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Synthesis, characterization and optimization of Silica nanostructures by use of structure modifiers and ultrasonication

ABSTRACT

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In recent years, using Sol-gel procedure for the purpose of laboratory and industrial synthesis of Nano-structures, and especially silica Nano-particles, has been significantly increased. In this research, silica particles were synthesized by Sol-gel procedure and their physical and chemical properties were studied by means of scanning electron microscopy (SEM), transmission electron microscopy (TEM) and thermo gravimetric analysis (TGA). The effect of structural modifiers on the morphology and diameter of Nano-particles was also investigated. In addition, the reaction was carried out in the presence of ultrasonic waves in periods of 10, 30 and 60 minutes and the effect of these waves on the different stages of reaction was studied by means of SEM. Moreover, spherical particles of 50 to 80 nanometer sizes were synthesized and characterized that can be very useful hosts for lanthanide complexes which can be used in drug delivery systems, radiotherapy, photo luminescence (PL), applications and manufacturing of special lasers. Different amounts of Lanthanum nitrate hexahydrate were also added to the mixture during the creation of nanoparticles. Then simulated body fluid (SBF) was produced to study both, the capability of these Nano-structures in regulated delivery of drugs such as lanthanides, and releasing of lanthanides in 10 minute periods for 80 hours. Finally, lanthanide concentration in SBF was studied by means of inductively coupled plasma (ICP). According to the obtained results from ICP analysis, loaded lanthanide does not release from silica network. These loaded lanthanides to mesoporous silica can be used in radiotherapy and particularly in liver cancer.

Keywords: *silica, modifier, Sol-gel, morphology, ultrasonic.*

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INTRODUCTION

In recent decades, great efforts have been made to develop new substances, particularly Nano-structure substances.

Because of their small size and high surface area, nano-particles show unique properties. Similarly, due to the large internal area and small cavity sizes, the mesoporous substances have found many applications. If the nanometer particles (semiconductors or metals) become porous inside the cavities, a new substance will be formed that with no doubt would contain some unique properties of Nano-particles and porous substance [1]. The porous structures show unique optical, electrical and mechanical properties in Nano-meter dimensions that would allow using them in large range of applications from photonics and electronic to biological and medical sensors. Synthesis of porous particles with less than one micro dimension, such as silica, is very important in expanding advanced technologies [2]. Since the time of discovering porous silica, most studies have been carried out to make them factored and have focused on homogenous distribution of the size of cavities and adjustability of cavity sizes to keep them between 1.5-30 nm due to their large surface area [3]. As a catalyst and absorber, mesopore silica has received large attention, due to its homogenous cavity structure; it can accommodate relatively large molecules that could not be put in zeolites. They could be used for producing conductor and magnetic nano wires [4]. Presently, the Sol-gel method has been recognized as highly suitable and applicable method for producing various types of ceramic and Non-ceramic materials. The most famous process includes hydrolyzing silicon dioxide, polymerization and agglomeration [5]. Specifications of synthesized products are totally dependent on their synthesis conditions [6]. Many studies have already been carried out on the relationship between synthesis conditions and specifications of the products [7]. It is evident that the spatial structure of those substances emerges in few subsequent stages [8]. This network is made of their prior initial structures that are much smaller than their final structure [9]. The existing cavities in mesopore, depending on their sizes, could be used for various types of atoms and small or large molecules [10]. Molecule loading into the mesopore cavity and sending medicine to the target cellular tissue increases the efficiency of the drug and lowers its dose. Today, studying controlled release of loaded medicine in particles has found large applications in medicine [11]. These applications consist of large range of regular

