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Synthesis of coated iron oxide nanoparticles and feasibility study of their use in magnetic hyperthermia

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ABSTRACT

The unique properties of magnetic nanoparticles have made them useful and important particles for use in various fields, especially in heat-based applications. This research presents a hopeful facet of magnetic hyperthermia by superparamagnetic Fe_3O_4/Alumina nanoparticles. We synthesized Fe_3O_4/Alumina nanoparticles of different sizes by sonochemical method and evaluated their ability to generate heat. We found by characterizations with Field emission scanning electron microscopy (FE-SEM), X-ray diffraction technique (XRD), and Transmission electron microscopy (TEM) the samples to be of spherical shapes and spinel structure whose diameter could be controlled in the range from 15 to 25 nm. The magnetic behavior of the samples determined using a vibration sample magnetometer (VSM) showed hysteresis loops with a coercivity (H_C) close to zero, suggesting superparamagnetic behavior at room temperature. The saturation magnetization (M_S) for sample 3 after synthesis is 23 emu/g. We also investigated the potential of the samples for magnetic hyperthermia using alternating magnetic fields at various frequencies. Samples 1, 2, and 3 achieved heat production rates of 0.22 °C/min, 0.41 °C/min, and 0.62 °C/min respectively under an alternating magnetic field with an amplitude of 120 Oe and a frequency of 250 kHz.

1. Introduction

Nanoscience is one of paramount the development areas and research of modern science. Nowadays Nanotechnology is employed extensively in the pharmaceutical, medical, electronics, robotics, and tissue engineering industries. The usage of nanoparticle materials offers many benefits owing to their unique physical properties and small size [1, 2]. These properties create exciting new possibilities for mechanical, optical, and magnetic applications. Among these nanoparticles, magnetic nanoparticles possess unique properties that fabricate them as excellent tools for biomedical applications, such as contrast agents, cell sorting, Magnetic resonance imaging (MRI), hyperthermia, and targeted drug delivery [3,4].

In biomedical applications, maghemite iron oxides (γ-Fe_2O_3) and magnetite (Fe_3O_4) are by far the most commonly used magnetic nanoparticles, as they have superparamagnetic behavior with high saturation magnetization and much lower toxicity than their metallic counterparts [4,5]. However, there is an unavoidable problem when using "bare" magnetite nanoparticles in biological applications, which is their instability over long periods due to easy oxidation in air, their high initial chemical activity, loss of dispersion, magnetism, and Intense accumulation [6,7]. Therefore, recently much attention has been paid to the fabrication of Fe_3O_4-based nanoparticles with a core-shell structure [3,6]. Biocompatible inorganic and organic materials are often considered potential candidates for magnetite surface modification. Such surface modification increases the biocompatibility of magnetite and provides the stability of the colloidal suspension for the required time [8,9].

