Maghemite (γ-Fe₂O₃) and γ-Fe₂O₃-TiO₂ Nanoparticles for Magnetic Hyperthermia Applications: Synthesis, Characterization and Heating Efficiency

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Abstract: In this report, the heating efficiencies of γ-Fe₂O₃ and hybrid γ-Fe₂O₃-TiO₂ nanoparticles NPs under an alternating magnetic field (AMF) have been investigated to evaluate their feasible use in magnetic hyperthermia. The NPs were synthesized by a modified sol-gel method and characterized by different techniques. X-ray diffraction (XRD), Mössbauer spectroscopy and electron microscopy analyses confirmed the maghemite (γ-Fe₂O₃) phase, crystallinity, good uniformity and 10 nm core sizes of the as-synthesized composites. SQUID hysteresis loops showed a non-negligible coercive field and remanence suggesting the ferromagnetic behavior of the particles. Heating efficiency measurements showed that both samples display high heating potentials and reached magnetic hyperthermia (42 °C) in relatively short times with shorter time (~3 min) observed for γ-Fe₂O₃ compared to γ-Fe₂O₃-TiO₂. The specific absorption rate (SAR) values calculated for γ-Fe₂O₃ (up to 90 W/g) are higher than that for γ-Fe₂O₃-TiO₂ (~40 W/g), confirming better heating efficiency for γ-Fe₂O₃ NPs. The intrinsic loss power (ILP) values of 1.57 nHm²/kg and 0.64 nHm²/kg obtained for both nanocomposites are in the range reported for commercial ferrofluids (0.2–3.1 nHm²/kg). Finally, the heating mechanism responsible for NP heat dissipation is explained concluding that both Neel and Brownian relaxations are contributing to heat production. Overall, the obtained high heating efficiencies suggest that the fabricated nanocomposites hold a great potential to be utilized in a wide spectrum of applications, particularly in magnetic photothermal hyperthermia treatments.

Keywords: iron oxide nanoparticles; maghemite; TiO₂; Sol-Gel synthesis; magnetic hyperthermia; heating efficiency; alternating magnetic field

1. Introduction

The unique properties of magnetic iron oxide nanoparticles (NPs) confirmed its use in several applications such as photocatalysis, photonic, magnetic storage and electronic
devices to biomedicine and theranostics [1,2]. Among these applications in clinical practice is their utilization in magnetic fluid hyperthermia (MFH) [3]. This is chiefly due to their excellent intrinsic magnetic properties, ultrasmall nanometer dimensions (5–15 nm) and their ability for dissipating heat using an alternating magnetic field (AMF). In particular, ferrites (mainly magnetite (Fe₃O₄) or maghemite (γ-Fe₂O₃)) are very promising materials for MFH and have been effectively utilized for cancer hyperthermia therapy [4–6]. Furthermore, a combination of iron-based nanoprobes with other transition metals (i.e., Ti, Au, Ag) at the nanoscale lead to formation of bifunctional materials which benefits from the unique properties of both components. Consequently, bifunctional iron oxide-based NPs, with both photo and magnetic properties, are expected to exhibit high potentials, particularly in multimodal photothermal therapies [7–9]. There is, therefore, a pressing need to understand the heat generated from such hybrid constructs and to show the influence of the added metal on the overall magnetism and heating properties of iron oxides.

The advantage of γ-Fe₂O₃, the rare form of iron oxides, over other metal doped ferrite NPs is their magnetism and relatively high saturation magnetization. γ-Fe₂O₃ is a spinel ferrite and has almost the same structure as Fe₃O₄, but it converts to alpha hematite (α-Fe₂O₃) at very high temperatures [10–12]. Thus, the impeccable synthetic routes to achieve a series of uniform, size-controlled, highly-magnetic, crystalline and stable γ-Fe₂O₃ NPs remain unambiguously challenging. To date, several different methods have been employed to synthesize iron oxide NPs including non-aqueous and aqueous sol-gel, spray/laser pyrolysis, sonochemical, microemulsion, hydrothermal, chemical precipitation and thermal decomposition [13]. However, preparation of γ-Fe₂O₃ NPs continues to be difficult and often leads to phase transitions and loss of crystallinity during the synthesis [14]. Another important factor relies on employing modest, feasible and cost-effective route to prepare big quantities of NPs on demand. On the other hand, among other oxide semiconductors, TiO₂ was the most interesting material due to its high photocatalytic activity, biochemical inertness, strong oxidizing power, relatively low price and long-term chemical and thermal stability against photo and chemical degradation. Therefore, the immobilization of TiO₂ onto magnetic ferrite NPs could serve as an excellent material that could be used for wide range of applications (water treatment, disinfection, pollutant degradation and photothermal hyperthermia therapy). Most of the reports on iron oxide-TiO₂ nanocomposites, however, focused their studies on the photocatalytic activities and showed that iron oxide NPs enhance the photocatalytic properties of TiO₂ [15–20]. Only few research works investigated the heating efficiency of these nanocomposites for possible use in magnetic hyperthermia applications [19,20]. Shariful Islam et al. [19] studied the thermal-photocatalytic cell killing efficiency of Fe₃O₄-TiO₂. It was found that the cancer cell killing percentage was enhanced by combining an alternating magnetic-field induction and UV–vis photoirradiation in comparison to only bare Fe₃O₄ or TiO₂. Lu et al. [20] investigated the hyperthermia abilities and photocatalytic activities of porous γ-Fe₂O₃ microspheres decorated with TiO₂. They reported a good heating ability of the composites, which make them promising candidate for magnetic hyperthermia applications.

