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A study of using manganese chloride (MnCl2) solution as an alternative of contrast medium for iodine in computed tomography (CT) imaging

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ABSTRACT

Iodine solution is the only contrast medium currently used in the computed tomography scan (CT scan) examination. In the present study manganese chloride (MnCl2) solution has been chosen as alternative contrast medium in computed tomography scanning (CT scan). It was found that using MnCl2 solution as an alternative contrast medium in rabbits which enhanced the CT scan imaging in the resolution and increasing the Hounsfield unit (HU) values of heart and kidney organs in comparison with the iodine compound at the same doses.

It was chosen the heart and kidney of rabbits to study the effect of using the iodine and MnCl2 solution as alternative contrast medium in CT scan imaging, the following results: the native has 45 HU for heart and 50.1 for kidney organ. While the results of using iodine solution at dose of 3 ml has 83 HU for heart and 164 HU for kidney organ. In the MnCl2 solution which used as alternative of contrast medium has 83 HU for heart and 70.3 HU for kidney at 2.5 ml of 0.5 molar of solution. From these results the resolution of CT scan image has well and clears when using the alternative contrast medium (MnCl2). We can concluded that the alternative contrast medium of MnCl2 solution has good HU values of both heart and kidney comparison with iodine solution.

Keywords: MnCl2 solution, contrast medium of CT scan, rabbits, Hounsfield unit, iodine

INTRODUCTION

Through the different studies of alternatives to the contrast media which used in different radiological techniques that have important effects on human health and to avoiding the side effects from the use of current contrasts media such as iodine and gadolinium harmful to the health [1-4]. Paramagnetic and hypo magnetic metals are used as contrast materials for magnetic resonance (MR) techniques. The metal gadolinium lanthanide (Gd) was the predominant and most prevalent semi-magnetic contrast agent until the discovery and association of the mineral with nephrogenic systemic fibrosis (NSF), a rare but serious side effect in patients with kidney or kidney problems. Manganese was one of the earliest reported examples of paramagnetic contrast materials for magnetic resonance imaging due to its positive active contrast enhancement [5]. Manganese-enhanced magnetic resonance imaging (MRI) is a well-established neuroimaging method for signal enhancement, and functional studies in the rat. Further, with the increasing availability of positron tomography (PET) and magnetic resonance imaging devices, interest in using Mn^{2+} as a contrast agent. In this work, we differentiate and compare the radioactive Mn^{2+} uptake in the brain of mice for MRI and PET, respectively. Additionally, we examined the Mn^{2+} in bioassay of mice [6]. Two of manganese polysulfide (II) complexes, Mn-DTPA cystamine polymers and Mn-EDTA cystamine polymers were synthe-

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sized and labeled as novel molecular contrast agents that could be degradable by MRI. Contrast enhancement of manganese-based contrast agents was evaluated in mice carrying with human breast cancer xenografts, compared with MnCl2 [7]. Clinical applications of manganese-based MRI contrast agents are intravenous (intravenous) and oral formulations. The preparation is a commercially available manganese-dimeridoxyl diphosphate chelate; whereas the oral formulation is a blend of MnCl2, alanine and vitamin D3, which is currently undergoing clinical trials. The formulations and preclinical and pharmacokinetic studies of both formulations are discussed. The main reported clinical difference between the two formulas is that intravenously. Administration exposes all organs, while oral ingestion only exposes the enterohepatic circulation [8]. Magnetic resonance imaging (MRI) is in increasing demand by researchers in many biological disciplines. Not only is the use of high field magnets to obtain satisfactory spatial resolution, but the achievement of adequate contrast between tissues also requires determination of applicable imaging parameters by cost and time- depreciation procedures. Systematically ingested manganese can act as an effective contrast agent in rapid imaging MRI. Due to the tendency of manganese ions to differentially accumulate in most soft tissues, higher overall signal intensity and strongly improved contrast between structures yield data well suited to digital post-processing in 3D models [9].

In this work, the enhancement of computed tomography imaging by chemical contrast media was studied by using an alternative of iodine contrast agent of a manganese compound.

