

## How Co-Precipitation Reaction Parameters Control the Characteristics and Features of Iron Oxide Nanoparticles

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The main purpose of this study was to find a simple reaction condition for reproducible synthesis of water-soluble superparamagnetic iron oxide nanoparticles (SPIONs) through the co-precipitation method. For this purpose, the effect of alkali solution, working atmosphere and final reaction temperature on type, size and magnetic properties of synthesized particles were examined. The characterization of chemical composition, structural and magnetic properties of the particles obtained was carried out by investigating suspension appearance, dynamic light scattering (DLS), scanning electron microscopy (SEM), UV-Vis spectrum, vibrating sample magnetization (VSM) and X-ray diffraction (XRD) results. The results reveal that from two different tested alkali precipitants including ammonia and 1 M NaOH, samples synthesized using ammonia demonstrate proper magnetic properties, while the latter agent leads to production of nonmagnetic brown suspensions in all reaction conditions. UV-Vis absorption spectrum and XRD peaks showed the typical magnetite pattern for samples synthesized by using ammonia as the alkali precipitant. In addition, the results show that higher reaction temperatures lead to the production of smaller size black particles with lower oxidation level, better crystallization, and higher saturation magnetization. The optimal results were obtained when the ammonia was used as an alkali precipitant and the reaction temperature was set to 80 °C under N<sub>2</sub> atmosphere. Furthermore, particles made under the air condition at 80 °C using 25% ammonia showed satisfactory dimensional and magnetic properties. The simple reaction condition used in this study could be applicable for large scale synthesis of stable SPIONs.

**Keywords:** Co-precipitation, Iron oxide particles, Superparamagnetism

### INTRODUCTION

Chemical reactions between iron and oxygen may result in ~16 distinct species of iron oxide compounds including oxides, hydroxides, and oxyhydroxides, depending on different reaction conditions [1,2].

Magnetite (Fe<sub>3</sub>O<sub>4</sub>), maghemite (γ-Fe<sub>2</sub>O<sub>3</sub>), and hematite (α-Fe<sub>2</sub>O<sub>3</sub>) are three common types of iron oxides among which magnetite is the most used form of iron oxide in biomedical applications due to its higher saturation magnetization, nontoxicity, biocompatibility, ease for biomolecule tagging, and simple collection from the

environment. Therefore, such unique properties have made the magnetite the only approved nanoparticle to be used in clinical studies [2-4].

Magnetite nanoparticles are also known as one of the most frequently-used ferrites (with a general formula of AB<sub>2</sub>O<sub>4</sub>) that form the common magnetic solid component of many magnetic fluids [3,5]. The important characteristics of magnetite nanoparticles (*e.g.*, uniform size distribution, good crystal structure, solubility, stable magnetic properties, and low toxicity) are highly dependent to the size, shape, and structure of the particles produced during the synthesis process that require strict controls over the production reaction methodologies [5].

As of now, a variety of methods including chemical,

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physical and biological approaches have been identified for the synthesis of iron oxide magnetic nanoparticles with a special focus on magnetite production. Among these methodologies, the chemical-based synthesis approach has been used in more than 90% of synthesis methods due to its ease of implementation, repeatability, tractability, short process time, and high efficiency [2]. Co-precipitation is the most common method for the magnetite IONs synthesis, in which the precipitation of magnetic nanoparticles occurs by mixing certain stoichiometric ratios of aqueous solutions of bivalent (ferrous) and trivalent (ferric) iron salts with an alkali solution under a given experimental atmosphere at a particular temperature [6]. In this method, the synthesis reaction occurs at atmospheric pressure and low temperatures (<100 °C) and it does not produce or use any toxic impurities or solvents [1]. Moreover, cost-effectiveness, repeatability and scalability of this method makes it a versatile and convenient method, not only for laboratory purposes but also for industrial use [7]. Although this method is the most suitable and convenient approach for mass production of magnetite nanoparticles, some issues may affect its performance. These issues including formation of unwanted nonmagnetic compounds and lack of uniformity in size and shape of iron oxide particles synthesized through co-precipitation can originate from the effect of various reaction conditions and the existence of different unknown pathways and intermediates involved in the formation of magnetite nanoparticles [8].

The effects of different parameters including iron types used in co-precipitation [5], ferrous to ferric ratio [3,9,10], reaction temperature, initial pH of the iron solutions [3,11], type of the alkali solution [12], rate and sequence of mixing iron salt solutions with alkali agent [1,8,12], working atmosphere [8], final pH of the reaction [1,3,12], stirring speed and stirring method [4,5,8], final temperature and duration of the reaction [10,12] on the particle type, crystal structure, size, magnetic properties, and stability of particles resulting from co-precipitation have been previously studied. However, despite numerous applications of the co-precipitation method in the production of iron oxide nanoparticles and the extensive research conducted in recent years on this method, the exact mechanism of the co-precipitation process and the effect of various factors influencing the characteristics of the particles produced in

the reaction are yet to be understood.

