

Preparation and Characterization of Magnetic Iron Oxide (Fe_3O_4) Nanoparticles with Different Polymer Coating Agents

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Abstract

In the present study, the influence of the organic stabilizers on the formation of magnetic iron-oxide nanoparticles was investigated. Polyethylene glycol (PEG), dextran (DEX), and chitosan was chosen as biocompatible surface modification agents for obtained magnetic nanoparticles. The structure of the coated Fe_3O_4 nanoparticles was learned by the X-ray diffraction and Fourier-transform infrared spectroscopic methods. It was explored that the PEG coated magnetic nanoparticles have relatively larger crystallite sizes, which indicate a more ordered crystal structure of these nanoparticles. Furthermore, FT-IR analysis showed that the Fe_3O_4 -PEG system possesses a stronger nanoparticle-stabilizer interaction at the supramolecular level. This study emphasizes the significance of optimizing the surface properties of magnetic nanoparticles when using them in biomedical applications.

Keywords: Magnetic Iron Oxide Nanoparticles, Surface Modification, Biocompatible Coating Agents, Polymer Stabilizers

Introduction

Magnetite nanoparticles (MNPs) have attracted significant attention for different biomedical applications, including heat mediators in hyperthermia, nanocarriers for drug delivery or biochemical molecules, and contrast agents in magnetic resonance imaging (MRI) [1-5]. In these applications, control of particle size, size distribution, shape as well as surface modification are critical steps required for effectively implementing the utilization of MNPs [6-10]. It was established that the unmodified MNPs have high surface energy which makes them thermodynamically unstable and grounds their agglomeration [11]. It is caused by the interaction of MNPs due to their strong magnetic dipole-dipole attraction and steric effects coming from van der Waals forces [12]. Aggregated MNPs are recognized by the reticuloendothelial system (RES) and are accordingly eliminated from the blood circulation [13]. Therefore, some coating procedures with various materials, for instance, long-chain-like polymer materials are required to improve their stability in highly ionic solutions [14-17]. For the obtaining of coated MNPs, polymers emerge as a priority among other materials due to their effortless and straightforward preparation and cost-effectiveness [18, 19]. Moreover, with an excellent hydrophilic feature, uncharged or weakly charged biocompatible polymers, such as polyethylenimine (PEI), polyethylene glycol (PEG), poly(lactic-co-glycolic acid) (PLGA), polyvinylpyrrolidone (PVP), polyvinyl alcohol (PVA), chitosan, starch, and dex-

tran (DEX) have been widely used as protective shells to decrease the agglomeration of MNPs in the presence of serum proteins [20-29]. In addition, the temperature and pH-sensitive characteristics of polymer coating materials could allow for the management of the drug release from the MNPs, for instance, in targeted drug delivery systems [19, 30].

In this study, magnetic iron-oxide nanoparticles were synthesized by the chemical co-precipitation synthesis method, and the samples were produced by using PEG, DEX, and chitosan as biocompatible coating agents. The samples' structure characterization is accomplished by Fourier-transform Infrared Spectroscopy (FT-IR) and X-ray powder diffraction (XRD) spectra, as well as, Scanning Electron Microscopy (SEM) images.

Materials and methods

Materials

Iron (III) chloride tetrahydrate ($\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$), iron (III) chloride hexahydrate ($\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$), polyethylene glycol (PEG), dextran (DEX), chitosan (degree of deacetylation <90%), ammonium hydroxide (NH_4OH , 23-25%) and acetic acid (CH_3COOH , 99%) were purchased from Karma Lab (Izmir, Turkey). All chemicals were of analytical grade.

Preparation of magnetite nanoparticles with various coating materials

Magnetic iron oxide nanoparticles were obtained via the co-precipitation method. In this synthesis, $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, and $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$, with a 2:1 mole ratio were each dissolved in 50 mL of deionized water. The two solutions were mixed into a 250 mL beaker glass and stirred and then heated until 70°C for 30 min under the nitrogen atmosphere. For coating with PEG appropriate amount of polymer was slowly added to the solution, and stirring was continuing about 1h. After it, 10-15 mL NH_4OH 23-25% was added drop-wise until the pH was 10 and the temperature was increased until 90°C and solution was vigorously stirred for about 1h [31-33]. Further liquid and precipitate separated using NdFeB magnet and washed with deionized water and ethanol several times. Finally, PEG coated magnetic iron oxide nanoparticles were put in an oven and subsequently dried for 4h at 80°C .