In fact, magnetic hyperthermia using iron oxide NPs is currently boosting as such probes can act as efficient and local nanoheaters through remote activation (i.e., by AMF), which leads to remarkable therapeutic effects. However, their success relies on the precise control of their magnetic properties, sizes, specific absorption rate (SAR) and intrinsic loss power (ILP), as well as tuning parameters such as concentrations and amplitude of the applied magnetic field. The heat dissipated using an AC magnetic field is characteristically known by SAR, which is the amount of heat generated per unit gram of magnetic material and per unit time [21,22]. Previous studies reported that SAR values could be influenced by different parameters, among them, size, structure, magnetic properties, preparation methods, concentration and the frequency and amplitudes of the applied magnetic field [23–27]. De la Presa et al. prepared γ-Fe₂O₃ NPs by the technique called coprecipitation and demonstrated the effect of different parameters on SAR [24]. They found
that the critical crystallite size to obtain maximum efficiency of heat was 12 nm. We previously investigated the heating efficiency of different sizes γ-FeO₃ NPs using sol-gel technique [25,26] and we obtained that 14 nm was the best size to acquire preferable heating efficiency. In addition to the above parameters, the magnetic particle-particle interactions could also affect SAR values. Despite the large number of reports on the effect of variable parameters on SAR, the key factors affecting the heat dissipation is still not very well understood.

Herein, we report a simple process using modified sol-gel strategy to synthesize maghemite and maghemite-TiO₂ nanocomposites. We tested whether the presence of TiO₂ affect particle-particle magnetic interactions and induce any effects on heating abilities. We then studied the influence of magnetic properties and amplitude of the exercised magnetic field on heating abilities (SAR values) for the acquired particles. Finally, we discussed the plausible heating mechanism responsible for the generation of heat from the obtained NPs. The best we know, there is no report systematically studying different effects on the heating efficiencies of γ-FeO₃ NPs and hybrid γ-FeO₃-TiO₂ NPs. These γ-FeO₃@TiO₂ nanocomposites, which integrate photo and magnetic properties, have great potential to be used in wide range of applications, particularly in medical photothermal hyperthermia.

2. Experimental

2.1. Synthesis of Maghemite and Maghemite-TiO₂ Nanoparticles

In the first step, γ-FeO₃ NPs were synthesized by a modified Sol-gel process in supercritical conditions of ethyl alcohol (EtOH) following similar procedure as in our previous work [25]. 5 g of iron (III) acetylacetonate [C₆H₅;FeO₉, 99%] obtained from Chemsavers was dissolved in a 30 mL of methanol (CH₃OH, 98%) obtained from SIGMA-ALDRICH, under magnetic stirring of 400 rpm at room temperature for 15 min. The solution was then placed in an autoclave and dried under supercritical conditions of ethanol (C₂H₅O, 96%) fabricated by Honeywell. The supercritical conditions of ethanol are Pₑ = 63.3 bar and Tₑ = 243 °C. The control of the heating of the autoclave was realised by temperature programmer.

In the second step, TiO₂ NPs enriched by FeO₃ particles were obtained by dissolving of 6.72 mmol of titanium (IV)-isoproxide (Ti(iOPr)₄, 97%, from Chemsavers) in a mixture of methanol and acetic acid (2 mL/2 mL). After 15 min of magnetic stirring, 50 mg of FeO₃ NPs prepared in the first step was added to the solution and introduced in ultrasonic bath for 10 min. The temperature range was varied from ambient to 250 °C. The resulted solution was then introduced in an autoclave and dried in the supercritical condition of ethanol by using 600 mL.

