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Study Zinc Oxide Nanoparticles Solution as an Alternative of Iodine Contrast Medium of CT-Scan Imaging of the Heart, Kidney, and Liver

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Abstract

Zinc oxide nanoparticles (ZnO NPs) solution was chosen as an alternative contrast medium in computed tomography scanning (CT-scan). ZnONPs solution has good electrochemical property, especially in blood medium. It was found that ZnO in the blood medium acts as an antioxidative detector because cyclic voltammogram imaging has only one reduction current peak at -0.75 volt, while iodine compounds are used as a common contrast medium in CT; they have an oxidation current peak in the blood medium at +1 volt. Additionally, iodine compounds caused many problems when used as a contrast medium, but they were the only contrast media used for this purpose. It was found that the use of ZnO solution as an alternative contrast medium in rabbits resulted in improved CT imaging in resolution and increased Hounsfield unit (HU) values for rabbit's organs (heart, kidney, and liver), compared to using iodine compound at the same dose.

Keywords: ZnONPs solution; CT-scan imaging; Hounsfield unit; Iodine solution, rabbit, kidney, liver, heart.

Introduction

In the recent period time, a focus has been made on the use of nanocomposites in the medical field, especially the use of alternative contrast media in different radiology techniques especially, computed tomography scan (CT-Scan) [1-5].

It was Evaluated the reported metal nanoparticles as a contrast agent for X-ray computed tomography, inclusion of improved in vivo contrast, targeted drug delivery and dual / multipurpose imaging characteristics of each metallic nanoparticle. The therapeutic effects of metallic nanoparticles studied, such as photo thermal therapy and magnetic hyperthermia. A diagram was produced showing the relative contrast enhancing properties of the nanoparticles [6].

In vitro imaging was performed on chicken breast tissue, with and without application of ZnONPs. Contrast improvements for ZnONPs were determined at different times of application time; with the dispersion coefficient and Contrast-to-Noise Ratio were calculated [7].

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Zinc oxide NP dispersion showed an increase in the dielectric constant compared to the background medium. Moreover, PEGylation of ZnO NPs could achieve a correct increase in the dielectric constant compared to water, which was shown to be concentration dependent. These results indicate that ZnOnanomaterials have the potential to be used in biomedical applications such as mammography to improve diagnostic capabilities [8]. It was advanced in the development of mono to multimodal NPs and their related biomedical applications in vitro and in vivo that range from imaging and tracer to cancer treatment, besides specific applications of classic imaging such as MRI, PET, CT, US, and PAI [9].

Differences in toxicity were associated with the chemical transformation of ZnO NPs, and Zn + played a major role in mutagenesis of alkaline NPs. These results indicate that NPs are converted chemically in the environment. These transformations lead to clear differences in toxicity, indicating that the NP conversion process should be considered more comprehensively when assessing toxicity [10]. They can be micelles-dependent agents and are used in conjunction with computed tomography. The required large contrast agent doses will require careful toxicology studies prior to clinical translation. The various green synthesis methods can be considered to provide evidence of the role of ZnO NP in many applications, in addition to which biomedical applications and toxicological effects have been reviewed. [11,12].

To provide T1 contrast, these particles must present certain physico-chemical properties while controlling the size, morphology and surface of the particles. In this review, we summarize the reported T1 iron oxide nanoparticles and critically review their properties, compositional protocols and applications, not only in MRI but also in multimodal imaging. In addition, we briefly summarize the most important Gd and Mn nanoparticle factors to assess whether T1 iron oxide nanoparticles can reach the Gd / Mn contrast potential [13].

In this study zinc oxide nanoparticles solution has been used to enhance the resolution of CT-scan imaging as an alternative contrast medium of iodine solution.

Experimental

Materials

Bayer Pharma AG Company from the German company (Berlin Germany) Iodine contrast as Iopromide (Ultravist 370) was used as contrast media in CT-scan. Zinc oxide nanoparticles (ZnO NPs) were used from US Research Nanomateials, Inc. (USA) as an alternative contrast medium. Anesthesia materials used to anesthetize animals such as ketamine 10% from Alfasan Company (Holland), xylazine 2% from Alfasan (Holland). Blood samples of rabbits, and other chemicals and solvents were of annular grade and were used as received by the manufacturers. Deionized water was used to prepare aqueous solutions.