To coat with dextran, 8 g polymer was added to the solution, and the whole process was repeated in the same way. Coating with chitosan was implemented, first, with the preparation of the chitosan solution. For this 0.25 g of fine chitosan powder was dissolved in the mixture of the 25 mL of deionized water and 1.25 mL of acetic acid. Chitosan coated magnetic nanoparticles were obtained in the above-described way.

Characterization of coated magnetite nanoparticles

The synthesized and coated magnetic iron-oxide nanoparticles were characterized by SEM, XRD, and FT-IR techniques. The SEM (JEOL JSM-7600 F) was used for the morphology and size characterization. The XRD (Rigaku Mini Flex 600) with $\text{Cu K}\alpha$ radiation was employed for the phase analysis. The FT-IR characterizations of magnetic Fe_3O_4 nanoparticles with various coating agents were determined with Varian 3600. FT-IR spectra were obtained with KBr pellets and the spectrum was taken from $4000\text{--}450\text{ cm}^{-1}$.

Results and Discussion

Figure 1 shows X-ray diffractograms of iron oxide nanoparticles coated with PEG, DEX, and chitosan. Characteristic X-ray lines are observed for magnetic nanoparticles prepared with all three coating agents. So, the d-spacing values of significant peaks match well with (ICDD DB card number 01-073-9877). Furthermore, the average crystallite size of Fe_3O_4 nanoparticles obtained by different coating agents was calculated using Scherrer's equation as follows:

$$d = 0,9\lambda / \beta \cos\theta$$

Calculations were carried out for $35,58^\circ$; $35,65^\circ$; $35,40^\circ$ values of 2 theta angles for nanoparticles stabilized by PEG, DEX, and chitosan. The average crystallite size for iron oxide nanoparticles obtained with different polymer coating agents is given in Table 1.