This simple and cost-effective synthesis allowed the production of large quantities of γ-FeO₃ NPs and γ-FeO₃-TiO₂ NPs on demand.

2.2. Structural Measurements

Using Bruker D8 Discover diffractometer (θ-2θ) equipped with Cu-Kα radiation (λ = 1.5406 Å), XRD analyses were made. The average crystallite size, D, of different samples was estimated by Scherrer’s formula [28]:

\[ D = \frac{K\lambda}{\beta \cos \theta} \] (1)

where θ is the Bragg angle (in degree), λ is the incident wavelength (1.5406 Å), K is a constant whose value is approximately 0.9 and β (rad) is the full width at half maximum (FWHM) of a diffraction peak. Fourier transform infrared (FTIR) spectra were obtained using a Perkin-Elmer 580B IR spectrometer. The morphology of the samples was studied by means of transmission electron microscope (Type JEOL JSM-200F atomic resolution microscopy operating at 200 kV, Tokyo 1968558, Japan).
2.3. Magnetic Characterization

Mössbauer spectra were recorded at ambient temperature (RT = 295 K) and 78 K in standard transmission geometry using a constant acceleration signal spectrometer equipped with a $^{57}$Co source in a rhodium matrix. The data were analyzed using a non-linear least-squares fitting program assuming a Lorentzian distribution. Isomer shifts are presented in reference to $\alpha$-Fe. Magnetic characterizations were performed in a Quantum Design MPMS-5S SQUID magnetometer (San Diego, CA 92121, USA). Zero-field-cooled and field-cooled (ZFC-FC) curves were recorded at magnetic field of 100 Oe.

2.4. Heating Efficiency

A commercial system “Nanotherics Magnetherm” was used to carry out the heating efficiency of the samples under alternating current (AC) magnetic field as reported in our previous report [28]. The heat generated by magnetic nanoparticles for magnetic hyperthermia measurement is quantified by the SAR, which can be determined by:

$$\text{SAR} = \frac{\rho C_w}{\text{Mass}_{\text{MNP}}} \left( \frac{\Delta T}{\Delta t} \right)$$  \hspace{1cm} (2)

where $C_w$ is defined as the specific heat capacity of water (4.185 J·kg$^{-1}$·K$^{-1}$), the density of the colloid is $\rho$, the concentration of the magnetic nanoparticles in the suspension is called Mass$_{\text{MNP}}$ and the heating rate is represented by $\frac{\Delta T}{\Delta t}$. By performing a linear fit of temperature increase versus time at the initial time interval (1 to ~30 s), the slope $\frac{\Delta T}{\Delta t}$ is obtained. The influence of concentration (10 and 20 mg/mL) has been studied. To show the effect of different amplitudes (40, 90 and 130) of the magnetic field and 170 Oe at 332.8 kHz on the heating ability of the as-prepared NPs, one has selected a concentration of 10 mg/mL. All the samples are dispersed in deionized water.

3. Results and Discussion

3.1. Structural Properties

XRD spectra of the obtained nanocomposites are shown in Figure 1. As can be seen in Figure 1a, XRD patterns of FeO$_n$ NPs indicated the presence of diffraction peaks which correspond to spinel structure, which could be indexed on the basis of $\gamma$-FeO$_n$ with space group P4132 (JCPDS No. 39-1346). No additional peaks have been observed suggesting that our synthetic method lead to the formation of a pure phase without any impurities that remain from the unreacted precursors. XRD patterns of $\gamma$-FeO$_n$-TiO$_2$ nanocomposite (Figure 1b) are similar to patterns obtained for $\gamma$-FeO$_n$ but new peaks appear at 2$\theta$ = 25.3°, 37.86°, 48.2°, 54.1°, 55.2° are attributed to anatase-TiO$_2$ [29], while the peaks located at 2$\theta$ = 27.57°, 41.02°, 54.3°, 68.96° are due to the rutile TiO$_2$ [30]. We can conclude from XRD results that the successful formation of $\gamma$-FeO$_n$-TiO$_2$ nanocomposite and that the addition of TiO$_2$ did not induce any significant phase changes on the $\gamma$-FeO$_n$ NPs. It is important also to note that the peaks for both samples are very broad indicating the formation of very fine particles. The average crystallite size obtained by using the Debye-Scherrer formula confirms this result. The average crystallite size estimated for $\gamma$-FeO$_n$ was 8.5 nm. This value increased to 10 nm after adding TiO$_2$ which has an average crystallite size of 16.5 nm and 22 nm for anatase and rutile phases, respectively.
FTIR was then extended to confirm the presence of Fe₂O₃ and Fe₂O₃-TiO₂ (Figure 2). FTIR spectrum of γ-Fe₂O₃ showed a broad band at 3434 cm⁻¹ and 1630 cm⁻¹ attributed to the O-H stretching and bending vibrations of surface hydroxyl, respectively. Another peak at 2927 cm⁻¹ may correspond to C-H groups stretching vibration. The band at 1420 cm⁻¹ is attributed to the C-O stretching vibration, while the bands at 635 cm⁻¹ and 583 cm⁻¹ are associated with the Fe-O vibrational modes confirming the presence of iron oxide. The γ-Fe₂O₃-TiO₂ shows a similar FTIR spectrum to that of γ-Fe₂O₃ with wide absorption band at 420–825 cm⁻¹. This wide absorption band is attributed to Ti-O vibrations [20].
Figure 2. FTIR spectra of γ-Fe₂O₃ (up) and γ-Fe₂O₃-TiO₂ (down) NPs.