MATERIALS AND METHODS

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. Manganese chloride ($MnCl_2$) was used from Chinese SCRC (China). 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 manganese chloride 0.5 M $MnCl_2$

A 0.5 molar solution of pure manganese chloride (Chinese SCRC) was prepared in a 10 ml volumetric flask, and the crystals were dissolved in deionized water to obtain a 0.5 molar solution of manganese chloride which used as alternative contrast medium.

CT scan apparatuses

The CT scan screw type General Electric (GE) model TC Revolution EVO 128 Slices, GE Healthcare.

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.

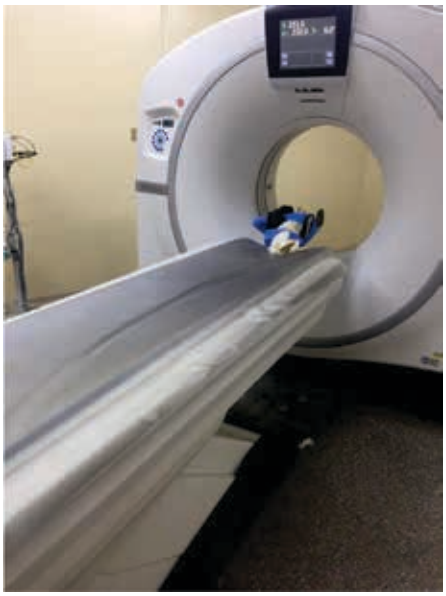

FIGURE 1. *Preparation of the rabbit in CT scan*

Cyclic voltammetric apparatuse

Ezstat series (potentiostat / glvanostat) NuVant Systems Inc. pioneering electrochemical technologies USA.

Pyrex cell measuring 10 milliliters and three electrodes was used:

a. Working electrode: where the glass carbon electrode (GCE) was used

b. Reference electrode: where Ag / AgCl silver electrode (3M KCl) was used

c. Counter electrode: Where to use a platinum wire (1 mm diameter)

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 2. The glassy carbon electrode (GCE) was used in this study after cleaning with alumina grand and sonic technique for 10-15 min [10].

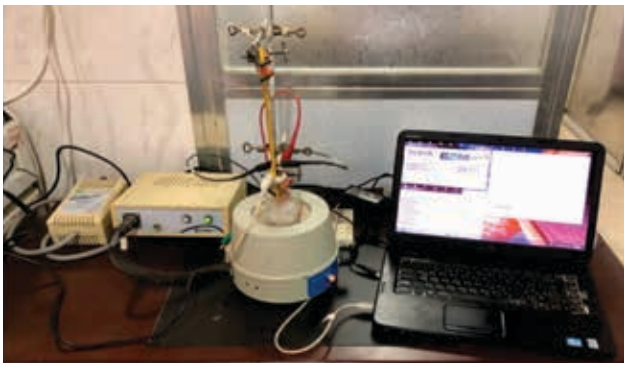

FIGURE 2. *Cyclic voltammetry parts*

RESULTS AND DISCUSSION

Study the rabbits by CT scan

The rabbits were chosen for a CT scan to check different organs of the rabbits' abdomen, especially the kidneys and the heart. The first group is the group that studied rabbits with CT scans without using (pre) contrast media. The second group, in which the spatial survey of rabbits was studied using an alternative contrast medium for manganese chloride solution, where the kidneys and heart of rabbits were studied via intravenous manganese chloride alternate contrast at a concentration of 0.5 mol at different doses (1, 1.5, 2, and 2.5 ml) and the tests were performed following using CT scanning.

CT scan examination of heart organ

This examination was taken for all members of the abdominal area of the body of the rabbits such as kidney and heart without using any contrast media, then the iodine contrast and the alternative contrast ($MnCl_2$ solution) were used for the examination was taken for the heart and kidney organs in the rabbits. The Hounsfield unit (HU) factor values can be used to determine the clarity of the CT scan image.

Hounsfield unit (HU): Absorption coefficient unit of radiolucency of a substance; HU is normalized to water, where water = 0 HU, air = -1000 HU and bone = 1000 HU, the HU values in the CT scan are reported for each case taken for the studied rabbits as in the following [3]:

1. The CT scan imaging of the heart Tests were taken to turn the rabbits into the following three cases: A. Checking the heart without using the contrast medium (native). It was found from the results as in Figure 3 of the rabbit's heart without using any contrast medium, and the value of the clarity of the heart of the HU value was 45 as illustrated in table 1.

