

Synthesis and Characterization of the First Generation of Polyamino-Ester Dendrimer-Grafted Magnetite Nanoparticles from 3-Aminopropyltriethoxysilane (APTES) via the Convergent Approach

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Abstract 3-aminopropyltriethoxysilane was acrylated using the Michael addition reaction. After that, magnetite nanoparticles were coupled with the silane dispersion. The structure of poly(amino-ester) dendrons grafted on the surface of magnetite nanoparticles was characterized by FTIR spectroscopy and thermogravimetric analysis. Generally, in the convergent method structural control is better than in the divergent one due to its relatively low number of reactions at each growth step. Therefore, the number of dendrons grafted onto the surface of magnetite nanoparticles increase via convergent synthesis. Moreover, the analysis showed that the prepared nanoparticles had nanometric size, low polydispersity and high yield.

Keywords Magnetic nanoparticles · Dendrimer · Iron oxide (Fe₃O₄) · Convergent method · 3-aminopropyltriethoxysilane

1 Introduction

Dendrimers are a relatively novel class of polymers with a well-defined molecular architecture, three-dimensional structure and highly branched and are being used for modifying iron oxide nanoparticles (MNPs) [1]. Dendrimers are highly ordered, globular monodisperse macromolecules composed of branched repeat units emanating from a central core [2]. As a result of their structural precision, globular shape and high functionality, dendrimers are currently being synthesized and investigated for applications in catalysis [3], light harvesting [4], molecular encapsulation [5], and drug delivery [6]. However, the synthesis of dendrimers often involves multiple steps of protection/deprotection and complicated purification, which limit their widespread use. Dendrimers are prepared using either a convergent approach or a divergent one [7, 8]. In the convergent method, the dendrimer is constructed stepwise, starting from the termination groups and progressing inwards. In convergent synthesis, the most determining parameter is the spatial structure of dendritic arms which could affect their adsorbing capability onto the surface of iron oxide nanoparticles (Fe₂O₃ and Fe₃O₄). The ability to prepare a careful structure of dendrimers is the most useful feature of the convergent approach [9–12]. With the speedy development of nanostructured materials in the fields of biomedicine and biotechnology in recent years, iron oxide nanoparticles, especially, have received considerable attention for their strong magnetic characteristics, low toxicity and biocompatibility [13–21]. Due to the different applications functionalized iron oxide nanoparticles with designed active sites have attracted more attention. The silane agents are frequently considered as potential candidates for modifying the surface of iron oxide nanoparticles directly. For example,

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by means of 3-aminopropyltriethoxysilane, the surface of magnetite nanoparticles can relatively easily be decorated with primary amine groups [22–27]. Pourjavadi et al. reported a new magnetic organocatalyst in which magnetite nanoparticles were coated by a sulfamic acid functionalized poly(amidoamine) dendrimer for modern pharmaceutical chemistry. Superparamagnetic Fe₃O₄ nanocrystals were prepared by a chemical coprecipitation method with a thin thickness-adjustable silica layer coated on the surface by hydrolysis of tetraethyl orthosilicate [28]. We have recently developed a series of magneto-dendrimers with OH and/or NH₂ functional groups based on poly(amino-ester) that were prepared via the divergent approach. The results confirmed that the nanoparticles with a high drug-loading amount could be useful in the application of biomedical fields, such as drug/gene delivery [29].

In continuation of our interest for the preparation and application of magnetic nanoparticles [30–33], in this study, we have reported the convergent synthesis of a dendrimer with hydroxyl functional groups based on poly(amino-ester) coated magnetite nanoparticles as pH-responsive dendrimers, and their characterizations were performed using Fourier transform infrared spectroscopy (FTIR). We have replaced the conventional coating with the grafting method that results in a stable magnetic nanocarrier in which a large number of dendrons are chemically bonded onto the surface of MNPs. The morphology and size of the nanoparticles were studied by scanning electron microscopy (SEM) and transmission electron microscopy (TEM). The crystalline structure of iron oxide nanoparticles was studied using powder XRD measurement. The presence and proportion of organic compounds on the Fe₃O₄ nanoparticles surfaces were investigated by TGA.

