

Full Paper

EDTA Capped Mn²⁺ Doped Superparamagnetic Fe₃O₄ Nanoparticles for Biomedical Application: Development of a Novel Electrosynthesis Route and Characterization

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Abstract- In this work, electrochemical synthesis was applied for the fabrication of ethylenediaminetetraacetic acid (EDTA) capped and metal-cations doped magnetite nanoparticles. The electro-deposition process was performed in the constant current mode using an aqueous electrolyte containing FeCl₂.4H₂O (0.5 g), Fe(NO₃)₃.9H₂O (2 g), MnCl₂.6H₂O (0.5 g) and 0.2 g EDTA capping agent. The prepared samples were examined by analyses of XRD, IR, TG, EDAX, FE-SEM and VSM. The XRD results proved the magnetite crystal structure of the deposited powder. All chemical bands of EDTA were observed in the IR spectrum of the sample. And EDAX data indicated the doping of iron oxide nanoparticles by Mn²⁺ cations during their electrochemical preparation. Based on the TG results, it was observed that EDTA capped layer has been formed onto the deposited iron oxide particles. The vibrating sample magnetometer (VSM) data (*i.e.* $M_s=41.77$ emu g⁻¹, $M_r=0.15$ emu g⁻¹ and $H_c=3.97$ G) was also confirmed the super-paramagnetic nature of the EDTA capped iron oxide nanoparticles. Based on the results, the cathodic electrochemical synthesis was proposed as a facile procedure for the preparation of EDTA-coated Mn²⁺ doped SPIONs.

Keywords- Iron oxide, Metal ion doping, Magnetic particles, Electrochemical synthesis

1. INTRODUCTION

During recent decade, superparamagnetic nanoparticles of iron oxides (SPIONs) i.e. Fe_3O_4 have attracted a great deal of research attention due to their practical use as targeted drug delivery [1,2], magnetic resonance imaging (MRI) contrast agents [3,4], hyperthermia [5,6], adsorbent in heavy metal removal [7,8] and energy conversion and storage (batteries [9-11] and super-capacitors [12-14]). The preparation of pure Fe_3O_4 has been explained through several techniques such as chemical precipitation or hydrothermal/solvothermal route [15-21]. In most case Fe_3O_4 is synthesized as a powder whose particle size can be controlled over a large dimension range [15-18]. The preparation parameters should be carefully selected to avoid production of other iron oxides and oxyhydroxides like as maghemite and/or hematite [17-21]. Due to its magnetic properties, Fe_3O_4 is often investigated in the various biomedical fields such as immobilization of bio-materials, bio-separation, environmental treatment, biomedical and bioengineering usage, and food analysis [22,23]. Furthermore, for these bio-applications, the charge, size, and surface groups/functions of the SPIONs are particularly important and directly affects their bioavailability within the body and the circulation time [15,22]. Also, magnetic actions and internalization of particles strongly related to the size of the Fe_3O_4 particles [17,23]. Although, many works have focused on SPIONs synthesis by three common methods of co-precipitation, hydrothermal and thermal decomposition, however, the control of the SPIONs size is very vital in order to tune their magnetic properties in the above mentioned fields [24-26].

As alternative and simple technique, electrochemical synthesis has been demonstrated for the preparation of metal oxide NPs [26-32]. In the case of iron oxide NPs, it was reported that uncoated and polymer coated SPIONs could be simply fabricated by one-step cathodic electro-deposition in both aqueous and organic electrolytes [33-36]. It should be noted that the functionalization or surface capping of SPIONs with biocompatible agents should be performed in order to provide the biocompatibility in biomedical uses [37]. The biocompatible coat on the surface of SPIONs give them the solution stability and fast magnetic response. It is worth noting that although the preparation of metal ion doped SPIONs has been recently developed by Aghazadeh et al. [38-41], however, the electrochemical synthesis has not been used for the fabrication of surface capped metal-ion doped SPIONs. Herein we report ethylenediaminetetraaceticacid (EDTA) capped Mn^{2+} -doped SPIONs for the first time. These SPIONs are prepared through one-step electrodeposition from the EDTA dissolved nitrate/chloride $\text{Fe}^{3+}/\text{Fe}^{2+}/\text{Mn}^{2+}$ electrolyte. The formation of EDTA capped Mn^{2+} -doped SPIONs are proved though XRD, FT-IR, FE-SEM, TGA and VSM analyses. The results validated the successful fabrication of EDTA capped Mn^{2+} -doped SPIONs via our simple applied electrochemical method.