B. The CT scan of cardiac examination using an iodine contrast medium which illustrated in Figure 4 with HU value of heart clearness have 53, 62, and 83 when using 1, 2, and 3 ml dose of iodine respectively, where diagnosis is possible.

C. Cardiac examination using alternative contrast medium of manganese chloride solution which illustrated in Figure 5, it was found an enhancement of the heart CT scan imaging by higher HU values compering with the HU values at iodine and native cases. Table 1 discuss the HU values when using alternative contrast agent ($MnCl_2$ solution) of 49.6, 65.1, 69.6, 70, and 83.3 at the doses of $MnCl_2$ solution of 0.5, 1, 1.5, 2, and 2.5 ml respectively, it is a good enhancement of CT scanning when using the alternative contrast medium comparison with iodine contrast, moreover the safety of using $MnCl_2$ solution.

TABLE 1. *HU values of heart and kidney of rabbits at different contrast media*

Contrast medium	Dose (ml)	Heart (HU)	Kidney (HU)
Native	-	45	50.1
Iodine	1	53	51.0
	2	62	70
	3	83	164
$MnCl_2$ (0.5 M)	0.5	49.6	56
	1	65.1	60.1
	1.5	69.6	65.3
	2	70	67.4
	2.5	83.2	70.3

CT scan examination of kidney organ

Other organ can be studied of the rabbit in CT scan examination to finding the differences of the imaging resolution under using different contrast media, with iodine and alternative contrast agent