2 Experimental

2.1 Materials

Iron (III) chloride hexahydrate (FeCl₃·6H₂O), iron (II) chloride tetrahydrate (FeCl₂·4H₂O), 25 % ammonia solution, 3-aminopropyltriethoxysilane, (APTES), acryloyl chloride and dimethylformamide (DMF) were purchased from Merck Chemical Co. Diethanolamine (DEA), triethylamine (TEA) and dichloromethane (DCM) were supplied from Sigma Aldrich Co (USA).

2.2 Synthesis of Magnetite Nanoparticles (MNPs)

Magnetite nanoparticles were prepared by the coprecipitation approach [15]. Briefly, FeCl₂·4H₂O and FeCl₃·6H₂O (Fe²⁺, Fe³⁺ = 1:2 molar ratio) were dissolved in 25 ml deionized water under nitrogen environment at

75 °C, then 10 ml of 25 % ammonia solution was added slowly into the above mixture under vigorous mechanical stirring at 1800 rpm for 2 h. The obtained black magnetite nanoparticles were separated by an external magnetic field and repeatedly washed with deionized water and ethanol. Then the final products were dried in a vacuum oven at 40 °C for 48 h, and the magnetite nanoparticles were finally obtained with 92 % yield.

2.3 Synthesis of Dendritic Layers (DE)

Synthesis of the DE consisted of the following four steps. Firstly, a solution of 1.86 ml 3-aminopropyltriethoxysilane (8 mmol) in 20 ml of DCM/DMF was placed in a round-bottom flask equipped with a dropping funnel, a nitrogen inlet, and a magnetic stirrer. 0.55 ml (4 mmol) of triethylamine and 0.66 ml (8 mmol) of acryloyl chloride were added slowly to the reaction media at 0 °C. After the addition of acryloyl chloride, the resulting mixture was stirred for 10 h at room temperature. The resulting product was filtered to remove triethylammonium chloride and acrylated APTES was obtained. Secondly, a solution of diethanolamine (0.96 ml, 10 mmol) in 5 ml of DMF was added to the reaction media dropwise over a period of 10 min. The resulting mixture was stirred for 6 days at room temperature and used in the next step without further purification.

2.4 Modifying of Magnetite Nanoparticles with Dendritic Layers (MNP-DE)

The magnetite nanoparticles (0.5 g) were dispersed in DMF (20 ml) under ultrasonic radiation for 10 min, and were added to the abovementioned dispersion solution. The deionized water (1 ml) was added as the catalyst to the reaction media dropwise over a period of 10 min and mechanically stirred. Afterwards the mixture was stirred for 2 days at room temperature (25 °C). Finally, the resulting product was separated by an external magnetic field and was washed carefully with deionized water and then dried under vacuum for 48 h at room temperature. The yield of this step was 91 %.

2.5 Characterization and Equipment

Fourier transform infrared (FTIR) spectra of the nanoparticles were taken by a (Nicolet 10-Thermo, USA) FTIR spectrometer. The nanoparticles were analyzed by scanning electron microscopy (SEM) (HITACHI S 4160). Their image reveals the surface morphology of the nanoparticles. The sample was placed on a stub and then sputter coated with gold before observation. Thermogravimetric analysis (TGA) was carried out using a TGA Q50 V6.3 Build 189.

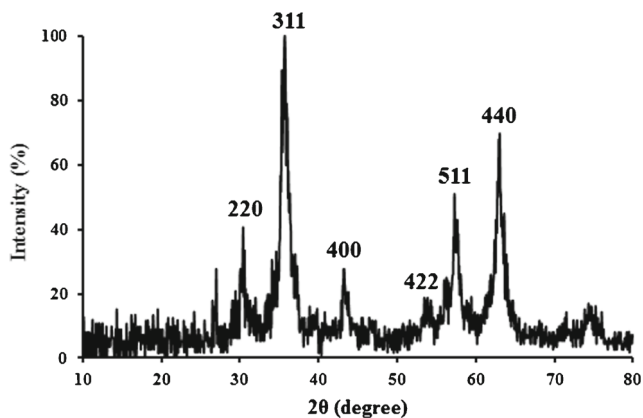


Fig. 1 X-ray diffraction pattern of MNP

The temperature of the sample increased from 25 °C to 800 °C at a rate of 10 °C/min under nitrogen atmosphere. The hydrodynamic size of the nanoparticles dispersion in distilled water was measured by dynamic light scattering (DLS) at 25 °C (Nano ZS, Malvern Instrument, UK). To obtain the size of the nanoparticles, transmission electron microscopy (TEM) images were taken using a CM 30 TEM (Philips, Germany). The sample for TEM observations was prepared by placing a drop of the dispersion of nanoparticles in deionized water onto copper grids. Powder X-ray diffraction (XRD) patterns for MNPs was obtained with a Philips X-ray diffractometer using Cu $K\alpha$ radiation ($\lambda = 1.54060 \text{ \AA}$).

