

Full Paper

Facile Electro-synthesis and Characterization of Superparamagnetic Starch Coated Gd³⁺ Doped Iron Oxide Nanoparticles for Biomedical Applications

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Abstract- Magnetic particles i.e. Fe₃O₄ nanoparticles have received great attention because of their potential biomedical applications like as MRI contrast agent, hyperthermia and biosensing magnetic labels. For these biomedical applications, Fe₃O₄ nanoparticles particles must have proper surface coatings and also acquire superparamagnetic properties with relatively high *M_s* values. Here, we performed Gd doping of iron oxide particles and their *in situ* surface modification through an electrochemical strategy. The prepared particles were examined using XRD, IR, TG, FE-SEM and EDAX analyses and their covering with starch and doping by Gd cations were approved. VSM data further proved the superparamagnetic behavior of the electrosynthesized iron oxide particles.

Keywords- Electrochemical synthesis, Iron oxide, Gd doping, Surface modification, Magnetic particles

1. INTRODUCTION

Iron oxides (IOs), Fe₃O₄ and Fe₂O₃, are interested candidates for use in many fields of medical, biological, environmental and energy storage [1-6]. Among these applications, the

potential use of iron oxides in the biomedical area has been recently more investigated, which includes magnetic resonance imaging contrast enhancement, hyperthermia, cell separation, and drug delivery, etc [7-11]. In this regard, nanoparticles of magnetite phase of iron oxide i.e. Fe_3O_4 , are more suitable and gained wide attention, which is related to their superparamagnetic behavior at room temperature [12-15]. In fact, for clinical applications, IO particles should provide major physical, chemical and pharmacological requirements, which include crystal structure, magnetic behavior, size uniformity, chemical composition, surface structure, solubility and low toxicity [16-18]. Due to hydrophobic interactions between the iron oxide particles, the IOs tend to be agglomerated through large clusters/particles formation. These tendencies yield bigger particles size with low colloidal stability. Also, the formed large IO clusters/particles show ferromagnetic behavior [19-21]. In order to improve and preserve the colloidal and magnetic stability, surface covering of IO with special biocompatible molecules like as PEG [22,23], PEI [24,25], chitosan [26,27], PVA [28,29], dextran [30], PVP[31,32] and saccharides [33,34] has been proposed.

As an saccharide, starch can also be used as a functional biocompatible-polymer, which is composed of repeating 1,4- α -D glucopyranosyl units: amylose and amylopectin [35,36]. The starch presents strong hydrophilic and biodegradable behaviors [37,38]; hence, the starch covering of iron oxide surfaces could be potential interest for biomedical uses. In addition to surface modification, which provides colloidal stability for the prepared IOs, the IOs doping with various transition metal ions have been also applied for improvement of their superparamagnetic behavior [39-47]. Based on these advances in the design of IOs for biomedical applications, here, we report Gd doping IOs and their surface modification with starch. For synthesis of these novel nanoparticles, the electrochemical deposition method was chosen due to its facility and simplicity in the fabrication of nanostructured inorganic materials [48-56]. The starch capped Gd doped iron oxide (starch/Gd-IO) was fabricated through two-electrode deposition system with applying constant current between anode and cathode electrodes. The obtained samples are characterized through by DSC-TGA, FE-SEM, FT-IR, XRD and VSM analyses.

2. EXPERIMENTAL PROCEDURE

2.1. Materials

Iron (III) nitrate nonahydrate ($\text{Fe}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$), Iron (II) chloride tetrachloride ($\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$), gadolinium chloride hexahydrate ($\text{GdCl}_3 \cdot 6\text{H}_2\text{O}$) and starch ($\text{C}_{12}\text{H}_{22}\text{O}_{11}$), were purchased from Merck company, Germany. The graphite plates and stainless steel sheets (316L) were provided from local companies.

2.2. Synthesis of iron oxide

A simple two-electrode electrochemical deposition procedure was chosen to prepare samples. The deposition solution was prepared through dissolving iron(II) chloride /iron(III) nitrate/ gadolinium(III) chloride salts with molar ratios of 0.5:2:0.5, and 1g starch in one liter distilled water. After applying constant current ($i=10 \text{ mA/cm}^2$), the black film was formed on the cathode side. Then, the film was washed with water and dried at $80 \text{ }^\circ\text{C}$ for 1h. In final, the dried film was removed from the steel cathode and the obtained powder was labeled starch/Gd-IOs.

