Magnetic Hyperthermia with cobalt ferrite nanoparticles: the Influence of Particle Size

S. H. A. ALLehyani[1], R. A. Hassan[1, 2] , A. A Alharbi [1] ,T.Alomayri[1] and H. Alamri[3]

[1]Department of Physics, Faculty of Applied Sciences, Umm Al Qura University, Makkah, Saudi Arabia.

[2]Department of Radiotherapy, National Cancer Institute, Cairo University, Cairo, Egypt

[3]Jamoum University College, Physics Department, Umm ALQura University, Jamoum, Saudi Arabia.

Abstract: Magnetic nanoparticles possess unique properties which can be applied in nanomedicine, they address targets such as cellular therapy, tissue repair, nanobiosensors, drug delivery, magnetic resonance imaging and magnetic fluid hyperthermia. In this work, different sized cobalt ferrite nanoparticls (CFNP) were selectively synthesized with narrow size distribution, by using chemical precipitation methods, to aim for finding the optimum particle size which has high heating efficiency in the applied magnetic field. The obtained powder was calcined at different temperature (600 °C, 800 °C, 900 °C, and 1000 °C). The sample which characterized by Transmission Electron Microscopy (TEM) confirmed the formation of single-phase CFNP in the range 10–115 nm depending on the annealing temperature. Localized magnetic particle hyperthermia treatment using ferrimagnetic nanoparticles continue to be an active area of medical research. So, homemade induction heater was designed. The heater was designed to be capable of generating high frequency, strong alternative magnetic fields (8 $kA \cdot m^{-1}$, 135 kHz). In vitro heating efficiencies in test tube, at a MNPs concentration of 250 mg $CFNP \cdot ml^{-1}$, were measured in the applied field. The temperature increase (ΔT) of the tube content at 60 s was 29.9 °C for MNPs of 18 nm, 26.7 °C for 25 nm, 25 °C for 60 nm and 22.9 °C for MNPs of 95 nm. The smallest nanoparticles (18 nm) exhibiting a high heating efficiency. In conclusion, it was found that the size of the CFNP increased with increasing the calcined temperature at which the synthesis of the nanoparticles was performed. The heating efficiency of the particles was improved with decreasing particle size from 95 nm to 18 nm in the alternating magnetic field.

Keywords: Cobalt ferrite, nanoparticls size, hyperthermia..

I. INTRODUCTION

Biologic and biomedical applications of nanoscale materials in health care have rapidly progressed, nanomaterials have attracted much attention because of their potential for use as efficient drug delivery carriers for diagnostic and therapeutic applications. Nanoparticles offer some attractive possibilities in biomedicine. First, they have controllable sizes ranging from a few nanometers up to tens of nanometers, which places them at dimensions that are smaller than or comparable to those of a human hair 60-120 μm wide, cells 10–100μm, a virus 20–450 nm, a protein 5–50 nm or a gene (2 nm wide and 10–100 nm long). Magnetic nanoparticles of spinel ferrites are of great interest in fundamental science [1]. Magnetic nanoparticles (MNPs) are being of great interest, for a wide range of disciplines, such as magnetic fluids, catalysis, biomedicine, magnetic energy storage [2, 3]. In many electronic and magnetic applications, it is mostly important to fabricate a ceramic material of desirable microstructure, with a high sintered density, a small particle size and a narrow particle size distribution [4]. Uses of MNPs in biotechnology and biomedicine have dramatically increased over the last few of years. They can be grouped into two broader categories, depending on the methodology: *in vitro* and *in vivo* procedures. For *in vitro* applications, the main use is in diagnostic and separation/labeling of biomolecules, such as protein, cell, Deoxyribonucleic Acid (DNA)/Ribonucleic Acid (RNA), microorganism, for *in vivo*, applications can be further split into (i) diagnoses (Magnetic Resonance Imaging (MRI)) and (ii) therapies (drug delivery and hyperthermia) [5].In the diagnoses medical field MNPs are used as contrast agents (CA) to enhance the contrast in MRI. In tumor therapy where they can be selectively introduced into the tumor cells and then their temperature is increased using an oscillating magnetic field; and finally used as site-specific drug delivery agents which involve immobilizing the drug on magnetic materials under the action of external magnetic field. Ferrofluids of nanoparticles were used in the treatment of solid tumors, and in the diagnosis and treatment of diseases [6]. The healing power of heat has been used to cure a variety of different diseases. This heat treating method which called hyperthermia was then recognized as new and promising form of cancer therapy aside from surgery, chemotherapy and irradiation. Magnetic hyperthermia is a method to induce hyperthermia using MNPs. In this approach, MNPs are firstly introduced into the desired tissues and then guided by an external magnetic field. An externally applied oscillating magnetic field induces the hyperthermia [7].The application of magnetic nanoparticles offers