2. EXPERIMENTAL PROCEDURE

2.1. Materials

$\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ (99.9%), $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ (99%), $\text{MnCl}_2 \cdot 6\text{H}_2\text{O}$ (99.5%) and ethylenediaminetetraacetic acid disodium salt dehydrate (EDTA- Na_2 , 99.9%) were purchased from Sigma Aldrich. All materials were used as received and without any purification.

2.2. Synthesis of iron oxide

The electrochemical deposition electrolyte was selected to be $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ (0.5 g), $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ (2 g) and $\text{MnCl}_2 \cdot 6\text{H}_2\text{O}$ (0.5 g) dissolved in the one liter deionized H_2O . Also, 1 g/L EDTA was added into this solution as capping agent. A two-electrode system including a stainless-steel and graphite plate was used as the cathode and anode electrodes, respectively. The deposition runs were performed in the constant current (CC) regime with a typical current density of 20 mA cm^{-2} . The deposition time and bath temperature were 15 min and $25 \text{ }^\circ\text{C}$, respectively. At the end of each run, black film was deposited onto the steel surface. After deposition time, the steel electrode was washed several times with deionized water. The deposited film were collected from the electrode surface and the extracted wet powder was dispersed in pure water solution. This solution was centrifuged at 6000 rpm for 5 min in order to removal of weekly bounded EDTA attached to the oxide surfaces. Notably, the product was collected from the solution by magnet. After drying at $70 \text{ }^\circ\text{C}$ for 1h, the obtained powder was named as EDTA Mn-SPIONs sample (as the final product of electrochemical synthesis procedure).

2.3. Sample characterization

The morphology of the prepared sample was observed by field-emission scanning electron microscopy (FE-SEM, Mira 3-XMU with accelerating voltage of 100 kV). Thermal behavior (DCS-TG) analysis was carried out in N_2 atmosphere between room temperature and $500 \text{ }^\circ\text{C}$ at a heating rate of $5 \text{ }^\circ\text{C min}^{-1}$ using a thermoanalyzer (STA-1500). The crystal structure of the prepared sample was studied by X-ray diffraction (XRD, Phillips PW-1800). The FTIR analysis was done at a resolution of 4 cm^{-1} from 400 to 4000 cm^{-1} using a Bruker Vector 22 Fourier transformed infrared spectroscope. The magnetic properties of the prepared sample were specified in the range of -20000 to 20000 Oe at room temperature using vibrating sample magnetometer (VSM, model: Meghnatis Daghigh Kavir Co., Iran).

3. RESULTS AND DISCUSSION

3.1. X-ray diffraction

Fig. 1 shows XRD pattern of the synthesized sample. The position of all observed diffraction peaks are related to the iron oxide with cubic spinel structure of (i.e. Fe_3O_4 , JCPDS 01-088-0315). No extra peak is observed, indicating the magnetite crystal structure for the deposited SPIONs. Using the Scherrer's equation ($D=0.9\lambda/\beta \cos(\theta)$), an average crystallite size (D) of 12.7 nm was calculated for the prepared SPIONs.

