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The Effect of Cobalt Oxide Nanoparticles on Improving the Quality of Computerized Tomography (CT) Scan Medical Imaging

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ABSTRACT

Introduction: Sometimes, a patient receives a poor quality medical image from a medical imaging center. Which the doctor orders to re-image with a drug contrast media agent. At this time, practical action is challenging to provide a proper image. Cobalt oxide nanoparticles show different activities based on different sizes and shapes. Objectives of this project is achievement a critical size of cobalt oxide nanoparticles between 5 to 10 nanometers for easy circulation in the blood and Investigation of the effect of cobalt oxide nanoparticles on the quality of CT from laboratory mice(Mus musculus).

Material and Methods: In this study, the coupling method was used to prepare the cobalt oxide nanoparticles. Co_3O_4 nanoparticle coatings are used for this purpose. They were investigated through the Fourier-transform infrared (FTIR) analysis, X-rays diffraction (XRD). In order to investigate the efficacy of cobalt oxide nanoparticles, we injected a suspension into the Mus musculus, and then the computerized tomography (CT) scans were taken before and after injection of the nanoparticles. Then, quantity evaluation was performed using the calculating the average local contrast media of the whole image.

Results: The average size of cobalt oxide nanoparticles was obtained about 5.8 nm, which is an appropriate size in the nanometer scale. After injecting of cobalt oxide nanoparticles into the mice and then CT scan imaging, we have obtained a better clarity.

Conclusion: Cobalt oxide nanoparticles behave well for use as a pharmacological contrast media agent in CT scan imaging.

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Introduction

The contrast media agents are used as a substance to enhance the contrast media of structures or fluids within the body and improve the visibility of features that would be difficult to detect in medical imaging [1]. The nanoparticle agents receive much attention for application as contrast media agents. Various pharmaceutical contrast media agents are available in markets, either orally or by injection [2].

One of the newest detectors is 18-F which is used for cancer patients, especially prostate cancer and is very common [3]. Many studies have been performed on the synthesis of new materials to increase the sensitivity of imaging techniques. Clark et al. significantly enhanced the contrast media of computerized tomography (CT) scan and used nanoparticles to detect the neoplasms using 15 nm gold nanoparticles [4, 5]. A computerized tomography (CT) scan combines a series of X-rays images taken from different angles around patient body and uses computer processing to create cross-sectional images (slices) of the bones, blood vessels and soft tissues inside patient body. CT scan images provide more-detailed information than plain X-rays do. Also, the iron oxide (Fe_3O_4) coatings have been used to improve pancreatic neoplasms diagnosis by CT scans and MRI [6-9]. All of the above compounds have short lifespans or require potent accelerators. Although, the use of cobalt in medical research has been considered in recent years, but, the toxicity and lattice structure of this material for diagnostic examinations are still debated.

In this study, the coupling method was used to prepare the cobalt oxide nanoparticles. The Co_3O_4 nanoparticle coatings are used for this purpose. They were investigated through the Fourier-transform infrared (FTIR) analysis, X-rays diffraction (XRD), and magnetization curve of the crystalline sample. In order to investigate the efficacy of cobalt oxide nanoparticles, a suspension was injected into the Mus musculus, and CT scans were taken before and after the nanoparticles injection. Since the Mus musculus's

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weight was 30 g, 0.1 cc suspension was injected into Mus musculus, and imaging was done after 15 min.

The results showed that cobalt oxide nanoparticles enhanced Reactive oxygen species (ROS) generation in lymphocytes. A protective function on lymphocytes death induced by Co_3O_4 nanoparticles was achieved using in vitro pretreatment with N-acetylene cysteine. In recent years, the anti-neoplasms activity of cobalt oxide nanoparticles has attracted much attention due to their sensitivity to neoplasms. Recently, cobalt oxide nanoparticles have been shown to be highly toxic to cancer cells while at the same concentrations they do not cause cytotoxicity in normal cells. [13]. After surface functionalization, no toxic effects from infiltration into blood cells and adverse effects were reported. As mentioned, iron oxide itself is not used as a tracer alone and is used as the primary tracer coating, and the maximum half-life of the tracer (with an Ethinyl glycol concentration) is achieved by using a cyclotron for 24 hours [14, 15]. Moreover, if the material is radioactive, it can be used for nuclear imaging.

