Synthesize and Characterization of a Novel Cadmium Selenide Nanoparticle with Iron Precursor Applicable in Hyperthermia of Cancer Cells

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Abstract

Many researchers have considered the idea of using heat to shrink cancer cells and treat cancer. However, efforts in recent years have led to creating novel material more practical in clinical application. The main reason for the synthesis and producing these materials is to raise the temperature in the right place so that healthy cells around the cancerous tissue are not harmed. Nowadays, this can be partly achievable with new devices and methods. Also, cadmium selenide (CdSe) nanoparticles with zinc selenide (ZnS) coating for special optical properties were investigated in this work. The CdSe nanoparticles have a wide application in biomedical engineering, including detecting cancer tumors and hyperthermia. There are various methods for synthesizing CdSe nanoparticles, such as precipitation, wet chemistry, mechanical activation, and mechanochemical technique. In this study, we have tried to use an economical method to control Cd ions' toxicity. After fabricating the nanoparticles, vibrating sample magnetometer (VSM), and hyperthermia analyses (HT), X-ray diffraction (XRD), and scanning electron microscopy (SEM) technique were performed to characterize the magnetization, thermal changes versus time, phase, and morphology of the synthesized nanoparticles. The obtained results indicated that the CdSe successfully synthesized using chemical segmentation for biomaterials applications.

Keywords: *Quantum dots, Hyperthermia, Radiation therapy, Magnetic nanoparticles, Chemical segmentation.*

1. INTRODUCTION

After cardiovascular disease and car accidents, cancer has the highest mortality rate among people depending on their genetics, air pollution, and nutrient habits.

Cancer is caused by cells' mutations enormously in the body, either bone or soft tissue [1-4]. The mutated cells proliferate faster than healthy and normal cells that can eliminate the cells' nutrients and oxygen [4-6]. Cancer is the main cause of premature deaths in recent years, and people have paid billions of dollars annually to treat cancer worldwide. There is a need to know about the cancer mechanism to address the cancer tumor for better treatment. The main problem with cancer is acidification and depletion of tissue oxygen [4-9]. Cancer cells are transformed from an advanced human cell to a primary cell. Healthy human cells become cancer cells in the absence of sufficient oxygen and nutrient that can increase with the support of sugars and blood [2-7]. Cancer cells are divided into two groups of malignant (MC) and benign cells (BC), in which the MC are the cell that grow and multiply when there are spontaneous genetic mutations. The size of these cells is maximally 1-2-1 mm^3 [5-9]. Tumors need blood vessels to get the necessary nutrients from the blood and spontaneously develop growth factors in the blood vessel by themselves that related with factors include vascular endothelial growth factor (VEGF), basic fibroblast growth factor (BFGF), and a bunch of proteins. These factors cause the capillary growth within the cancer cell, which is spontaneous and causes blood vessels to grow in a cancer cell as tumor angiogenesis [10-13]. There are several ways to fight cancer cells that are focused on energy - based approaches. Recently, hyperthermia and radiotherapy treatment are two adjunctive methods used to fight cancer cells [14-16]. This study aims to synthesize nanoparticles that can be used in adjunctive therapy with a lower cost, better efficiency, and safe response. For this purpose, quantum dot (QD) nanoparticles that have unique thermal, chemical, and optical properties were used [18-24]. When all three dimensions of a matter are on a nanometer scale, the resulting structure is called a quantum dot [25-32]. These points' excitation is usually caused by ultraviolet (UV) radiation, which results in visible light. The performance of these points is due to the adjustable wavelength that emits the lights. The QD materials are semiconductor nanoparticles with small bond points and a large bandgap. They also exhibit size and composition dependent optical and electronic properties. The size range is between 1.5 and 10.0 nm [33-39]. The optical and chemical evidence suggested that increasing or decreasing one type of atom can alter the bandgap and consequently the intensity of light emitted by these nanoparticles [40-47]. In addition to UV rays, excitation of these points is also done by heat or electric field. The width of these points is about 2-10 nm, equivalent to 10-50 atoms. The application of QDs in various applications has limitations such as particle aggregation, toxicity and lack of bioaccumulation, and inaccessibility. After synthesizing these points, the researchers refined their surface factors by performing complementary operations and the surface treatment process [48-57]. In this regard, CdSe QDs are used in a wide range of specialized fields. One of the widespread applications of these nanoparticles is in biomedical imaging. Rays with wavelengths close to UV rays have the ability to penetrate human tissue. Therefore, by injecting CdSe nanoparticles properly into the damaged tissue, it is possible to image the tissue in those damaged areas. Also, the role of metal coatings on these nanoparticles in amplifying the magnetic field is of particular importance. Coating the QDs with a layer of another semiconductor (shell) with a larger energy band can enhance the luminescence properties of the complex. Zinc sulfide-coated CdSe has recently received much attention due to its adjustable gap band, high conductivity, high chemical stability, and special optical properties [54-58]. As mentioned, this study's ultimate goal is to investigate the optical and thermal properties of synthesized nanoparticles for their use as a destructive agent for cancer cells. In fact, this research is preliminary to the hypothesis that the local release of heat by a mechanism described above can increase the temperature in the cancer cells, however; the hyperthermia at the desired temperature and, to some extent, affect DNA can be sufficiently treated the abnormal cells [23-25, 56-60]. This heat also causes electron transfer and radiation in the QD. The aim of this work is to synthesize and characterize novel CdSe nanoparticles for hyperthermia and photothermal therapy application. The XRD and SEM analysis are used to characterize the phase and morphological properties of the fabricated nanoparticles.