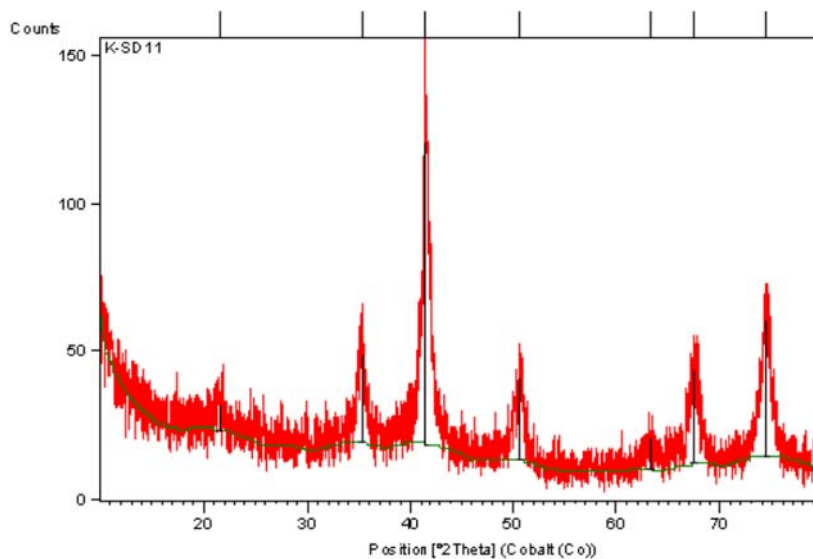


Fig. 1. XRD pattern of the prepared sample

3.2. Morphology and particle size

Morphological observations and EDS data of the prepared sample are provided in Fig. 2. The FE-SEM observations in Figs. 2a and b exhibited a particle-like morphology with some degree of agglomeration. The size of the agglomerated particles was estimated to be about 25 nm, as seen in Fig. 2a. The elemental analysis of the prepared sample was examined through Energy-dispersive X-ray spectroscopy (EDAX), and the obtained graph and data are presented in Fig 2c. As seen in this graph, the presence of Fe, Mn, C, O and N elements was proved by EDAX results. In fact, this graph in Fig, 2c showed that the prepared sample has elemental composition of 24.61% oxygen, 6.45% carbon, 2.57% nitrogen, 52.618% iron, and 14.21% manganese. The SPIONs doping was proved via the manganese presence in our sample composition. In fact, it is stated that the prepared SPIONs are doped with manganese cations. Hence, the applied electrochemical strategy was successful. Furthermore, the presence of C and N elements in sample composition indicated that the EDTA capping agent

and support the surface capping of the SPIONs prepared during the electrochemical deposition process.

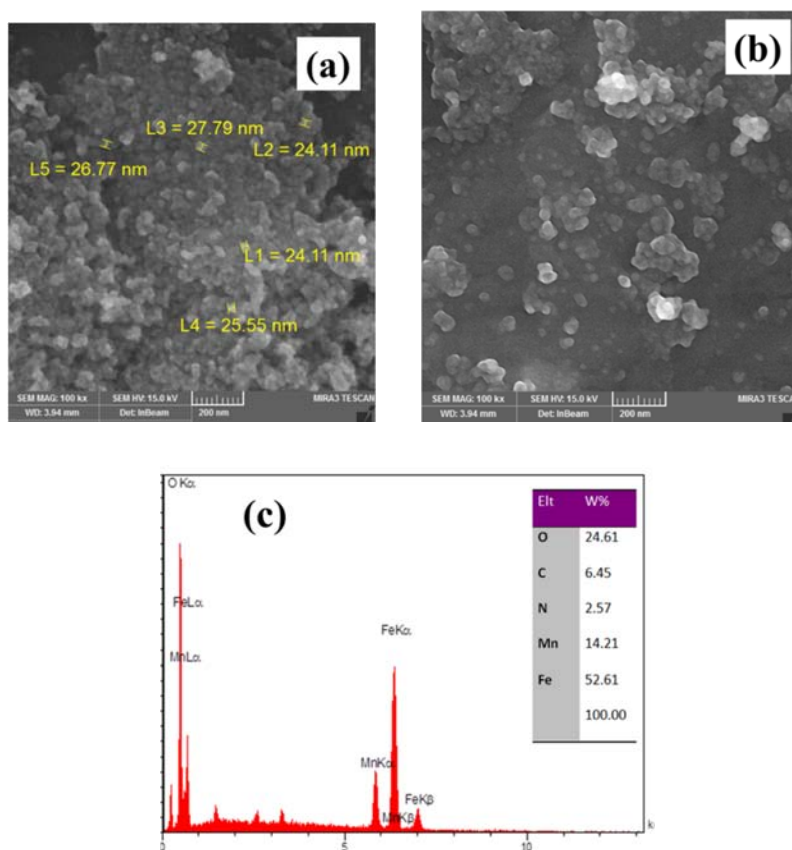


Fig. 2. (a,b) FE-SEM images and (c) EDS data of the synthesized EDTA capped Mn²⁺ doped IONPs