medicines to cancer treatment via radiotherapy as well as sending medicine and controlled medicine release. Owing to its many advantages, the controlled medicine release has found large applications [12]. Medicine release is studied in SBF as being a buffer with special conditions. The ability of a controlled medicine direction in regulating medicine release has many advantages for both patients and medical centers. Few number of medicine injection, leading to less referral to the medical centers, decrease in the costs of medicine prescription, improvement in efficiency and medicine absorption and reducing medicine loss are among the advantages. Another type of sending medicine is the entry of medicine to the target tissue without releasing it in the body. This method is used for medicines that would lead to intoxication if released in body however, their medicinal properties such as radioactive radiations of some of them are necessary for treating some diseases such as cancer. Today many medicines are used in radiotherapy of cancer patients; some of them include ^{64}Cu , ^{32}P , ^{153}Sm and ^{131}I . In addition, a number of Lanthanides such as Samarium and Holmium have become widely used due to their suitable amount, radiation time and half-life, as needed by the radiation receiver [1]. They have more important role in cases such as treating cancer by using Beta or Gamma medicine sending systems. That system should enclave the radiation diffuser pool and do not allow those particles, including lanthanide as it is most suitable one, to release; for, even very small amount of those particles in body causes acute intoxication in medicine receiving patients. On the other hand, the medicine carriers should be neutral and sustained in both chemical and thermal terms and do not become affected by radiation. Therefore, this research tried to synthesize silica carriers with high physical and chemical sustainability that could be easily changed due to their high surface and controllability of particles size and cavities, followed by loading lanthanum nitrate that has many physiochemical similarities with other lanthanides including samarium and holmium. Their release in the SBF was then studied thoroughly [13].

EXPERIMENTAL

Materials and Methods

Lanthanum nitrate hexahydrate with P.a. purity degree was supplied from Sigma Aldrich Company. Tetraethylorthosilicate (TEOS) with 98% purity, glacial acetic acid and other chemicals with P.a. purity as used in the experiment were supplied from Merck Germany Company. Scans were taken from samples by using (SEM) model XL30, Phillips, Holland. In addition, centrifuge model Hettich, Rotofix3 Japan was used for separating synthesized products from reaction environment (TEM), model FEG.CM20, Philips, Holland, (TGA) model PL-STA.1640 England and (PL), model perkin-Elmer, LS-5 USA to identify the Nano-materials. The quantity of released lanthanides from nano-particles was studied by (ICP), model DV 2100, Perkin-Elmer model, made in England. In this research, deionized water produced by Milli-RO15 apparatus, Switzerland was used.

Synthesis of prototypes by using Sol-gelMethod

Prototypes were obtained by mixing acetic acid, water and Tetraethylorthosilicate (TEOS) with 9, 1.6 and 4.5 ml values respectively. Mixture was stirred for 30 seconds. The sample was left for 6 hours so the reaction and the gel made in the initiation of reaction could be completed. The product was obtained by using a centrifuge at 600 rpm acceleration. Then, in order to remove the surface of product from unreacted substances, the product was washed with 20 ml ethanol four times and the product was obtained by using centrifuge. The samples were then dried and studied by SEM[9]. (Figure 1)

Adding various quantities of sodium carbonate to reaction environment

Four parallel reactions were performed in Sol-gel method by adding 0.01, 0.05 and 0.2 grams sodium carbonate to the reaction environment 1, 2, 3 and 4. (Table 1) The products were obtained according to the previous method and their morphology and size of particles were studied by SEM, as shown in Figure 2.

Table 1. Adding various quantities of sodium carbonate to reaction environment

Deionized water (ml)	TEOS (ml)	Acetic acid (ml)	Sodium carbonate (gr)
1.6	4.5	9	0.01
1.6	4.5	9	0.05
1.6	4.5	9	0.1
1.6	4.5	9	0.2

Ethylene Glycol

Three parallel reactions were performed in Sol-gel method by adding 0.01, 0.05 and 0.1 Molar ratios of ethylene glycol to Tetra Ethyl Ortho silicate respectively, to the reaction dishes. (Table 2) The products were obtained in accordance with the method and their morphology and size of particles were studied by using SEM.

Table 2. Adding various quantities of Ethylene Glycol to the reaction environment

Deionized water (ml)	TEOS (ml)	Acetic acid (ml)	Ethylene glycol (gr)
1.6	4.5	9	0.01
1.6	4.5	9	0.05
1.6	4.5	9	0.1

Nitrobenzene

The three parallel reactions were performed in Sol-gel method by adding 0.01, 0.05 and 0.1 Molar ratios of nitrobenzene to TEOS respectively, to the reaction environment. (Table 3) The products were obtained in accordance with the method and their morphology and size of particles were studied by using SEM. Table shows results of adding similar amount of ethylene glycol and nitrobenzene to the reaction environment and compares their results.