Materials and Methods

Materials

The chemicals used in this article are: Cobalt chloride manufactured by Merck Company, sodium hydroxide (KOH), and citric acid (C6H8O7) manufactured by Qatran Shimi Company, all purchased from the Razi Chemical Institute of Iran at the Isfahan University of Technology (IUT).

Preparation

For synthesizing, dissolve 5 mmol of cobalt chloride in 40 ml of distilled water. Add the solution of potassium dropwise to the previous solution to obtain a green color. The resulting mixture was added to a 100 ml Teflon and kept in an autoclave for 6 hours at 180 °C. After cooling, the resulting dried mixture was washed with distilled water and passed through a strainer. Then we dried the material in powder for 6 hours at 90 °C [16]. The particle size has been reduced by a ball mill. The chloric acid solution was added dropwise to a pH of 6.5. After that, the sample was dispersed in distilled water for 10 minutes at room temperature to obtain a uniform and stable surfactant. Bath ultrasonic broke the bonds between the patches and increased the quality of the solution. The desired solution concentration is adjusted to 0.4 mmol. The material prepared by the laboratory of Zarrinshahr Payame Noor University (PNU) in the Isfahan city, made by ball Mill Company, was transformed for 6 hours by the nano measurement. In this study, the laboratory small white mice were used. One was used for CT scan imaging weighing approximately 30 grams. The necessary reactions are as follows

$$CoCl_2 + 2KOH \rightarrow Co(OH)_2\downarrow + 2KCl, \quad (1)$$

$$3\ Co(OH)_2\downarrow + H2O2 \rightarrow Co_3O_4\downarrow + H_2O \quad (2)$$

The Mus musculus were raised in the Isfahan Royan Laboratory. Neoplasms induction in mice was performed by injecting cancer cells. The specified method suppresses the immune system of mice before the injection. The growth of the neoplasms took three weeks. During this time, the Mice were fed a diet of 30% carbohydrates and 40% cereals and vitamins. Moreover, if this material becomes radioactive, the half-life of the nanoparticle can be obtained as [17]

$$\tau_{1/2} = \frac{\ln 2}{\lambda}, \quad (3)$$

which, λ is the decay constant.

Characterization

FTIR spectra of samples were measured with KBr pellet in the wave number range of 4000–350 cm^{-1} by an FTIR-ATR spectrometer (Bruker, Tensor II). The XRD patterns were recorded by a Bruker D8ADVANCE X-rays diffraction spectrometer with a Cu K α target from 5 to 80 °C.
The morphologies of nanoparticles were investigated using SEM (Philips, XL30, SE detector). The magnetic properties of the samples were determined by a vibrating sample magnetometer (model LBKFB, Kavir Magnet Co., Kashan, Iran). The CT scanner used was Siemens, Munich, Germany (Voltage 61 kV, Current 50 µA).

Results

Fourier-transform infrared spectroscopy

In order to investigate the molecular bonding of the surface of cobalt oxide nanoparticles, the Fourier-transform infrared (FTIR) analysis was performed on suspended sediment. This analysis was performed using a Nicolet-Magna 500 spectrometer. The coated cobalt oxide nanoparticles were washed, dried, and powdered several times for the FTIR test. As shown in Fig. 1, the nanoparticles are well coated, and C=O is observed at the wavenumber of 1638 cm-1. The small peak at the low wavenumber of 542 cm-1 belongs to C-H.

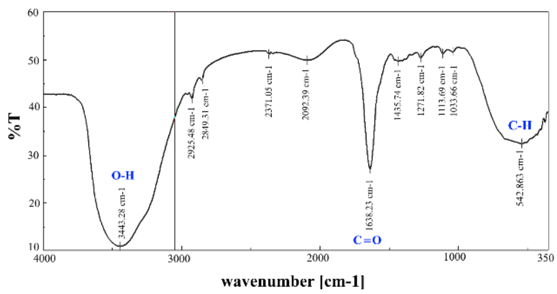

Figure 1. FTIR analysis of cobalt oxide nanoparticles.

X-rays Diffraction

The sample was subjected to x-rays diffraction (XRD) to measure the crystallinity of material. The XRD test was performed with a wavelength of 1.55266 copper lamps. All the diffraction peaks of Co_3O_4, are sharp, indicating a high degree of crystalline. XRD device model is D8 ADVANCE from Germany Bruker Company.