Preparation of 0.5M ZnO NPs solution

A 0.5 molar solution of pure zinc oxide NPs (US Research Nanomateials, Inc.) was prepared in a 10 ml volumetric flask, and the crystals were dissolved in deionized water to obtain a 0.5 molar solution of zinc oxide nano solution which used asan alternative contrast medium.

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CT-Scan apparatuses

Philips Brilliance 64 Slice CT-Scanner was manufactured; 2012, Cleveland, USA. After preparing the rabbit for examination and in the case of anesthesia with the specified dose of the contrast, the rabbit was lying on the examination table to perform the spiral CT-Scan as shown in Figure 1 and 2.

Preparing rabbits for CT-Scan imaging

The groups of rabbits, Balbo type (white), number 11, were selected, with an average weight of 2.5 to 3 kg, and were divided into three groups:
A. Group I: One rabbit for the test without using any contrast media (control sample).
B. GroupII: Five rabbits using the alternative contrast medium zinc oxide nanoparticles at a concentration of 0.5 M ZnO NPs in different doses:
C. GroupIII: Five rabbits using the contrast currently used in hospitals and examination centers with the CT-Scan, which is the iodine contrast medium (370 mg/ml) in different dosages:
Where the three groups of rabbits were studied in their natural condition (i.e. healthy and without any injury) using Philips Brilliance 64 Slice CT-Scanner, Cleveland USA.
All rabbits were anesthetized with Xylazine 2% (1ml / 20mg from Alfasan (Woerden Holland) at a dose of (0.15mg / gm) according to the weight of the rabbit in the hip muscle (im) of the rabbit.
Then, after making sure that they were completely anesthetized and without any movement, the rabbits were injected into the heart region with iodine contrast medium (370 mg/ml) in volumes of 1, 2, 3, 4, and 5 ml of the contrast, and then injected with alternative contrast medium ZnO NPs solution at a concentration of 0.5 Min volumes of 1, 1.5, 2, 2.5, and 3 ml, then study the different organs of the rabbits by CT-scan imaging (Philips Brilliance 64 Slice CT-Scanner, Cleveland USA) such as heart, kidney, and liver to finding the HU values of each organs.

Cyclic Voltammetric technique

Ezstat series (potentiostat/glvanostat) NuVant Systems Inc. pioneering electrochemical technologies USA were used.
Pyrex cell measuring 10 milliliters and three electrodes was used:
a. glass carbon electrode (GCE) was used as working electrode.
b. silver electrode (3M KCl) Ag / AgCl was used as reference electrode.
c. platinum wire (1 mm diameter) was used as Counter electrode.
All three electrodes were dipped in the solution under study and linked to the potentio- stat, which in turn was connected with the personal computer to identify the properties of the materials studied in the blood medium as shown in Figure 3. The glassy carbon electrode (GCE) was used in this study after cleaning with alumina grand and sonic technique for 10 - 15 min [14].

Results and Discussion

Computed tomography is one of the most widely used clinical imaging methods. In order to increase the sensitivity of CT scans, iodine compounds are used as injectable contrast agents.

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However, iodinated contrast media are excreted through the kidneys and have short time periods. This rapid renal cleansing not only restricts in vivo applications that require long turnover periods but also occasionally results in serious adverse effects related to the excretory pathway. In addition, X-ray iodine attenuation is not effective in clinical CT scans that use high-energy X-rays. Due to these limitations, iodine-fortified nano-contrast media have been developed that can increase circulation time and reduce adverse effects. In addition to iodine, nanoparticles based on heavy atoms such as gold, lanthanides and tantalum are used as more efficient CT contrast agents [15].

CT-scan study

The rabbits were chosen for a CT scan to checking the image of the heart, kidney, and liver. The rabbits were divided in to three groups; the first group is the group that studied rabbits with CT-scan without (pre) using contrast media. The second group was injected with different doses of iodine (370 mg/ml) contrast medium 1, 2, 3, 4, and 5 ml. The third group was injected with different doses of alternative nanocontrast medium of 0.5M zinc oxide NPs solution 1, 1.5, 2, 2.5, and 3 ml.The tests were performed following using CT-scan.

1.CT-scan examination of rabbit's heart

This examination was taken for the heart organ without using any contrast media, then the iodine contrast (370 mg/ml) and the alternative contrast ZnO solution (0.5 M). The Hounsfield unit (HU) factor values can be used to determine the resolution of the CT-scan images.