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For instance, Tekiye *et al* [11]. Reported the successful synthesis of Fe_3O_4/Alumina nanoparticles through the co-precipitation method and used them as catalysts for alcohol oxidation. By examining the effects of several oxidation reaction parameters such as catalyst concentration, solvent type, and reaction temperature on the oxidation percentage, they found that this type of nanoparticles had an oxidation efficiency of over 91 % and also could recycle the ideal organic catalyst in such a way that it can be recycled up to five times without Losing significant re-use activities. Tsai-Jung Yu *et al* [12]. Reported on alumina-coated iron oxide magnetic nanoparticles as an efficient photothermal tool for selective killing of bacteria. They also stated that these nanoparticles can increase the temperature of their suspension by 20 °C for 5 min under infrared light, and as a result, they can prevent more than % 95 of bacterial cell growth. Rajan et al [13] were able to synthesize CTAB (cetyltrimethylammonium bromide) functionalized Fe_3O_4 nanoparticles using iron oxyhydroxide precursor through a facile reduction process to achieve improved magneto-thermal efficiency and magnetic behavior, and colloidal stability. Also, they found that these nanoparticles have very good stability in solutions and 5 mg/ml of nanoparticles under the applied alternating magnetic field strength of 800 Oe and frequency of 315 kHz has a specific loss power of ~ 1036 W/g. The effect of heat on biological tissue has been known for a long time [14]. In the 19th century, it was discovered that heating cancerous tissue can injure it with minimal damage to healthy tissue [14,15]. Thus began research into the healing effects of hyperthermia. There are several methods to induce hyperthermia, including Radiofrequency (RF), ultrasound, microwave antennas, water baths, and high-frequency currents. The mentioned methods have shortcomings that have kept them from being the primary cancer treatment [16,17]. Perhaps the most effective of these methods is microwave hyperthermia, which can only be used on superficial tumors. However, with the development of nanoscience in recent years, an effective and new method of hyperthermia has been developed. This method uses relaxation losses and hysteresis losses to generate heat [18,19]. Considering the importance of this issue, we decided to evaluate the potential of Fe_3O_4/Alumina nanoparticles for use in magnetic hyperthermia and if they are effective, introduce them as a good option for direct destruction of cancer tissues. Therefore, to achieve this goal in this study, Fe_3O_4/Alumina nanoparticles were prepared by the sonochemical method, and using their magnetic and structural properties and their ability to generate heat were investigated by VSM, XRD, FE-SEM, TEM, and magnetic hyperthermia.

2. MATERIALS AND METHODS

2.1. Materials and instruments

Iron (II) chloride tetrahydrate ($FeCl_2•4H_2O$, 99% w/w), Iron (III) chloride hexahydrate ($FeCl_3•6H_2O$, 99% w/w), Alumina (Al_2O_3), ammonium hydroxide solution (NH_4OH), and were used for preparation of Fe_3O_4/Alumina nanoparticles. All materials listed in this section were purchased from Merck Co.

2.2. Synthesis Method

2.2.1. Synthesis of Fe_3O_4 / Alumina nanoparticles

The chemical co-precipitation method was used to prepare Fe_3O_4 nanoparticles. By adjusting the concentration of initial salt solutions ($FeCl_2.4H_2O$ and $FeCl_3.6H_2O$) and the reaction temperature, we obtained different sizes of Fe_3O_4 / Alumina particles. We dissolved 3.83 g of iron (III) chloride hexahydrate and 1.75 g of iron (II) chloride in 80 ml of deionized water, then the salt concentration was 0.2 M, 0.1 M, and 2 M at solution temperatures of 80, 100 °C, respectively. They were mixed at 40 °C and stirred for 20 min at 900 rpm and the samples were named sample 1, sample 2, and sample 3 respectively. Next, 15 ml of ammonium hydroxide was slowly added to the three solutions and they were kept on a magnetic stirrer for 50 min. After cooling to room temperature, the solutions were removed from the magnetic stirrer and washed four times (twice with deionized water and twice with ethanol). Finally, the black residue was dried in an oven at 95 °C for 2 h.

Finally, Fe_3O_4/Alumina nanoparticles were prepared using the Sonochemical method [5]. To form Fe_3O_4/alumina core/shell nanoparticles, Alumina (1.0 g) was dissolved in ethanol (50 mL) to produce a homogeneous solution. Then all the samples (0.2 g) were added to the solution under the influence of ultrasonic waves for 15 min. Then a mixture of water (5 mL) and ethanol (25 mL) (1:5 v/v) was added dropwise to the solutions with vigorous stirring for about 20 min. At the end of the synthesis, the obtained samples were magnetically separated using a permanent magnet, washed several times with ethanol, and dried in an oven at 90 °C for 3 h.

