surrounding these cores that is silica coating shell with thickness of about 5 nm.

Table 1. The obtained structural parameters of XRD analysis.

(hkl)	2θ (deg.)	FWHM (deg.)	D _{XRD} (nm)	a (Å°)	d _{hkl} (Å°)
(311)	35.61	0.689	12.6	8.32	2.51
(440)	62.84	0.756	12.9	8.31	1.47

FT-IR analysis

In order to testify the presence of the silica coating and citrate groups on Fe₃O₄ NPs surface, FT-IR analysis of synthesized samples was performed (Figure 5). In Fig.5(a)

the presence of intense absorption bands at 425, 591 and 624 cm⁻¹ wavenumbers which respectively attributed to Fe-O stretching vibrations of Fe²⁺ and Fe³⁺ ions placed in tetrahedral sites and Fe³⁺ ion placed in octahedral sites, indicates formation of Fe₃O₄ structure (14). Again observation of these absorption peaks in citrate-modified and silica-coated MNPs (Figures. 5(b) and 5(c)) implies that MNPs don't change chemically or physically after surface modification and coating processes.

Compared to pristine MNPs, appearance of a new absorption peak in the range of 1307-1463 cm⁻¹ and also intensification of peak with 1620 cm⁻¹ wavenumber are observed in FT-IR spectrum of citrate-modified MNPs, which are characteristic of the carboxylate. It indicates that trisodium citrate has been successfully bonded on the surface of MNPs (15). In Figure. 5(c), absorption bands at 801 and 1094 cm⁻¹ are also characteristic peaks of the symmetrical and asymmetrical vibrations of Si-O-Si bond that attest silica matrix formation (4).

It must be mentioned that in all FT-IR spectra demonstrated in Figure. 5, two absorption bands centered at 1624 and 3432 cm⁻¹ can also be seen which are related to O-H stretching vibration of free water molecules and surface hydroxyl groups or adsorbed water on samples surface (9,16). All the aforementioned absorption bands are outlined in Table 2 with the assignments of the associated functional groups.

Table 2. FT-IR absorption wavenumbers with the assignments of the associated functional groups.

IR Wavenumbers (cm ⁻¹)			Assignment of absorption bands
MNPs	Citrate-modified MNPs	Silica-coated MNPs	
425, 591 and 624	419, 584 and 617	464, 590 and 677	ν(Fe-O)
1624 and 3432	1620 and 3432	1610, 1653 and 3270	ν(O-H)
-	1307-1463	1339-1425	ν _s (-COO-)
-	1620	1610 and 1653	ν _a (-COO-)
-	-	801	ν _s (Si-O-Si)
-	-	1094	ν _a (Si-O-Si)

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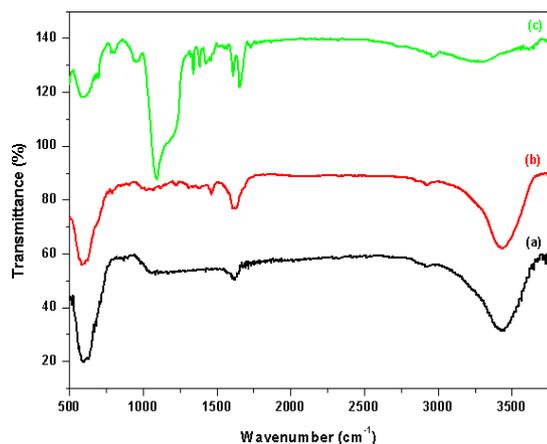


Figure 5. FT-IR spectra of: (a) pristine MNPs, (b) citrate-modified MNPs and (c) Fe₃O₄@SiO₂ nanocomposite.

Magnetic properties analysis

VSM technique was employed to study magnetic properties of synthesized Fe₃O₄ NPs and Fe₃O₄@SiO₂ nanocomposite at room temperature, whose resultant magnetization curves are shown in Fig. 6. The magnetization curve indicates magnetization as a function of applied magnetic field.

Based on these curves, data related to coercivity field (H_c), remnant magnetization (M_r), saturation magnetization (M_s) and initial magnetic susceptibility (χ_i), as the magnetic characteristics of samples were calculated whose the obtained results are summarized in Table 3.