Hounsfield unit (HU): the absorption coefficient unit of the radiative transparency of a material; HU is normalized to water, where water = 0 HU, air = -1000 HU and bone = 1000 HU, the HU values are reported in CT for each case taken for the studied rabbits as follows [16]

The CT-scan imaging of the heart examination was taken to study the rabbits into the following three cases:

A. Checking the heart without using the contrast medium (native).

B. The CT-scan of cardiac examination using an iodine contrast medium .

C. Cardiac examination using alternative contrast medium of zinc oxide nanoparticles (0.5 M) solution .

2.CT-scan examination of rabbit's kidney

The CT-scan imaging of the kidney organ was examined at three cases as in the following:

A. studies the kidney organ without using the contrast medium (native).

B. The CT-scan of kidney organ examination using an iodine contrast medium .

C. kidney examination using alternative contrast medium of zinc oxide nanoparticles (0.5 M) solution .

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3.CT-scan examination of rabbit's liver

The CT-scan imaging of the liver organ was examined at three examination cases as in the following:

A. studies the liver organ without using the contrast medium (native).

B. The CT-scan of liver organ examination using an iodine contrast medium.

C. liver examination using alternative contrast medium of zinc oxide nanoparticles (0.5 M) solution .

Table 1: HU values of heart, kidney, and liver of rabbits at different contrast media

Contrast medium	Dose(ml)	Heart(HU)	Kidney(HU)	Liver(HU)
Native	**---**	**45**	**48**	**49**
Iodine (1.4M)	**1**	**58**	**57**	**58**
	2	**146**	**58**	**65**
	3	**210**	**61**	**69**
	4	**353**	**65**	**72**
	5	**407**	**67**	**75**
ZnOnps(0.5M)	**1**	**83**	**61**	**67**
	1.5	**177**	**70**	**74**
	2	**268**	**73**	**82**
	2.5	**360**	**79**	**85**
	3	**465**	**87**	**93**

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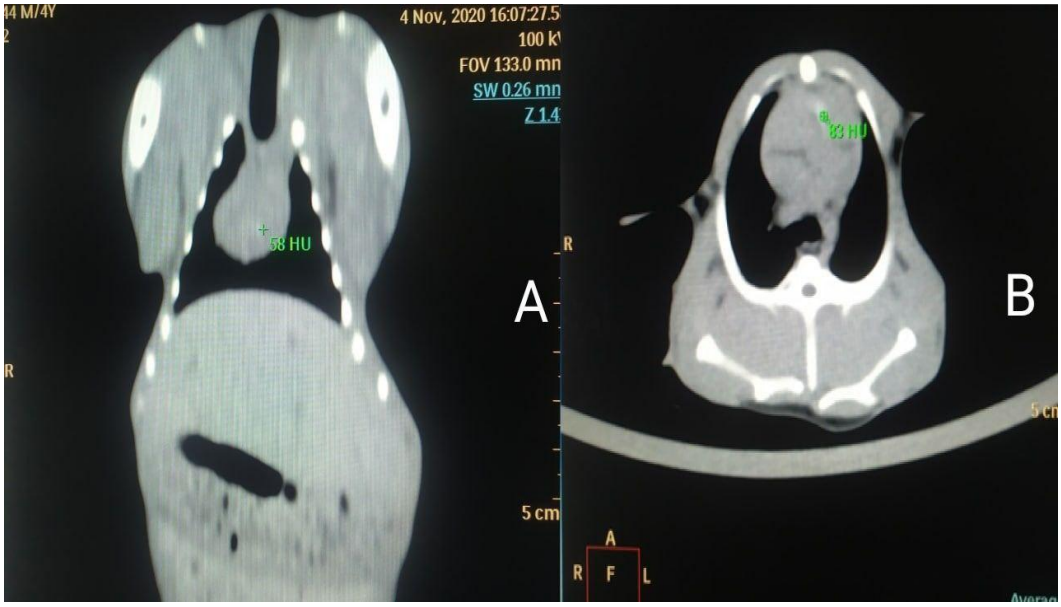

Figure 1: CT-scan images of rabbit's heart with A. iodine(1.4M) and B. with alternative contrast medium (0.5 M) ZnO NPs of 1 ml.