3. Results and discussion

Fig. 1 demonstrates the XRD patterns for Fe_3O_4/Alumina superparamagnetic nanoparticles of different sizes. The presence of characteristic peaks at 2θ: 30.1°, 35.4°, 43.1°, 53.4°, 56.9°, 62.5° is related to Fe_3O_4 and 45.5°, 67.1° is related to crystalline phase of Alumina. It can be seen the XRD patterns illustrate the structure of an inverse cubic spinel. Also, the sharp peaks show the crystal structure of the synthesized Fe_3O_4/Alumina samples [20,21]. To calculate the mean grain sizes, the Scherrer equation was used, which resulted in obtaining the sizes of about 12, 14, and 18 nm for sample 1, sample 2, and sample 3, respectively. These results revealed that the metal oxides formed a single composite.

Based on the FESEM images of the three samples shown in Figure 2a-c, we found that the average particle sizes for Sample 1, Sample 2, and Sample 3 are 15, 17, and 25 nm, respectively. The mean grain sizes calculated from XRD data differ slightly from those estimated from FESEM images. TEM technique was used as a powerful technique to understand the surface morphology of these samples. The TEM image determines the core@shell structure and the uniform spherical shape of the Fe_3O_4/Alumina as shown in Figure 2d. With more attention in Figure 2d, the non-magnetic Alumina layer with an outer coating around the core, in a lighter color (grey), and Fe_3O_4 nanoparticles are exhibited in the inner part (black) as the core.

The dependence of the samples' magnetization on the applied magnetic field at room temperature was measured as shown in Figure 3. All samples exhibit hysteresis loops with coercivity (Hc) close to zero, indicating superparamagnetic behavior at room temperature [23]. The results reveal high saturation magnetization (Ms) values of 14, 16.5, and 23 emu/g for samples prepared with diameter sizes of 15, 17, and 25 nm respectively.

To prove the suitability of Fe_3O_4/Alumina nanoparticles for generating heat under the magnetic field, a hyperthermia experiment was performed with particles dispersed in an aqueous solution. Dispersion of nanoparticles in aqueous solution was achieved using distilled water as a biocompatible environment similar to the human biological body. The Fe_3O_4/Alumina nanoparticles were dispersed in the aqueous solution using a magnetic stirrer and an ultrasonic device to a particle concentration of particles of 0.3 mg/ml. The thermal effect of a solution of particles dispersed in an alternating magnetic field was investigated using a high-frequency generator with a system of water-cooled magnetic coils. Variable magnetic fields with a magnetic field strength of 120 Oe and a frequency of 150 and 250 kHz were applied to the samples. The temperature of solutions containing nanoparticles was measured and recorded as a function of the time of exposure to the magnetic field with an optical fiber sensor, and it is shown in Figure 4. A clear heating effect was observed for all samples in the alternating magnetic field applied with a strength of 120 Oe and frequencies of 150, 250 kHz. Under the AC magnetic field with a frequency of 150 kHz and a field magnitude of 120 Oe, the samples with sizes 13, 17, and 23 reached the heating rate of 0.17, 0.30, and 0.49 °C/min, respectively. At the maximum applied magnetic field of the frequency of 120 Oe and 250 kHz, the heating rate reached values of 0.22 °C/min, 0.41 °C/min, and 0.62 °C/min for samples with sizes of 15, 17, 25 nm, respectively. In other words, the thermal effect of sample 3 is higher than that of other samples. It can be judged from the obtained data that at the frequency of 250 kHz, the thermal effect of sample 3 is greater than that of other samples due to the higher saturation magnetization. It is expected that by increasing the frequency, the faster rotation of the magnetic moments and the nanoparticles themselves in the solution will be achieved, which will increase the temperature of the samples.