To better analyze the size and morphology of the obtained nanocomposites, transmission electron microscopy (TEM) was conducted. Figure 3a,b shows TEM images of γ-Fe₂O₃ and γ-Fe₂O₃-TiO₂ nanocomposites, respectively. The images clearly indicate the quasi-cubic morphology of the samples with average core sizes of γ-Fe₂O₃ equal to 8.5 nm and slightly increases for γ-Fe₂O₃-TiO₂ to 11 nm. The particle size distribution associated with the TEM images confirm the good uniformity of the as-synthesized NPs (Figure 3c,d).
Figure 3. TEM photographs (a,b) particles size distribution (c,d) γ-Fe₂O₃ and γ-Fe₂O₃-TiO₂ nanocomposite respectively.

3.2. Magnetic Characterization

3.2.1. SQUID Measurements

Hysteresis loops and ZFC-FC curves for γ-Fe₂O₃ and γ-Fe₂O₃-TiO₂ NPs are shown in Figure 4. The saturation magnetization (Ms), remanence (Mr), remnant to saturation magnetization ratio (Mr/Ms) and coercive field (Hc) values are presented in Table 1. It can be seen that the samples exhibit a non-negligible coercive field at room temperature, indicating that the particles do not behave as superparamagnetic (Figure 4a,b). The saturation magnetization at room temperature estimated for γ-Fe₂O₃ (Ms = 84.5 emu/g) is higher than the standard value reported for bulk maghemite γ-Fe₂O₃ (Ms = 74 emu/g) but comparable to those reported in previous studies [24]. This is because of the spin disorder in surface that can be aligned readily in the applied magnetic field direction [31]. It might be also due to the presence of magnetite phase which has high magnetization, but XRD and Mossbauer results (discussed later) confirm the absence of this phase in the sample. The observed decrease of saturation of γ-Fe₂O₃-TiO₂ NPs (Ms = 58.77 emu/g) is due to the non-magnetic nature of TiO₂. Previous studies reported similar behavior of saturation after coating magnetite and maghemite with TiO₂ [18,32]. To further understand the magnetic behavior of the samples, magnetization as a function of temperature using the zero-field-cooled and field-cooled (ZFC-FC) were performed (Figure 4c,d). The ZFC-FC curves indicate that blocking temperature (Tₛ) for γ-Fe₂O₃ NPs is above room temperature, while Tₛ is around 240K for γ-Fe₂O₃-TiO₂ NPs.
Figure 4. Hysteresis loops of (a) γ-Fe2O3 and (b) γ-Fe2O3-TiO2 nanocomposites. ZFC/FC curves of (c) γ-Fe2O3 and (d) γ-Fe2O3-TiO2 nanocomposite.

Table 1. Magnetic parameters deduced from hysteresis loops and anisotropy constant ($K_{\text{eff}}$) for γ-Fe2O3 and γ-Fe2O3-TiO2 nanocomposites.

| Samples         | $M_s$ (emu/g) 10 K | $M_s$ (emu/g) 300 K | $M_s/M_r$ | $H_c$ (Oe) | $K_{\text{eff}}$ (erg/cm$^3$) | D (nm) |
|-----------------|--------------------|---------------------|-----------|------------|-------------------------------|-------|
| Fe2O3           | 97.76              | 84.55               | 17.51     | 2.69       | 0.179                         | 23    |
| Fe2O3-TiO2      | 68.11              | 58.77               | 12.25     | 3.11       | 0.18                          | 27    |