Table 3. Addition of various quantities of nitrobenzene to the reaction environment

Deionized water (ml)	TEOS (ml)	Acetic acid (ml)	Nitro benzene (gr)
1.6	4.5	9	0.01
1.6	4.5	9	0.05
1.6	4.5	9	0.1

Synthesis of simulated body fluid (SBF)

SBF contains mineral ions with similar concentration as their concentration in human blood plasma. Table 4 lists concentration of those ions [13].

Table 4. Concentration of ions existing in the SBF and human blood plasma

Ion	Concentration (mmol/dm ³)	
	SBF	Blood plasma
Na ⁺	142	142
K ⁺	5	5
Mg ²⁺	1.5	1.5
Ca ²⁺	2.5	2.5
Cl ⁻	147.8	103
HCO ₃ ⁻	4.2	27
HPO ₄ ²⁻	1	1
SO ₄ ²⁻	0.5	0.5

The pH of SBF at 36.5°C is taken as 7.25. To synthesize such solution, special substances should be used, as their names and quantities are listed in Table 5 [13].

Table 5. Amount of reactors for synthesizing SFB

No	Reagent	Concentration
1	Ultra-pure water	750 ml
2	NaHCO ₃	0.350 gr
3	NaCl	7.996 gr
4	KCl	0.224 gr
5	K ₂ HPO ₄ .3H ₂ O	0.228 gr
6	MgCl ₂ .6H ₂ O	0.305 gr
7	HCl (1kmol/m ³)	40 cm ³
8	CaCl ₂	0.278 gr
9	Na ₂ SO ₄	0.071 gr
10	(CH ₂ OH) ₃ CNH ₂	6.057 gr
11	HCl (1kmol/m ³)	Enough amount to adjust pH to 7.25

Loading Nitrate Lanthanum in samples

Various quantities of lanthanum nitrate were added to the initial synthesized samples to study amount of lanthanum loading in them. The lanthanum nitrate hexahydrate 0.02, 0.05 and 0.1 Molar ratios to TEOS contained 0.18, 0.35 and 0.9 grams lanthanum nitrate hexahydrate respectively was dissolved in 1.6 ml. water and 9 ml acetic acid

was added to each. The mix was stirred and in the process of stirring, 4.5 ml. TEOS were added to each dish. (Table 6) The mixture was stirred for 30 seconds and after 6 hours, the products of the reactions were extracted, washed and then dried. No product was made in samples with 0.35 and 0.9 grams lanthanum nitrate. To remove that problem, the amount added to the reaction environment was taken as to be half of the initial quantity and syntheses were repeated. By that correction, the reaction led to production of substance. The amount of loaded Lanthanum on samples was then measured by using ICP.

Table 6. Study amount of Lanthanum loading in presence of various concentrations of Nitrate Lanthanum hexahydrate

Lanthanum Nitrate hexahydrate (gr)	Acid	Retention time (h)
0.18	Acetic acid	6
0.35	Acetic acid	6
0.9	Acetic acid	6

Adding same amount of Lanthanum Nitrate to the synthesized samples by using ultrasonic in various time intervals

In order to study the effects of ultrasonic waves on lanthanides loading, reactions have been made by using 0.02, 0.05 and 0.1 Molar Lanthanum Nitrate that contained 0.18, 0.35 and 0.9 grams of that sold in the presence of those waves. The reactions products were separated and washed after 30 and 60 minutes from starting the reaction in presence of waves. (Table 7) Reactions were performed in similar conditions as before. The effects of existence of that salt on the size of particles as well as amount of loaded Lanthanum on particles with various concentrations of Lanthanum Nitrate were studied. In addition, the percent of loading was compared with the loaded amount on ordinary samples (without ultrasonic waves). (Figure 4, 5, 6 and 7)

Table 7. Effects of ultrasonic waves in size and shape of particles and amount of Lanthanum loading in samples

Ultrasonic waves (min)	Lanthanum Nitrate hexahydrate (gr)	Acid
10	0.18	Acetic acid
30	0.35	Acetic acid
60	0.9	Acetic acid