2.3. Instrumental Analysis

FT-IR spectra of samples in the form of KBr pellets were recorded by a Bruker Vector 22 IR spectrometer. X-ray powder diffraction (XRD) patterns were recorded in a Rigaku diffractometer, model X Pert Phillips PW-1800 using $\text{Co K}\alpha$ radiation. Field-emission scanning electron microscopy (FE-SEM) images were obtained on VEGA/TESCAN-Mira 3-XMU and elemental analysis was performed through Energy Dispersive X-ray Spectroscopy (EDAX). The thermal behavior data was recorded in an N_2 atmosphere between RT and 500°C at a heating rate of $5 \text{ }^\circ\text{C min}^{-1}$ using a thermoanalyzer (STA-1500). Magnetization measurements were performed in a magnetic field (H) of up to 20 kOe using a vibrating sample magnetometer (VSM, Lakeshore-7400).

3. RESULTS AND DISCUSSION

3.1. Crystal structure

The XRD pattern was used to identify the iron oxide phase of the electrodeposited powder. In Figure 1, all the peak positions at 18.1 (111), 29.4 (200), 35.7 (311), 42.7 (400), 54.1 (422), 57.5 (511), and 63.2 (440) are consistent with the standard X-ray data for the magnetite phase (JCPDS no. 19-0629). No additional peaks were observed. So, the XRD pattern verified the magnetite phase of starch/Gd-IO sample.

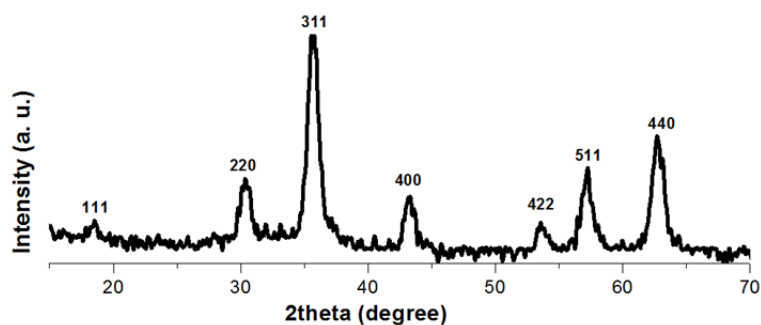


Fig. 1. XRD pattern of the electrodeposited iron oxide/starch composite

3.2. Thermogravimetric analyses

Fig. 2 shows the DSC and related TG profiles for the prepared sample at temperature range of 25-500 °C. The DSC profile has two contentious endothermic peaks at temperature ranges of 25-150 °C and 150-350 °C. The first one is related to the removal water and hydroxyl groups attached to the Gd-IO particles [47,56]. The weight loss due to this step is about 4.5%. The second peak is assigned to the starch degradation [57,58]. TG curve (in Fig. 2b) shows 16.5% weigh loss. After this step, TG curved has a small weigh loss (about 2.3%), which is due to the conversion of magnetite to the FeO. The total weight loss of sample is observed to be 23.3%. These observations proved the presence of starch onto the electrodeposited Gd-IO particles.

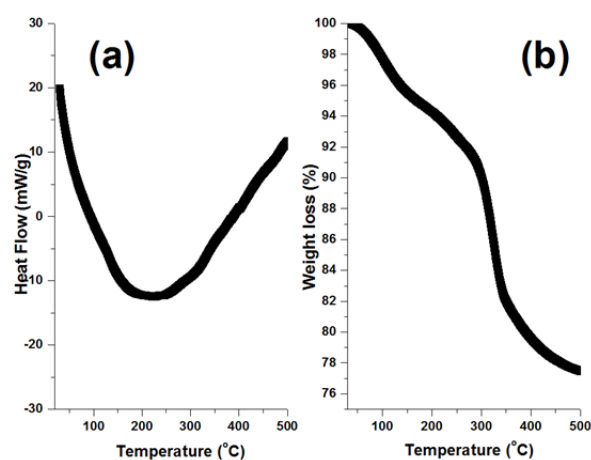


Fig. 2. (a) DSC and (b) related TG curves of the electro-synthesized starch capped iron oxide

