

A COLLOIDAL Zn-DOPED Fe₃O₄ AS CONTRASTING AGENT FOR MRI DIAGNOSTICS

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Stabilized colloidal solutions of sol-gel derived Fe₃O₄ and Zn_{0.18}Fe_{2.82}O₄ nanosized oxides were studied as potential contrasting agents for MRI. The samples were characterized by TEM, SEM, XRD, PMR- and IR-spectroscopy. The Zn-doped Fe₃O₄ was shown to have higher magnetization and T_2 -relaxivity as compared to pure Fe₃O₄. A low concentration threshold of the contrasting activity has been achieved for both samples.

1. Introduction

Advances in nanotechnology and molecular biology are rapidly enabling the development of nanoparticles (NPs) with specific functional properties that address the shortcomings of traditional disease diagnostic and therapeutic agents [1–2]. Brighter, tissue-specific magnetic resonance imaging (MRI) probes are being developed with NP technology to visualize and help diagnose diseases at the earliest stages. Gd-based MR contrast agents are widely employed although they suffer from an inherent high threshold of detectability and high toxicity [3].

Magnetic nanoparticles have gained significant attention due to their intrinsic magnetic properties, which enable tracking through the MRI [4]. This class of NPs include metallic, bimetallic, and superparamagnetic iron oxide nanoparticles (SPIONs) [4, 5]. The latter of which has been widely favored because of its inoffensive toxicity profile and reactive surface that can be readily modified with biocompatible coatings [6].

Currently, a number of SPIONs are in early clinical trials or experimental study stages [4, 5, 6], and several formulations have been approved for clinical use for medical imaging and therapeutic applications (e.g. Ferridex IV, Lumiren, Combidex). Specifically, magnetic NPs have been formed from iron oxides, including magnetite (Fe₃O₄) and maghemite (γ -Fe₂O₃) [6]. They have also been doped to enhance their magnetic properties to form $M\text{Fe}_2\text{O}_4$ structures where M is a +2 cation such as Mn, Co or Ni [7, 8]. However, these materials are potentially toxic that makes them poor candidates for clinical use.

Herein, we represent a study on the preparation of stabilized colloidal solutions of magnetite and Zn-doped magnetite as non-toxic contrasting materials for medical and biological MRI examinations.

2. Experimental

Nanoparticles of Fe_3O_4 and $\text{Zn}_{0.18}\text{Fe}_{2.82}\text{O}_4$ were prepared by an inorganic sol-gel approach. Water solutions of $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$, $\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ and $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ taken in the corresponding proportions was added to a solution of NaOH under stirring. The precipitates were washed with water. Stable sols were obtained under ultrasonification of the suspension with the addition of citric acid.

The powdered samples dried at 60°C were characterized by scanning (SEM) and transmission electronic microscopy (TEM), X-ray diffraction (XRD) and infrared spectroscopy (IR). Grain size and morphology were estimated on a LEO 906E and a LEO 1420 microscopes. The XRD analysis was carried out on a DRON-2 diffractometer using Co-K α radiation. IR spectra were recorded from powdered samples on an AVATAR FTIR-330 spectrometer.

Magnetization measurements were performed with a Cryogen Free Measurement System (CFMS) Cryogenic Ltd ($T = 7\text{--}300\text{ K}$, $B_{\text{max}} = 18\text{ T}$).

Proton magnetic resonance (PMR) measurements were carried out on an ADVANCE 500 high-resolution spectrometer.

3. Results and Discussion

The XRD patterns of the synthesized Fe_3O_4 and Zn-doped Fe_3O_4 ($\text{Zn}_{0.18}\text{Fe}_{2.82}\text{O}_4$) powders are shown in Fig. 1. For all samples, the only reflections attributed to a cubic spinel structure were observed. The diffraction lines are diffuse and broad, as expected for nanosized and poorly crystallized materials. The lattice parameter a was calculated for the Fe_3O_4 and $\text{Zn}_{0.18}\text{Fe}_{2.82}\text{O}_4$ powders to be 8.369 and 8.391 Å, respectively. All this indicates the formation of a substitutional solid solution in the case of the magnetite slightly doped with Zn (7 mol. %)

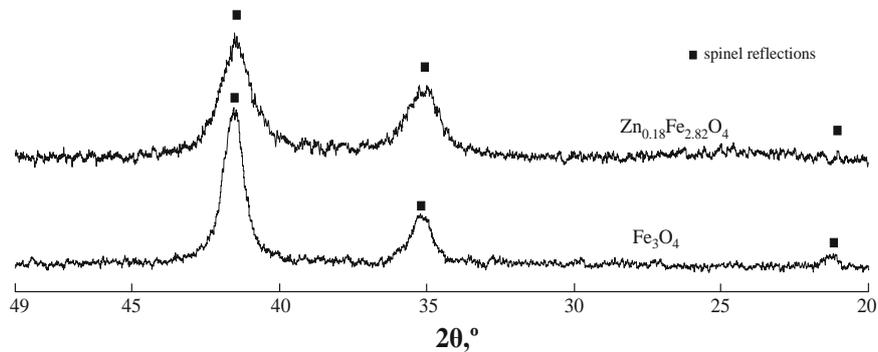


Figure 1. Fragments of the XRD patterns the pure and Zn-doped magnetites.