Transmission Electron Microscopy

The particle size was determined by the transmission electron microscopy (TEM) at the University of Isfahan, shown in Fig. 2. This figure shows that the synthesized particles are quasi-spherical, which is desirable. Also, the particle size distribution graph and mean particle size are plotted with 50 particles in the bottom panel of Fig. 2. According to this figure, the average sizes of the particle are about 5.8 nm, which is an appropriate size.

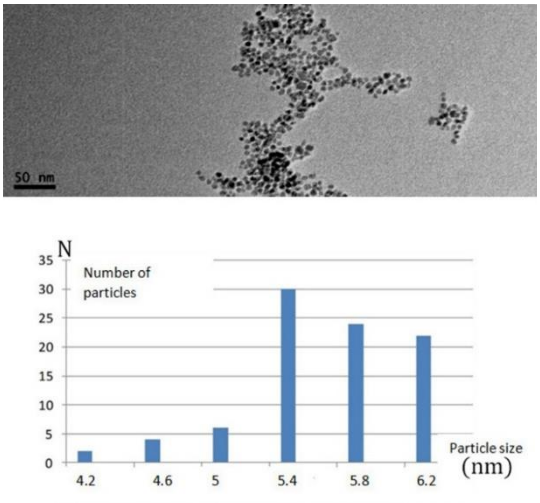

Figure 2. Distribution diagram of the particles by their size

Cobalt oxide and iron oxide nanoparticles performance comparison in CT-scan images

In order to study the efficacy of cobalt oxide nanoparticles, a suspension was injected into the Mus musculus, and CT scan was taken before and after the nanoparticles injection. Since the Mus musculus weight was 30 g, 0.1 cc suspension was injected intravenously into the Mus musculus, and imaging was done after 15 min. The imaging was performed with a Siemens CT scan with a 61 kV voltage profile, 500 μA current, 440 ms irradiation time and 0.09 mm voxel size at Kashani hospital in Isfahan (see Fig. 3). Figure 4 shows the results of these two views (a and b). In both figures, in the left images, none of the rat's viscera, including the bladder and the kidneys, are visualized, but in the right images, the bladder and kidneys are completely clear. The results show that suspension solution prepared from cobalt oxide nanoparticles can be a right contrast media agent for CT scanning imaging. An essential feature of this nanoparticle is its easy preparation, availability, and cheapness.

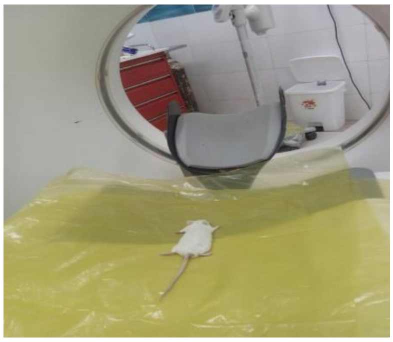

Figure 3. The picture of Mus musculus on a CT scan bed.

Figure 4. View a,b of CT scan images: left and right panels are for before and after contrast media injection respectively. (a: Color effect and 45 ° view, b: Black and white effect and 0 ° view)

Discussion

Quantitative Evaluation

The images in Fig. 4 illustrate the effect of contrast media injection for improving image contrast media, but there are limitations to quantifying the amount of contrast media improvement. In most quantitative methods, the image contrast media is compared before and after the image processing algorithm. For quantitative evaluation of medical images, a proposed method with modifications has been used [18]. In this method, a gamma correction is first performed on the image, and the pixel size of the image from 0 to 255 is mapped to the range [1, 0].

$$l = (\frac{k}{255})\gamma, \quad (4)$$

which is each pixel value in the image before mapping and the pixel value after mapping and gamma correction? The value obtained for the pixel is then scaled as follows

$$L = 100\sqrt{l} = 100 \times \sqrt{(\frac{k}{255})^{\gamma}}. \quad (5)$$

The amount of local contrast media is calculated as the average value of the absolute magnitude of the difference in brightness of each pixel from its adjacent pixels, as follows for each pixel (see Fig. 5)

$$lc_{i,j} = \frac{|L_{i,j}-L_{i-1,j}|+|L_{i,j}-L_{i+1,j}|+|L_{i,j}-L_{i,j-1}|+|L_{i,j}-L_{i,j+1}|}{4}. \quad (6)$$