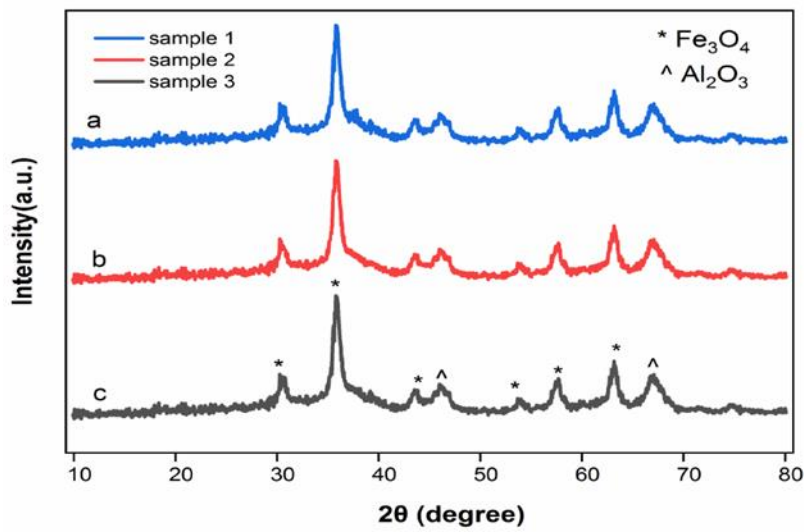

Fig. 1. XRD patterns of Fe_3O_4/Alumina core-shell nanoparticles: (a) sample 1, (b) sample 2, and (c) sample 3