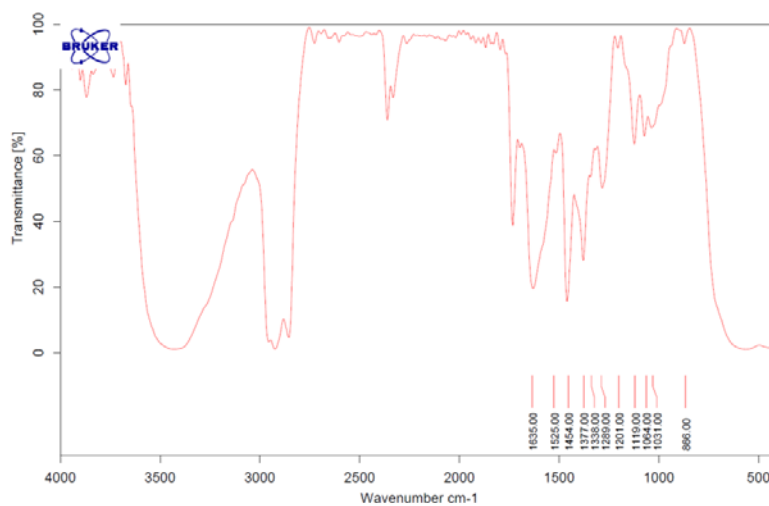


Fig. 3. IR spectrum of the synthesized iron oxide nanoparticles

3.3. FT-IR

IR spectrum of the prepared iron oxide sample is presented Fig. 3. Generally, the vibration modes of metal-oxygen-metal (i.e. Fe-O-Fe) are appeared at the wavenumbers below 700 cm^{-1} [42-45]. Hence, the observed IR bands at 562 cm^{-1} is due to the Fe-O-Fe and/or Fe-O-Mn vibrations in tetrahedral sites and the next one at 428 cm^{-1} is related to the Fe-O-Fe vibration at octahedral sites in the magnetite crystal structure [43-46]. At higher wavenumbers, several IR band are observed, which could be originated from the EDTA capped layer on the Mn^{2+} doped SPIONs. These IR bands are as follows: (i) 1064 cm^{-1} and 925 cm^{-1} due to C-N and C-C stretching vibrations [42,44], (ii) a peak at 2864 cm^{-1} corresponding to the N-C-H asymmetric stretching [45], (iii) a broad band at $3450\text{-}3500\text{ cm}^{-1}$ arising from OH stretching modes [33,34], (iv) a bands at 1377 cm^{-1} , 1289 cm^{-1} and 1119 cm^{-1} are due to the $-\text{CH}_2$ and C-H stretching and waging vibration modes [34,41,46], (v) a band at 1683 cm^{-1} is own to the C-O scissoring vibration [33], (vi) a sharp peak at 1635 cm^{-1} shows the C=O bending vibration [34,47,48] and (vii) peaks at $\sim 1525\text{ cm}^{-1}$ and $\sim 1454\text{ cm}^{-1}$ due to C=O and C-OH stretching vibrations [47,49]. All of these observed IR bands are completely related to the EDTA structure i.e. vibrations of its chemical bonds. Hence, EDTA capped layer onto the surface of SPIONs is proved.

3.4. Thermo-gravimetric analysis

Fig. 4 shows the TG curve of the prepared EDTA capped SPIONs. In the TG curve, there is a weight loss of 4.84% at temperatures below $150\text{ }^\circ\text{C}$, which is due to the elimination of OH^- groups attached onto the surface of SPIONs and physically water molecules [42-44]. After that, there is also a main weigh loss at the temperature range of $200\text{-}400\text{ }^\circ\text{C}$, as clearly observable in Fig. 4.

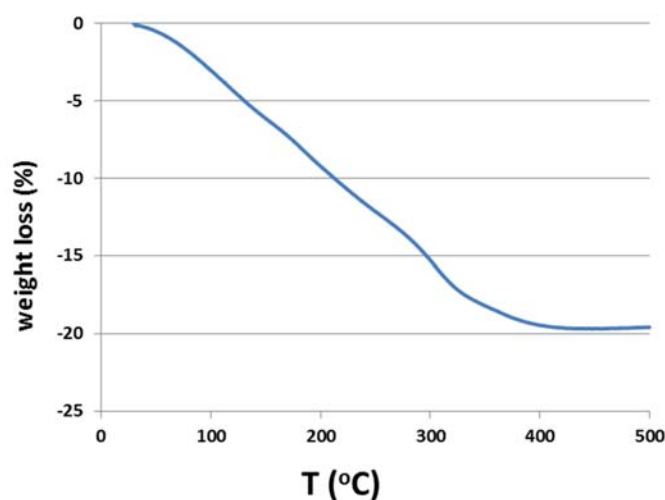


Fig. 4. TG curves for the prepared EDAT capped Mn^{2+} doped iron oxide nanoparticles