In this study, the effect of working atmosphere (N<sub>2</sub> or air), final reaction temperature (25 or 80 °C), and type of alkali solution (ammonia 25% or 1M sodium hydroxide) on the properties of resulted particles are studied using a simple optimum condition for the synthesis of water-soluble iron oxide magnetite nanoparticles.

## MATERIALS AND METHODS

The chemicals FeCl<sub>3</sub>·6H<sub>2</sub>O, FeSO<sub>4</sub>·7H<sub>2</sub>O, NaOH, ammonia, and citric acid were purchased from Merck Co, (USA). Using the eight experimental treatments shown in Fig. 1, the present study examined the effects of reaction atmosphere, type of the alkali precipitant, and final reaction temperature on the production of iron oxide magnetic nanoparticles. Other constant parameters during the experiments were selected based on the best level of each variable reported in the previously published articles. Table 1 provides a summary of different studied parameters affecting the co-precipitation reaction and the selected level.

The synthesis reactions were performed in two-neck flasks with a capacity of 50 ml and a final reaction volume of 30 ml. The required solutions for the synthesis reaction including ferrous iron salt solution (245 µl of 36% hydrochloric acid and 1.65 g of FeSO<sub>4</sub>·7H<sub>2</sub>O added to 1.5 ml of distilled water, with a final volume of 3 ml), ferric iron salt solution (2.43 g of FeCl<sub>3</sub>·6H<sub>2</sub>O dissolved in water with a final volume of 2 ml), and 1 M NaOH (1 g of NaOH salt dissolved in 25 ml of distilled water) were freshly prepared just before the synthesis reaction. The reverse co-precipitation was conducted in all the treatments by suddenly adding the separately prepared iron salt solutions to the stirring alkaline solution. To this end, 25 ml of alkaline solution (ammonia 25% or 1 M NaOH) was charged in the reactor flask. The desired reaction temperature was adjusted to the required temperature (25 or 80 °C) while the solution was stirred under a steady flow of N<sub>2</sub> or atmospheric air. The ferrous and ferric iron salt solutions were simultaneously added to the alkaline solution in the reactor, and the solution was then mixed by a magnetic mixer at a speed of 900 RPM. After adding the iron solutions to the alkaline medium, the reaction proceeded for 30 min under 900 RPM magnetic stirring.