In order to ensure the existence of Lanthanum Nitrate in samples, the synthesized sample fluorescence was compared with the fluorescence of pure Lanthanum oxide by using of Lanthanum Nitrate. (Figure 8)

The Study of the release of loaded Lanthanum inside synthesized samples

Since no release of loaded lanthanides inside samples is of high importance, samples have to be studied in terms of lanthanum release. Since the half-life of ^{166}Ho and ^{188}Re radio isotopes is 17 and 26.8 hours, respectively therefore, by basic ^{188}Re as the criteria with longer half-life, after 80 hours, only 12% of the loaded radioisotopes remained while 88% of it vanished by disintegration. Hence, in order to determine amount of probable release of lanthanum, 0.5 grams of one sample with highest loaded Lanthanum was poured in SBF and was stirred for 80 hours at 37°C temperatures. Samples of the mix were taken in 1, 5, 10, 20, 40, 60 and 80 hours and their Lanthanum was measured by ICP.

RESULTS AND DISCUSSION

The Study of the samples synthesized by using general Sol-gel method

The SEM pictures of these samples show that there are many differences between the sizes of synthesized particles, varying from 500 nanometers to few microns. (Figure 1)

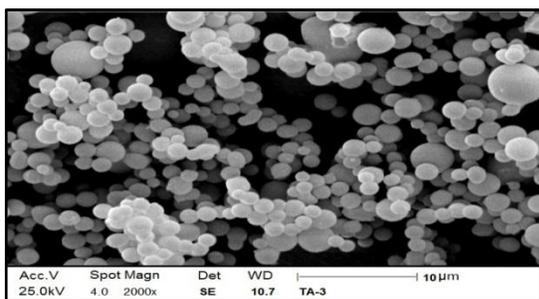


Fig. 1. The SEM picture of the sample synthesized by using general Sol-gel method

The effects of adding sodium carbonate

Since hydrolysis and condensation form the two key stages in the reaction and in the digestion design, the diameter of associated ion

layer as formed on particles has direct relations with the type and amount of ions in the reaction environment, therefore, existence of substances with the ability of correction and controlling the ion power and ion concentration in environment could have direct effects in the size and form of particles. As an example, it is possible to use sodium, potassium, calcium carbonate. In this research, sodium carbonate was used as a corrector, that is, partial amounts of this substance was dissolved in a ratio of 0.01, 0.05 and 0.1 to TEOS that equals to 0.09, 0.45 and 0.9 grams, respectively in 1.6 ml water and the reaction was continued in ordinary way. By increasing that modifier, morphology of particles was modified to a large extent and particles with same sizes were obtained, however, the particles which were obtained had diameters higher than 500 nanometers. (Figure 3) In addition, the amount of products obtained in these conditions was very low. This process could be justified as the existence of those modifiers in the reaction environment caused intensive reduction of hydrolysis and in turn, that effect caused a reduction in the speed of core creation. However, the speed of density process was higher than hydrolysis. As a result, particles formed in this method had much less number but better morphology and larger size.

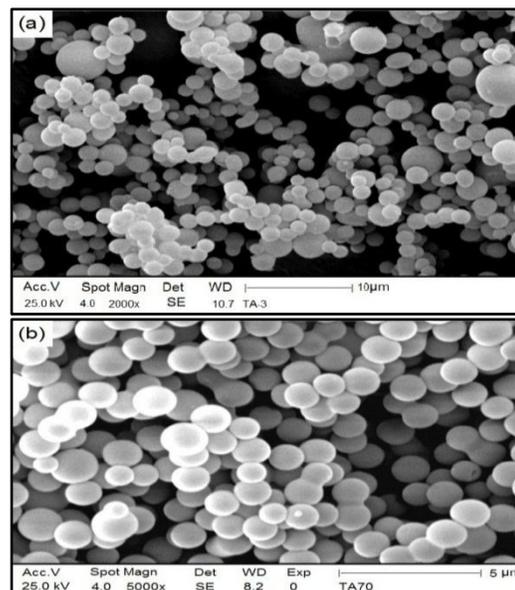


Fig. 2. The sample of synthesis with 0.09 gram (A) and 0.9 gram (B) sodium carbonate

