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Synthesis and physical characterization of magnetic nano-particles functionalized with β-cyclodextrin

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The synthesis and characterization of magnetite nanoparticles suspended in neutral pH colloidal fluid intended for medical purposes is presented. The ferrophase was prepared by chemical precipitation from ferric and ferrous hydrated salts in alkali medium, being further coated with β – cyclodextrin, so that neutral pH could be reached following the suspension in water. Measurements of magnetization and magnetic susceptibility were performed revealing the suitability for utilization as magnetic carrier in medical diagnosis or therapy. The microstructural analysis was carried out by transmission electron microscopy (TEM). Infrared absorption spectra have been recorded aiming to get some supplementary information on the core-shell interaction within the colloidal nanoparticles. Physical tests have been applied in order to reveal the rheological features of the magnetic colloidal suspension. The interpretation of all measurements was fulfilled with respect of the literature data regarding the stability and biocompatibility of functionalized magnetic nanoparticles.

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1. Introduction

Biophysicists pay more and more attention to the magnetic nanoparticles functionalized with a nonmagnetic molecular surfactant that prevents the irreversible aggregation of the magnetic cores and makes them suitable for biomedical applications. Stable colloidal suspensions of core-shell system can be assured by controlling the physical diameter - in the nanometric range so that each particle represents a magnetic mono-domain. Nanoparticles made of iron oxide cores and hydrophilic macromolecules are of particular interest as contrast agents in magnetic resonance imagistic or as hyperthermia mediators [1-2]. In the last years the magnetic labeling and cell separation was developed as a useful technique in molecular and cellular medicine [3]. Among the earliest detailed studies on aqueous dispersions of magnetite colloidal particles were those performed by Massart [4], who proposed the auto-catalysis reactions which result in the co-precipitation of ferric and ferrous oxide particles with narrower size distribution. To get magnetic nanoparticles for medical applications producers usually work with magnetite cores which are known as biocompatible. Their coating in single or double shell with organic hydrosoluble and biodegradable molecules is carried out. While for biological research, focused on various types of cells either vegetal, animal or microorganisms, investigated either *in vitro* or *in vivo*, acid or basic magnetic nanoparticles suspensions might be of equal interest, in the case of nanoparticles injection into the human body the neutral colloidal suspensions are required such as those stabilized with dextran or different polymers. Cyclodextrins are widely applied in the medicine, pharmaceutical industry, environmental protection food and chemical industry due to their ability to form inclusion compounds by coating various organic and inorganic structures. In the next we present the preparation and characterization of magnetite coated with β-cyclodextrin to get aqueous dispersion for medical research purposes.

2. Experimental

Magnetic nanoparticles preparation. The synthesis of magnetic nanoparticles has been carried out via a controlled chemical precipitation approach, at room temperature [5]. Aqueous mixture of ferric and ferrous salts and NH_3 as an alkali source were prepared as stock solutions. The stock solution of ferric and ferrous salts was prepared in presence of 2M HCl solution since the acidic conditions prevent formation of iron hydroxides. 6.0ml of acidic solution of $FeCl_2 \cdot 4H_2O$ (7.95g in 10ml HCl 2M) with 24.0 ml of acidic solution of $FeCl_3 \cdot 6H_2O$ (13.52g in 50 ml HCl 2M) were magnetically mixed up. Continue stirring was assured throughout the slow addition into the beaker of 300 ml aqueous 0.7M NH_4OH solution. A black precipitate, i.e. the magnetite, was separated immediately. The magnetite was decanted in an inhomogeneous magnetic field the supernatant being eliminated. Further, the magnetite was washed several times with 800 ml deionized water until the pH of the washing liquid remained neutral. After filtration the obtained ferrophase (2.16g) was vigorously mechanically mixed with 0.1g β-cyclodextrin ($C_{42}H_{70}O_{35}$) and 6ml deionized water at neutral pH.

Structural investigation. TEM and IR investigations were carried out. Transmission electron microscopy was the main investigation method for the assessing of the ferrophase particle size. Image analysis was accomplished on about 1000 particles. TESLA device with a resolution of 1.0nm was utilized (sample deposition of collodion sheet after 10^{-4} dilution).

Infrared absorption spectra have been recorded in the 4000-400 cm^{-1} range aiming to get some information on the composition of magnetic colloidal particles, using a Bruker Vertex 70 FT-IR infrared spectrometer, and KBr disks.