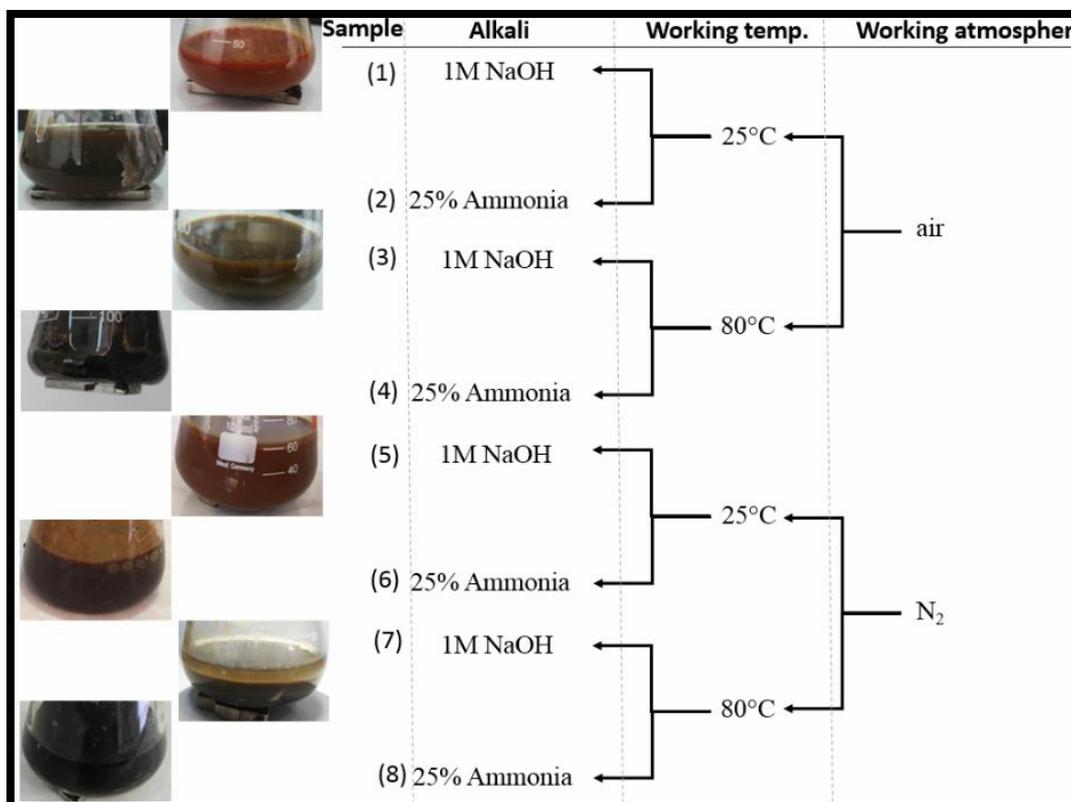


Fig. 1. Different parameters investigating optimization of the synthesis conditions of iron oxide nanoparticles.

Thereafter, iron oxide particles were separated with a permanent magnet and the resulting supernatant was removed.

The remaining precipitate was washed 3 times with 25 ml of ethanol (96% aqueous solution). For each washing step, the container was placed on a magnetic mixer at 900 RPM and 80 °C for 10 min. The magnetic particles were then separated by placing the reaction container on a permanent magnet and the resulting supernatant was removed and discarded using a pipette. The washing process for non-magnetic products was accomplished by centrifugation.

After washing, 65 ml of 0.02 g ml<sup>-1</sup> citric acid solution was added to the precipitate and the reaction pH was set to 5.4 by adding 25% ammonia. The temperature was raised to 80 °C under continuous stirring at 900 RPM for 90 min. At the end of the 90-minute period, a small amount of precipitate was collected and discarded. The pH of the

obtained suspensions was adjusted to 7 by adding 25% ammonia, and the resulting suspensions were stored at 4 °C.

The obtained particles were characterized through the investigation of suspension appearance, ultraviolet-visible (UV-Vis) spectrum, dynamic light scattering (DLS), surface electron microscopy (SEM), vibrating sample magnetization (VSM), and X-Ray diffraction (XRD). The UV-Vis spectra were recorded using Rayleigh instrument, Model UV2601 (Beijing Rayleigh Analytical Instrument Corporation, China) which is a double beam spectrometer and is capable of recording spectra in the range of 190 nm to 1100 nm with a resolution of 0.3 nm. The DLS measurements were performed at 25 °C using a Zetasizer Nano ZS instrument (Malvern Instruments Ltd., Malvern, Worcestershire, UK) equipped with a helium-neon laser and a scattering angle of 173°. The measurements were done by adding 5 µl of sample to 995 µl of water. The magnetic properties were measured at room temperature using

**Table 1.** Summary of the Studied and Selected Levels of Parameters Influencing the Co-precipitation Reaction

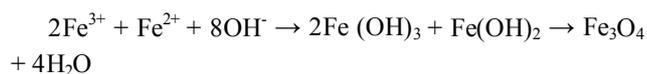
Variable	Studied levels in publications	Selected level	Ref.
Ferrous salt (Fe(II))	FeCl <sub>2</sub> .4H <sub>2</sub> O, FeSO <sub>4</sub> .7H <sub>2</sub> O	FeSO <sub>4</sub> .7H <sub>2</sub> O	[5]
Ferric salt (Fe(III))	FeCl <sub>3</sub> .6H <sub>2</sub> O	FeCl <sub>3</sub> .6H <sub>2</sub> O	[5]
Fe(II)/Fe(III) ratio	1:2, 2:3, 3:1	2:3	[3]
Initial temperature of iron salt solutions	25 °C, 30 °C, 60 °C	25 °C	[3]
Initial pH of iron salt solutions	0.7, 1.5, 3, 4.7, 5.7, 6.7	Initial pH was adjusted to 1.5	[3,6]
Working atmosphere	N <sub>2</sub> , AIR	Was investigated as a variable	[9]
Alkali solution	Ammonia solution 25%, NaOH < 1 M, NaOH 1 M, NaOH 2 M, KOH 0.9 M, 4NaOH(C <sub>2</sub> H <sub>5</sub> ) 0.9 M	25% Ammonia and 1 M sodium hydroxide solutions were investigated	[9,12]
Iron solutions addition rate	FAST(suddenly) or SLOW(dropwise)	FAST (suddenly) addition	[1,8,12]
Final pH	5, 10, 10.34, 12, 12.6	Based on the used alkali solution PH was 10 or 12	[1,3,6, 10,12]
Stirring method	Mechanical or magnetic	Magnetic	[4]
Stirring time	5 min, 10 min, 30 min, 60 min	5 min	[11,12]
Final reaction temperature	5 °C, 25 °C, 47 °C, 80 °C, 90 °C	25 and 80 °C were investigated	[10, 2]
Precipitate collection method	Centrifugation or permanent magnet	Permanent magnet and centrifugation	[4]
Precipitate washing method	3 times with 25 °C distilled water, 3 times with ethanol and then with distilled water, 3 times with 60 °C distilled water, 3 times with 1 M nitric acid and then 3 times with distilled water	3 times with ethanol and then with distilled water	[1,3, 6,10,12]
Functionalization	Oleic acid or citric acid	Citric acid	[3,6]
Precipitate storage	Liquid or powder	Liquid in 4 °C	[3,6]