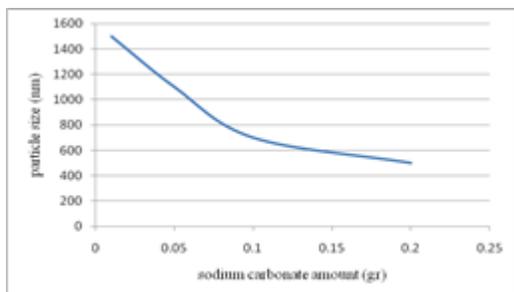


Fig. 3. The Diagram of the effect of adding different values of sodium carbonate on the size of similarity of particles

Addition of ethylene glycol and nitrobenzene

The two substances, due to having electrophile end groups could cause absorption of positive ions in the reaction environment and the concentration of existing active positive ions in environment; and subsequently, effects on the speed of reaction and amount of its progress. The speed of reaction and the amount of its progress in the process of Sol-gel have direct impact on the size and shape of nanoparticles that were formed as well as amount of adhesion and their conglomeration. In this research, ethylene glycol and nitrobenzene were added to the initial substances mixture with 0.1 and 0.01 molar ratios than TEOS and the reaction was performed. The products of reaction were studied by SEM after exiting reaction environment. **Figures 2-a** and **b**, show the synthesized samples with 0.1 molar ratio of ethylene glycol and nitrobenzene, respectively. As it could be seen in **Figure 2-a**, ethylene glycol causes flatness of particles surface, and therefore, adhesion in particles is rarely observed, that in turn too, was limited to the formation of bi-nucleolus granules. The size of particles; too, is very small. This effect has occurred due to the two supplementary effects of ethylene glycol in the reaction. First, the correction of ions concentration in the reaction environment that prevented the non-reacted free ions around formed nucleus. The second is the physical prohibition of this substance that prevents adhesion of newly established nucleolus. In another word, the ethylene glycol in the first stage of reaction; that is, core creation or hydrolysis with correction of ion structure causes an increase in nucleolus and production of more nucleus. However, as **Figure 2-b** shows, the products of reactions made with nitrobenzene help were totally different from products controlled by

using ethylene glycol. The SEM pictures show that formation of multi-nucleus groups and agglomeration of particles has increased. However, the particles could be separated isolated. This is due to the less spatial prevention of nitrobenzene than ethylene glycol. However, the nitrobenzene has been able to adjust the ion structure of environment. For that reason, the particles which are formed have small size and many of them have similar shape and size.

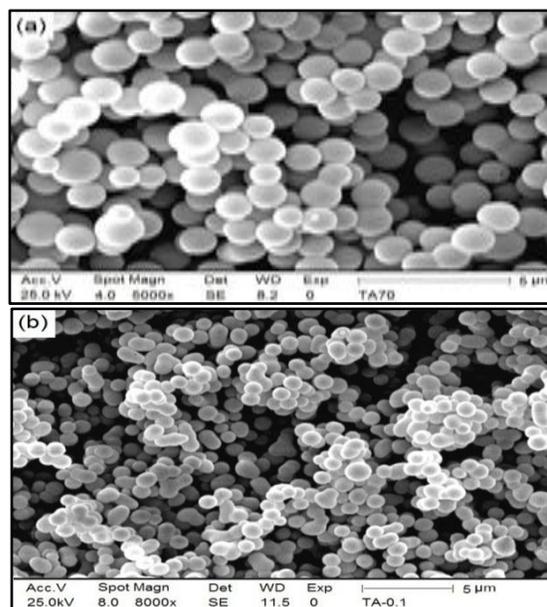


Fig. 4. The synthesized sample with ratio (A) 0.1 molar ethylene glycol (B) 0.01 molar nitrobenzene

Addition of different values of Lanthanum salt to the initial synthesized sample

As it could be seen in **Figure 5**, by increasing the concentration of Lanthanum nitrate in the reaction environment, the amount of loaded Lanthanum in the synthesized samples increases as well. In addition, the curve slope of the loaded amount of Lanthanum decreases as the concentration of Lanthanum Nitrate in the environment increases. In case of high increase in the concentration of Lanthanum nitrate in environment, no reaction is made. The reason could be an increase of ion power in the environment along with the increase in amount of Lanthanum nitrate that leads to an increase in hydrolysis reaction speed, associated with core creation.