The coercive field $H_c$ increases with decreasing temperature for both samples due perhaps to the blocking of magnetic moments. The behavior of $H_c$ at room temperature for the two samples can be analyzed in term of size. It can be seen that coercivity at room temperature increase slightly for γ-Fe2O3-TiO2 nanocomposite ($H_c = 27$ Oe) compared to γ-Fe2O3 ($H_c = 23$ Oe). This behavior can be understood on the basis of model describing the magnetic behavior in the monodomain regime; where coercivity follow the relation [24,33]:

$$H_c = \left(\frac{2K_{\text{eff}}}{\mu_0M_s}\right)\left[1 - \frac{25K_bT}{K_{\text{eff}}V}\right]$$

(3)

where $K_{\text{eff}}$ is effective anisotropy constant, $M_s$ is the saturation and $V$ is the volume of the nanoparticles. It can be seen from the relation (3) that the coercive field depends on saturation, the volume and effective anisotropy constant. All these parameters are size dependent and that can explain the decrease of the coercivity with decreasing size.

Using the law of approach to saturation (LAS), we attempt to calculate the anisotropy constant $K_{\text{eff}}$ which characterize the magnetization close to the saturation as below [34,35]:

$$M(H) = M_s\left(1 - \frac{b}{H^2}\right)$$

(4)

where $b$ is a parameter used to determine $K_{\text{eff}}$ by using the following equation [25]:

$$K_{\text{eff}} = \mu_0M_s\sqrt{\frac{15b}{4}}$$

(5)

The calculated value of $K_{\text{eff}}$ for both samples at 10 K and 300 K are summarized in Table 1. As can be seen, the effective anisotropy constant obtained for γ-Fe2O3 NPs at room temperature ($K_{\text{eff}} = 5.68 \times 10^4$ erg/cm$^3$) is close to that reported for bulk γ-Fe2O3 ($K_{\text{eff}} = 4.7 \times 10^4$ erg/cm$^3$) [36].
3.2.2. Mössbauer Spectroscopy

We indexed the phase of the obtained NPs as $\gamma$-Fe$_2$O$_3$ from XRD, but it could be also indexed as Fe$_3$O$_4$ given that XRD patterns of $\gamma$-Fe$_2$O$_3$ and Fe$_3$O$_4$ are almost the same. In order to differentiate between the two phases ($\gamma$-Fe$_2$O$_3$ and Fe$_3$O$_4$) and to confirm that the obtained phase is $\gamma$-Fe$_2$O$_3$, Mössbauer spectroscopy studies were carried out. It is well known that the hyperfine parameters such as isomeric shift and hyperfine field of both Fe-oxides are different. The Mössbauer spectra of the two samples at 78 K and 295 K are shown in Figure 5a and as can be observed, all the spectra show well-defined magnetic sextet pattern. The best fit was obtained by considering two dominating sextets and one small magnetic component A, B and C, respectively, as shown in Figure 5b. As can be seen from Table 2, the isomeric shift values of the main components A (0.40 mm/s) and B (0.43 mm/s) of Fe$_2$O$_3$ at 78 K are typical of ferric (Fe$^{3+}$) iron [37]. In addition to the isomer shift values, the hyperfine field and quadrupole shifts of both components are the typical characteristics of Fe$^{3+}$ ions in maghemite $\gamma$-Fe$_2$O$_3$ nanoparticles [38]. Furthermore, the hyperfine parameters of the third component C is also attributed to the Fe$^{3+}$ ions. It is important to highlight the absence of ferrous (Fe$^{2+}$), which is characteristic of magnetite (Fe$_3$O$_4$). Thus, it can be concluded that the synthesized NPs are indexed as $\gamma$-Fe$_2$O$_3$ with space group P4132 (JCPDS No. 39-1346). The A and B components are attributed to the tetrahedral and octahedral sites of maghemite, respectively, while the third component C is attributed to the iron ions in the surface layer. The spectrum of Fe$_2$O$_3$-TiO$_2$ at 78K was fitted with same components and no changes are observed except slight decreases in the hyperfine field values due to the effect of TiO$_2$, which is non-magnetic. This is in agreement with magnetization measurement that clearly shows a decrease of Fe$_2$O$_3$-TiO$_2$ saturation.
Figure 5. (a) The $^{57}$Fe Mössbauer spectra of γ-Fe$_2$O$_3$ and γ-Fe$_2$O$_3$-TiO$_2$ nanocomposite at 78 and 295 K; (b) The calculated spectrum components for both samples corresponding to the tetrahedral (A), octahedral (B) sites of Fe$^{3+}$ ions and iron ions at the surface of the NPs (C).