Princeton Applied Research VSM, Model No. 155 (Ametek Inc., USA). The X-ray diffraction patterns were measured at room temperature using a RINT/DMAX 2200 H/Pc (Rigaku, Japan). The XRD peaks were recorded at 2-theta.

## RESULTS AND DISCUSSION

Parameter combinations used to optimize the synthesis of magnetic iron oxide nanoparticles are presented in Fig. 1. In this experiment, the effects of working atmosphere, working temperature and alkali type were investigated simultaneously.

Based on the following chemical reaction that takes place during co-precipitation of magnetite, the ideal ratio of  $\text{Fe}^{2+}/\text{Fe}^{3+}$  is 1/2.



Due to the probable oxidation of  $\text{Fe}^{2+}$  to  $\text{Fe}^{3+}$  and performance of some experiments under air condition, an initial molar ratio of 2/3 for  $\text{Fe}^{2+}/\text{Fe}^{3+}$  was used in all the experiments. Furthermore, in order to reduce the ferrous oxidation process before initiation of the precipitation reaction, the initial pH of ferrous solution was adjusted to 1 using 2 M HCl [3]. Reverse co-precipitation reaction was initiated with the rapid addition of iron solutions to stirring alkali precipitant and reactions proceeded for 30 min under the defined conditions.

The results of 8 different conditions examined for the synthesis of iron oxide nanoparticles using the co-precipitation method showed that in 4 conditions, where 1 M NaOH was used as basic precipitant, the resulting products were unstable suspensions with light orange (samples 1 and 5) or red-brown colors (samples 3 and 7), suggesting the formation of non-magnetite impurities (Fig. 2). The products obtained from these 4 synthesis conditions did not show any observable magnetic behavior under the external magnetic field induced by a permanent magnet [4,13].

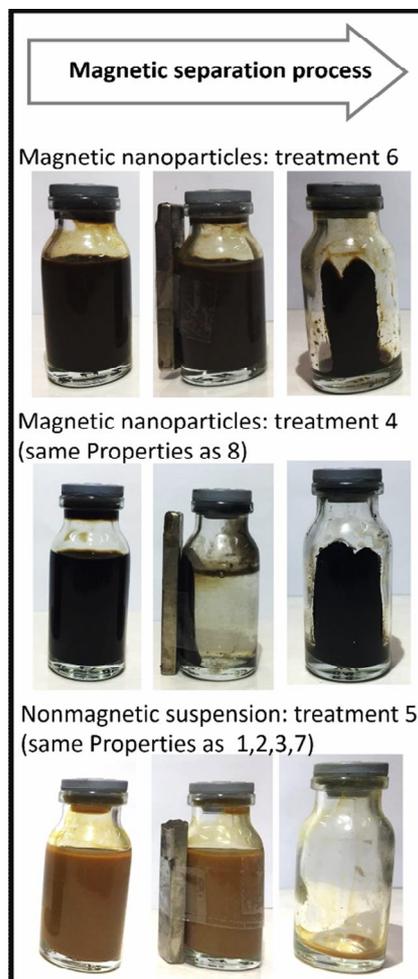
The formation of nonmagnetic particles in the presence of NaOH as the basic precipitant was previously reported by Gnanaprakash *et al.* According to this article, unlike 25% of ammonia as a weaker basic agent, when 1 M NaOH was

used in the co-precipitation reaction, the XRD spectrum showed the additional peaks, indicating the presence of nonmagnetic goethite [3]. Another study comparing five different concentrations of NaOH solution as a precipitating agent showed that the lowest concentration of this solution that leads to a pH of about 10 (that is almost the same as the pH created by 25% ammonia) maximizes the magnetite production and minimizes the non-magnetic impurities. In addition, it was proposed that higher concentrations of the basic agent prevent the formation of magnetite due to the disrupted stoichiometric ratios of ferrous and ferric iron salts [12]. Another explanation for the effect of 1 M NaOH was that the conversion of ferrihydrite to goethite is accelerated at extreme low and high pH levels that could be the reason for the production of non-magnetic particles with 1 M NaOH [14].