3 Results and Discussion

3.1 Synthesis and Characterization of Magnetite Nanoparticles and Dendrimer

The dendrimer with a dendritic shell and magnetite core was prepared by the convergent method. The magnetite nanoparticles were synthesized through the co-precipitation approach by addition of 25 % ammonia to a solution of

Fe (II) and Fe (III) salts under nitrogen atmosphere to prevent oxidation. The crystalline structure of nanoparticles was examined using powder the XRD measurement. Figure 1 shows XRD pattern of the prepared iron oxide nanoparticle. X-ray powder diffraction analyses of Fe_3O_4 nanoparticles appeared with diffraction peaks of (220), (311), (400), (422), (511), (440), and (533). It is demonstrated that the obtained nanoparticles have the standard face-centered cubic structure.

The surface morphology of bare MNPs and MNP-DE nanoparticles was studied by SEM (Fig. 2). It could be seen that the Fe_3O_4 nanoparticles have a spherical morphology and the average diameter calculated from the SEM image was approximately $\sim 15 \text{ nm}$ (Fig. 2a). As shown in Fig. 2b, dendrimer-modified magnetite nanoparticles have a semi spherical shape with a smooth surface and are nanoscale in size.

Figure 3 shows FTIR spectra of bare MNPs. The strong stretching band at 597 cm^{-1} is attributable to the Fe-O group which indicates the formation of the magnetite nanoparticles.

Acrylated 3-aminopropyltriethoxysilane (AC-APTES) was synthesized through a condensation reaction between APTES and acryloyl chloride.

FTIR spectroscopy was used to confirm the formation of the acrylate group. The characteristic peaks of acrylated APTES are N-H stretching band at 3424 cm^{-1} , C-N stretching band at 1498 cm^{-1} , C-H symmetrical stretching band at 2848 cm^{-1} , C-H asymmetrical stretching band at 2932 cm^{-1} , =C-H bending band at 919 cm^{-1} , CH_2 bending band at 1450 cm^{-1} , CH_3 bending band at 1390 cm^{-1} , C=O stretching bond at 1663 cm^{-1} , C=C stretching band at 1604 cm^{-1} and the stretching vibration of Si-O at 1080 cm^{-1} . The presence of a peak at 1663 cm^{-1} corresponded to the C=O stretching bond, a characteristic peak at 1604 cm^{-1} related to the C=C of the acrylate group and the other one at 919 cm^{-1} is assigned to the =C-H bending band indicating the formation of the vinylic linkage. This result confirms the reaction between the amine end

Fig. 2 SEM images of bare MNP (a) and MNP-DE (b)