| Samples               | Component | Isomer Shifts δ ± (0.01) mm/s | Quadrupole Shifts ε ± (0.002) mm/s | Magnetic Hyperfine Field Bh (±0.1) | Area A (±1) % |
|-----------------------|-----------|------------------------------|------------------------------------|----------------------------------|--------------|
| Fe$_2$O$_3$           | A         | 0.40                         | −0.007                             | 49.7                             | 34           |
| Fe$_2$O$_3$-TiO$_2$   |           |                              |                                    |                                  |              |
The Mössbauer spectra for both samples show well-defined magnetic sextet pattern, but the lines become broadened (Figure 5), indicating that the samples conserved their magnetic order remain. This is in agreement with SQUID measurements, which indicated that both samples are ferromagnetic at room temperature. The phase is confirmed again by fitting the spectra with the same components corresponding to Fe³⁺ ions in the tetrahedral, octahedral and in the surface layer. For γ-Fe₂O₃-TiO₂ sample, the best fit was obtained by adding paramagnetic doublet component D (Table 2), which is attributed to the transition of some part of NPs from magnetic ordering to a paramagnetic state (Figure 6b). This paramagnetic component is due to part of the NPs, where their blocking temperature $T_B$ is below 295 K. ZFC/FC measurements corroborated this hypothesis and showed that γ-Fe₂O₃-TiO₂ sample has $T_B$ around 240K, while $T_B$ for γ-Fe₂O₃ is above room temperature.

In summary, the Mössbauer results indicated that the phase is maghemite and that both samples are ferrimagnetic at room temperature, which is in agreement with magnetic measurements.
Figure 6. Temperature increases at $H_0 = 170$ Oe and $f = 332.8$ kHz for γ-Fe$_2$O$_3$ and (b) γ-Fe$_2$O$_3$-TiO$_2$ nanocomposite: (a) 10 mg/mL, (b) 20 mg/mL and (c) SAR values as function of concentration.

3.3. Heating Efficiency Measurements

3.3.1. SAR as Function of Concentration

The heating efficiencies of γ-Fe$_2$O$_3$ and γ-Fe$_2$O$_3$-TiO$_2$ nanocomposites dispersed in de-ionized water at different concentrations under AMF with frequency and amplitudes that satisfy the magnetic hyperthermia safety condition ($H_x f \leq 5 \times 10^8 \text{A/m.s}$) [24] were conducted (Figure 6). The main heating parameters obtained from the temperature rise are summarized in Table 3. As can be seen in Figure 6a,b, all the samples show high heating ability and reach magnetic hyperthermia temperature (42 °C) in short time. For instance, γ-Fe$_2$O$_3$ reached magnetic hyperthermia temperature in only 3 min, while γ-Fe$_2$O$_3$-TiO$_2$ took around 4.5 min to reach the same temperature at the same concentration. As expected, the rise in temperature decreases with decreasing the concentration for both samples. While 20 mg/mL sample of γ-Fe$_2$O$_3$ could reach high temperatures up to 73 °C in 15 min, temperature up to 62 °C was achieved for 10 mg/mL concentration of the same sample. This increase can be explained by the additional amount of magnetic nanostructure, which is generally the main source of heat dissipation. The calculated values of SAR as function of concentration are shown in Figure 6c. It can be seen that SAR values of γ-Fe$_2$O$_3$ are higher than that obtained for γ-Fe$_2$O$_3$-TiO$_2$ nanocomposites but both samples have
considerable SAR values. As reported by previous reports, interparticles dipolar interaction increases with increasing concentration of NPs and that could induce such effect on the heating [22,39,40]. Abbasi et al. [39] claimed that increase of dipolar interaction with enhancing concentration has a considerable influence on the Neel relaxation time (which will be discussed later).

### Table 3. Heating characteristics at \( H_0 = 170 \) Oe and \( f = 332.8 \) kHz.

| ILP (nH m²/kg) | SAR (W/g) | Time Needed to Reach Hyperthermia Temperature 42 °C (min) | Maximum Temperature (°C) | Concentration | Samples            |
|---------------|-----------|-------------------------------------------------------|--------------------------|---------------|-------------------|
| 1.57          | 92.3      | 4.8                                                   | 62                       | 10 mg/mL      | \( \gamma \)-FeO₃ |
| 0.64          | 39        | 10.5                                                  | 46                       |               | \( \gamma \)-FeO₃-TiO₂ |
| 0.73          | 44.46     | 3                                                     | 73                       | 20 mg/mL      | \( \gamma \)-FeO₃ |
| 0.67          | 41.15     | 4.6                                                   | 57.5                     |               | \( \gamma \)-FeO₃-TiO₂ |