The results of the present study revealed that in the reaction conditions designed in this experiment, the 1 M NaOH used as a strong basic precipitant can lead to nonmagnetic products. Therefore, further analysis of these samples was avoided due to unfavorable results.

From the 4 samples synthesized *via* 25% ammonia as the alkali precipitant, samples 2 and 6 which were synthesized at 25 °C under air (sample 2) or  $\text{N}_2$  (sample 6) atmosphere, led to the production of dark brown suspensions, whereas sample 2 did not show any magnetic behavior under the external magnetic field. However, a large portion of the particles in sample 6 was collected using an external magnetic field.

On the other hand, at reaction temperature 80 °C, the color of the suspensions formed under either air (sample 4) or  $\text{N}_2$  (sample 8) working atmosphere turned into black, suggesting the formation of iron oxide consisting of mainly magnetite. Particles prepared under these conditions showed excellent magnetic properties with black sediment and a relatively clear supernatant was detectable inside the reaction flask under an external magnetic field. All particles resulting from condition 2 and part of the particles resulting from condition 6 were precipitated after almost an hour when stored at room temperature without applying an external magnetic field. The stability analysis of the synthesized particles in samples 4 and 8 showed visible magnetic properties in the presence of an external permanent magnet and their stability maintained up to

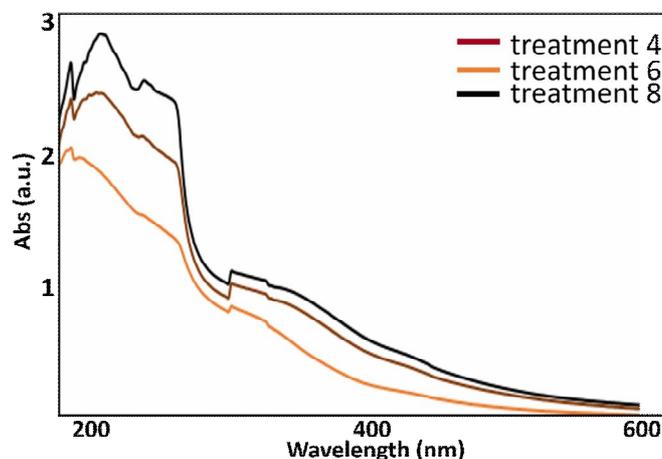


**Fig. 2.** Comparison of the appearance and magnetic properties of particles prepared through co-precipitation under different conditions; First row: magnetic nanoparticles synthesized using condition 6 (25% ammonia as the alkali precipitant, 25 °C reaction temperature, N<sub>2</sub> atmosphere). B and C Photographs were taken 2 min after placement of the magnet, Middle row: magnetic nanoparticles resulted from condition 8 (25% ammonia as the alkali precipitant, 80 °C reaction temperature, N<sub>2</sub> atmosphere) which is similar to condition 4 (25% ammonia as the alkali precipitant, 80 °C reaction temperature, air atmosphere). Last row: nonmagnetic suspension resulted from treatment 5 (1 M NaOH as the alkali precipitant, 25 °C reaction temperature, N<sub>2</sub> atmosphere) which shows properties similar to samples 1, 2, 3 and 7.

6 months. Low levels of sedimentation over time was observed. When we compared the results obtained from samples 2 and 6 synthesized at 25 °C with those from samples 4 and 8 synthesized at 80 °C, it is clearly evident that increasing the reaction temperature has a positive effect on the magnetic properties of obtained iron oxide particles.

Similar results on the effect of higher reaction temperature on the magnetic behavior of synthesized iron oxide nanoparticles were previously observed by Roth *et al.* [10].

After examining the suspensions of all the samples, samples 4, 6 and 8 which showed normal magnetite appearance (dark color) and good magnetic behavior were



**Fig. 3.** UV-Vis absorption spectra of iron oxide nanoparticles synthesized in different reaction conditions. Sample 6 spectrum showed the lowest absorbance intensity and blue shift to smaller wavelengths which can originate from more oxidation occurring at 25 °C reaction temperature.

