

RESEARCH PAPER

Core-shell nanoparticles for medical applications: effects of surfactant concentration on the characteristics and magnetic properties of magnetite-silica nanoparticles

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ABSTRACT

Objective(s): The use of cationic surface-active agents (surfactant) in the synthesis of nanoparticles, with formation of micelle, can act as a template for the formation of meso-porous silica. Changes in the concentration of surfactants can affect the structures and properties of the resulting nanoparticles.

Materials and Methods: Magnetite nanoparticles were prepared as cores using the coprecipitation method. Silica shells were formed on the prepared cores using sol-gel through the single-step process. During synthesis, cetyltrimonium bromide (CTAB) was used as a surfactant at low (0.1 g), medium (1 g), and high concentrations (7 g), and the effects on the properties of the nanoparticles were investigated. The core-shell nanoparticles were analyzed using X-ray diffraction (XRD), scanning electron microscopy (SEM), and transmission electron microscopy (TEM). In addition, the surface porosities of the nanoparticles were evaluated using the BET and BJH methods. The vibrating sample magnetometer (VSM) was also employed to assess the magnetic characteristics of the synthesized samples.

Results: The results of XRD indicated that the nanoparticles were composed of magnetite and silica, while the SEM and TEM images confirmed the presence of uniform spherical particles with a core-shell structure. According to the results of the VSM tests, all nanoparticles showed super-paramagnetic behaviors. Moreover, the increased concentration of CTAB led to an increment in saturation magnetization (Ms), size, and volume of the surface pores, while the specific surface area of the nanoparticles decreased.

Conclusion: According to the results, the properties of the silica shell could be adjusted in terms of pore characteristics and magnetic behavior by changing the concentration of the surfactant.

Keywords: Core-shell, Magnetite-silica, Magnetic behavior, Nanoparticle, Surfactant

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INTRODUCTION

With the emergence of nanotechnology in the field of diagnostic and therapeutic processes, use of nanoparticles has been on the rise. Such example is the use of magnetic nanoparticles in magnetic resonance imaging (MRI). Contrary to conventional contrast agents, which only intensify the vascular signal during imaging, magnetic nanoparticles increase the signals from tissues and cells to a recognizable level [1]. Furthermore, magnetic nanoparticles provide imaging contrast by affecting the relaxation properties of water

protons. In general, it could be denoted that magnetic iron oxide particles are able to enhance the ability of MRI-based imaging in cellular systems [2]. Another advantage of magnetic nanoparticles is the ability to attach to identifier biomolecules, so that the particles could be specifically targeted toward the cells and tissues that may produce certain molecules known as biomarkers in case of disease, thereby facilitating the identification and diagnosis of diseases [3]. Magnetic nanoparticles are of paramount importance in drug delivery in terms of the practical applications. A drug delivery system is able to carry and release agents in a desirable position at a specific rate [4]. At room temperature, magnetite and

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hematite nanoparticles have super-paramagnetic behaviors. Therefore, iron oxide nanoparticles could adopt the ability of drug delivery without deviation from the specific path in the body under an applied magnetic field [2, 3]. Some of the prominent features of magnetite nanoparticles in medical applications include chemical stability, uniform size, and proper distribution in the base liquid. Due to their high surface energy, these nanoparticles tend to agglomerate, thereby losing their properties. In addition, their reactivity increases by size reduction, and the potential of rapid biodegradation increases in contact with biological systems. Therefore, the formation of suitable coatings (e.g., polymer, silica, and gold) on iron oxide nanoparticles could effectively prevent these limitations [5, 6]. In this regard, the core-shell nanocomposites of metal oxide and mesoporous silica have been extensively studied. Iron oxide nanoparticles covered with mesoporous silica are also classified in this group of nanocomposites [7].

Formation of silica coatings on the surfaces of magnetite nanoparticles could improve their distribution in the liquid medium, enable their activation of various functional groups (e.g., amine, thiol, and carboxyl) [8], and increase the surface area of the nanoparticles without significantly reducing the magnetic properties [9]. Among the other important features of silica are the safety of silica for the human body (no chemical reaction) [8, 10], adjustable properties of silica shell, thermal stability, mechanical strength, and low specific weight [11]. Recent studies on metal oxide/mesoporous silica nanocomposites have been focused on tuning the properties of these particles [12]. In this regard, several studies have investigated the methods to control the thickness of mesoporous silica shells [13, 14]. Further studies have also been focused on increasing the size and volume of porosity in the shell structure to enhance drug loading [15, 16]. Several efforts have been made to control the particle size and morphology of silica nanoparticles using various surfactants as templates [17, 18]. In the preparation of silica nanoparticles, the degree of hydrolysis reaction is largely influenced by the reaction conditions [19, 20]. Therefore, the difference in the reaction conditions leads to differences in the morphology of the synthesized products as reported by Brinker and Scherer [21]. Accordingly, primary alkoxide particles are trapped in the micelle's structures during the sol-gel process in the presence of the