the possibility of a self-limitation of the temperature enhancement by using a magnetic material with suitable Curie temperature, Such magnetic nanoparticles can bind to drugs, proteins, enzymes, antibodies, or nucleotides and can be directed to an organ, tissue, or tumor using an external magnetic field [8,9]. Ferrites are magnetic ceramics of great importance in the production of electronic components, since they reduce energy losses caused by induced currents acting as electric insulators. Their applications range from simple function device, such as small permanent magnets to sophisticated devices for the electro-electronic industry [10]. Ferrites were discovered thousands of years ago. The spinel ferrites are very much important magnetic materials due to their combined electrical and magnetic properties, makes ferrite useful in many technological applications. The basic electrical and magnetic properties of ferrite can be modified so as to suit the desire application [11]. The properties of ferrites have been improved through extensive research. In 1950, ferrites attract worldwide attention because new applications such as microwave devices, electronic media, computer and telephone industry were rapidly expanding [12]. They have potential applications in high-density magnetic recording devices especially those with high coercivity in electronic devices and in medicine. One of the most recent applications studied is the complete decomposition of CO_2. This decomposition has been significantly improved by developing ultra-fine ferrite particles with high surface area as a catalyst [13]. Magnetic nanoparticles being subjected to a magnetic AC field may show remarkable heating effects related to losses during, different processes of magnetization reversal in systems of magnetic nanoparticles. There are various theories which explain the reasons for the heating of the MNPs when subjected to an oscillating electromagnetic field. There exist at least four different mechanisms by which magnetic materials can generate heat in an alternating field, which depend in different manners on the applied magnetic AC field strength and frequency. The Magnetic losses to be utilized for heating arise [14, 15]. If a magnetic sample is placed in a liquid of low viscosity and exposed to an oscillating field, the sample reacts with oscillating or rotating movements, as a whole (because of the torque exerted on the magnetic moment by the external AC magnetic field), towards the field with the moment locked along the crystal axis under the effect of a thermal force against a viscous drag in a suspending medium, in order to achieve the position of lowest energy, which lead to losses in the surrounding liquid [15,16,17]. The physical and chemical properties of spinel nano-particles are greatly affected by the synthesis route. Therefore a large number of research reports are available concerning the preparation techniques. Quality ferrites continued to be prepared having new properties [12, 13, 18]. Among the various methods for producing nanoparticles, precipitation method are highly interesting, have been widely used, for their versatility, due to their straightforward nature and their potential to produce large quantities of the final product, low temperature for preparation, relatively simple and providing good control over particle properties. Realizable particle sizes range in size from nanometers to micrometers [19, 20, 21]. Most studies suggested that the cobalt ferrites ($CoFe_2O_4$) could be promising materials for various applications [22]. $CoFe_2O_4$ nana -particles are of interest because of their unique optical, electronic and magnetic, physical properties such as high Curie temperature, large magneto crystalline anisotropy, large magnetostrictive coefficient, excellent chemical stability. (Metal & alloys unstable under atmospheric conditions); good thermal stability; high electrical resistivity (high frequency devices, memory cores, recording media), and mechanical hardness, also for its catalytic properties. This kind of ferrite is a spinel (cubic spinel structure) In addition to the precise control on the composition and structure of $CoFe_2O_4$ [10, 13, 21, 23, 24, 25].

II. MATERIAL AND METHOD

Cobalt ferrite nanoparticls (CFNP) were selectively synthesized with narrow size distribution, by using chemical precipitation methods, Cobalt nitrate hexahydrate $(Co(NO_3)_2.6H_2O)$, ferric nitrate nonahydrate $(Fe(NO_3)_3.9H_2O)$, was purchased from Sigma-Aldrich Company, and sodium hydroxide (NaOH) was used as the precipitating agents, and deionized water as solvent.