2. MATERIALS AND METHODS

CdSe QDs were synthesized in this study, and their unique radiation release properties and other thermal, optical and morphological characterization were investigated. Required materials for the synthesis of CdSe include cadmium acetate ($CdC_4H_6O_4$, 99.99%, sodium selenite (Na_2O_3Se, 99.99%), ferric chloride ($FeCl_3.6H_2O$, NaOH, TGA (Thioglycolic Acid), ethanol) purchased from Merck company with 98% purity. Equation 1 shows the general physical and chemical reaction of the formation of CdSe nanocrystals as below;

$$CdC_4H_6O_4 + \text{Acid (Thioglycolic acid)} + Na_2O_3Se + FeCl_3 \rightarrow CdSe\,(Fe) + \text{Oxide products} \quad (1)$$

Initially, to prepare solutions of equal molarity from cadmium acetate and sodium selenite in 20 ml of deionized water, according to thermodynamic calculations, 0.046 g and 0.034 g of cadmium acetate and sodium selenite were poured into a beaker with deionized water to reach 20 ml. Then, the solution containing cadmium precursor solution and solution containing selenite precursor solution was prepared. To create 5 wt% of iron nanoparticles, the weighed 0.011 g of hexachloride iron was added to solution number one. Then, 0.5 ml of TGA was added to the above solution. Due to the chemical stability of cadmium selenide (CdSe) nanoparticles at pH = 11.2 with 2 molars of NaOH solution, the solution's pH was also adjusted. After that, the number one solution was mixed with the number two solution and stirred for 35 min in a water bath at 65°C and 1100°C with 650 rpm. At the time of mixing, the solution was measured to determine the transposon pH suitability and found that the environment was suitable for synthesizing stable CdSe nanoparticles. Afterward, the solutions were centrifuged in four faucets and placed in a centrifuge at 6000 rpm for 5 min. The precipitate particles from the centrifuge were washed twice with ethanol and dried after the leaching step. The resulting nanoparticles were transferred to an environment of 4°C to prevent agglomeration. Two samples were synthesized for phase and morphological characterization. In the second sample, the amount of surfactant used to investigate its role in the nanoparticles' size was reduced by 12 ml. The percentage of the magnetic precursor was increased slightly to investigate the magnetization value. The final product was characterized using X-ray diffraction (XRD) analysis, the crystal morphology was determined by scanning electron microscopy (SEM) technique. To obtain the magnetic properties, vibrating-sample magnetometer (VSM), hyperthermia analyses (HT) at room temperature, and an AC field with a frequency of 100 kHz were performed. The HT device with ethanol suspension with 15 mg/ml in the center of the copper coil, which is cooled by water. A variable frequency alternating current (AC) magnetic field is then applied, and the temperature changes of the samples were evaluated by a non-contact fiber optic probe connected to a thermometer (LUXTRON, USA). This device's frequency is adjustable at 100, 200, 300, and 400 Hz, and the maximum power is 300 W. It also has an inductor with a diameter of 5 cm, a height of 4 cm, and a thermistor thermometer. Phase characterization of powder and composite samples was performed by XRD (XRD, Philips X Pert-MPD System). The diffraction pattern was obtained using Cu-Kα lamp with wavelength λ = 1/5406 A in the range of 100<2θ<90°, step 0.02 and time for each step 1 second. To determine the crystallite size of CdSe using the Shearer method to measure the nanoparticles crystal size. For this purpose, three peaks from each phase in the XRD pattern were selected, and peak width was calculated:

$$0.89\lambda/t = B \cos\theta \qquad (2)$$

where L is the grain size in nanometers, λ the wavelength used (for 0.1542 nm copper tube), the K-shaped factor (0.89), B the peak width chosen at half height in radians, and θ the peak angle in degrees. In this method, by drawing Ln B diagrams in terms of Ln (1/Cos θ) and obtaining the width of the source, which is actually Ln (Kλ/L), one can obtain the average value of L crystals. However, given that the values of k, λ are 1.54 and 0.89, respectively. The microstructure, particle distribution, and morphology of powder and composite samples were investigated by scanning electron microscopy (Zaies 00947B). Before examining the specimens, a very thin gold coating was applied. Figure 1 shows the schematic of the preparation of CdSe nanoparticles using a centrifuge and wet chemistry technique. To understand the magnetic nanoparticle's (MNPs) behavior, the amount of heat release from the samples was investigated in an external magnetic field (EMF).

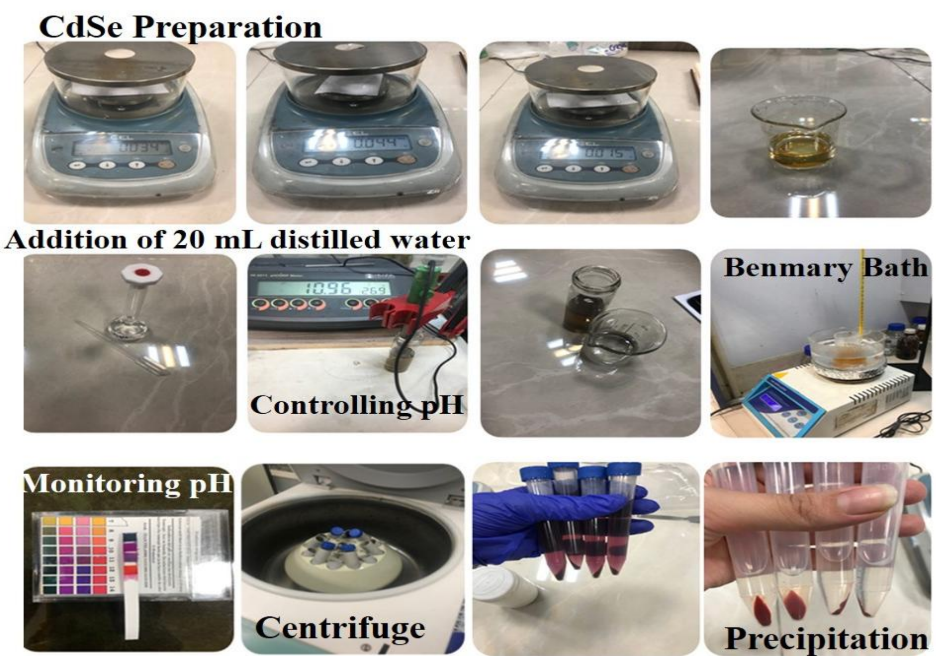

Figure 1. *Schematic preparation of CdSe nanoparticles using centrifuge and wet chemistry technique.*

3. RESULTS AND DISCUSSION

The XRD pattern of the synthesized nanoparticles are shown in Figure 2. The first, second, and third peaks represent the (111), (220), and (311) pages. The XRD pattern shows the synthesized sample successfully doped the iron into the sample.