surfactant. As such, cationic surfactants could act as a template for the synthesis of mesoporous silica by the formation of micelles, and the altered concentration of the surfactant could affect the structure and properties of the shell structure. Given the importance of the synthesis of core/shell nanoparticles (especially in medical applications) and effects of surfactants on their structure and properties, core-shell (magnetite-silica) particles were synthesized using the coprecipitation method and sol-gel in the current research. Moreover, we investigated the effects of low (0.1 g), medium (1 g), and high (7 g) surfactant concentrations on the chemical composition, morphology, particle size, and magnetic properties of the nanoparticles.

MATERIALS AND METHODS

The materials used for the synthesis process included deionized water, iron(II) chloride tetrahydrate ($\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$), iron(III) chloride hexahydrate ($\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$), NH_4OH (28%), tetraethyl orthosilicate (TEOS; $\text{Si}(\text{OC}_2\text{H}_5)_4$), cetyltrimethylammonium bromide (CTAB; $[(\text{C}_{16}\text{H}_{33})\text{N}(\text{CH}_3)_3]\text{Br}$), and triethanolamine (TEA; $\text{C}_6\text{H}_{15}\text{NO}_3$). All raw materials were obtained from Merck, Germany.

Initially, the magnetite nanoparticles were synthesized through the coprecipitation of the iron chloride salts in the ammonium hydroxide solution. Afterwards, the core-shell structure was formed with the addition of the CTAB and TEA surfactants using the pattern removal method, and TEOS was also formed through the sol-gel process. To this end, 100 ml of deionized water was heated to the temperature of 80°C in a 250-ml round-bottom flask in nitrogen atmosphere, and oxygen was removed by homogenization at 12,000 rpm for 15 minutes. At the next stage, 0.338 gram of $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ and 0.919 gram of $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ were added and stirred for five minutes in the same conditions. With the addition of 20 ml of ammonium hydroxide solution and performing the coprecipitation reaction, the caramel color of the solution rapidly turned into black due to the formation of magnetite nanoparticles. Mixing continued for 15 minutes. Following that, various concentrations of the CTAB (0.1, 1, and 7 g) were added to the mixture, and after stirring for five minutes, 0.5 ml of TEA was also added. The reaction continued for 15 minutes. Finally, with the addition of one ml of TEOS, the sol-gel process was initiated. After 15 minutes, the solution was

centrifuged, and the synthesized products were collected using a magnet. Following that, the nanopowders were washed with deionized water three times. The formation mechanism of the core-shell structure has been described previously [22]. The product was dried in an oven at the temperature of 35°C. In order to remove the CTAB and obtain a porous structure, the synthesized samples were calcinated in a furnace in nitrogen atmosphere at the temperature of 550°C for six hours. The chemical composition of the synthesized particles was analyzed using X-ray diffraction (XRD; BRUKER D8-Advance X-ray Diffractometer). The surface area and pore size of the nanoparticles were determined using nitrogen adsorption/ desorption isotherms (BET). The measurements were conducted using the Micromeritics' TriStar II Plus, operated at the temperature of 196°C. In addition, the size and morphology of the nanoparticles were examined using a field emission scanning electron microscope (FE-SEM, HITACHI S-4160) and transmission electron microscope (TEM). In addition, shell-layer thickness was measured using an image analyzer by various images based on the measurement of a minimum of 100 nanoparticles. The magnetic behavior of the core-shell structures was assessed using a vibrating sample magnetometer (VSM).