**3.3.2. SAR as Function of Field Amplitude**

Figure 7a,b shows the temperature rise of the samples with concentrations of 10 mg/mL in frequency of 332.8 kHz and for different strength of AC magnetic field. When the field amplitude increases from 90 Oe to 170 Oe and as expected, an increase of the temperature is observed (Figure 7c), indicating that the heating efficiency of the NPs can be tuned by changing the field amplitude. As can be observed also in Figure 8a, SAR increases with increasing field amplitude and reached their higher values at field amplitude of 170 Oe for both samples. The same trend of SAR with the field amplitude was reported for many NP systems [22,24,25]. Furthermore, we investigated that the linear response theory (LRT) was valid for the two samples. In this model, SAR varies linearly as a function of square of field amplitude and given as below [24]:

\[
SAR = c f H^2
\]

where \( c \) is a constant, \( f \) is the frequency and \( H \) is amplitude of the field.

Figure 8b shows that field amplitude dependence of experimental SARs has a quadratic behavior as expected by the LRT model. The coefficient of determination \( R^2 \), which should be near 1 for better fit is around 0.998 for both samples and this affirms the high fit accuracy.
Figure 7. Temperature increases at $f = 332.8$ kHz and different AC magnetic field of (a) $\gamma$-Fe$_2$O$_3$, (b) $\gamma$-Fe$_3$O$_4$-TiO$_2$ and (c) Temperature vs field amplitude.
3.3.3. Comparison of Heating Ability

Both samples reached magnetic hyperthermia (42°C) in a relatively short time but the time needed to reach this temperature is shorter in the case of γ-Fe₂O₃ compared to γ-Fe₂O₃-TiO₂ nanocomposites. Furthermore, the SAR values achieved for γ-Fe₂O₃ are higher than that obtained for γ-Fe₂O₃-TiO₂, indicating better heating for γ-Fe₂O₃ NPs. This high heating efficiency could be explained mainly by the high saturation of γ-Fe₂O₃ NPs (Ms = 84.55 emu/g) compared to 58.77 emu/g obtained for γ-Fe₂O₃-TiO₂. Other parameters such as size of NPs and the effective anisotropy constant (Keff) can also affect SAR. However, the effect of size can be neglected due to almost comparable sizes obtained from TEM measurements, while Keff of γ-Fe₂O₃ (5.68 × 10⁴ erg/cm³) is about 16-fold larger than γ-Fe₂O₃-TiO₂ nanocomposite value (3.43 × 10³ erg/cm³).

The comparison of the heating ability of our NPs with other systems through the SAR values is depicted in Table 4. However, this comparison of SAR values does not give much information on the heating efficiency given that each study has its own experimental conditions such as concentration, magnetic properties, field amplitude, frequency etc.

Table 4. Comparison of ILP values for different magnetic NPs.

| Magnetic Nanoparticles | Synthesis Method       | Frequency (kHz) | Field (Oe) | Medium            | ILP (nH m²/kg) | Ref |
|------------------------|------------------------|-----------------|------------|-------------------|----------------|-----|
| γ-Fe₂O₃                | Modified Sol-gel       | 332.8           | 170        | distilled water   | 1.57           | This work |
| γ-Fe₂O₃                | Modified Sol-gel       | 523             | 100        | distilled water   | 1.3            | [25] |
| γ-Fe₂O₃-TiO₂           | Modified Sol-gel       | 332.8           | 170        | distilled water   | 0.64           | This work |
| Fe₂O₃                  | Hydrothermal           | 55              | 86.7       | Physiological saline | -             | [20] |
| Zn₄1Fe₉0FeO₄           | coprecipitation method | 339             | 92         | distilled water   | 5.4            | [41] |

To allow a logic comparison of the heating efficiency, we used the intrinsic loss power (ILP), which is given by [38]:

\[
ILP = \frac{SAR}{fH_0^2}
\]

where \( f \) is the frequency and \( H_0 \) is magnetic field.
It can be seen from Table 3 that ILP values for 10 mg/mL sample of $\gamma$-Fe$_2$O$_3$ (1.57 nHm$^2$/kg) is larger than that achieved for the same concentration of $\gamma$-Fe$_2$O$_3$-TiO$_2$ (0.64 nHm$^2$/kg) showing again the high heating efficiency of $\gamma$-Fe$_2$O$_3$ compared to $\gamma$-Fe$_2$O$_3$-TiO$_2$ nanocomposites. However, the ILP values for both samples are in the range reported for commercial ferrofluids (0.2–3.1 nHm$^2$/kg) [42].