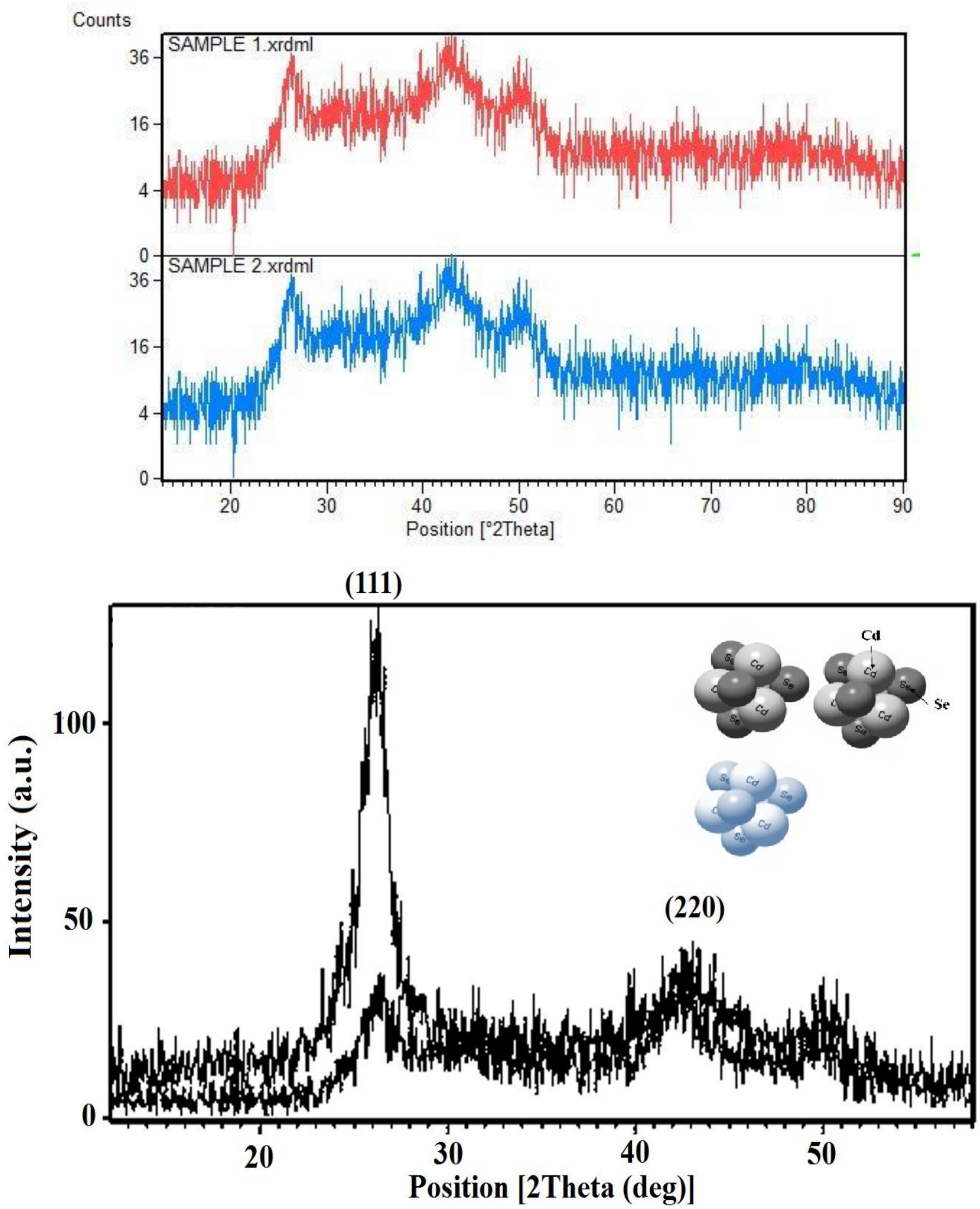

Figure 2. XRD pattern of sample 1 and sample 2 of CdSe with various amount of surfactant.

The intensity of the peaks in sample 1 shows that the nanoparticles have high crystallinity without any cubic phase effect. The peak intensity shows the amorphous nanoparticles due to the decrease in the amount of surfactant compared to the first sample and a change in the precursors' mixing process. It can be concluded that the nanoparticles are in agreement with the constant lattice parameter to the mentioned results [25]. The XRD patterns show that the nanoparticles' average grain size were calculated by the Debye-Scherrer formula and estimated to be about 100-150 nm. Figure 3(a-d) shows the SEM micrograph of the synthesized nanoparticles with semispherical shape and irregular nano-structure.