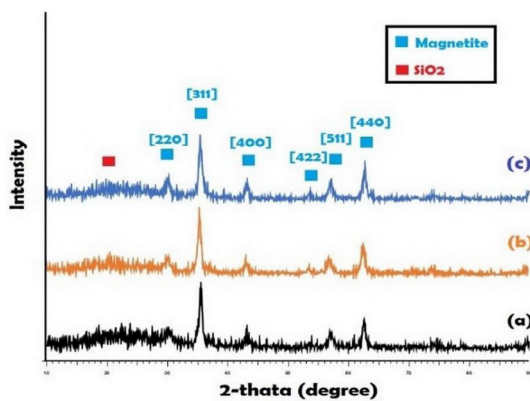


Fig 1. X-ray diffraction (XRD) pattern of synthesized magnetite-silica core-shell nanoparticles Sample No. 1, (b) Sample No. 2 and (c) Sample No. 3

RESULTS AND DISCUSSION

In order to evaluate the test results, the samples with 0.1, one, and seven grams of the surfactant were numbered one, two, and three, respectively. Fig 1 depicts the results of the XRD analysis in the three samples with various CTAB values. In all the samples, a wide peak was

observed within the range of 15-28°, indicating that the silica was formed in all the samples. The peaks observed at 30°, 35.5°, 43°, 53.5°, 57°, and 62.5° were associated with the standard magnetite peaks (JCPDS card: 01-1111). Therefore, the obtained results confirmed the presence of silica and magnetite in all the synthesized nanoparticles, which is consistent with the previous studies in this regard [23, 24]. The surface porosity of the synthesized nanoparticles was characterized using the BET and BJH methods, as well as adsorption-desorption isotherms (Table 1).

Table 1. Specifications of surface pores obtained from BET and BJH analysis

Sample number	1	2	3
surface area (m ² g ⁻¹)	265	244	177
porosity internal volume (cm ³ g ⁻¹)	0.34	0.40	0.48
pore size(nm)	3.72	3.99	5.25

According to the information in this table, higher CTAB was associated with increased size and volume of the pores and their reduced specific surface area. The adsorption-desorption isotherm curves for sample number two are shown in Fig 2.

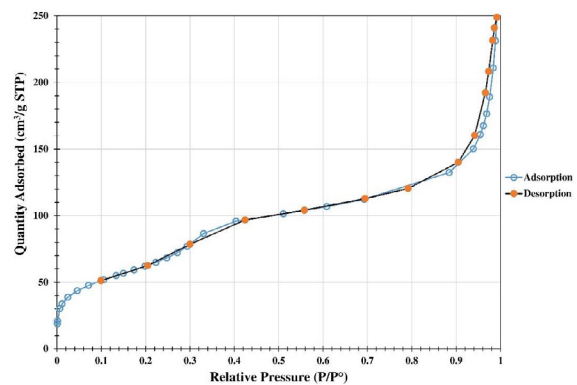


Fig 2. Nitrogen adsorption-desorption isotherm of synthesized nanoparticles for sample No. 2

As can be seen, desorption and adsorption branches did not follow the same path, thereby demonstrating hysteresis.

This was also observed in all magnetic-silica samples that were synthesized in various concentrations of the surfactants. The hysteresis patterns for the samples were type IV isotherms based on the IUPAC classification with an H1 hysteresis loop; this type of hysteresis is associated with mesoporous materials [25].

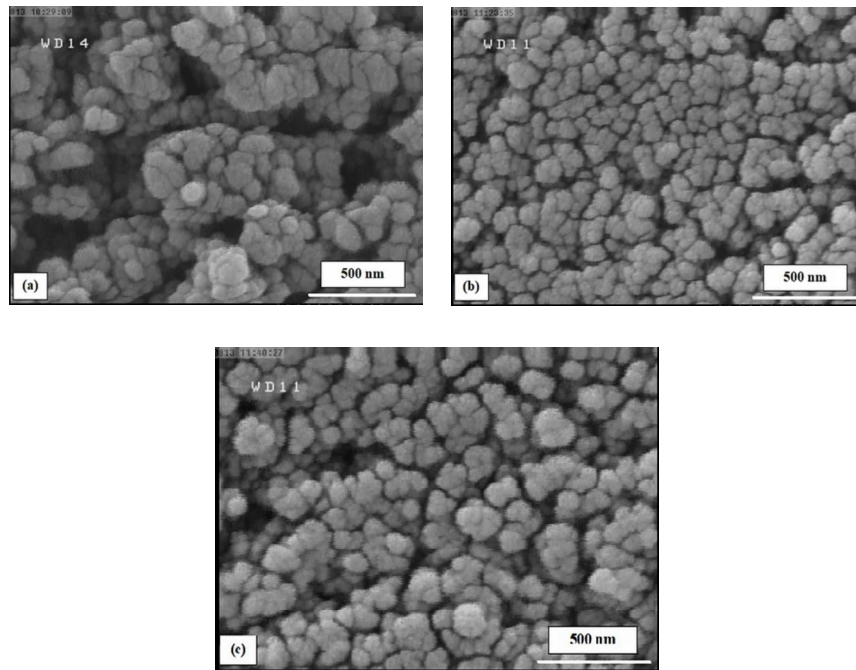


Fig 3. Scanning electron microscope images of magnetite-silica nanoparticles; (a) Sample No. 1, (b) Sample No. 2 and (c) Sample No 3