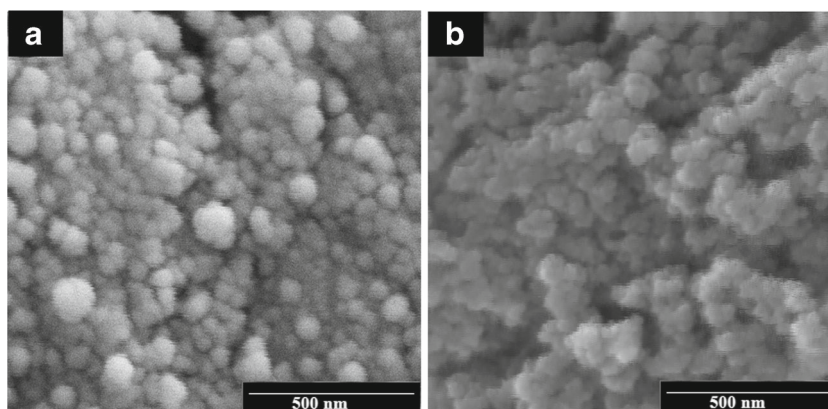
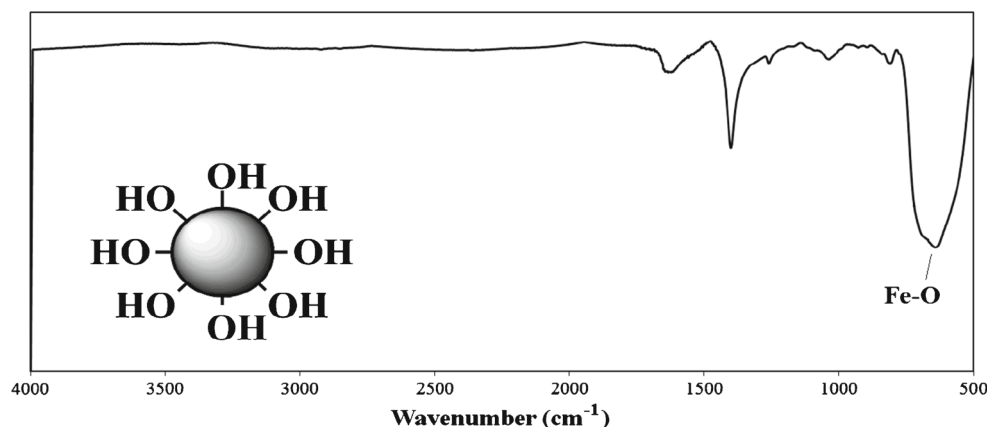


Fig. 3 FTIR spectra of bare MNPs



group of 3-aminopropyl triethoxysilane and acryloyl chloride (Fig. 4a). Dendrimer-modified magnetite nanoparticles were synthesized via a two-step method. In the first step, acrylate end groups ($-\text{CH}=\text{CH}_2$) of APTES-AC are reacted with amine groups of diethanolamine through the Michael addition reaction at room temperature to produce a dendron (Scheme 1). Figure 4b displays the FTIR spectrum of this dendron (DE). The disappearance of the $\text{C}=\text{C}$ peak at 1604 cm^{-1} , $=\text{C}-\text{H}$ peak at 919 cm^{-1} and the occurrence of a wide absorption signal at $3100\text{--}3600\text{ cm}^{-1}$ belonging to the hydroxyl end groups confirm the Michael reaction between the amino group of diethanolamine and the vinyl group of APTES-AC.

In the next step, the dendrons were condensed at the outer surface of the MNPs (core) via the convergent approach. The presence of dendrons on MNPs surface was characterized by FTIR spectroscopy (Fig. 4c). The disappearance of the IR peak corresponding to the methyl group and the

appearance of new absorption peaks at 597 cm^{-1} and at 1634 cm^{-1} are attributable to the Fe-O stretching band as the characteristic peak of magnetite nanoparticles (MNPs) and the amide group respectively, indicating that dendrons have been grafted onto the surface of MNPs.

Particle size, size distribution and zeta potential of dispersed nanoparticles in deionized water were determined using dynamic light scattering (DLS). The as-prepared dendrimer-modified magnetite nanoparticles have a size of 51.5 nm with narrow size distribution and a zeta potential of -25 mV . Moreover, the presence of dendrons on the magnetite nanoparticle surface was confirmed by thermogravimetric analysis (TGA). The TGA thermograms of bare MNPs and dendrimer-modified magnetite nanoparticles (Fig. 5) show that the weight loss of bare MNPs is about 2.2% which is presumably due to the loss of residual water in the final product. According to Fig. 5, in MNP-DE, the weight loss is about 12.90% which indicates the