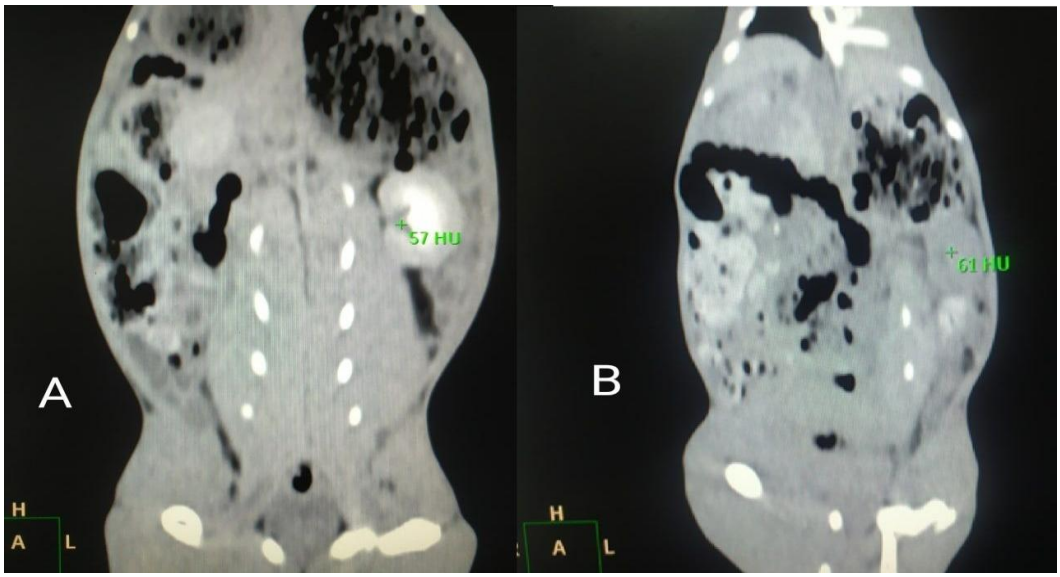

Figure 2: CT-scan images of rabbit's kidney with A. iodine(1.4M) and B. with alternative contrast medium (0.5 M) ZnO NPs of 1 ml.

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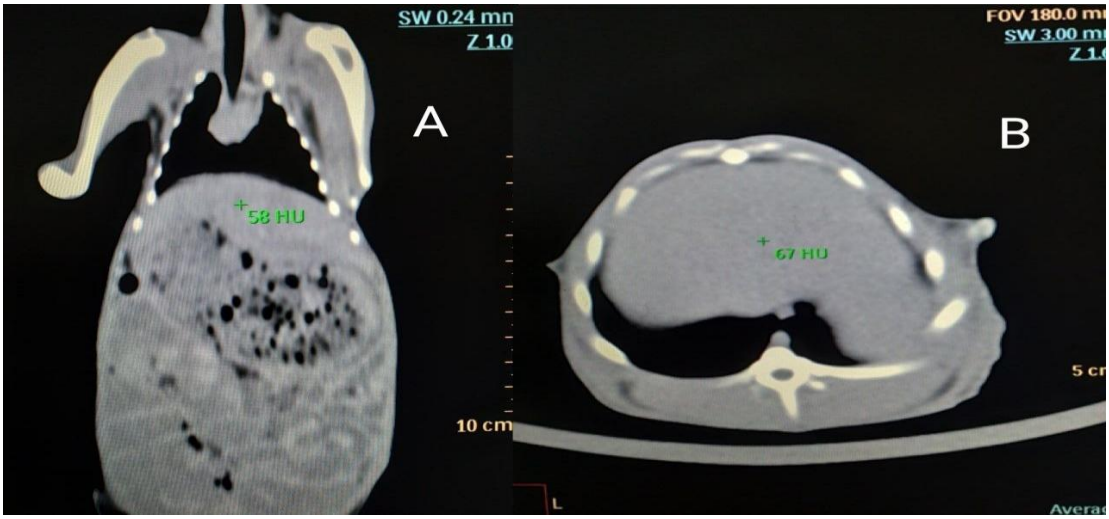

Figure 3: CT-scan images of rabbit's liver with A. iodine(1.4M) and B. with alternative contrast medium (0.5 M) ZnO NPs of 1 ml.