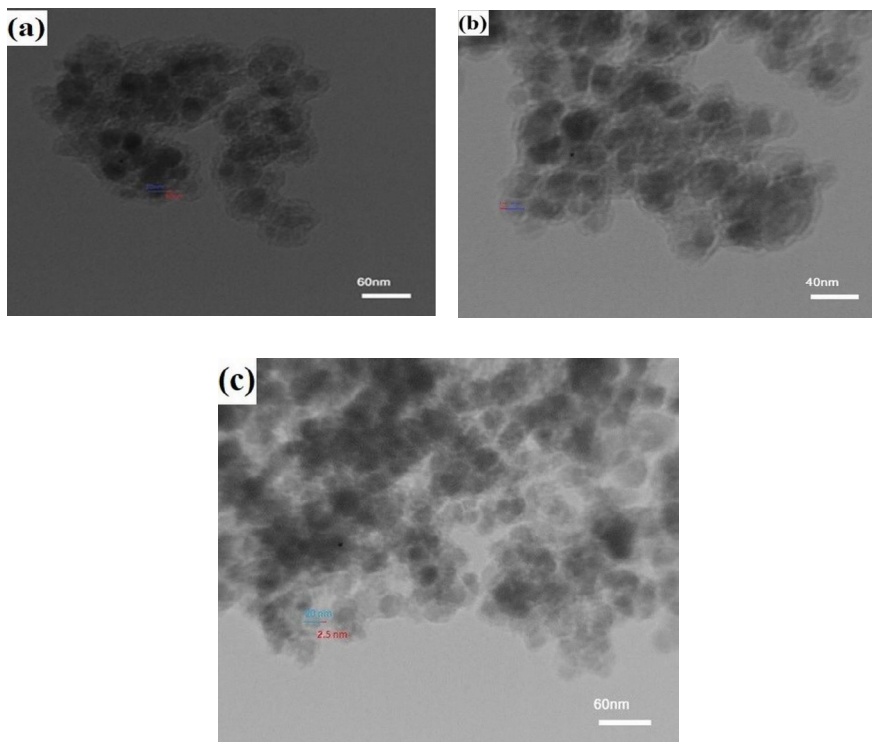


Fig 4. Transmission electron microscope images of magnetite-silica core-shell; (a) Sample number 1, (b) Sample number 2 and (c) Sample number 3

Figs 3 and 4 show the SEM and TEM images of the samples synthesized by various concentrations of the surfactants, respectively. As is observed, the

SEM images confirmed the presence of spherical nanoparticles in all samples. As expected, these images demonstrated that higher concentration

of the surfactant had no significant effects on the size and morphology of the magnetite cores. The TEM images confirmed the formation of core-shell structure. According to the obtained results, the mean size of the cores was approximately 20 nm, and the shell thickness was estimated at 10, 5, and 2.5 nm in samples one, two, and three, respectively. It is also notable that the particle size in the SEM images appeared to be larger than TEM due to agglomeration. According to the findings of the current research, increasing the concentration of the surfactant from 0.1 g to seven g decreased the thickness of the silica shell by 75%, while the diameter of the surface pores increased. Seemingly, increasing the concentration of the surfactant was associated with the higher accumulation of the surfactant molecules in the micelles, which could in turn increase the diameter of the pores. This is schematically shown in Fig 5.

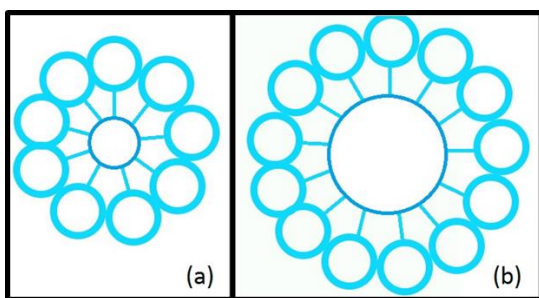


Fig 5. Micelles schematic images (a) A sample with a lower concentration of surfactant, (b) A sample with a higher concentration of surfactant

Fig 6 depicts the results of the VSM tests (magnetic behavior) of the synthesized samples. According to the resulting curves, the width of the hysteresis loops was zero (S-type curves).