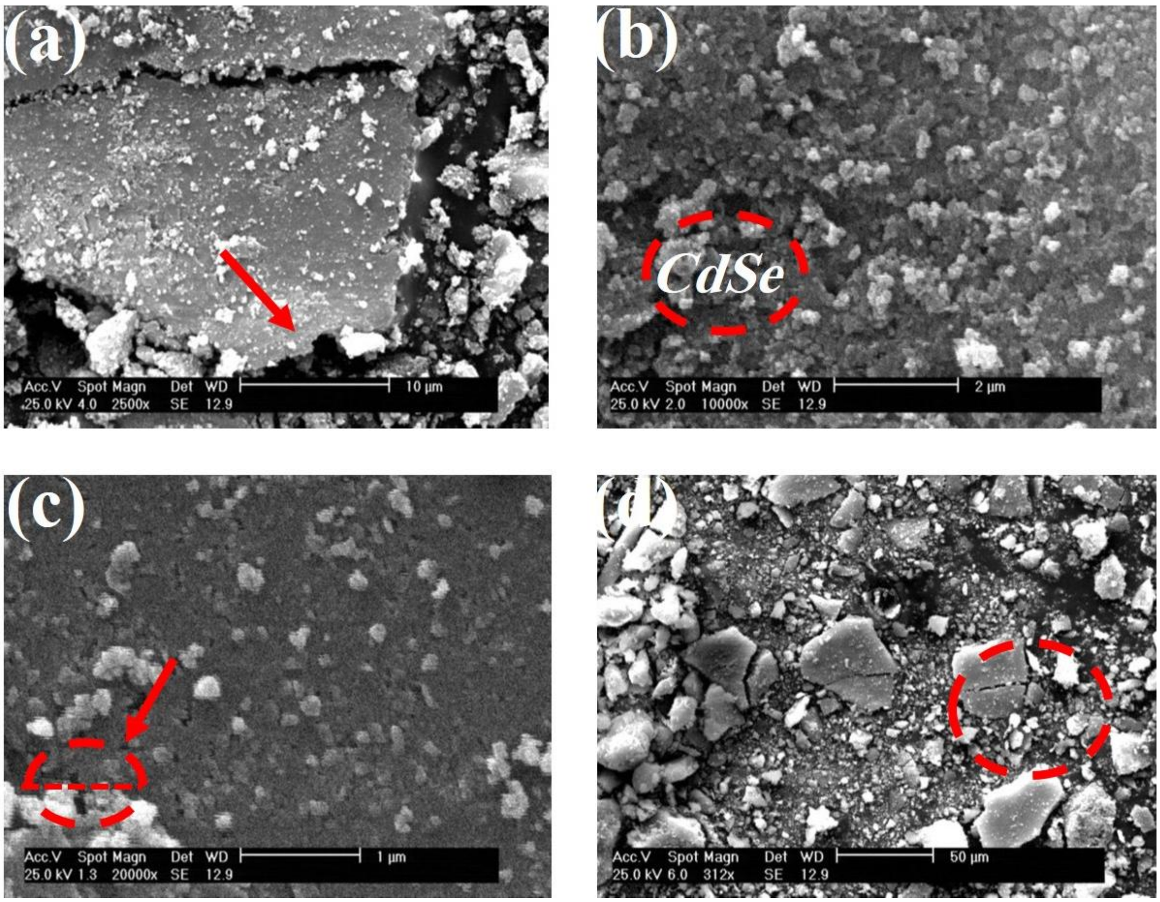

Figure 3. *SEM images of CdSe nanoparticles under different conditions.*

Although, it considers first and second case which shows that sample 2 have higher crystal size. The SEM images show that both samples have agglomeration particles bonded with chemical reactions in the fabrication process. The VSM results measure superparamagnetic response's magnetic properties in various forms of single solid crystal and liquid thin films. From the magnetic phase point of view, the materials are divided into three forms such as ferromagnetic, diamagnetism, and superparamagnetic property. Paramagnetic materials consist of atoms that have a permanent magnetic moment but act separately without any interaction. These materials' magnetization orientation is positive but small and affected by an EMF in an approximate direction. Ferromagnetic materials have spontaneous magnetization in the absence of an EMF. The magnetization obtained in antiferromagnetic materials is eliminated in the absence of the magnetic field, and their magnetic orientation becomes such that the total magnetization becomes zero. In ferromagnetic materials, the magnitude of the magnetic moment in one direction is larger than others, resulting in a net magnetism of zero.