In order to characterize the crystalline structure of the magnetite nanoparticles X-rays diffraction measurements were performed on magnetite powder, using a DRON 2.0 X-rays diffractometer and Cu-Kα radiation at 1.5418 Å.

Magnetic properties. Magnetic susceptibility and magnetization measurements were carried out by Gouy method. Magnetic field intensity was measured by means of Walker Scientific MG 50D Gaussmeter with Hall probe. For sample weight an electronic balance ACULAB-200 with 10^{-4}g accuracy was used. The measurements were performed at constant temperature ($22.0 \pm 0.1^{o}C$) using in all cases the same air-tight nonmagnetic cylindrical sample holder with 3mm diameter and 25cm length, placed perpendicular to the magnetic field.

Rheological investigation. The density of the magnetic colloidal suspension (picnometric method), the dynamic viscosity (capillary method with an Ubbelohde viscosimeter) and the surface tension (stalagmometric method) were measured using standard methods. The electrical conductivity measurements using a standard universal device LCR were performed. The samples have been placed in a special holder for electrical measurements.

Measurements of pH values were carried out with high quality Merck indicative paper.

3. Results and discussions

TEM microphotographs showed that the size of coated magnetite nanoparticles ranges between 1 and 30 nm, exhibiting mostly spherical shape, with minimal agglomeration. Image analysis was carried out on about 1000 nanoparticles. A TEM image of as-prepared β-cyclodextrin coated magnetite is shown in Fig. 1.

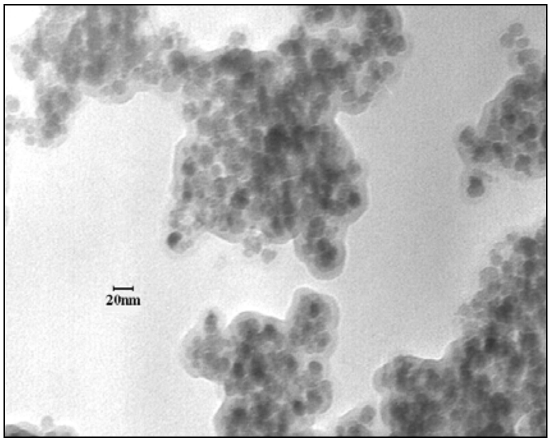

Fig.1. TEM image for magnetite particles functionalized with β-cyclodextrin.

In Fig. 2 the histogram of size particles distribution and the log-normal fit are presented. The average value of the magnetite particle physical diameter was equal to 12.3 nm.

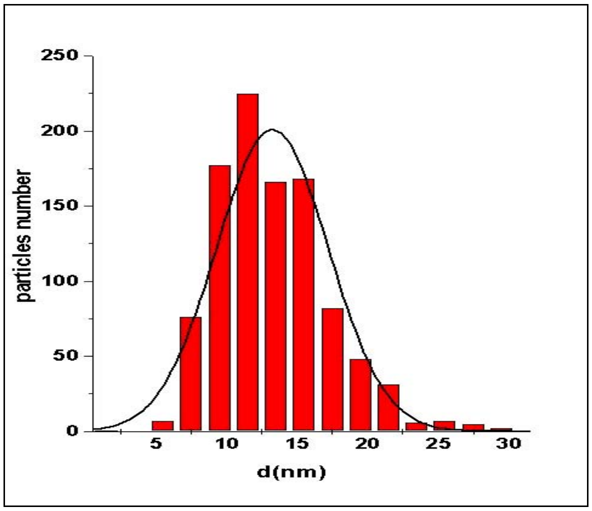

Fig. 2. Diameter distribution of magnetic nanoparticles functionalized with β-cyclodextrin

Further analysis was carried out by means of FT-IR spectra (4000 cm^{-1} – 400cm^{-1}) which are presented in Fig. 3. The FT-IR spectra of the nanoparticles functionalized with β-cyclodextrin shows intense absorption beyond 600 cm^{-1} associated with the stretching and torsional vibration modes of the magnetite. The assignments are concordant with Keiser et al. [6]. We can notice the presence of the absorption bands in the 850-1600 cm^{-1} range, that are corresponding to characteristic vibrations of β-cyclodextrin molecules. This observation may suggest that the β-cyclodextrin molecule structure remains intact beyond magnetite nanoparticles coating reactions. The intense band at 1600cm^{-1} may be assigned to the deformation vibrations of water molecules trapped onto the magnetite colloidal particles while the large and intense absorption band from 3450cm^{-1} corresponds to the symmetric and asymmetric stretching of OH groups from β-cyclodextrin molecule.