Therefore, all samples exhibited super-paramagnetic behavior. It is also noteworthy to mention that the occurrence of super-paramagnetic behavior in the nanoparticles enabled their accurate control since super-paramagnetic particles are more sensitive to external magnetic fields [26, 27].

The saturation magnetization of the super-paramagnetic magnetite-silica nanoparticles with core-shell structure plays a key role in determining the magnetic properties of materials. In the present study, this value was estimated at 50, 55, and 60 emu/g in sample one, two, and three, respectively. As can be seen, increasing the surfactant led to the higher value of saturation

magnetization, indicating the improvement of the magnetic properties.

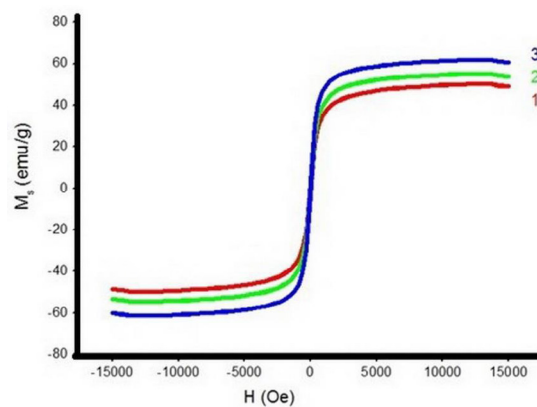


Fig 6. Magnetization versus applied field curves for nanoparticles with different surfactant concentrations; 1) 0.1 g, 2) 1 g, and 3) 7 g

Among super-paramagnetic nanoparticles, particles with higher saturation magnetization are preferable for medical applications owing to their higher sensitivity and efficacy [26, 27]. As is depicted in Fig 6, the M values declined at saturation and high applied fields (>12,500 Oe), which could be due to the diamagnetic nature of the silica shells [22]. On the other hand, increasing the concentration of the surfactant was observed to decrease the shell thickness, thereby incrementing the saturation magnetization of the nanoparticles by reducing the contribution of the diamagnetic shells. The obtained results of the present study indicated that the higher ratio of the core diameter to the shell thickness was associated with higher saturation magnetization which would be closer to the magnetization of the core [28].

Since the surfactant is consisted of a hydrophilic head and hydrophobic tail, increasing its concentration led to the higher accumulation of the surfactants per micelle. Since the pores were formed following the outflow of the surfactants during calcination, The diameter and volume of the pores were expected to increase with the accumulation of the surfactants [29]. According to the results of BET analysis, the higher CTAB content was associated with increased pore volume of the synthesized nanoparticles. Consequently, the mesoporous silica layer of sample number three had more pores compared to the shell layers of other samples. As such, sample number three was expected to have the highest magnetic saturation

(M_s); This was confirmed by the results of the VSM tests. Since the silica shell is non-magnetic, the magnetite core was more exposed to the magnetic field. According to the results of the present study, increasing the surfactant concentration caused the silica to be involved in preventing agglomeration, biocompatibility, and core protection, while the magnetic properties of the nanoparticles were maintained. Therefore, in the diagnostic applications where magnetic properties are more important, sample number three had the highest surfactant concentration (7 g) compared to other samples and was considered to be the optimized sample. Considering that the pore diameters of 2-10 nm allows the loading of various drugs [30]. Sample number three was observed to have the optimal magnetic properties and pore size and could be a candidate for such applications.

CONCLUSION

In the current research, nanoparticles with magnetite core and silica shell were successfully synthesized using a single-step synthesis method consisting of coprecipitation and sol-gel processes. Furthermore, we evaluated the effects of surfactant concentration on the chemical composition, morphology, core-shell structure, surface porosity, and magnetic properties. According to the results, the properties of the silica shell could be altered in terms of pore characteristics and magnetic behavior by changing the concentration of the surfactant, which was suggestive of the ability to tune the characteristics of the core-shell nanoparticles for the desired applications.

The most important findings of the current research were as follows:

- XRD analysis indicated the presence of magnetite and silica in the synthesized nanocomposite particles.
- SEM and TEM images indicated the formation of a structure consisting of the magnetite core and silica shell.
- Evaluation of the pores in the silica shell confirmed the increased pore volume and size, as well as the reduced specific surface area at the higher concentrations of the surfactants.
- All the synthesized samples had superparamagnetic behaviors, which rendered them useful for medical applications for disease diagnosis and treatment.
- The decreased shell thickness and increased saturation magnetization in the synthesized

samples were caused by higher surfactant concentrations.

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