Scheme 1 Synthesis of acrylated APTES, dendron and MNP-DE

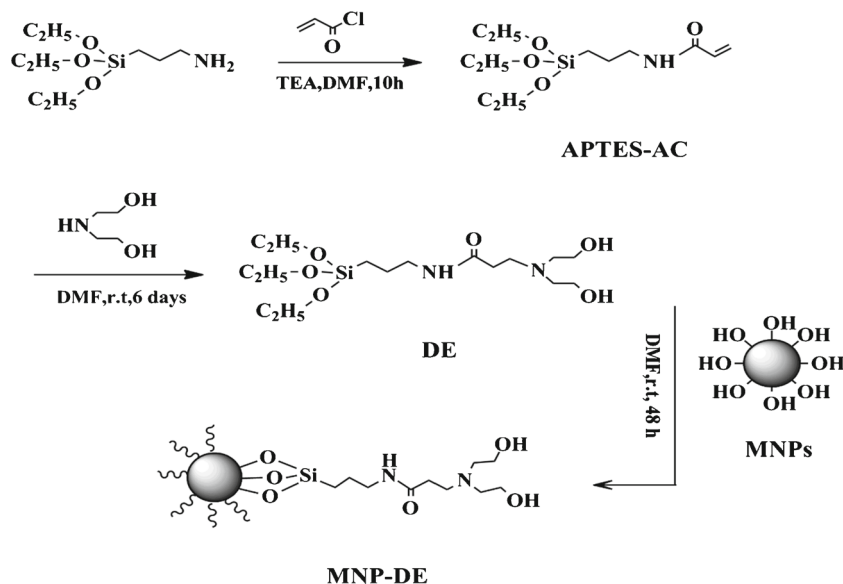
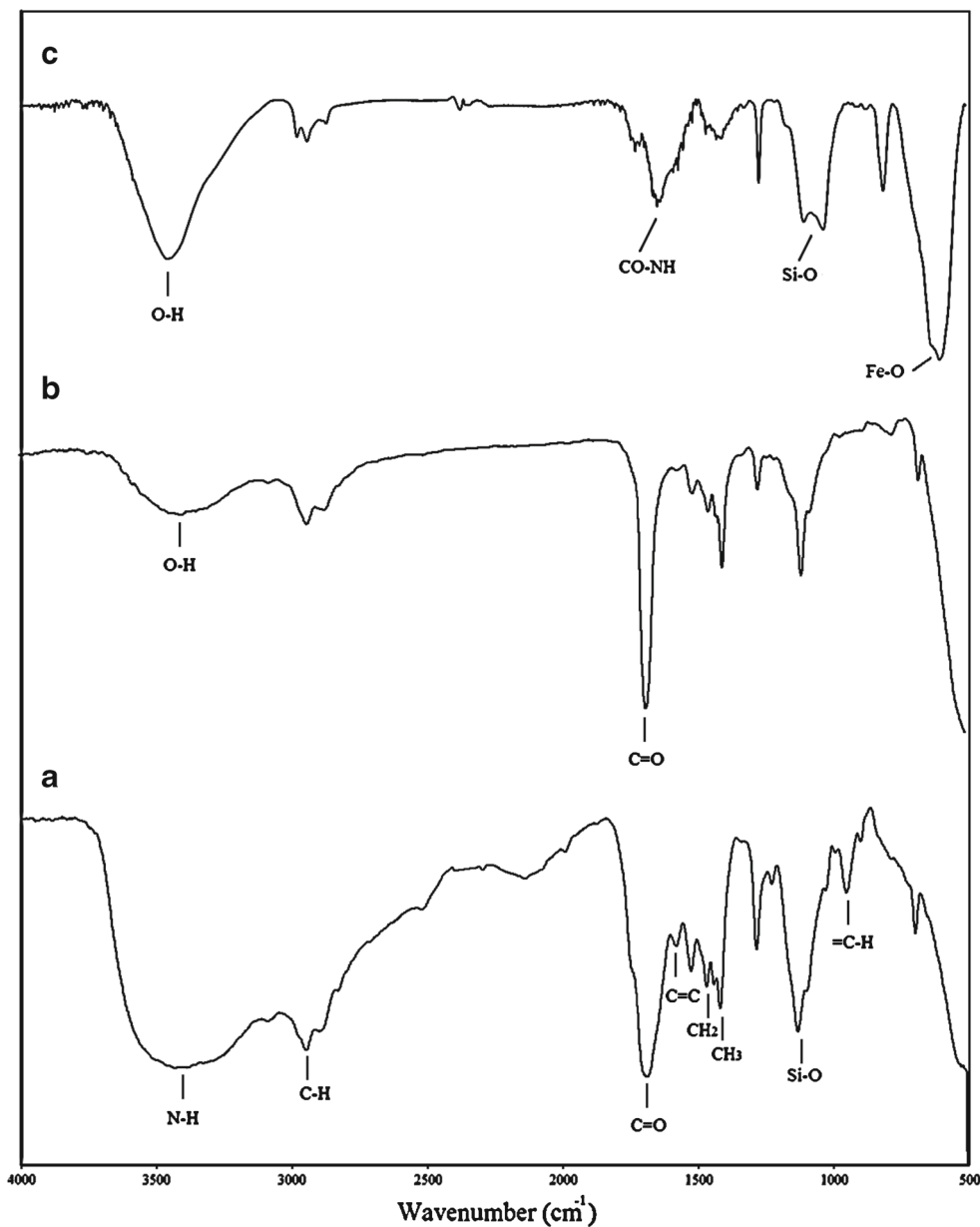