The XRD investigation was carried out on the uncoated magnetite, synthesized as presented above, dried until constant weight at 100°C. Using XRD data, the average crystal size of magnetite was estimated following the Scherrer's equation ($D_{hkl} = 0.9\lambda / B\cos\theta$), where λ is the X-ray wavelength, θ is the Bragg angle and B is effective full width at half maximum of the XRD diffraction line [7]. The value provided by the above formula was 7.6 nm. These results agree with the previous results regarding the average crystalline size of magnetite particles.

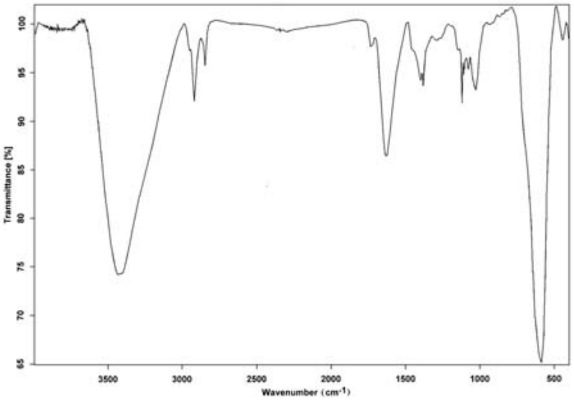

Fig. 3. FT-IR spectra for magnetite functionalized with β-cyclodextrin.

Magnetization curves can be used for the study of both particle interactions and agglomerate formation, processes which strongly influence the rheological behavior of magnetic colloidal suspensions.

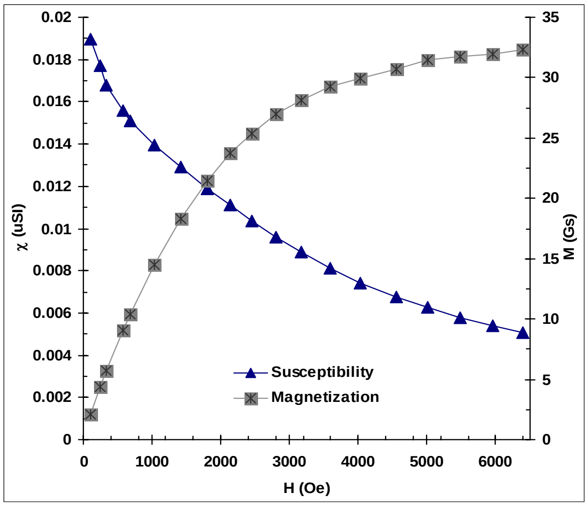

Fig.4. Magnetization and susceptibility curves of the magnetite nanoparticles coated with β-cyclodextrin.

The saturation magnetization was obtained from magnetization versus $1/H$ curves, by extrapolating to $1/H = 0$. The initial susceptibility χ_i was determined from the susceptibility curve registered by extrapolating the initial linear curve to $H = 0$. The saturation magnetization value was of 35 Gs while initial magnetic susceptibility value was of 0.022. In Fig.4 are presented the magnetization and susceptibility curves check in for magnetite functionalized with β-cyclodextrin.

The volume fraction Φ of ferrophase particles in the magnetic colloid was determined from mass density measurements according to $\Phi = \frac{\rho_F - \rho_L}{\rho_S - \rho_L}$ equation, where ρ_F is the density of the nanoparticles suspension, ρ_L the density of the carrier liquid, and ρ_S that of the solid particles.

Densities values, measured by means of picnometric method at T = 295K in Table I are given together with rheological data (average values calculated following ten repetitions of every measurement).

Table 1. The rheological measurement values.

Φ	Density (kg/m^3)	Surface tension (*10^{-3} N/m)	Viscosity (*10^{-3} kg/ms)	Electrical conductivity (S/m)
0.023	1082.77 ± 1.9%	89.20 ± 1.06%	4.01 ± 6%	0.018

We can observe that the density, viscosity and surface tension have relatively high values compared to similar nanoparticles suspension discussed in literature [8].

4. Conclusions

Magnetic nanoparticles suspension, prepared by using the β-cyclodextrin as stabilization substance in water dispersion, was adjusted in order to get some physical parameters concordant with the literature data. The availability for biological purposes is assured by the fine ferrophase diameter while the magnetic properties were evidenced also. Its future destination for living tissues applications will be accompanied by adequate measurements of the biological effects. Deeper investigation is planned within the future research project which is designed to optimize the preparation details in order to yield functionalized biocompatible magnetic nanoparticles.

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