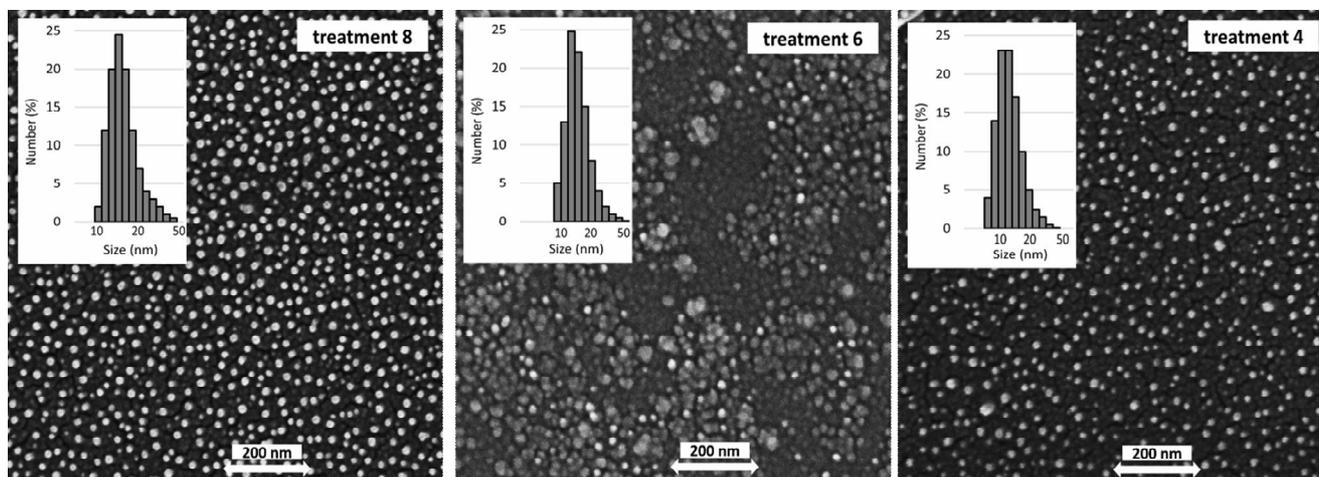
selected for additional instrumental characterization.

Figure 3 shows the UV-Vis absorption spectrum of samples prepared from conditions 4, 6 and 8. The spectra obtained for samples 4 and 8 show a considerable similarity to the spectrum previously reported for maghemite iron oxide particles. The samples exhibited a broad absorption in the visible region with a tail extending to more than 560 nm. No absorption was observed beyond 700 nm which is consistent with previously reported spectra for magnetic iron oxide compounds [16]. It also revealed the difference between the resulting patterns with the hematite spectrum [15]. The absorption spectrum resulting from sample 6 had a slightly different structure than the other two samples. UV-Vis spectrum obtained from this sample showed a blue shift to smaller wavelengths, which can be due to the probable changes in the particles phase and size [17]. The absorption intensity values of the three samples were compared and sample 8 was found to have the highest value followed by sample 4 and sample 6.

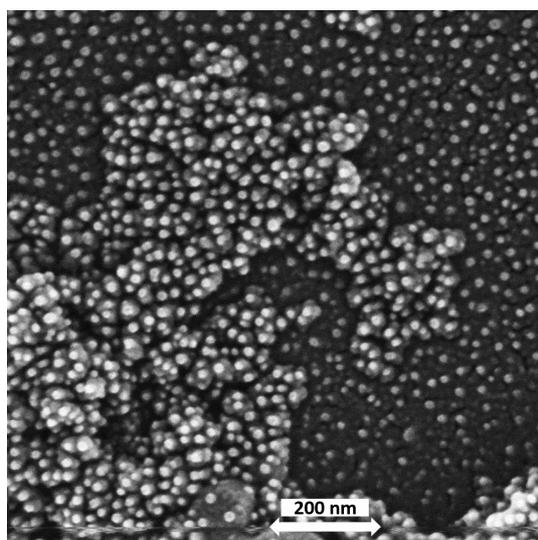
It has been reported that lower stability and higher oxidation degree of iron oxide particles can increase the diffuse reflectance and cause lower absorption in UV-Vis spectrum [16]. It is clearly observed that sample 8 which is synthesized at 80 °C under N<sub>2</sub> atmosphere has a higher

absorbance intensity which can show the lower oxidation degree. In contrast, lower reaction temperature used in sample 6 promoted the iron oxide oxidation and caused the lowest absorption values. Comparison of the UV-Vis spectrums of sample 4 (synthesized under air condition at 80 °C) and sample 6 (synthesized under inert atmosphere at 25 °C) indicates that the degree of oxidation at 25 °C in sample 6 is even higher than that of sample 4 which is synthesized under air condition.