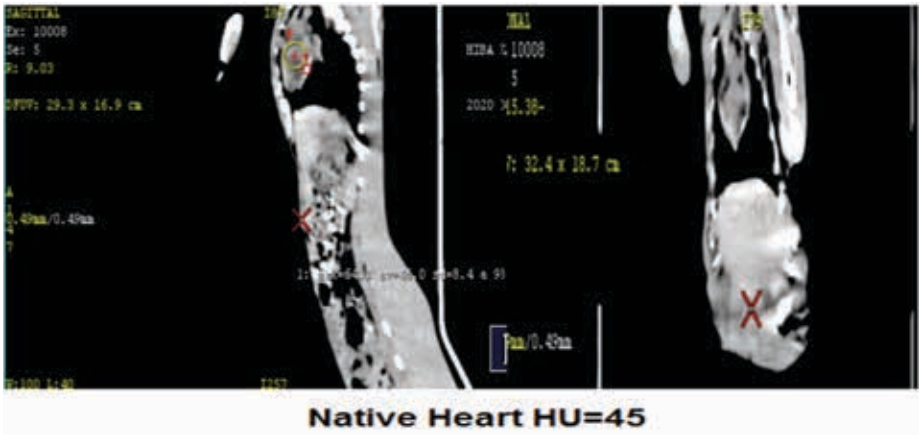

FIGURE 3. *CT scan imaging of rabbit's heart without contrast media (HU = 45)*

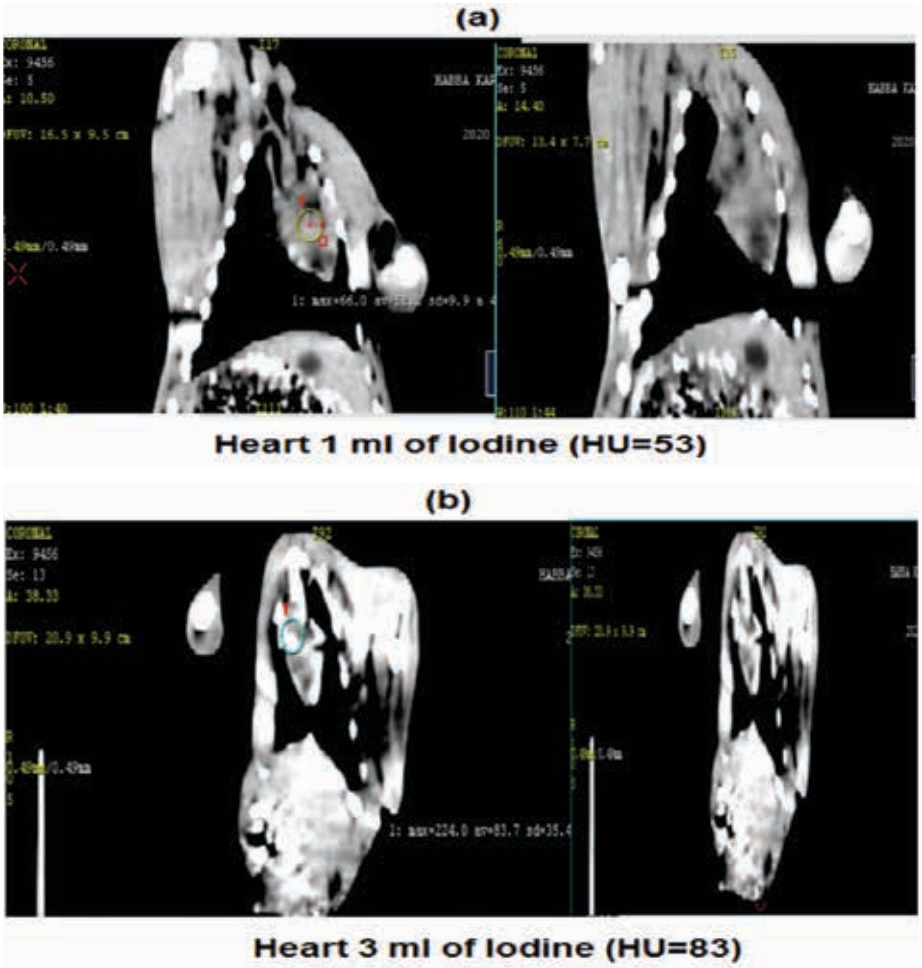

FIGURE 4. *CT scan imaging of rabbit's heart using iodine contrast medium at different dose (a) at 1 ml (HU = 53), and (b) at 3 ml (HU=83)*

of $MnCl_2$ solution by using HU values to evaluation which contrast more active in the resolution of kidney organ of rabbit. The HU values in the CT scan are reported for each case taken for the studied rabbits as in the following:

A. Native examination

The native exam of CT scan for kidney organ has 50.1 of HU value as shown in table 1 and Figure 6. The resolution of CT scan imaging for native exam is still low in the HU value because no contrast used in both heart and kidney.

B. Iodine contrast medium examination

It was used iodine contrast medium at different doses for the kidney organ of rabbit of 1, 2, and 3 ml. the resolution of CT scan imaging has HU values at 52, 70, and 164 respectively as shown in Figure 7, the resolution of CT scan gradually enhanced with increasing the iodine dose, but the