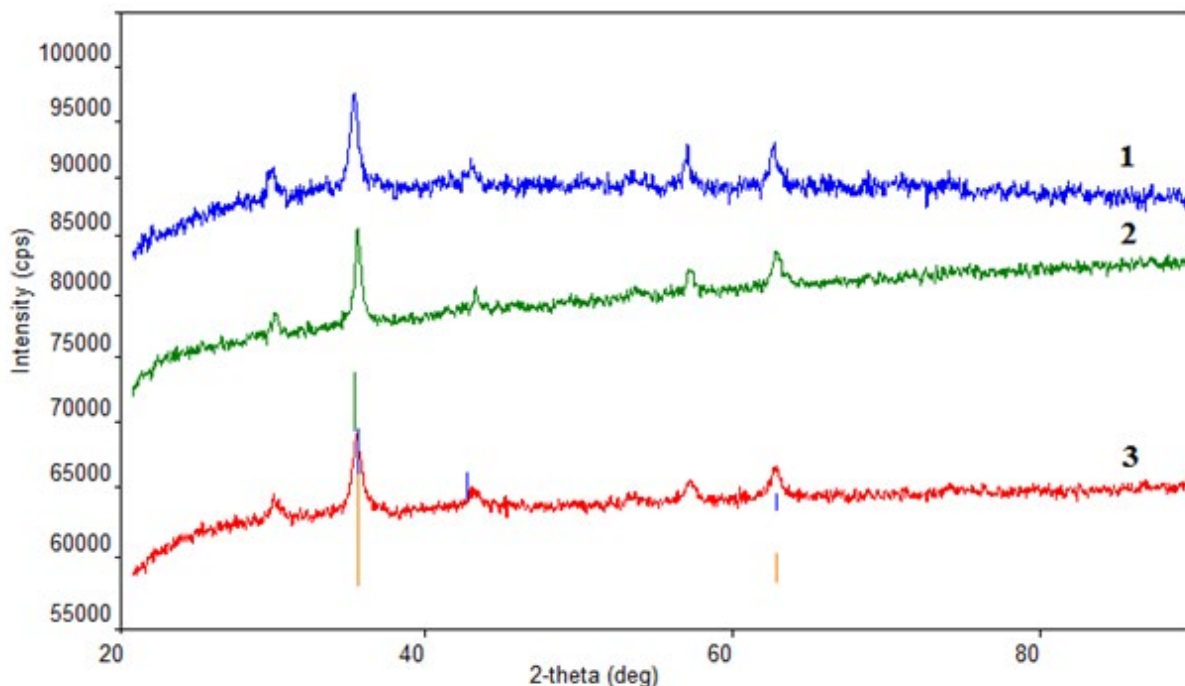


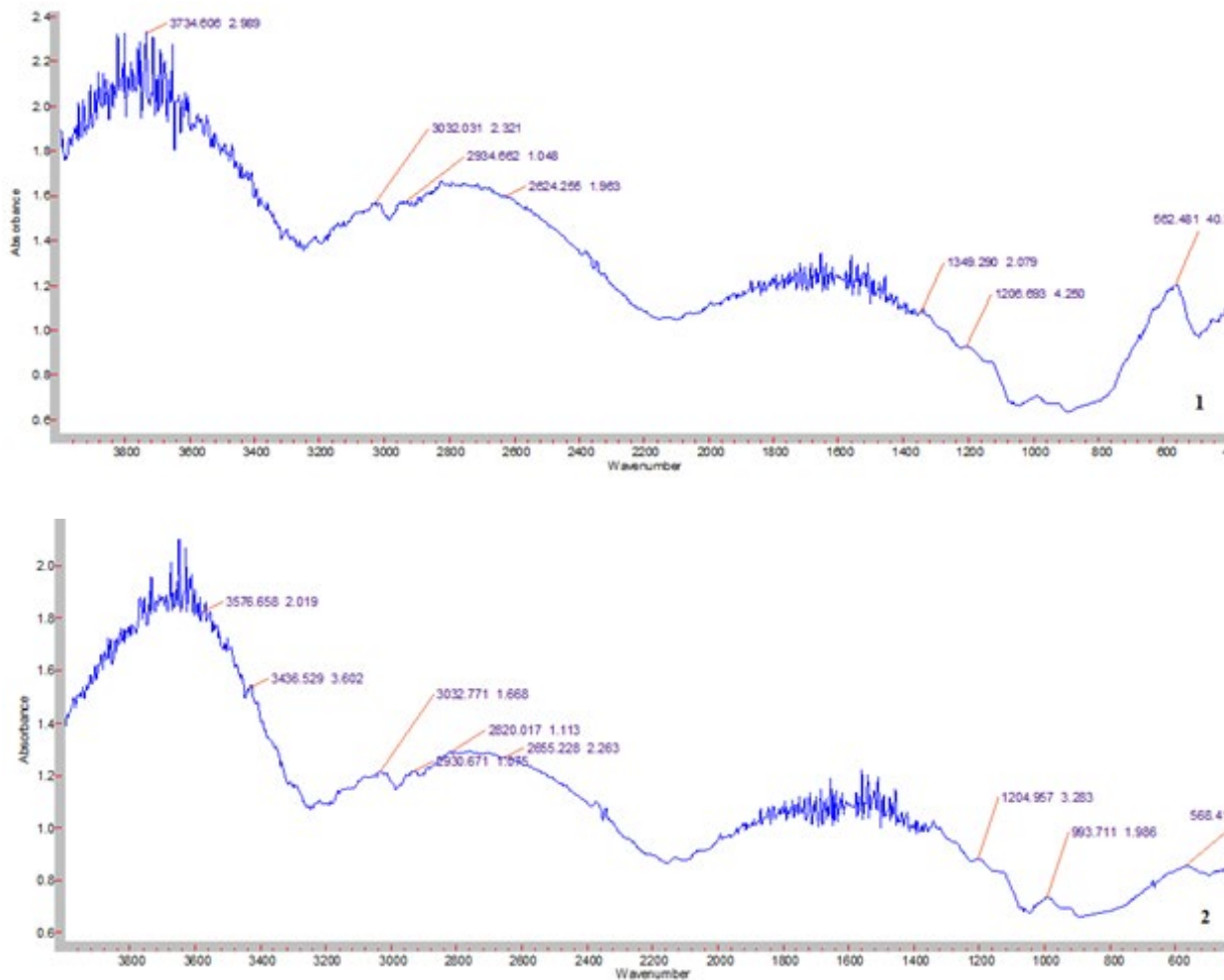
Figure1: X-ray diffractogram of iron oxide nanoparticles obtained by different coating agents: Fe_3O_4 +PEG (1); Fe_3O_4 +chitosan (2); Fe_3O_4 +DEX (3).