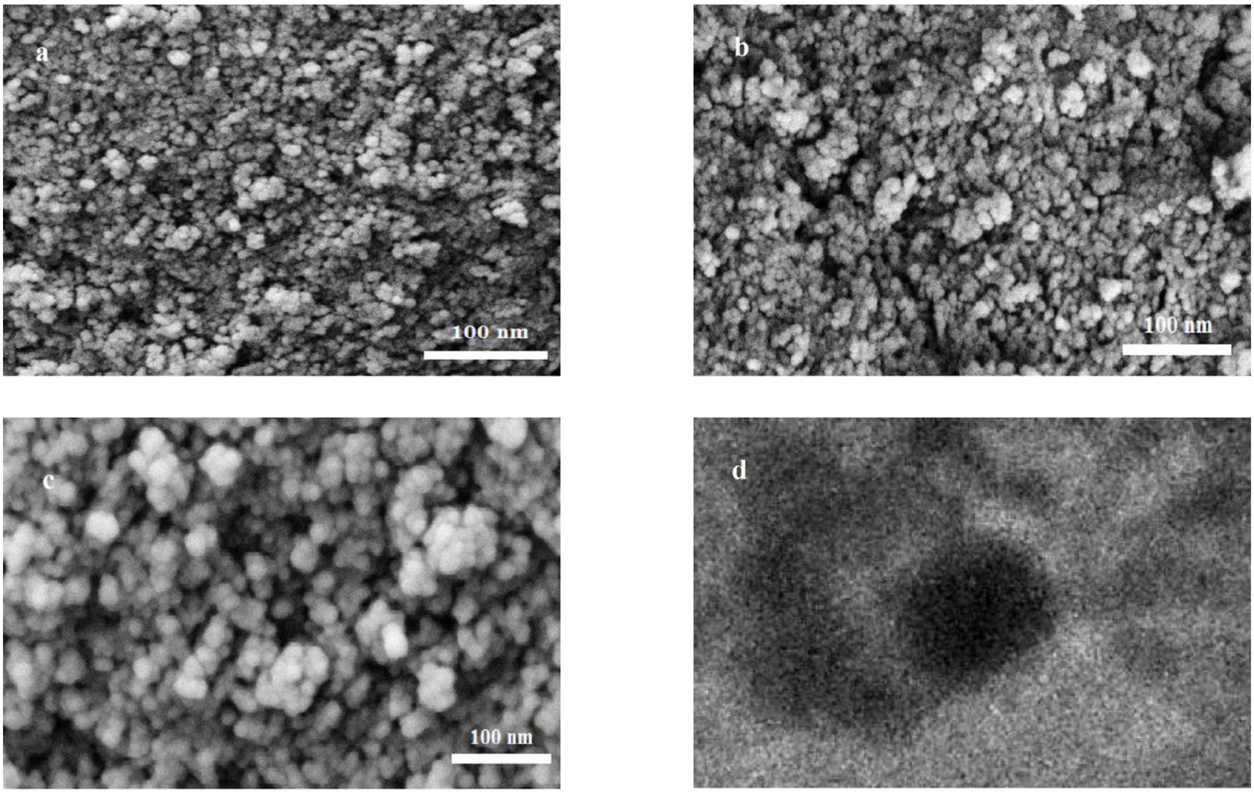

Fig. 2. a-c. FE-SEM images of Fe_3O_4/Alumina core-shell nanoparticles: (a) sample 1, (b) sample 2, (c) sample 3, and Fig. 2d. TEM image of Fe_3O_4/Alumina core-shell nanoparticle.

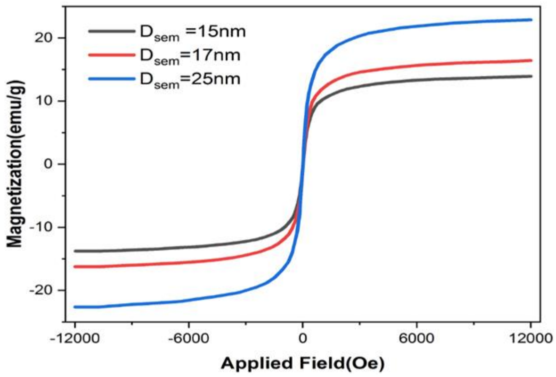

Fig. 3. VSM curves of samples at room temperature.

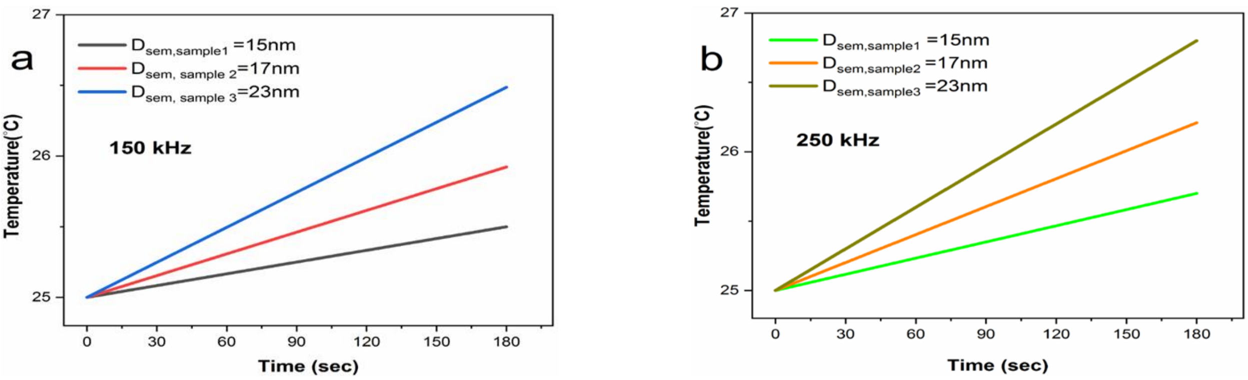

Fig. 4. Temperature vs. time plots of an aqueous suspension with 0.3 mg/mL concentrations of Fe_3O_4/Alumina nanoparticle at a field of 120 Oe and frequencies of (a) 150 kHz and (b) 250 kHz

4. Conclusion

The present work provided a new type of compound for potential thermal applications. Fe_3O_4/Alumina magnetic nanoparticles are efficient for magnetic hyperthermia. The product has been achieved by the reaction of fe_3O_4 and Alumina compounds using an ultrasonic device. The prepared product was evaluated by VSM, XRD, TEM, FE-SEM, and magnetic hyperthermia analyses, and their results showed the core-shell structure, successful synthesis, superparamagnetic behavior, and acceptable heating power of nanoparticles. Finally, it can be stated that research findings highlight the potential of Fe_3O_4/Alumina MNPs such as small size, superparamagnetic behavior with high saturation magnetization, and good heat generation rate for use in the field of magnetic hyperthermia of nanoparticles.

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