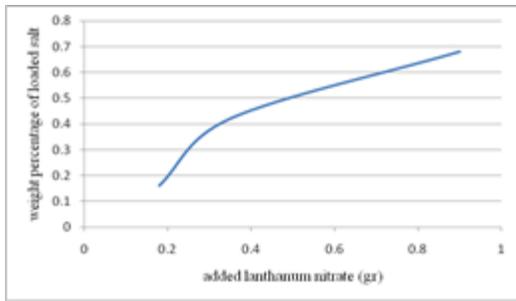


Fig. 5. The relationship between amount of added salt to the reaction environment and weight percent of loaded salt on synthesized samples

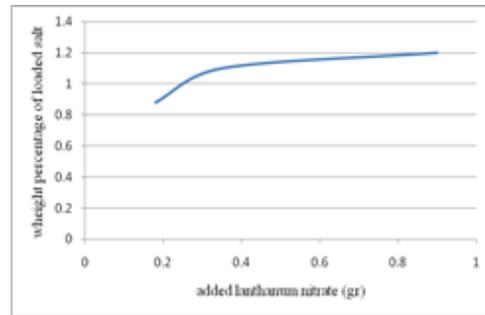


Fig. 7. Diagram of amount of Lanthanum loading in samples by using ultrasonic

Addition of similar quantity of Nitrate Lanthanum salt to the synthesized samples by using ultrasonic in different time intervals

According to Figure 7, the loaded Lanthanum in samples when ultrasonic waves are used is significantly higher than synthesis without using those waves. However, as it is seen in figure 8, the slope of loaded Lanthanum curve in samples is less in that state. This could be explained in this way, that the ultrasonic waves cause acceleration in hydrolysis and density processes. (Figure 6) Consequently, by the acceleration of hydrolysis reaction, the core creation speed increases and since the Lanthanum ions exist in core creation in environment; they enter in the initial nucleuses. Therefore, the amount of loaded Lanthanum in samples is much higher by using the waves than in ordinary state. However, due to increase in the density speed, the amount of Lanthanum loaded in the samples in this state is less than ordinary state; and, therefore, the slope of loaded curve is very little. The fluorescence spectrum of oxide Lanthanum and few sapless with Lanthanum that has become agitated in 258 nanometer wave length [14]. Figure 9 confirms the existence of lanthanum in synthesized samples.

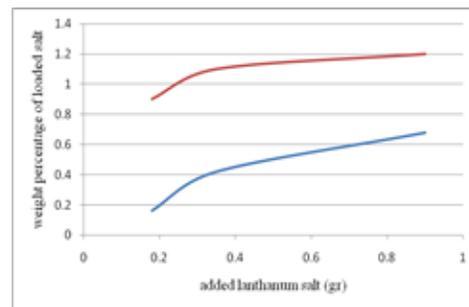


Fig. 8. Diagram of comparing the loaded Lanthanum on ordinary samples and the samples which have been adjunct to ultrasonic

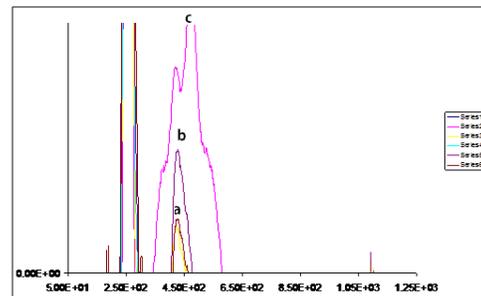


Fig.9. Diagram of fluorescence of oxide Lanthanum and sapless containing Lanthanum

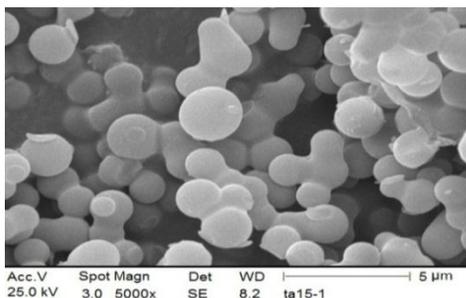


Fig.6. The synthesized samples with 0.18 gram Lanthanum and 30 minutes ultrasonic