In order to obtain 6 gm weight of $CoFe_2O_4$, an amount of 7.4 g of $Co(NO_3)_2$ was dissolved in 50 ml of distilled H_2O. The solution was mixed and stirred at constant temperature (80^0C) in shaking water bath; using a stirring rate of 120 rpm for 15 minute. An amount of 20.6 g of $Fe(NO_3)_3$ was dissolved in 50 ml of distilled H_2O. The solution was mixed and stirred at constant temperature (80^0C) in shaking water bath; using a stirring rate of 120 rpm for 15 minute. And after that, $Co(NO_3)_2$ solution was mixed with the $Fe(NO_3)_3$ solution at 80^0C in a shaking water bath using a stirring rate of 120 rpm for 30 minute. A 10 g of *NaOH* was dissolved in 1/4 liter of distilled H_2O and then added stepwise to the reaction mixture. When the reaction was completed, precipitate was shown at the bottom of the reaction mixture, and then, 4 or 5 drops of oleic acid solution as a coating agent was mixed

with the reaction mixture at temperatures 80 ^{0}C in a The weight of all samples were made similar (4x 1g), the samples were heated at 600 ^{0}C, 800 ^{0}C, 900 ^{0}C, 1000 ^{0}C respectively for 12 hours. Each of these samples is subdivided into another 4 samples (4x 250 mg) for TEM characterization and hyperthermia application. Transmission electron microscopy (TEM) is the premier tool for understanding the internal microstructure of materials at the nanometer level. It allows one to obtain real-space images of materials with resolutions on the order of a few tenths to a few nanometers, TEM used to analysis cobalt ferrite synthesized by co-precipitation, in order to determine shape and average of particle. The induction heater circuit build and tested in our medical physics laboratory Umm Al-Qura University, it has alternating magnetic field 8 kA·m^{-1}, 135 kHz (Figure 1.A). Suspensions tubes of cobalt ferrite nanoparticles samples in water with thermal insulator material are holding within the coil as figure 1 B, where we put the same amount of cobalt ferrite (250 mg/ml) which calcination at different temperature (600 ^0C -800 ^0C -900 ^0C -1000 ^0C). The hyperthermia done for one minute, and then we measure temperature by digital temperature meter. The ambient temperature was measured before each evaluation.

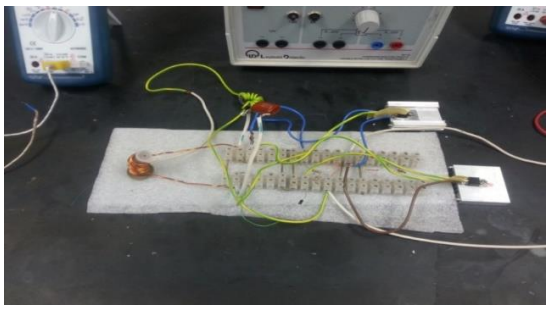


Figure 1.A: Magnetic Hyperthermia Unit

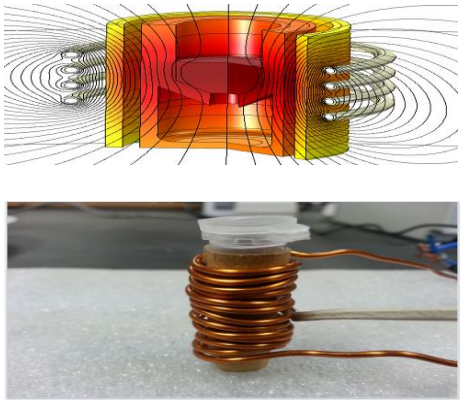


Figure 1.B: Sample in Magnetic Hyperthermia coil

III. RESULT AND DISCUSSION

1- Transmission Electron Microscope Results

TEM which we used to analysis cobalt ferrite synthesized by co-precipitation, in order to determine shape and average size of particle.

TEM images display different morphologies and size of cobalt ferrite nanoparticles, where calcination at various temperature (600, 800, 900, 1000 ^{0}C) respectively for 12 hours.

In Figure 2.A&B the substance involves dispersion of nearly spherical particles with narrow size distribution, which spurring their natural of nanoparticle. The size of particle as shown by TEM is including with mean size distribution of 10 to 25 nm.

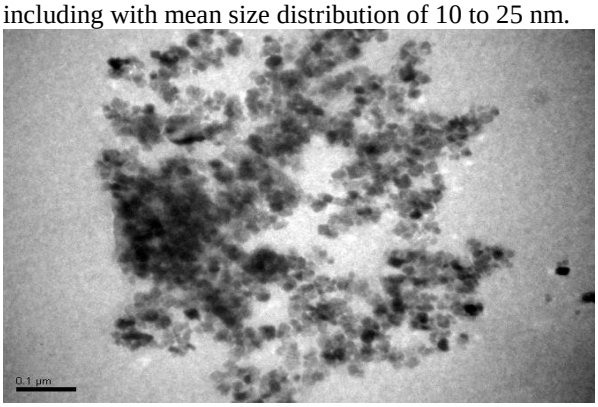


Figure 2.A: TEM micrograph of nanosize $CoFe_2O_4$ particle with an average particle size of 10-25 nm at 600 ^0C