In order to calculate the ultimate saturation magnetization (M_s), the magnetization (M) was plotted against $1/H$ (M at $1/H \geq 0$). From extrapolation of this curve, the magnitudes of M_s when $1/H \approx 0$, were obtained of 70 emu/g and 33.80 emu/g for Fe₃O₄ NPs and Fe₃O₄@SiO₂ nanocomposite, respectively. The $\chi_i = (dM/dH)_{H \rightarrow 0}$ value was also determined

from the magnetization curves by curve-fitting to the linear portion ($H \approx 0$) of data.

The negligibility of H_c (field strength required to bring the material back to zero magnetization) and M_r (value of magnetization at zero field) values in absence of an external magnetic field (inset in Figure. 6) indicates that both samples possess superparamagnetic property at room temperature although M_s value of Fe₃O₄@SiO₂ nanocomposite is significantly less than pristine MNPs.

The reason of observed reduction could be explained by the presence of diamagnetic silica shell surrounding MNPs that has weakened magnetic moment of inner magnetic core and diminished the inductive effect of the magnetic field (15, 9).

One of the parameters calculable by magnetic data is magnetic particle size or magnetic domain size, D_m , which can be determined using the following formula (17):

$$D_m = \left[\frac{18 k_B T}{\pi \rho} \times \frac{\chi_i}{M_s^2} \right]^{1/3} \quad (3)$$

Where k_B is the Boltzmann constant (1.38×10^{-23} J/K), T is the absolute temperature (300K) and ρ is the density of Fe₃O₄ (5.18 g/cm^3).

Using the calculated χ_i (0.1971 emu/g Oe) and M_s (70 emu/g) values, a magnetic particle size of 12.25 nm was obtained at 300K for MNPs which is less than that estimated from TEM images ($D_{\text{TEM}} = 14.29 \text{ nm}$).

This difference can be attributed to presence of the canted spins in the surface layers due to decrease in the exchange coupling which leads to formation of magnetically dead surface layers around the magnetic cores (18).

Table 3. Magnetic characteristics obtained from VSM analysis.

	M_r (emu/g)	M_s (emu/g)	H_c (Oe)	χ_i (emu/g Oe)
Fe ₃ O ₄	1.11	70	5	0.1971
Fe ₃ O ₄ @SiO ₂	0.11	33.80	0.74	0.1121

Conclusion

In this work, we successfully synthesized $\text{Fe}_3\text{O}_4@\text{SiO}_2$ core/shell nanocomposite by a sol-gel approach, using electrostatically stabilized magnetite NPs as seeds.

Magnetic and structural properties of the prepared

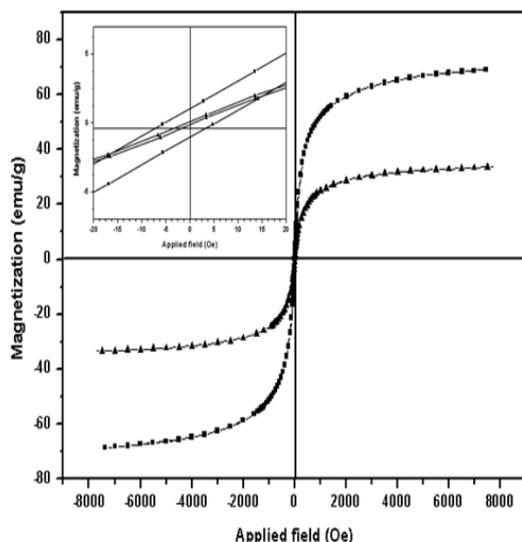


Figure 6. Magnetization curves of Fe_3O_4 NPs (■) and $\text{Fe}_3\text{O}_4@\text{SiO}_2$ nanocomposite (▲) at 300K. Inset: the enlarged curves from -20 to 20 Oe.

samples were investigated by XRD, TEM, FT-IR and VSM techniques whose results are mentioned below:

1. The results of XRD analysis imply that the prepared nanocomposite consists of crystalline magnetite cores and an amorphous silica shell that formation of their core/shell structure was confirmed by TEM images. TEM images show also improvement in dispersibility of the MNPs after surface modification with citrate groups.

2. The presence of the silica coating and citrate groups on MNPs surface attested from the FT-IR absorbance peaks.

3. The synthesized magnetite-silica nano composite exhibits superparamagnetic behaviour at room temperature although its M_s value is significantly less than pristine MNPs.

It is believed that the prepared nanocomposite with its magnetic potential can be considered for different biomedical applications.

Acknowledgments

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