3.3.4. Mechanism of Heating

Heat dissipation from magnetic nanoparticles under AC magnetic field is caused by three major mechanisms, namely: Hysteresis loss; Brownian relaxation and Néel relaxation as discussed in our previous report [22,25]. We and others [41,43] believe that all the three mechanisms are collaboratively effective in the heat generation. However, some aspects are more dominant over the others as discussed below.

Generally, hysteresis losses are in proportion with the area (A) of the hysteresis loop. As can be observed from M-H curves (Figure 4), both samples present a minor hysteresis loop area due to the low values of coercivity and remanence. It is therefore reasonable to deduce that the contribution of hysteresis loss in the heat dissipated by the samples can be neglected.

In Néel relaxation, the magnetic moment of NPs suspended in fluid can relax after magnetic field removal and relaxation time is given by:

$$\tau_N = \tau_0 e^{K_{\|}/k_B T}$$

(8)

where $\tau_0 = 10^{-8}$ s, $V$ the particle volume, $K_{\|}$ magnetic anisotropy constant, $k_B$ the Boltzmann constant and $T$ the absolute temperature.

The entire nanoparticles can rotate through Brownian relaxation during time $\tau_B$:

$$\tau_B = \frac{3\eta V}{k_B T}$$

(9)

where $\eta$ is the viscosity of the fluid and $V$ the particle volume.

It can be seen that Néel relaxation time depends exponentially on volume and magnetic anisotropy whereas the Brownian relaxation varies linearly with the volume and the media viscosity.

In most cases, the combination of the two mechanisms is more suitable, but the quick relaxation mechanism is prevalent and an effective relaxation time may be known as:

$$\frac{1}{\tau_{\text{eff}}} = \frac{1}{\tau_N} + \frac{1}{\tau_B}$$

(10)

Previous studies showed that Néel relaxation is more dominating in the case of particles with smaller sizes, while larger particles relax in liquid medium mainly by a Brownian mechanism [24,25,43,44]. The NP sizes deduced from XRD and TEM for our samples allow us to suppose that the contribution of Néel relaxation is more dominant than that of Brownian relaxation. In order to confirm the contribution of Brownian relaxation in the heat dissipated by NPs, the temperature rise was measured in different carrier liquids as shown in Figure 9. It is expected that Brownian relaxation time in liquid with lower viscosity will decreases as described by Equation (9) and that would induce an increase of heating efficiency. It can be observed from Figure 9, that the sample dispersed in acetone reach magnetic hyperthermia (42 °C), while sample in deionized water does not reach this temperature. The heating efficiency clearly increase for NPs dispersed in acetone which has lower viscosity (0.295 mPa.s) compared to deionized water (0.89 mPa.s). Thus, we can conclude that Brownian relaxation mechanism is also contributing to the heat production.
Figure 9. Increase in temperature at $H_0 = 170$ Oe and $f = 332.8$ kHz for $\gamma$-Fe$_2$O$_3$-TiO$_2$ NPs (5 mg/mL) dispersed in deionized water and in acetone.

4. Conclusions

In conclusion, a modified sol-gel method was employed to synthesize $\gamma$-Fe$_2$O$_3$ and $\gamma$-Fe$_2$O$_3$-TiO$_2$ nanocomposites with small sizes and good uniformity for magnetic hyperthermia applications. Magnetization measurements and heating efficiencies were investigated in detail. The influence of concentration, magnetic field amplitude and carrier liquid on heating efficiency was presented. Our results show that the ILP and SAR values differ slightly between the two samples, but both have high heating efficiency and reach magnetic hyperthermia temperature ($42 \, ^\circ$C) in relatively short times. While $\gamma$-Fe$_2$O$_3$ NPs reached magnetic hyperthermia temperatures in 3 min, $\gamma$-Fe$_2$O$_3$-TiO$_2$ NPs require around 10 min for reaching the same temperature. SAR values indicated that the heating efficiency of the NPs can be tuned by changing the field amplitude or concentration of the NPs. The dependence of SAR values with field amplitude follows linear response theory (LRT). Moreover, the ILP values of 1.57 nHm$^2$/kg and 0.64 nHm$^2$/kg obtained for $\gamma$-Fe$_2$O$_3$ and $\gamma$-Fe$_2$O$_3$-TiO$_2$, respectively, are in the range reported for commercial ferrofluids (0.2–3.1 nHm$^2$/kg), showing their good heating efficiency. The high crystallinity, good SAR and ILP values make these NPs promising candidates for hyperthermia application.

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