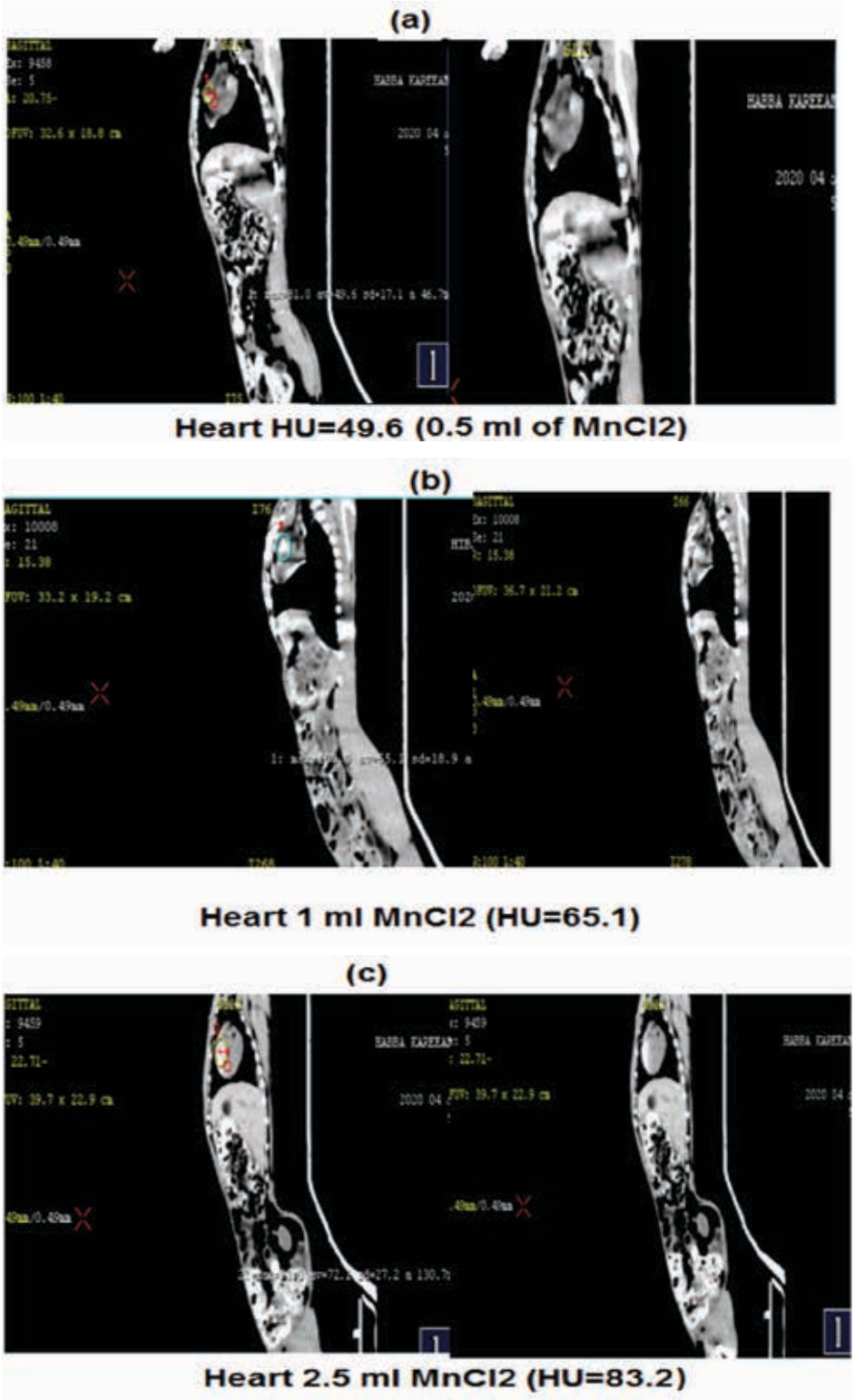

FIGURE 5. *CT scan imaging of rabbit's heart using an alternative contrast medium MgCl2 at different dose (a) at 0.5 ml (HU = 45), (b) at 1ml (HU=65.1) and (c) at 2.5 ml (HU=83.2)*

side effects of iodine compound increased for the patients [11].

C. Alternative contrast medium of $MnCl_2$ solution examination

From table 1 can be found the results of using the alternative contrast medium of MnCl2 solution for diagnosis of kidney imaging at different doses of 0.5, 1, 1.5, 2, and 2.5 ml with HU values of 56, 60.1, 65, 67.4, and 70.3 respectively as shown in Figure 8. It was found the resolution of CT scan imaging has been enhanced with increasing the dose of MnCl2 solution, so the alternative contrast

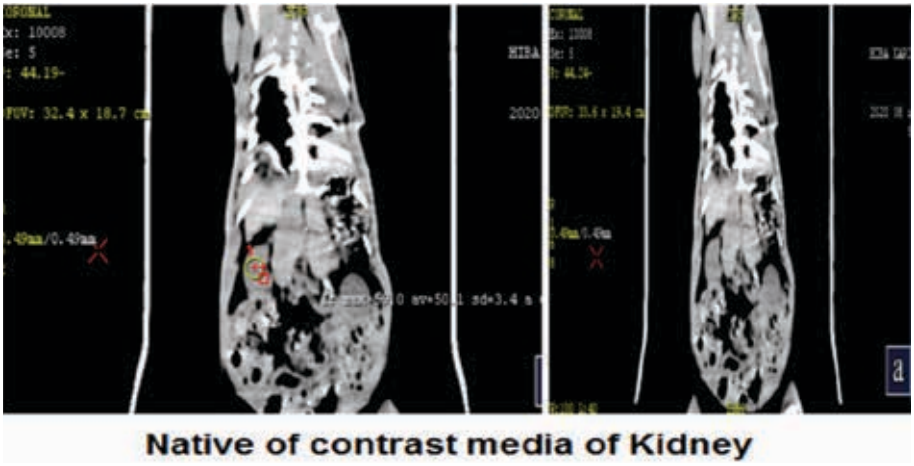

FIGURE 6. *CT scan imaging of rabbit's kidney without contrast media (HU = 50.1)*