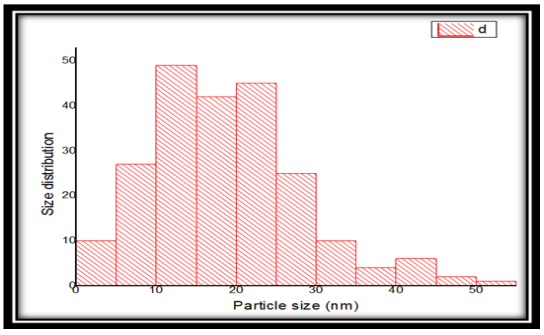


Figure 2.B: Size distribution of nanosize $CoFe_2O_4$ particle with an average particle size of 10-25 nm at 600 ^0C

Figure 3 A&B Shown the existence of large few agglomerates including hundreds of particles. The mean of particle size is about 15-35 nm, as evident in this figure sample involves dispersion of nearly spherical particles.

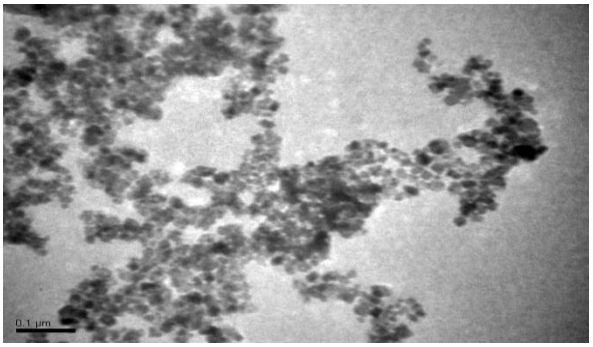


Figure 3.A: TEM micrograph of nanosize $CoFe_2O_4$ particle with an average particle size of 15-35 nm at 800 ^0C .

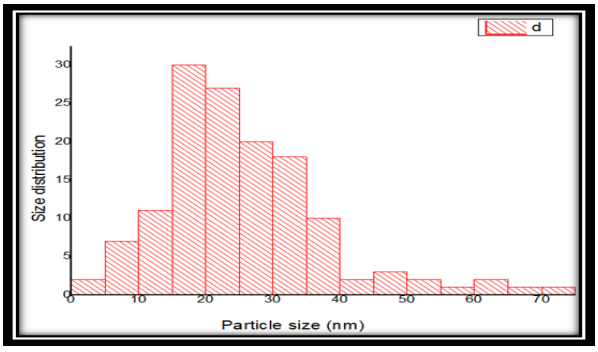


Figure 3.B: Size distribution of nanosize $CoFe_2O_4$ particle with an average particle size of 15-35 nm at 800 ^0C

Figure 4: Shown the existence of large agglomerates including hundreds of particles. The mean of particle size is about 20-100 nm. As evident in this figure sample involves dispersion of nearly spherical particles.

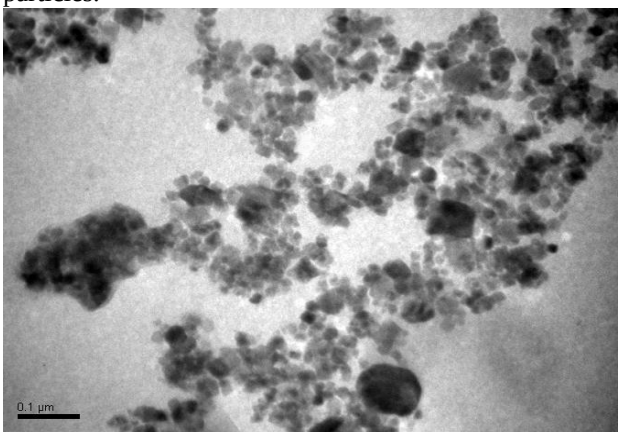


Figure 4.A: TEM micrograph of nanosize $CoFe_2O_4$ particle with an average particle size of 20-100 nm at 900 ^0C

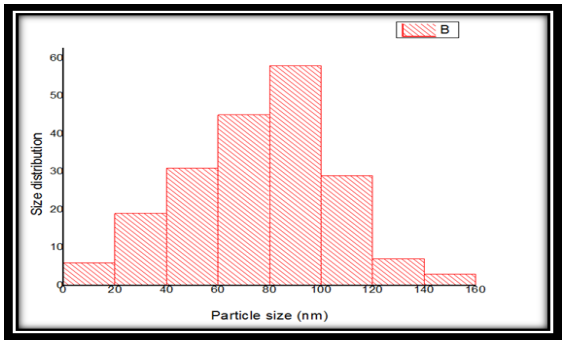


Figure 4.B: Size distribution of nanosize $CoFe_2O_4$ particle with an average particle size of 20-100 nm at 900 ^0C

Figure 5: As evident the existence of largest agglomerates including hundreds of particles. The mean of particle size is about 75-115 nm. There are majority of particles appears spherical in the shape although some elongated particles are also existence.