Figure 4 shows the magnetic field diagrams in terms of inductive flux in samples 1 and 2, which is ideal for biomedical engineering applications. Obviously, the CdSe magnetic nanoparticles are solid-phase materials that respond to the magnetic field, which can be single nanoparticles or aggregates of micro and nanoparticles. The composition, size, and route of synthesis of magnetic nanoparticles vary according to their type of application [64-67].

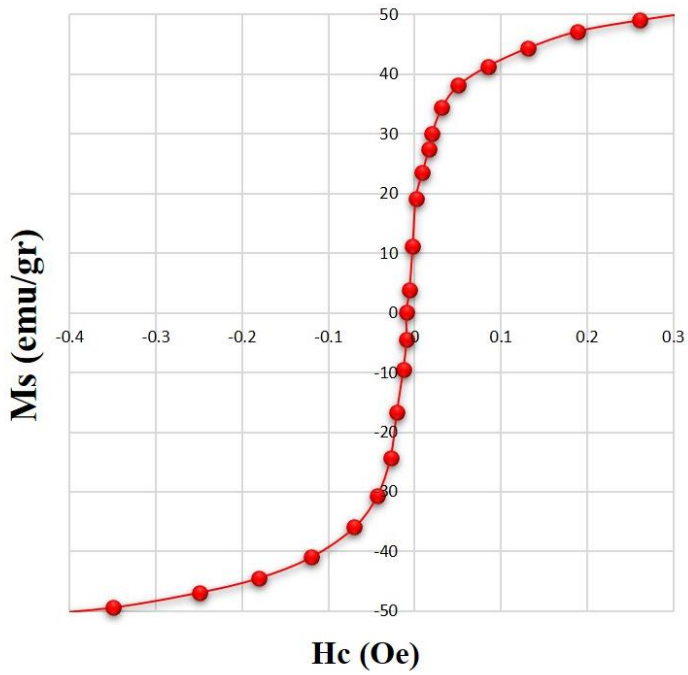

Figure 4. *Magnetization behavior of CdSe nanoparticles synthesized in the first step.*

Still, superparamagnetic, ferromagnetic, and ferromagnetic particles are applicable for a variety of drug applications. These materials are strongly affected by the EMF due to the magnetic moment of the lattice unit and the nanostructure of the domains so that they act as a passive particle in the absence of the EMF. The single-domain and superparamagnetic properties of CdSe magnetic nanoparticles are the sources of many unique properties. The domain walls have a certain width and separate a group of homogeneous spins that operate in a single domain. The formation and stability of domains are associated with energy consumption. As the particle size is reduced to the critical diameter, single-domain particles are formed, which is not suitable for energy formation in these conditions. MNPs have a bright future due to the reduction of magnetic fields and creating superparamagnetic properties. For the use of MNPs in medical applications, those that exhibit superparamagnetic phenomena at room temperature are preferred. Because these particles' magnetic properties are lost in the absence of the EMF that does not persist. The magnetic residues in these materials can also cause them to clot, blocking blood in the veins. Therefore, for such applications, it is necessary to employ superparamagnetic compounds. In general, as mentioned above, the superparamagnetic property is a kind of magnetic property seen in small ferromagnetic or free MNPs. In small nanoparticles, magnetization can be randomly shifted by temperature. In the absence of an EMF, when the time used to measure the nanoparticles', magnetism is much longer than the Nile relaxation time.