It was reported that the uncoated [44,50] and metal ion doped [11,51,52] iron oxide nanoparticles exhibit no special weight loss in the thermogravimetric analysis. Furthermore, it was reported that the decomposition of EDTA coated onto the iron oxide NPs is occurred at the temperatures of 200-400 °C [53-56]. Hence, the main source for the observed weight loss in TG curve could be assigned in to the EDTA capped layer onto the iron oxide particles. And it is stated that the observed weigh loss of about 16% is originated from the decomposition of EDTA layer capped on the SPIONs. At higher temperatures, no weigh change is seen indicating the complete decomposition of EDTA layer. These results proved the successful electrochemical preparation of EDTA capped Mn^{2+} doped iron oxide.

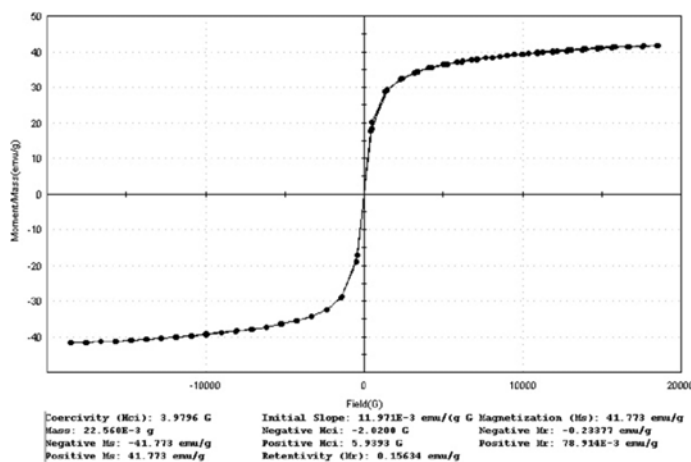


Fig. 5. Hysteresis profile and the related magnetic data for the prepared EDAT capped Mn doped iron oxide nanoparticles

3.5. Magnetic evaluation

The prepared sample were investigated through vibrating sample magnetometer (VSM), and its magnetic properties (i.e. saturation magnetization (M_s), remnant magnetization (M_r) and coercivity (H_c)) were determined within a magnetic field range of -20000 to 20000 Oe. Fig. 5 presents the hysteresis profile of the prepared sample. The completely reversible S form proved the superparamagnetic property of the prepared nanoparticles. The M_s , M_r and H_c values for the prepared sample are 41.77 emu g^{-1} , 0.15 emu g^{-1} and 3.97 G , respectively. These data showed the superparamagnetic nature of the prepared sample.

4. CONCLUSION

In summary, an easy and facile electrochemical synthesis was developed for the preparation of EDTA capped manganese cations doped iron oxide nanoparticles. The magnetite crystal structure and particle morphology of the prepared sample was examined

though XRD and FE-SEM analyses. Mn^{2+} doped cations into the Fe_3O_4 structure was confirmed using EDAX and XRD results. The existence of EDTA agent onto the surface of the prepared iron oxide was confirmed through FT-IR and TG data. Magnetic evolution by VSM was also proved the superparamagnetic nature of the prepared nanoparticles.