SEM image and particle size distribution of the magnetic iron oxide nanoparticles prepared from conditions 4, 6 and 8 are shown in Figs. 4 and 5. As determined by dynamic light scattering (DLS), it must be outlined that samples 4 and 8 exhibited a hydrodynamic diameter with a median size of about 30 nm, which is the critical size for superparamagnetic behavior [9,10,18]. The average hydrodynamic diameter measured by DLS for the samples prepared from conditions 4, 6 and 8 are 24.9, 37.4 and 28 nm, respectively. SEM images showed that samples 4 and 8 consist of single particles smaller than 20 nm with a nearly spherical shape. For sample 6, aggregation led to the formation of larger particles that could be visualized in SEM images. The structure of precipitated particles from sample 6 is shown in Fig. 4. It can be observed that for sample 6 synthesized at 25 °C, the particle size is larger than



**Fig. 4.** SEM images and Hydrodynamic particle size distribution of magnetite nanoparticles prepared at conditions 4, 6 and 8.

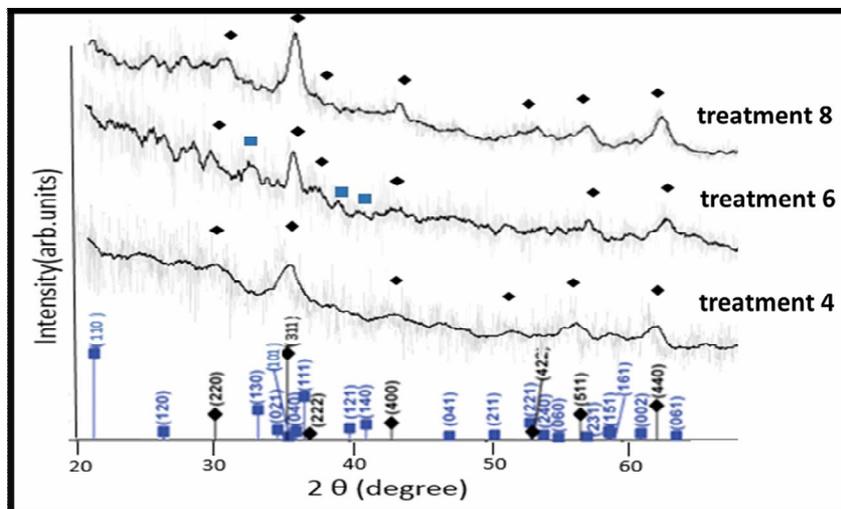


**Fig. 5.** SEM images of precipitated particles from sample 6.

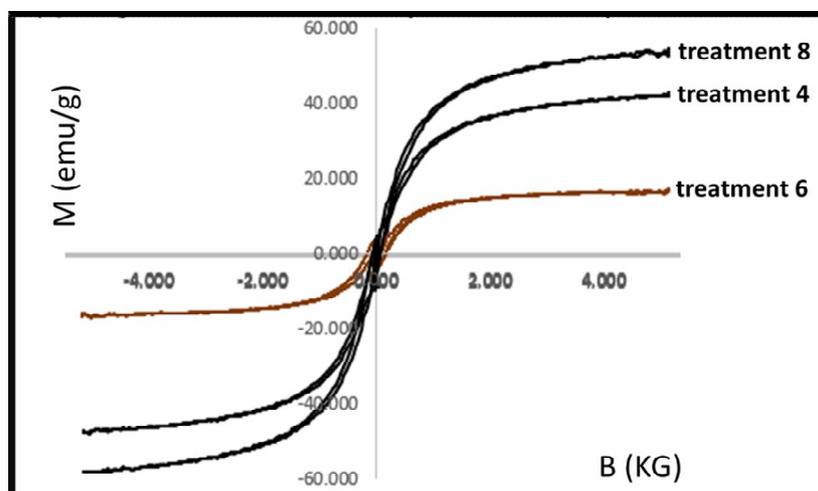
the particles synthesized at 80 °C. By combining the above mentioned results with the data obtained from UV-Vis spectra, it can be concluded that reduction of the reaction temperature promotes the oxidation process of iron oxide nanoparticles and consequently increases the particles size. It is noteworthy to mention that the smallest size of particles was obtained from the reaction condition 4. It showed that in higher reaction temperatures, magnetic particles

may appear with smaller diameters compared to lower temperatures.

The crystal structure of iron oxide nanoparticles prepared under three selected conditions was obtained through X-ray diffraction. Figure 6 shows the XRD patterns of the particulate samples synthesized at various conditions as well as standard patterns for magnetite (JCPDS 19-0629) and goethite (JCPDS 29-0713). In all three spectra, the



**Fig. 6.** XRD patterns for samples synthesized under various conditions. (a) sample 4, (b) sample 6 and (c) sample 8. The reference pattern was obtained from [1]. Blue Squares show the goethite (JCPDS 29-0713) and black diamonds show the magnetite (JCPDS 19-0629) pattern.