Fig. 4 FTIR spectra of APTES-AC (a), DE (b), MNP-DE (c)



modification of dendrimer on the surface of Fe₃O₄ nanoparticles. The number of dendrons coating each particle was calculated using the following equation [34]

$$N = \frac{wNa\rho\frac{4}{3}\pi R^3}{(1 - w)M_{den}} \tag{1}$$

Where N is the dendritic arms number on each particle, R is the mean radius of magnetite nanoparticles, ρ is the density of magnetite, Na is Avogadro’s number, M_{den} is the relative molecular weight of the dendritic arm, which is calculated according to their chemical structure (Scheme 1), and w is the weight loss of the dendrimer-modified magnetite nanoparticle. As a result, there are about 40 dendrons on each particle after dendrimer modification.

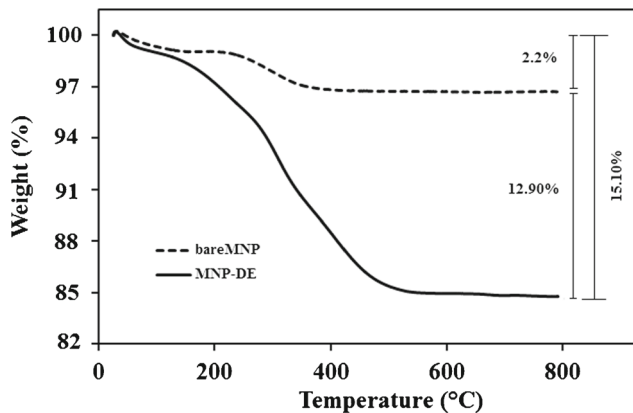


Fig. 5 TGA thermograms of bare MNP and MNP-DE nanoparticles

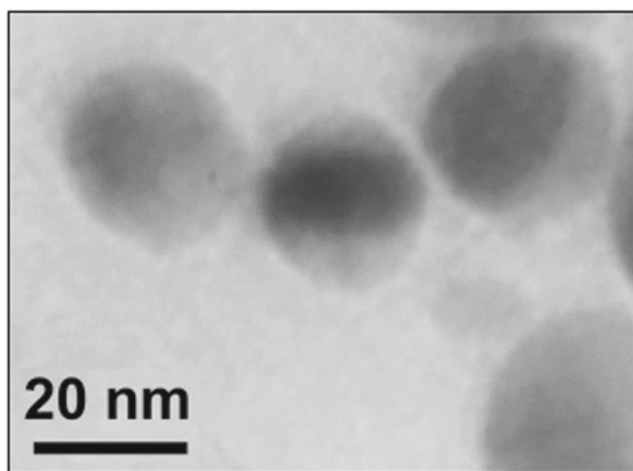


Fig. 6 TEM image of MNP-DE

Morphology of MNP-DE samples has been investigated by transmission electronic microscopy (TEM). The TEM image (Fig. 6) shows that MNP-DE is monodisperse with about 20 nm average diameter and the nanoparticles have a regular spherical shape.

4 Conclusion

A dendrimer with magnetite core and dendritic shell was prepared by the convergent approach. To prepare the MNP-DE, 3-aminopropyltriethoxysilane was first reacted with acryloyl chloride and then a Michael reaction was carried out between the amino group of diethanolamine and the vinyl group of APTES-AC. After that, a condensation reaction was performed between the triethoxysilyl-terminated dendrons and hydroxyl groups on the surface of magnetite nanoparticles (Fe_3O_4). The results of the present study indicate that the convergent dendrimer has the most density of grafted structures on the magnetite core relative to the divergent ones. Therefore, due to the small particle size (~ 20 nm) and low polydispersity as well as high biocompatibility this generation can be proposed as an appropriate nanocarrier for biomedical applications.

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