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REFERENCES

- [1] C. Scialabba, M. Licciardi, N. Mauro, F. Rocco, M. Ceruti, and G. Giammona, *Eur. J. Pharmaceut. Biopharm.* 88 (2014) 695.
- [2] J. Chomoucka, J. Drbohlavova, D. Huska, V. Adam, R. Kizek, and J. Hubalek, *Pharmacol. Res.* 62 (2010) 144.
- [3] Z. Atashi, B. Divband, A. Keshtkar, M. Khatamian, and N. Gharehaghaji, *J. Magn. Magn. Mater.* 438 (2017) 46.
- [4] K. Hola, Z. Markova, G. Zoppellaro, J. Tucek, and R. Zboril, *Biotechnol. Adv.* 33 (2015) 1162.
- [5] G. Kandasamy, A. Sudame, P. Bhati, A. Chakrabarty, and D. Maity, *J. Molecular Liquids* 256 (2018) 224.
- [6] Z. Q. Zhang, and S. C. Song, *Biomater.* 132 (2017) 16.
- [7] F. Lu, and D. Astruc, *Coord. Chem. Rev.* 356 (2018) 147.
- [8] N. Dhiman, Markandeya, F. Fatima, P.N. Saxsena, S. Roy, P.K. Rout, and S. Patnaik, *RSC Adv.* 7 (2017) 32866.
- [9] Q. Wu, R. Zhao, W. Liu, X. Zhang, X. Shen, W. long Li, and G. Diao, M. Chen, J. *Power Sources* 344 (2017) 74.
- [10] J. He, L. Luo, Y. Chen, and A. Manthiram, *Adv. Matter.* 29 (2017) 1702707.
- [11] M. Aghazadeh, and M.R. Ganjali, *Ceram. Int.* 44 (2018) 520.
- [12] M. Aghazadeh, and M.R. Ganjali, *J. Mater. Sci.* 53 (2018) 295.
- [13] M. Aghazadeh, and M.R. Ganjali, *J. Mater. Sci.: Mater. Electron.* 29 (2018) 2291.
- [14] M. Aghazadeh, and M.R. Ganjali, *J. Mater. Sci.: Mater. Electron.* 29 (2018) 4981.
- [15] M. Aghazadeh, and M.R. Ganjali, *J. Mater. Sci.: Mater Electron.* 28 (2017) 8144.
- [16] W. Lei, Y. Liu, X. Si, J. Xu, and J. Lin, *Phys. Lett. A* 381 (2017) 314.
- [17] L. Zhu, X. Zeng, X. Li, B. Yang, and R. Yu, *J. Magn. Magn. Mater.* 426 (2017) 114.
- [18] A. Radoń, A. Drygała, Ł. Hawelek, and D. Łukowiec, *Mater. Characterization* 131 (2017) 148.
- [19] Z. Chen, Y. Du, Z. Li, K. Yang, and X. Lv, *J. Magn. Magn. Mater.* 426 (2017) 121.
- [20] B. Bateer, Y. Qu, C. Tian, S. Du, Z. Ren, R. Wang, K. Pan, and H. Fu, *Mater. Res. Bull.* 56 (2014) 34.

- [21] Z. F. Yang, L. Y. Li, C. T. Hsieh, and R. S. Juang, *J. Taiwan Institute Chem. Eng.* 82, (2018) 56.
- [22] J. K. Xu, F. F. Zhang, J. J. Sun, J. Sheng, F. Wang, and M. Sun, *Molecules* 19 (2014) 21506.
- [23] M. Sonmez, M. Georgescu, L. Alexandrescu, D. Gurau, A. Ficai, D. Ficai, and E. Andronescu, *Curr. Pharmaceut. Design* 21 (2015) 5324.
- [24] C. Goujon, T. Pauporté, C. Mansour, S. Delaunay, and J. L. Bretelle, *Electrochim. Acta* 176 (2015) 230.
- [25] F. Chen, Q. Gao, G. Hong, J. Ni, *J. Magn. Magn. Mater.* 320 (2008) 1775.
- [26] J. Santoyo Salazar, L. Perez, O. de Abril, L. Truong Phuoc, D. Ihiawakrim, M. Vazquez, J. M. Greneche, S. Begin-Colin, and G. Pourroy, *Chem. Mater.* 23 (2011) 1379.
- [27] A. Barani, M. Aghazadeh, and M. R. Ganjali, *Mater. Sci. Semicond. Process* 23 (2014) 85.
- [28] M. Aghazadeh, and S. Dalvand, *J. Electrochem. Soc.* 161 (2014) D18.
- [29] M. Aghazadeh, T. Yousefi, and M. Ghaemi, *J. Rare. Earths* 30 (2012) 236.
- [30] M. Aghazadeh, M. Asadi, M.R. Ganjali, P. Norouzi, B. Sabour, and M. Emamalizadeh, *Thin Solid Films* 634 (2017) 24.
- [31] M. Aghazadeh, M. R. Ganjali, and P. Norouzi, *J. Mater. Sci.: Mater. Electron.* 27 (2016) 7707.
- [32] M. Aghazadeh, M. G. Maragheh, M. R. Ganjali, and P. Norouzi, *RSC Adv.* 6 (2016) 10442
- [33] I. Karimzadeh, H. Rezagolipour Dizaji, and M. Aghazadeh, *J. Magn. Magn. Mater.* 416 (2016) 81.
- [34] I. Karimzadeh, M. Aghazadeh, M. R. Ganjali, P. Norouzi, S. Shirvani-Arani, T. Doroudi, P. H. kolivand, S. A. Marashi, and D. Gharailou, *Mater. Lett.* 179 (2016) 5.
- [35] I. Karimzadeh, H. Rezagolipour Dizaji, and M. Aghazadeh, *Mater. Res. Express* 3 (2016) 095022.
- [36] I. Karimzadeh, M. Aghazadeh, M. R. Ganjali, and T. Dourudi, *Curr. Nanosci.* 13 (2017) 167.
- [37] O. J. Fakayode, N. Tsolekile Sandile, P. Songca Oluwatobi, and S. Oluwafemi, *Biophys. Rev.* 10 (2018) 49.
- [38] M. Aghazadeh, I. Karimzadeh, M. R. Ganjali, and A. Behzad, *J. Mater. Sci.: Mater. Electron.* 28 (2017) 18121.
- [39] M. Aghazadeh, I. Karimzadeh, and M. R. Ganjali, *J. Mater. Sci.: Mater. Electron.* 28 (2017) 19061
- [40] M. Aghazadeh, I. Karimzadeh, and M. R. Ganjali, *J. Electronic Mater.* 47 (2018) 3026.