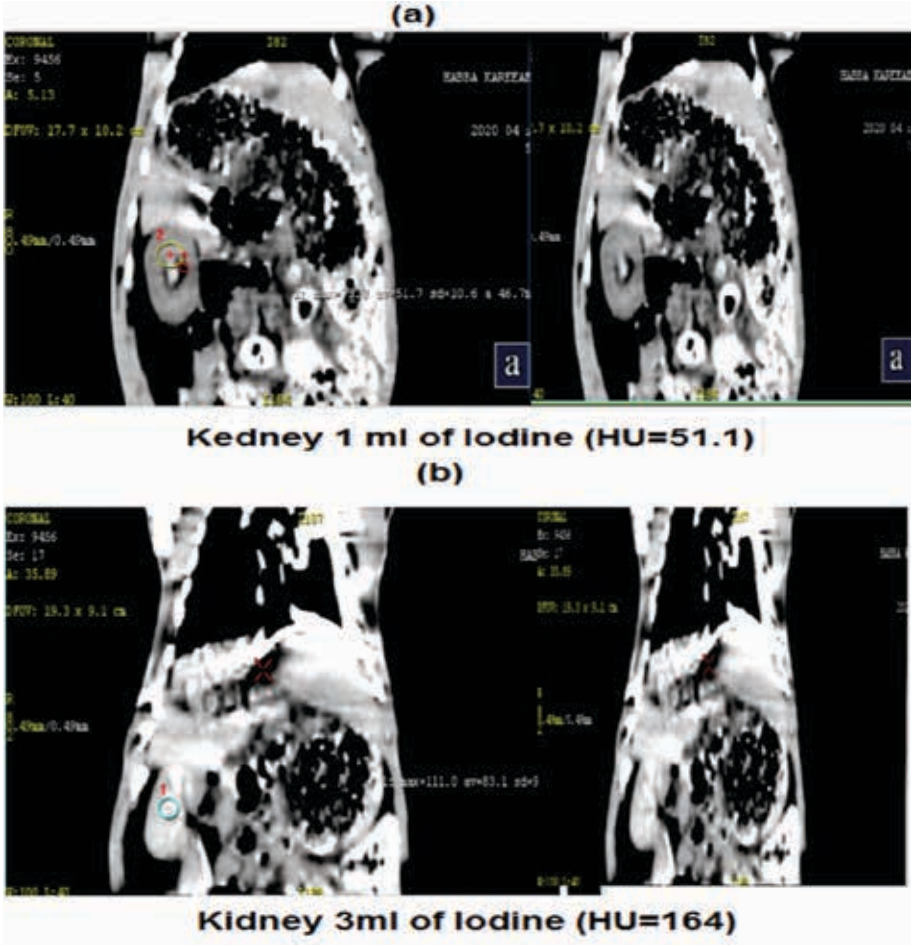

FIGURE 7. *CT scan imaging of rabbit's kidney using iodine contrast medium at different dose (a) at 1 ml (HU = 51), and (b) at 3 ml (HU=164)*

agent has safety using for humans because manganese ion is one of Nutritional supplements in the human body [12].

Voltammetric study – Electrochemical study of the iodine compound in the blood medium

An iodine compound has been used as one of the popular and only contrast media used in images using X-ray and spiral computed tomography at the present time. It also showed electrochemical properties in the blood medium as an oxidizing reagent, it showed several oxidative peaks in the blood and enhanced the two peaks of the oxidation current by increasing the concentration of the iodine compound added to the blood as shown in Figure 9. It can be concluded from this important