Cyclic voltammetric study

Electrochemical study of the iodine compound in the blood medium

The iodine compound has been used as one of the common and only contrast medium used in computed tomography at present. It also showed the electrochemical properties in the blood medium as an oxidizing compound, showed many peaks of the oxidation current in the blood, and strengthened the peak as shown in Figure 8. It can be concluded from this important analysis that all compounds containing iodine oxidize harmful substances through their interaction with blood composition, which causes unwanted symptoms when administered intravenously to all patients who undergo diagnostic x-rays and computed tomography, in addition to the dangerous symptoms it causes for those with kidney, liver or heart failure. To avoid complications of contrast iodine intermediates that may cause death in certain cases or permanent diseases, and at the same time, the diagnosis required for this technique is not used [17, 18].

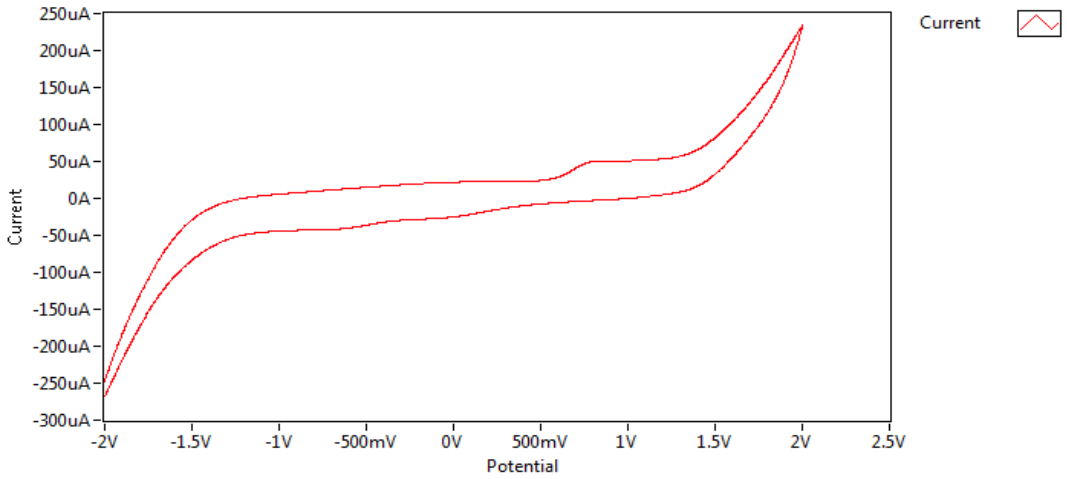

Figure 4: cyclic voltammogram of Iodine in rabbit's blood medium on GCE versus Ag/AgCl as reference electrode at 0.1 Vsec-1

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Effect of zinc oxide nanoparticles solution in the rabbit's blood medium

A solution of zinc oxide nanoparticles was used as an alternative contrast medium in computed tomography, and it was studied using an electrochemical method by measuring cyclic voltammetry. ZnO NPs solution has good electrochemical properties, especially in blood medium. It was found that ZnO NPs in the blood act as an antioxidant agent as shown in Figure 9, that the current limit peak of Zn (II) is in the potential region of -0.75 V without any oxidation peak appearing, so the ZnO NPs can be considered as an antioxidant agent because Free radicals receive an electrochemical reaction with hematopoiesis. Therefore, solution ZnO NPs can be used as an alternative contrast medium in safety behavior in blood medium [19-21].