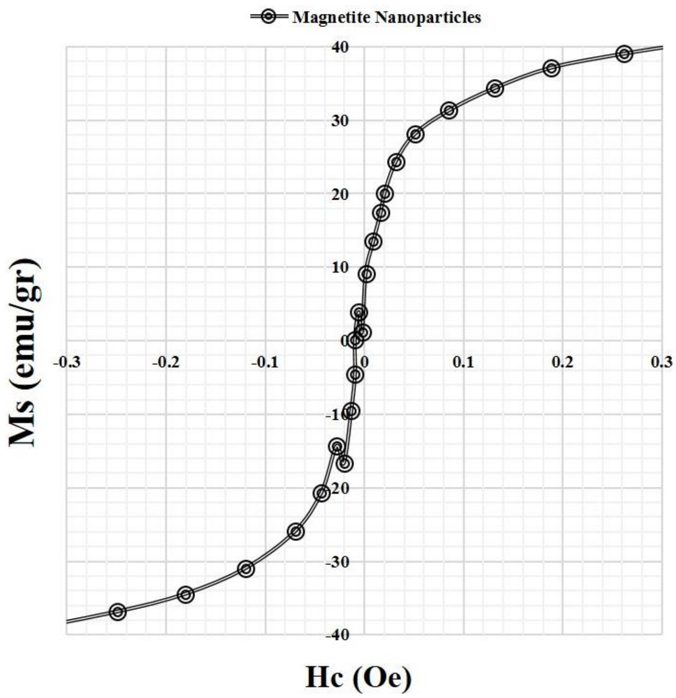

Figure 5. *Magnetization behavior of CdSe nanoparticles synthesized in the second step.*

The MNPs in the EMF act like a paramagnetic substance but with a very large magnetic moment. Therefore, their magnetization can be higher than the paramagnetic. Figure 5 indicates the magnetization behavior of CdSe nanoparticles synthesized in the second step.

Figure 6 shows the samples' temperature changes versus time plotted over time by a non-contact fiber optic probe connected to a thermometer (LUXTRON, USA) with a dot diagram. It is observed that with passing the time, the temperature of all samples increases. One of the unique features of the synthesized CdSe nanoparticles is the production of heat under alternating current (AC) magnetic fields by amplifying MNPs in synthetic material structures. The heat generated can be overly tolerable for cancer cells and cause them to die over time. According to the diagrams, sample number one has more favorable conditions compared to sample 2. As the slope of the hyperthermia term of sample 1 moves slower than sample 2, which contains a higher percentage of iron oxide. As mentioned above, hyperthermia means that the cancer tissue's temperature increases by 5°C to 6°C [38-44].

One can say that these spots are directly in the cancerous tissue, and the radiation released from them directly affects the cancer cells. Those nanoparticles can be used in radiation therapy that reach the target tissue by crossing other tissues and are supposed to lose some of their energy after passing the time [27, 45-53]. Therefore, it is desirable to calculate the maximum amount of iron because increasing the iron content decreases the nanoparticles' size and increases the bandgap size. Consequently, it reduces the wavelength of the light emitted and increases its energy, as shown in Figure 7.

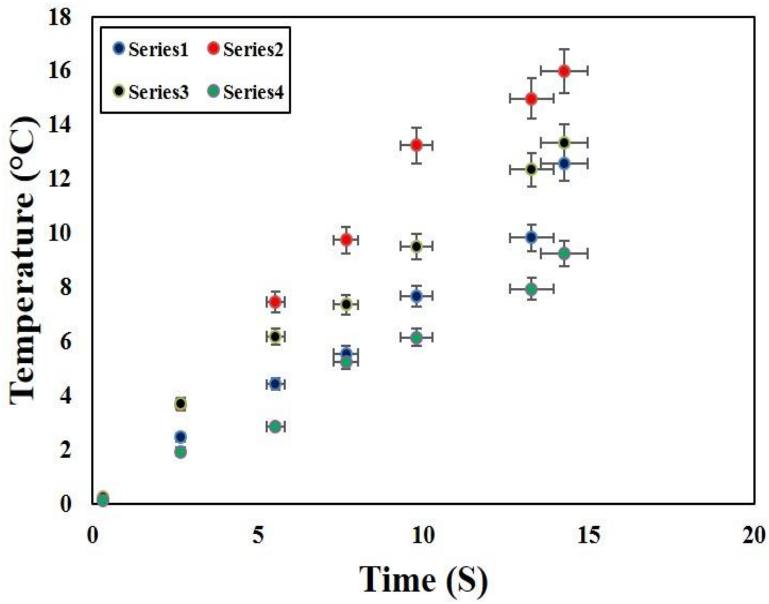

Figure 6. *The hyperthermia test of CdSe nanoparticles for 15 seconds and 15°C temperature.*

Figure 7 demonstrates the MNPs heat; heat release the samples were investigated in an external magnetic field (EMF). The VSM results are used to measure the magnetic properties of superparamagnetic response in various forms of single solid crystal and liquid thin films. It is also important to note that the energy emitted when the electron is recharged less than the energy absorbed by the electron, which is equivalent to the energy difference between the capacitance and conductivity bands. Since iron is a transition metal, finding the maximum amount of iron can also improve the luminescence properties [52-60]. As the synthesized basic nanoparticles with the optimum percentage of iron and surfactant achieved, then their toxicity is discussed to eliminate the phagocytic system. The obtained results show that high levels of cadmium increase the risk of cervical cancer, as the cadmium is a "very stable" toxic metal and can be accumulated in the body over time [34-40, 61-73]. Exposure to cadmium has adverse effects on health, including kidney damage, impaired calcium balance, and increased risk of pancreatic and breast cancer.