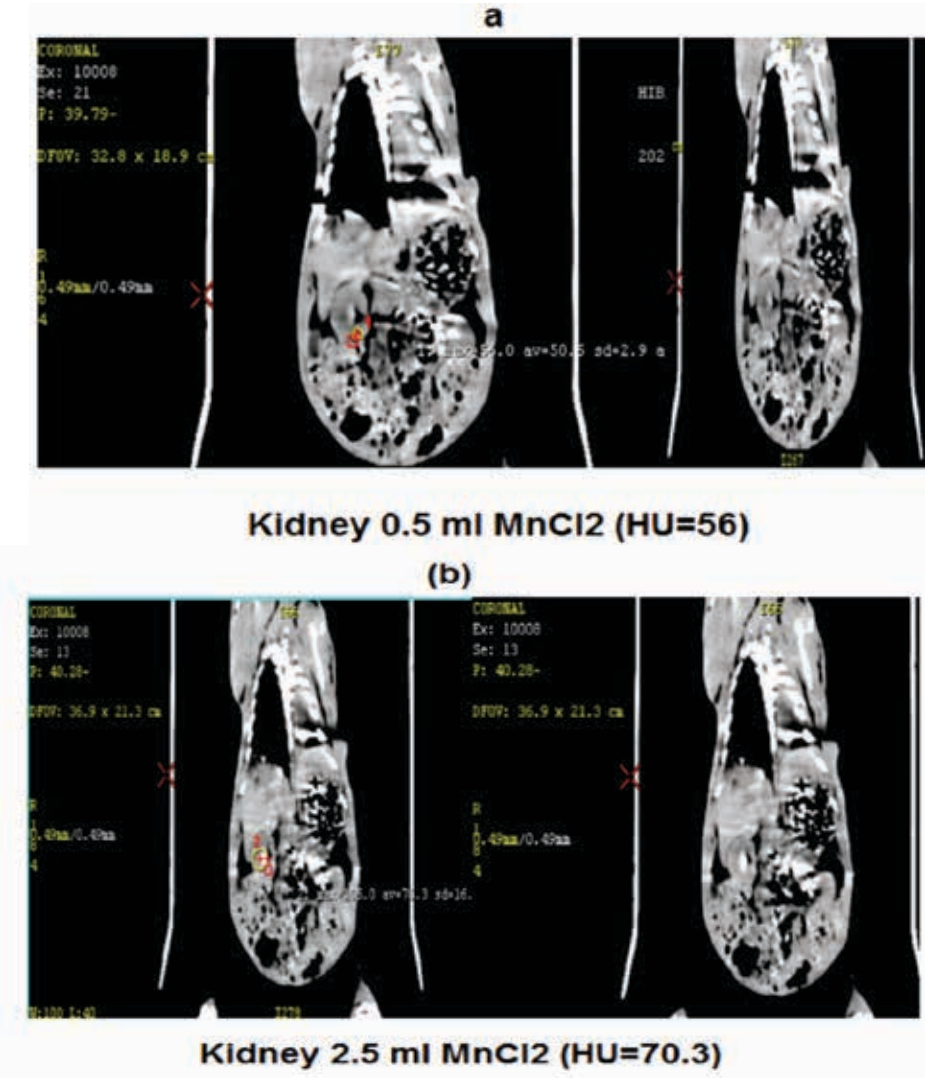

FIGURE 8. *CT scan imaging of rabbit's kidney using an alternative contrast medium MgCl2 at different dose (a) at 0.5 ml (HU = 56), and (b) at 2.5 ml (HU = 70.3)*

analysis that all compounds containing iodine They are harmful oxidizing substances through their interaction with the blood composition, which causes undesirable symptoms when administered intravenously to all patients who undergo diagnosis with both X-ray and tomography techniques, in addition to the dangerous symptoms they cause for those suffering from kidney or liver failure or heart disease Iodine should not be given for contrast to avoid complications that may cause death in certain cases or permanent diseases, and at the same time, the diagnosis required for this technique is not used [13,14].

Voltammetric effect of manganese chloride in the serum blood medium

Manganese chloride ($MnCl_2$) the alternative contrast medium was used in CT scan, it was studied using an electrochemical method by cyclic voltammetry. Manganese chloride solution has good electrochemical properties, especially in the blood medium. It has been found that Mn(II) in the blood which acted as an anti-oxidative agent as shown in Figure 10 illustrated the appearance of reduction current peak of Mg(II) in potential region at -0.55 V, so MnCl2 solution can be considered as anti-oxidant agent because it received the free radical in the electrochemical reaction with blood composition. So, it can be used MnCl2 solution as alternative contrast medium in safety behavior in blood medium [15,16].