Table1. The average crystallite size for iron oxide nanoparticles obtained with different coating agents

Samples	Fe ₃ O ₄ +PEG	Fe ₃ O ₄ +DEX	Fe ₃ O ₄ +chitosan
The average crystallite size of nanoparticles (nm)	25,30	25,17	25,10

The relatively narrow and sharp peaks in the XRD patterns of the Fe₃O₄+PEG indicate better crystalline characteristics of this sample than Fe₃O₄+DEX and Fe₃O₄+chitosan samples. Table 1 demonstrates that the magnetic nanoparticles modified by PEG have relatively larger crystallite sizes. It can be explained that a more ordered crystal structure is formed during the nucleation process of the iron oxide nanoparticles coated with PEG molecules [34,35]. Electrical neutrality, significant spatial repulsion, and high hydrophilicity of PEG molecules may have had a positive effect on the magnetic nanoparticles modification by this polymer [36]. It should also be noted that the effect of the molecular weight of PEG macromolecule on the average crystallite size of the magnetite nanoparticles is negligible [34].

Figure 2 shows the IR spectra of iron oxide nanoparticles obtained with different coated agents. The characteristic absorption bands of Fe₃O₄ nanoparticles in the IR region are in the range of 400-600 cm⁻¹ [37]. The absorption lines at 570 cm⁻¹ on the FT-IR spectrum of DEX-coated iron oxide nanoparticles correspond to the vibrational oscillations of the Fe-O bond [38]. The same band was observed at 568cm⁻¹ on the spectrum of chitosan-coated nanoparticles [39]. On the spectrum of the PEG-coated Fe₃O₄, the band corresponding to the Fe-O bond was blue-shifted. The shift can be explained by the strengthening of the interaction between the stabilizer and the nanoparticle at the supramolecular level, the decrease in the degree of freedom of the atoms of the nanoparticle, in other words, the decrease in the frequency of oscillations of the Fe-O bond.



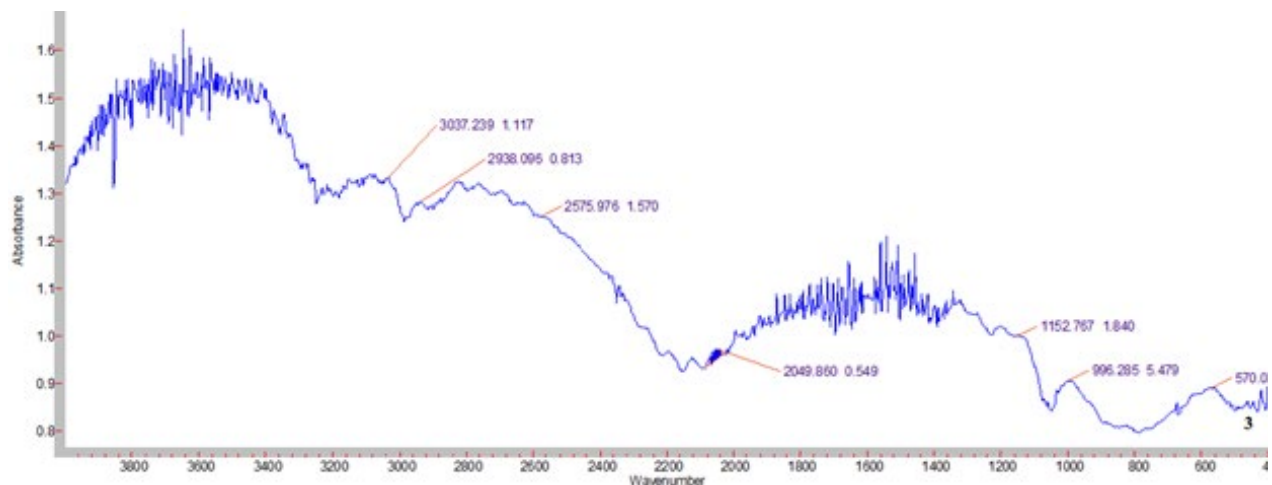


Figure 2: FTIR spectra of iron oxide nanoparticles obtained with different coating agents: Fe₃O₄+PEG (1); Fe₃O₄+chitosan (2); Fe₃O₄+DEX (3).