**Fig. 7.** Magnetization curves at room temperature for samples (a) sample 8, (b) sample 4 and (c) sample 6.

presence of magnetite prominent peaks at 35.5 (3 1 1) and 62.9 (4 4 0) are clearly observable[3]. The XRD patterns confirm the cubic crystal structure with the characteristic peaks at 30.2, 35.5, 43.3, 53.7, 57.2 and 62.9 corresponding to (2 2 0), (3 1 1), (4 0 0), (4 2 2), (5 1 1) and (4 4 0) crystal planes which may be indexed to either magnetite or maghemite [9]. The X-ray diffraction patterns of samples

4 and 8, synthesized under air and N<sub>2</sub> atmospheres at 80 °C, were completely matched the magnetite spectrum (JCPDS 19-0629). In sample 8, all the magnetite characteristic peaks were sharp and high in intensity while in patterns obtained from sample 4 magnetite prominent peaks were broader that can be due to the lower production yield obtained from this synthesis condition. The diffraction peaks for both samples

4 and 8 can be indexed to the cubic phase of magnetite without any secondary phase. However, the XRD pattern of sample 6 prepared under N<sub>2</sub> atmosphere at 25 °C demonstrates the presence of both goethite and magnetite peaks revealing that, in addition to the cubic phase of magnetite, goethite with an orthorhombic phase (JCPDS file No. 29-0713) is also found [8,16]. These results demonstrate the dependency of oxidation and crystallization of magnetite to the reaction temperature.

Magnetic properties of samples resulted from 3 synthesis conditions were characterized by VSM at room temperature with the maximum field applied reaching 5 KG. Figure 7 shows the typical magnetization curves and hysteresis loops for iron oxide nanoparticles that have been synthesized under 3 conditions. The results indicate that the saturation magnetization (M<sub>s</sub>) values obtained from samples 4, 6 and 8 were 40, 12 and 52 emu g<sup>-1</sup>, respectively. The saturation magnetization for all three samples is lower than that for the bulk state Fe<sub>3</sub>O<sub>4</sub> (~90 emu g<sup>-1</sup>), that could be attributed to the decrease in the particles size, crystal and shape anisotropy. These results are consistent with the earlier reports that showed a 20-50% decrease in saturation magnetization between bulk state and nanometer scales ferromagnetic materials [19,20]. Furthermore, the higher M<sub>s</sub> value observed in sample 8 (compared to sample 4) can be a result of particle size and its direct impact on magnetic properties. The results also showed that the saturation magnetization values decreased from 52 to about 12 emu g<sup>-1</sup>, as the reaction temperature was decreased from 80 °C to 25 °C under N<sub>2</sub> atmosphere. According the XRD analysis, it is evident that there were goethite impurities in samples synthesized at 25 °C and the reduction in the saturation magnetization values is expected to be due to the presence of goethite which is known to be an antiferromagnetic compound [3]. In the magnetization curves obtained from samples 4 and 8, residual magnetization and coercivity are almost zero at room temperature. This result may indicate that the obtained black precipitates from two aforementioned conditions properly reflect the magnetic behavior of magnetite nanoparticles, as a soft superparamagnetic substance. On the other hand, for sample 6, M<sub>s</sub> value reached 12 emu g<sup>-1</sup> which is considerably lower than that for the two other samples.

Combining the dark brown color (non-black) of the

precipitate resulting from sample 6 with the different absorption spectrums of the sample in the UV-Vis range and the results obtained from XRD pattern which shows broad and ambiguous peaks, the formation of non or poorly magnetic iron oxide impurities under this synthesis condition are confirmed.

## CONCLUSIONS

In this study, we determined optimum synthesis conditions for superparamagnetic iron oxide nanoparticles. The effect of various synthesis parameters (working atmosphere, final reaction temperature, and types of basic precipitant) on the type, size, and magnetic properties of each synthesized nanoparticle was studied by various analysis techniques. Utilizing 25% ammonia as the alkali precipitant gave better results and led to the production of dark brown and black particles with an acceptable magnetic behavior under the influence of an external magnetic field. In addition, the ideal temperature for obtaining the best particles with regard to size, morphology, and magnetic character was at 80 °C in the N<sub>2</sub> atmospheric condition. Therefore, basic precipitant and reaction temperature are critical parameters in controlling the formation of magnetic nanoparticles under either oxidative or inert atmospheres. These optimized reaction conditions can serve as a simple and low-cost operating condition for large-scale production of water-soluble iron oxide magnetic nanoparticles and can have potential applications in the biomedical field.

## ACKNOWLEDGMENTS

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## CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

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