The average local contrast media of the whole image is calculated according to as follows

$$C_i = \frac{1}{w\times h}\sum_{i=1}^{h}\sum_{j=1}^{w} lc_{i,j}. \quad (7)$$

In the proposed method, after calculating the average local contrast media of the whole image, the image resolution is reduced to load, and each time the average local contrast media of the new image is obtained. The final criterion for the weighted sum is the average local contrast media of all images

$$GCF = \sum_{i=1}^{N} w_i C_i, \quad (8)$$

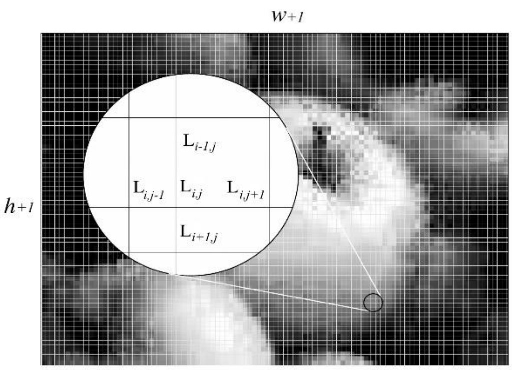

Figure 5. Pixel indices of Eq. (6).

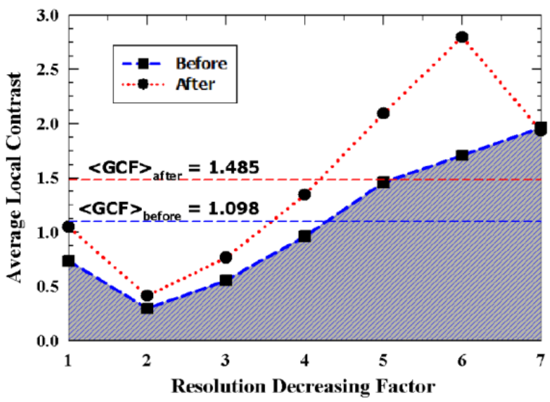

Figure 6. Numerical comparison of contrast media and Average global contrast media factor (GCF) for cobalt oxide the dashed line diagram for pre-injection values and the red line diagram for after injection values.

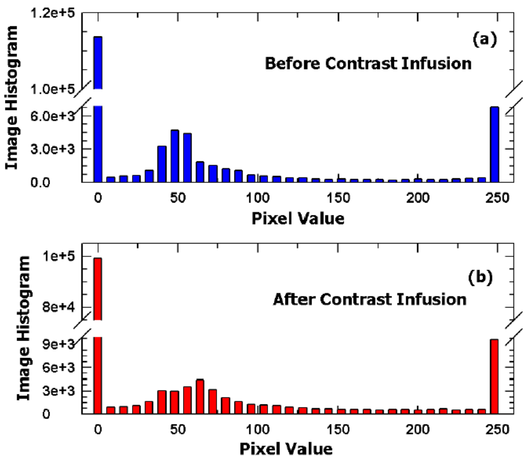

Figure 7. Quantitative comparison of contrast medias (a) before injection and (b) after injection of cobalt oxide nanoparticle contrast media agent in CT scan imaging.

Depending on the image's size, it is done up to 7 levels, and plotted the average local contrast media values of the entire image for all resolutions on a graph, as shown in Figure 6. The figure shows the dash line diagram for pre-injection values and the red line diagram for after injection values. At all resolutions, higher values are obtained for the image after contrast media injection. The mean global contrast media factor (GCF) values for the image before and after injection were 1.079 and 1.4849, respectively. The histogram of the images is shown in Figure 7.

Conclusion

In the present work, the efficiency of Co_3O_4 nanoparticles in CT scans was investigated. The coupling method was used to prepare the cobalt oxide nanoparticles. Co_3O_4 nanoparticle coatings were used for this purpose. They were investigated through FT-IR analysis, X-rays diffraction and magnetization curve of the crystalline sample. The particle size measured by electron microscopy was 5.8 nm on average. Injection of the sample into the Mus musculus and obtaining a CT scan showed that cobalt oxide nanoparticles could be used as a suitable contrast media agent for detecting visceral domestic animals. Moreover, it is marked at the Mus musculus and does not show contrast media in the blood vessels and organs of mice. The most related research is done by Ahmadi et al [6], who has studied the effectiveness of iron oxide in CT scan imaging, which our results are consistence to them. The sample magnetization curve shows excellent superparamagnetic properties for Co_3O_4 nanoparticles. Therefore, these nanoparticles may also be the right contrast media agent for MRI imaging. This can be investigated by MRI imaging.

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