The results obtained from the IR spectra are in agreement with the XRD patterns. Among the considered coated agents, the most optimal coating for magnetic nanoparticles synthesized for biomedical purposes is PEG .

Figure 3 shows the SEM image of the surface morphology PEG-coated iron oxide nanoparticles. The scanning process was performed in SEI mode at an accelerating voltage of 15 kV and a working distance of 4.5 mm.

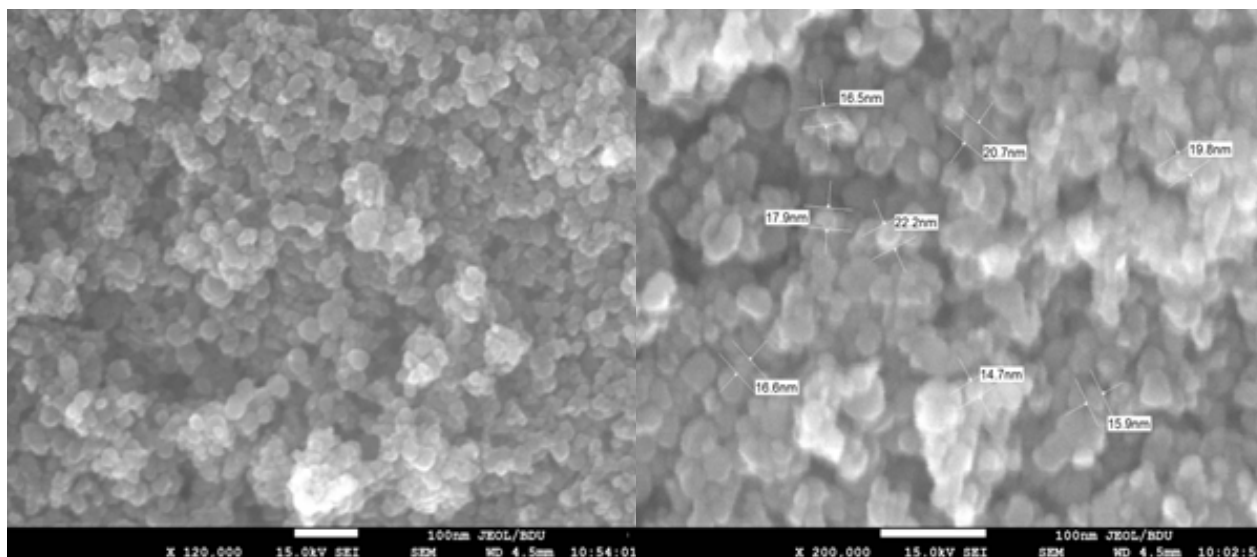


Figure 3: SEM images of PEG coated iron oxide nanoparticles.

As can be seen from the picture, the average size of Fe₃O₄ nanoparticles is 18-20 nm. This showed that the synthesized nanoparticles meets the size requirements for biomedical application [40, 41].

Conclusion

In the present study, magnetic iron-oxide nanoparticles was synthesized with the help of different biocompatible coating agents, namely, PEG, DEX, and chitosan. The structure of the produced nanoparticles was investigated by X-ray diffractometer, FT-IR spectrometer and Scanning Electron Microscope. It was explored that magnetic nanoparticles coated by PEG macromolecules are more suitable for biomedical application. The nanoparticles stabilized by PEG have relatively larger crystallite sizes, which in-

dicates a more ordered crystal structure of these nanoparticles. Furthermore, FT-IR analysis showed that the Fe₃O₄+PEG system possesses a stronger nanoparticle-stabilizer interaction at the supramolecular level. The size of the PEG-coated nanoparticles was about 18-20 nm which is suitable for their biomedical application.

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Competing Interests

The authors declare no conflict of interest.

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