- [41] M. Aghazadeh, A. Bahrami-Samani, D. Gharailou, M Ghannadi Maragheh, and M. R. Ganjali, *J. Mater. Sci.: Mater. Electron.* 27 (2016) 11192.
- [42] M. Aghazadeh, I. Karimzadeh, M. R. Ganjali, and M. Mohebi Morad, *Mater. Lett.* 196 (2017) 392.
- [43] I. Karimzadeh, M. Aghazadeh, M. R. Ganjali, P. Norouzi, T. Doroudi, and P. H. Kolivand, *Mater. Lett.* 189 (2017) 290.
- [44] M. Aghazadeh, *Mater. Lett.* 211 (2018) 225.
- [45] M. Aghazadeh, and I. Karimzadeh, *Current Nanosci.* 14 (2018) 42.
- [46] M. Aghazadeh, A. A. M. Barmi, H. M. Shiri, and S. Sedaghat, *Ceram. Int.* 39 (2013) 1045.
- [47] I. Karimzadeh, M. Aghazadeh, T. Doroudi, M. R. Ganjali, P. H. Kolivand, and D. Gharailou, *Curr. Nanosci.* 13 (2017) 274.
- [48] A. G. Magdalena, I. M. B. Silva, R. F. C. Marques, A. R. F. Pipi, and M. Jafelicci, *J. Phys. Chem. Solids* 113 (2018) 5.
- [49] C. Su, *J. Hazardous Mater.* 322 (2017) 48.
- [50] M. Aghazadeh, A. A. M. Barmi, and M. Hosseinifard, *Mater. Lett.* 73 (2012) 28.
- [51] M. Aghazadeh, R. Ahmadi, D. Gharailou, M. R. Ganjali, and P. Norouzi, *J. Mater. Sci. Mater. Electron.* 27 (2016) 8623.
- [52] M. Aghazadeh, M. R. Ganjali, and P. Norouzi, *Mater. Res. Express.* 3 (2016) 055013.
- [53] Y. Huang, and A. A. Keller, *Water Res.* 80 (2015) 159.
- [54] A. Barth, *Prog. Biophys. Mol. Biol.* 74 (2000)141.
- [55] P. R. Desai, N. J. Jain, R. K. Sharma, and P. Bahadur, *Colloid Surf. A* 178 (2001) 57.
- [56] E. Shah, P. Upadhyay, M. Singh, M. S. Mansuri, R. Begum, N. Shethd, and H. P. Soni, *New J. Chem.* 40 (2016) 9507.