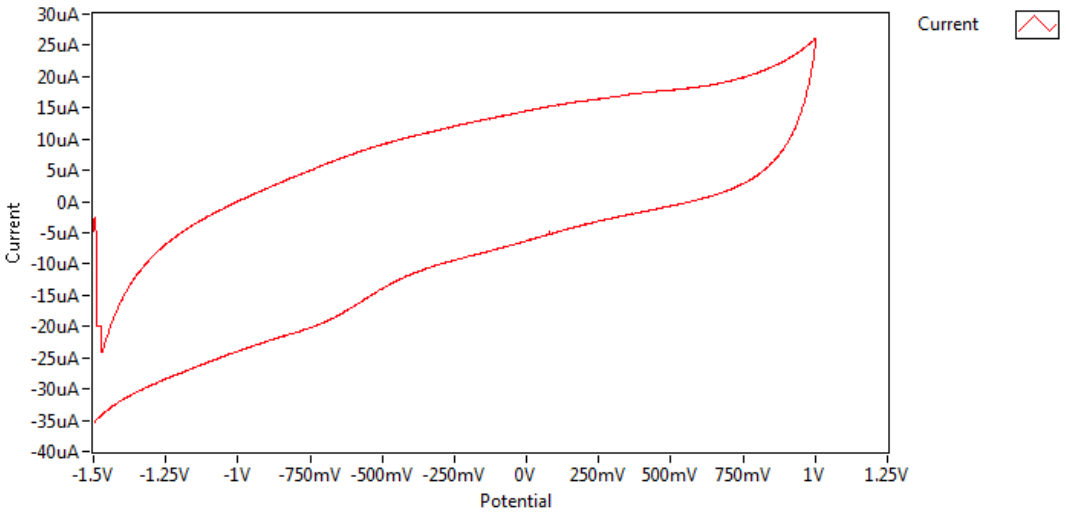

Figure 5: cyclic voltammogram of ZnONPs solution in rabbit's blood medium on GCE versus Ag/AgCl as reference electrode at 0.1 Vsec-1.

Discussion

This examination was taken for the heart , kidney and liver organs without using any contrast media, then the iodine contrast (370 mg/ml) and the alternative contrast ZnO solution (0.5 M). The Hounsfield unit (HU) factor values can be used to determine the resolution of the CT-scan images. It was found from the results of the rabbit's heart without using contrast medium, the HU values of the heart was 45, as illustrated in table 1. when using different doses of iodine (370 mg/ml) 1, 2, 3, 4 and 5 ml respectively the HU values of the heart organ of 58, 146, 210, 353, and 407, as illustrated in figure1. when using alternative contrast agent of ZnO NPs solution of different doses of 1,1.5, 2,2.5, and 3 ml. respectively the HU values of the heart organ was 83, 177, 268, 360, and 465 as illustrated in figure1.

It was found from the results of the rabbit's kidney without using contrast medium, the HU values of the heart was 48, as illustrated in table 1. when using different doses of iodine (370 mg/ml) 1, 2, 3, 4 and 5 ml respectively the HU values of the kidney organ of 57, 58, 61, 65, and 67, as illustrated in figure2. And when using alternative contrast agent of ZnO NPs solution of different doses of 1,1.5, 2,2.5, and 3 ml. respectively the HU values of the kidney organ was 61, 70, 73, 79, and 87 as illustrated in figure2.

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It was found from the results of the rabbit's liver without using contrast medium, the HU values of the heart was 49, as illustrated in table 1. when using different doses of iodine (370 mg/ml) 1, 2, 3, 4 and 5 ml respectively the HU values of the liver organ was 58, 65, 69, 72, and 75, as illustrated in figure3. And when using alternative contrast agent of ZnO NPs solution of different doses of 1,1.5, 2,2.5, and 3 ml. respectively the HU values of the liver organ was 67, 74, 82, 85, and 93 as illustrated in figure3. It is noted that the results of the examination when using the alternative contrast medium (ZnO solution) gave encouraging results (higher HU values and using low doses) than that shown in the case of using iodine solution , moreover the safety of using ZnO solution.

Conclusion

ZnO NPs solution is a safe compound that can be used as an alternative contrast medium without any side effects in a CT scan. In the electrochemical analysis of ZnO NPs solution which only showed one peak of reducing current in blood medium, while iodine compound contains oxidation current peak, so ZnO NPs is antioxidant compound and iodine is oxidizing compound. On the other hand, the solution of ZnO NPs has been used as a good alternative contrast medium due to the improved imaging to diagnose the abdominal organs as in rabbit heart, kidneys and liver. The Hounsfield unit (HU) values have the high values when using an alternative nano contrast medium (ZnO NPs) comparison with iodine contrast medium which gives high resolution of CT-scan imaging. The HU value is 683 for the heart organ when an alternative contrast medium is used while the value HU is 407 for the iodine compound. The resolution of CT scan imaging has the low in iodine solution, but ZnO NPs has high resolution without any side effect for the patients. On the contrary, many side effects happened for the patients through using iodine solution. Therefore we recommend using ZnO NPs solution as an alternative method in diagnosing via CT-scan.

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