To clarify the character of zinc distribution in the synthesized ferrites, IR spectroscopy was used. The IR data testify for the formation of a substitutional solid solution in the $\text{Zn}_{0.18}\text{Fe}_{2.82}\text{O}_4$ sample. The poor crystallinity and the high concentration of structural and adsorbed OH-groups were confirmed for both the Fe_3O_4 and the Zn-doped Fe_3O_4 samples prepared by the method used here.

As expected, both the pure and the doped magnetites demonstrate similar morphology. Thus, TEM micrographs of the samples given in Fig. 2 show the diameter of the grains to be in a range from 5 to 13 nm. The grains have a nearly spherical shape with an average diameter of about 7 nm.

The specific magnetization of the powdered samples were measured as a function of the applied magnetic field. It was revealed that that the magnetization of all the samples is not completely saturated at the maximum value of the external magnetic field (50 kOe).

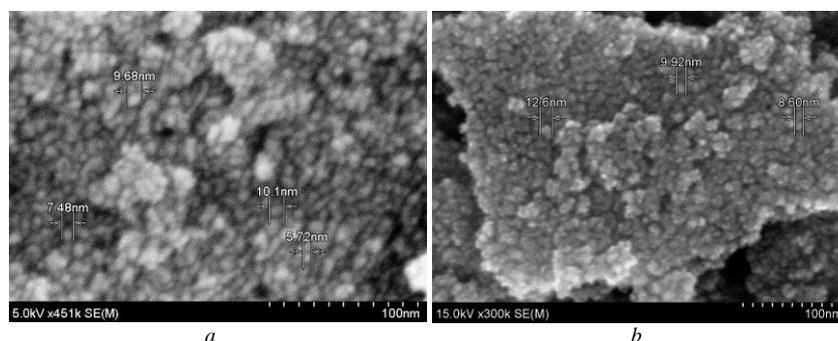


Figure 2 SEM images of the Fe_3O_4 (a) and $\text{Zn}_{0.18}\text{Fe}_{2.82}\text{O}_4$ (b) powders.

At 5 K, the samples show a hysteresis behavior with small coercivities. In contrast, at 300 K, all the samples display no hysteresis. This indicates that in the prepared powders the majority of the particles have a diameter below the size critical for a superparamagnetic behavior, which is in an agreement with the TEM and XRD data given above. It was found that the doping of Fe_3O_4 with 7 mol. % of Zn causes an increase in its magnetization due to a redistribution of the cations between the octahedral and the tetrahedral sites in the spinel lattice. The maximum magnetization values were measured at 300 K for the Fe_3O_4 and the $\text{Zn}_{0.18}\text{Fe}_{2.82}\text{O}_4$ powders to be about 50 and 60 $\text{A} \cdot \text{m}^2 \cdot \text{kg}^{-1}$, respectively.

Proton magnetic resonance (PMR) analysis of the prepared samples shows that the sols of Fe_3O_4 and $\text{Zn}_{0.18}\text{Fe}_{2.82}\text{O}_4$ are characterized by a low detecting threshold (C_{tr}) and a high contrasting ability in magnetic resonance imaging (MRI) (Table 1). The effectiveness of contrasting materials for MRI could be

estimated with a relaxivity: $r = (T_0 - T_s)/C_s$, where T_0 and T_s – times of proton relaxation in water and in the sols of the contrasting agents, C_s – concentration of the contrasting agent.

Table 1. The characteristics of the synthesized contrasting materials

Sample	Mode	T_0 , s	T_s , s	r , mole ⁻¹ ·l·s ⁻¹	C_s , mole·l ⁻¹	C_{tr} , mole·l ⁻¹	M_{sat} , A·m ² ·kg ⁻¹
Zn _{0.18} Fe _{2.82} O ₄	T_1	14.44	12.63	2.0	$8.57 \cdot 10^{-3}$	$7.5 \cdot 10^{-3}$	~60
Fe ₃ O ₄	T_1	14.44	11.33	2.2	$8.64 \cdot 10^{-3}$	$6.8 \cdot 10^{-3}$	~50
Zn _{0.18} Fe _{2.82} O ₄	T_2	3.37	0.09	1220	$8.57 \cdot 10^{-3}$	$2.4 \cdot 10^{-4}$	~60
Fe ₃ O ₄	T_2	3.37	0.11	1070	$8.64 \cdot 10^{-3}$	$2.7 \cdot 10^{-4}$	~50

MRI contrasting agents based on nanosized metal oxides show a moderate activity in a T_1 (spin-lattice) relaxation mode [4, 5]. The highest relaxivities were achieved for both the studied samples examined in a T_2 (spin-spin) relaxation mode. The doping of magnetite with Zn results in an increase in the relaxivity by 150 mole⁻¹·l·s⁻¹, which is likely caused by an enhanced magnetization of the Zn_{0.18}Fe_{2.82}O₄ as compared to the pure Fe₃O₄ (see Table 1).

4. Conclusion

A stabilized colloidal solution of a nanosized (~7 nm) Zn_{0.18}Fe_{2.82}O₄ solid solution as a potential contrasting material for MRI has been synthesized via an inorganic sol-gel technique. The sample is characterized by a superparamagnetic behavior at 300 K. The Zn-doped magnetite demonstrates a higher magnetization values (60 A·m²·kg⁻¹) as compared to the pure magnetite (50 A·m²·kg⁻¹). The nanocrystalline nature and the high magnetization of the synthesized ferrite particles result in their advanced features for MRI – the low concentration threshold and the high relaxivity in T_2 relaxation mode.

References

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