3.3. FT-IR

The presence of the coating agents on the surface of the IO nanoparticles was also supported by the FT-IR spectroscopy analysis. FTIR spectral pattern of starch/Gd-IO sample is shown in Fig. 3. The band observed at 519 cm^{-1} and 565 cm^{-1} are related to the Fe–O–Fe/or Gd–O–Fe vibrations [59-61], which proved the magnetite structure of the prepared sample. The broad characteristic band from 3450 to 3100 cm^{-1} could be assigned to O-H stretching vibration arising from hydroxyl groups on nanoparticles and adsorbed starch, and water [62]. The peaks around 2915 and 2862 cm^{-1} , assignable to asymmetric and symmetric vibrations of C-H in $-\text{CH}_2-$, can be obviously found [63]. The absorption regions observed at 3145 and 1631 cm^{-1} were due to the presence of water molecules, and the peak at 1412 cm^{-1} reflects the bending modes of O-C-H, C-C-H, and C-O-H angles [64,65]. The absorption region at 1085 and 1025 cm^{-1} relates to C-C and C-O stretching modes of the polysaccharide backbone [64,66]. Furthermore, the peaks at 1478 cm^{-1} , 1150 cm^{-1} and 860 cm^{-1} are due to the CH_2

bending, C–C stretching, CH₂ deformation, respectively [65,66]. These IR data verified the fabrication of starch capped Gd-IO particles.

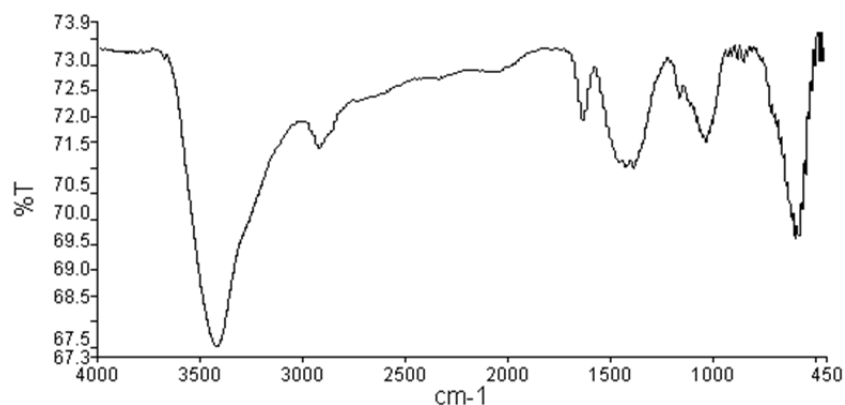


Fig. 3. IR spectrum of the electrodeposited iron oxide/starch composite

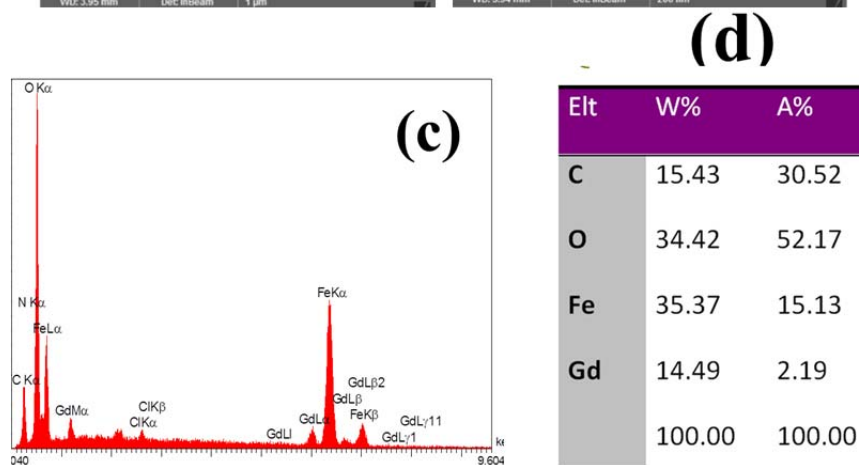
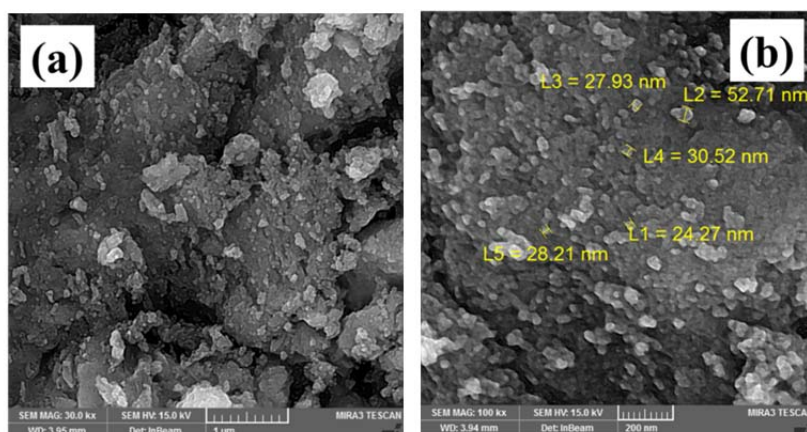