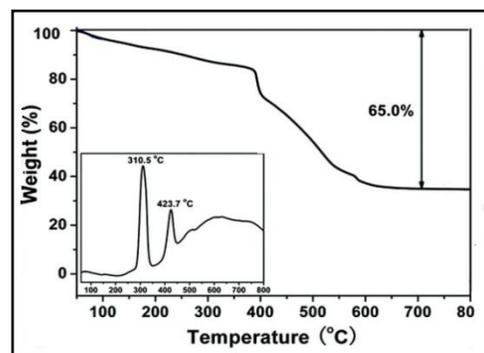


Fig. 10. The TGA curves of the synthesized sample with 30 minutes of ultrasonic effect

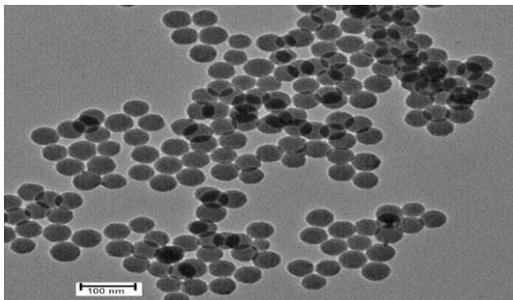


Fig. 11. The TEM picture of synthesized samples with 30 minutes of ultrasonic effect

Figure 10 shows the TGA curves of synthesized sample with 30 minutes of ultrasonic effects. In 100°C, the curve shows a sensible lowering in weight that could be caused by the absorbed water by the surface layer of particles. The eventual gradual reduction of samples is because of formation of network structure in the samples. Figure 11 shows the TEM picture of samples with approximate size of 50 nanometers. This picture confirms the size of particles.

Study the release of loaded Lanthanum inside synthesized sapless

The samples taken in different intervals were analyzed by ICP to study the probable Lanthanum that was released in the environment from samples. No Lanthanum was observed in any of the samples. With respect to the detection limit of ICP apparatus (0.01ppm) one could conclude that either no Lanthanum is released from the samples or the released Lanthanum is so low that its concentration is below the detection limit of ICP apparatus.

CONCLUSION

Using of sodium carbonate in silica synthesis lowers core creation speed. Therefore, the number of nucleus produced is fewer and their sizes are larger. The morphology of particles is spherical with more than 500 nm diameter. Therefore, using this corrector could have direct and suitable effects in the particles morphology. The evident disadvantage is greater particles size than the required sizes. Due to their large size, these particles are not suitable in radiotherapy application; however, they could be used in

photoluminescence. Using ethylene glycol could have good effects in modifying the reaction environment and controlling the size and morphology of particles. This substance flattens surface of granules and minimizes its conglomeration. The advantage of using ethylene glycol is to obtain sphere particles with very flat surface; however, its disadvantage is obtaining large sized particles with 150 to 200 nm. Those particles are not suitable for radiotherapy due to their large size. The effect of nitrobenzene in modifying the structure of those particles less than ethylene glycol as when this substance is used, there are abundant multi-nucleus agglomeration. The size of particles varies from 50 to 80 nanometers. A large number of them have same shape and size. Therefore, particles obtained when adding that modifier are unsuitable in terms of size and morphology. Adding different lanthanide salts could have two major impacts on the reaction products; one is the reduction in the size of synthesized particles and configuration of those particles and second is placement of different quantities of those salts inside the structure with physical or chemical bonds. Since this research peruse the loading of Lanthanum salts in synthesized samples, the effect of second case is studied. By adding various quantities of lanthanide salts into reaction environment, amount of loaded Lanthanum in synthesized sample will be more. Using ultrasonic could accelerate the general process of reaction as much that the ordinary reaction takes 6 hours and reaction made by ultrasonic would take one hour. In addition, amount of lanthanides loading in sample will be increase. This loading will be suitable for lanthanide when the loaded lanthanide do not exit the nanoparticles. As the ICP results show, the loaded salts did not leave nanoparticles. Those nanoparticles with loaded lanthanides could be used for radiotherapy and diagnostic cases, particularly in liver cancer.

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