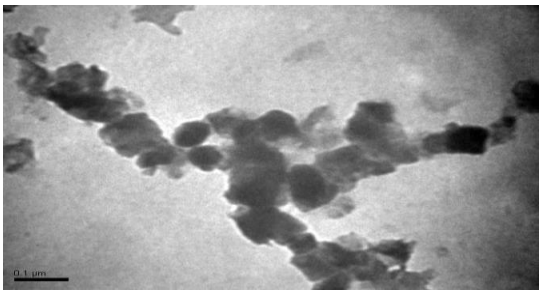


Figure 5.A: TEM micrograph of nano size $CoFe_2O_4$ particle with an average particle size of 75-115 nm at 1000 ^0C

shaking water bath using a stirring rate of 120 rpm, which was kept at least for 12 hours. The precipitate separated from the solution, and it was washed for several times with distilled H_2O and ethyl ether, finally the precipitate was dried at 100 ^{0}C for 12 hours. After this stage, the sample is divided into 4 samples A, B C, D

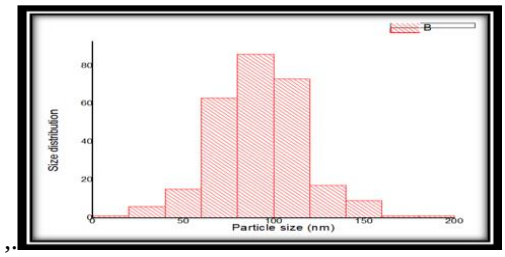


Figure 5.B: size distribution of nanosize $CoFe_2O_4$ particle with an average particle size of 75-115 nm at 1000 ^0C

In general particle size increment with increment temperature of reaction due to ratio of reaction is increment, where these magnetic nanoparticles tend to

agglomeration towards each other because magnetic dipole-dipole interaction between particles. In order to achieve better sample to produce hyperthermia, we made electrical circuit (induction heater) as evident in figure (1A) where we put the same amount of cobalt ferrite which calcination at different temperature (600 ^0C -800 ^0C -900 ^0C -1000 ^0C) and distilled water into four different small tubes. And then we test these small tubes by putting a small tube inside a coil of electrical circuit to measure temperature by digital temperature meter.

2- Hyperthermia Temperature

To recognized Temperature of cobalt ferrite (^0C) as a function of MNP diameter (Table 1) we was measured using hyperthermia system.

Table 1: Induction heat generating with different MNP size

	Average size (nm)	Ambient T (^{0}C)	T1 (^{0}C)	T2 (^{0}C)	T3 (^{0}C)	Mean T (^{0}C)	ΔT (^{0}C)
A	18	21.8	46.3	55.56	53.245	51.7	29.9
B	25	21.9	43.5	52.2	50.025	48.58	26.68
C	60	21.9	42	50.4	48.3	46.9	25
D	95	21.9	40.1	48.12	46.115	44.78	22.88

We can notes from table 1 that the temperature (hyperthermia) changes with different size of $CoFe_2O_4$, where the temperature decreases with increasing the particle size of $CoFe_2O_4$.

IV. CONCLUSION

TEM measurement show that size of the samples that were syntheses by Co- precipitation method are in Nano size .The existence of stabilizer encapsulate atoms (oleic acid),which prevent agglomeration and precipitation and thus get a smaller size. The size of particles increases with increase the preparation temperature. We noted that the size of $CoFe_2O_4$ nanoparticles was 10-25 nm, 15-35 nm, 20-100 and nm, 75-115 nm for the samples prepared at 600 ^oC and 800 ^oC ,900 ^oC , 1000 ^oC respectively.The measured magnetization curve for sample that was syntheses by co-precipitation method display clearly ferrimagnetic behavior & the magnetic property of CFNP depend on the particle size. . The temperature increase (ΔT) of the tube content at 60 s was 29.9 °C for MNPs of 18 nm, 26.7 °C for 25 nm, 25 °C for 60 nm and 22.9 °C for MNPs of 95 nm. The 18 nm exhibiting a high heating efficiency.

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