Fig. 4. (a,b) FE-SEM images and (c,d) EDS graph and data for the prepared iron oxide/starch sample

3.4. Morphological characterization

FE-SEM images (Figs. 4a-b) and Energy Dispersive X-ray graph and data (Figs. 4c-d) are provided to determine the morphology and composition of the fabricated sample. For the synthesized starch/Gd-IO sample, the particulate-shape texture is seen in the SEM observations (Figs. 4a-b). The observed particles have an average size of 30 nm in diameter (Fig. 4b). The elemental graph and data collected from EDAX analysis are presented in Figs. 4c-d. For our sample, the presence of carbon, oxygen, gadolinium and iron is confirmed through EDAX graph. These elements have weight percentage of 15.43% (for C), 34.43% (for O), 14.49% (for Gd) and 35.37% (for Fe). The presence of carbon and gadolinium in the composition of the electrodeposited powder established two facts: (i) doping of iron oxide with Gd cations during their electrochemical deposition, and (ii) *in situ* surface capping of iron oxide particle with starch during their electrosynthesis. Hence, it is concluded that the applied electrochemical strategy has successful performance in the fabrication of starch/Gd-IO nanoparticles.

3.5. Magnetic analysis

Magnetic properties of the prepared sample were investigated by VSM and the related magnetization curves are depicted in Fig. 5. It is observed that magnetic hysteresis loop of both samples exhibits superparamagnetic characteristic at RT condition. Saturation magnetization (M_s) value of starch/Gd-IO particles is 38.44 emu g^{-1} (as seen in Fig. 5a), where this value for the uncapped Gd-IO has been reported to be 40.67 [61]. The prepared sample exhibited low remanent magnetization and coercivity at condition of removing the applied field as clearly observable in Fig. 5b. These data indicated that although M_s value decreases after covering of Gd-IO with starch, it is still high enough to be readily separated by an external magnetic field.

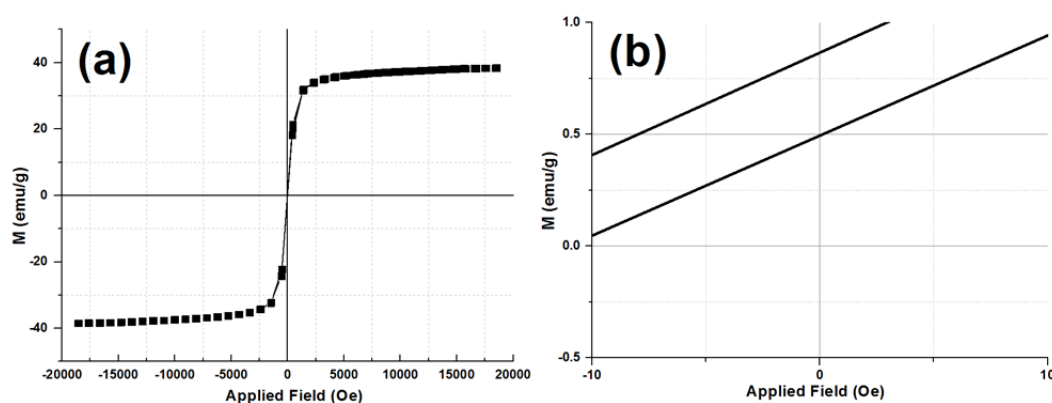


Fig. 5. Room temperature M-H curves for the fabricated sample

The other magnetic factors for the prepared sample are: $M_r=0.18 \text{ emu g}^{-1}$ and $C_e=3.92 \text{ Oe}$. These data further verified the superparamagnetic nature of the electrodeposited sample and their proper magnetic behavior for use in various biomedical applications.

4. CONCLUSION

In summary, we developed an electrochemical route for Gd doping and in situ surface coating of iron oxide particles during their synthesis. Using these method, starch capped Gd-iron oxide particles was prepared and their superparamagnetic properties, magnetite crystal phase and particle morphology were approved through VSM, XRD, FT-IR and FE-SEM analyses. The findings approved that the prepared polymer capped Gd doped iron oxide particles have proper physico-chemical properties for biomedical applications.

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