Also, the small nanoparticle diameter of the QDs can be attributed to the ratio of surface atoms to central atoms made inside the nucleus. This dominates the properties of the surface atoms over the properties of the entire nanoparticle. Surface atoms have different chemical properties from the atoms that result from the termination of the semiconductor network at the QD level performed. Atoms of the QDs that have not been deactivated with strong bands and adsorbed or transduced with organic, oxygen, and semiconductor molecules. This has specific effects on the optical properties of QDs by binding to these free cells [58-67]. ZnS mineral shells can completely inactivate surface atoms, and coating the core of nanoparticles with a layer of ZnS can create a larger bandgap. In addition to improving their photolumin-escence properties, it prevents direct cadmium exposure. For non-detection and removal of nanoparticles by the phagocytic system, the nanoparticles can also be coated with Polyethylene glycol (PEG) polymeric. This coating improves the nanoparticles' half-life in the bloodstream and is not detected and eliminated by the immune system [55-60. 67-73].

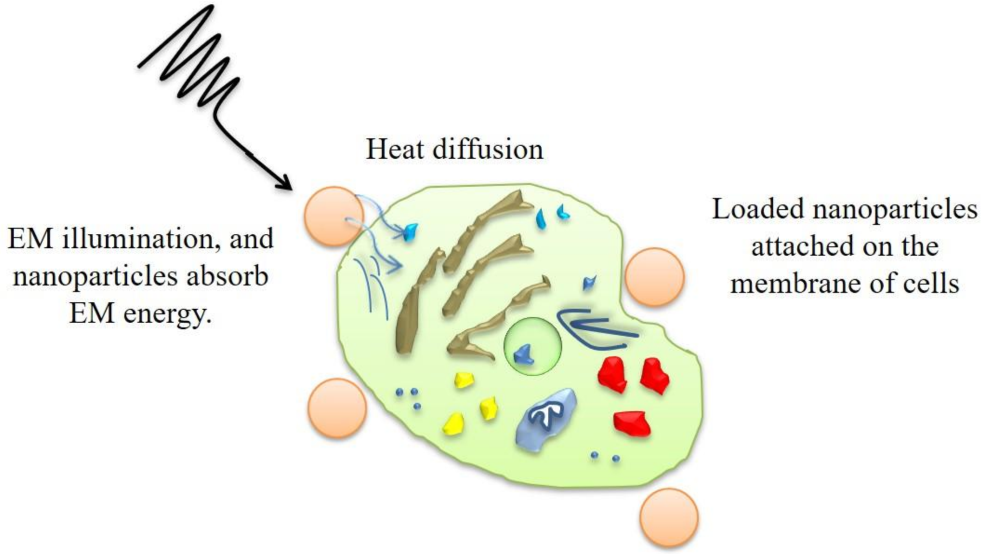

Figure 7. *A schematic nanoparticle loading, EM illumination and heat diffusion on cells.*

4. CONCLUSIONS

The results obtained from synthesized CdSe nanoparticles showed that the nanoparticles have the optimum size, morphology, magnetic phase and thermal properties. The synthesized nanoparticles can be used as basic nanoparticles for the desired purposes by modifying them to the desired nanoparticles. The small size of the nanoparticles improves the optical and thermal properties. As the amount of surfactant increased in the procedure method, it influences the nanoparticles' final size. Changes in the surfactant amount can be more desirable for cancer treatment with suitable desired heat release. A specific amount of heat release plays an important role in hyperthermia treatment. The photoluminescence properties of the CdSe nanoparticle exhibits higher value as the heat increased. Optimal iron content can also be determined by varying the sample effect's iron content on the magnetic field. While the radiation's wavelengths used in the radiation range from gamma to ultraviolet, it is desirable to obtain nanoparticles that emit the lowest wavelength. However, the maximum energy emitted by QDs is less than the minimum energy released by the utilized energy waves.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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