CONCLUSIONS

Manganese chloride ($MnCl_2$) solution has good electrochemical properties and is safe to be used as

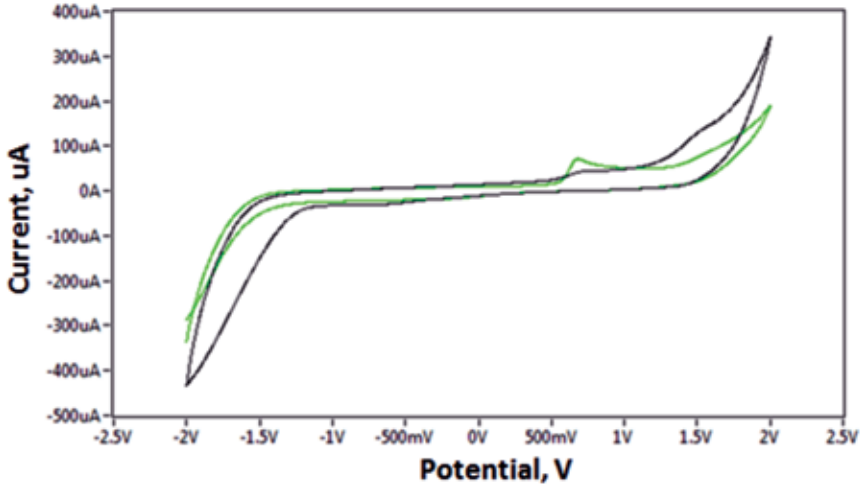

FIGURE 9. *Cyclic voltammogram of Iodine solution at different concentrations in blood medium*

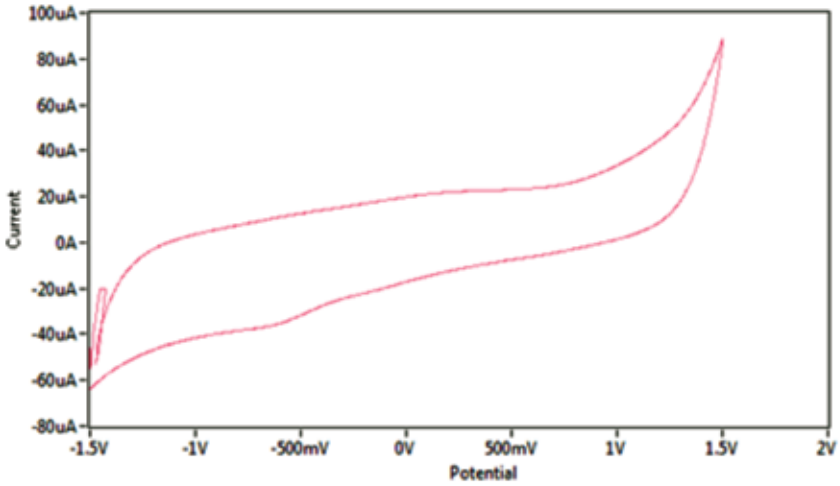

FIGURE 10. *Cyclic voltammogram of $MnCl_2$ solution in blood medium*

an alternative contrast medium without side effects for CT scan examination. The $MnCl_2$ solution contains only the peak of the reducing current in the blood medium, while the iodine complex contains two oxidation current peaks, so manganese chloride is an antioxidant compound and iodine is an oxidizing compound. On the other hand, the $MnCl_2$ solution has been used as an alternative contrast medium due to the improved imaging for diagnosing the abdominal organs as founding in the rabbit heart of the value of HU = 83.2 when using alternative contrast medium and the same value when using iodine contrast medium. The HU value is 70 for kidney organs when using the alternative contrast medium and iodine compound. The resolution of CT scan imaging has the same in iodine and $MnCl_2$ but the side effect is high in iodine compound and safe in $MnCl_2$, so we recommend using $MnCl_2$ solution as an alternative medium in the diagnosis by CT scan.

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