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Evaluation Study: The Effect of Using Ascorbic Acid with and without Contrast Agent on Patient Blood Samples Exposed to Different X-Ray by Cyclic Voltammetry

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Abstract

Ascorbic acid commonly referred to as vitamin C, a naturally occurring antioxidant, can lessen the negative effects of ionizing radiation. With regard to medical imaging, contrast agents are frequently employed to improve the visibility of particular body structures throughout X-ray examinations. The purpose of the presented work is using cyclic voltammetric analysis to assess the impact of utilizing contrast medium (iodine solution), both without and with ascorbic acid (AA), on patient blood samples exposed to different X-rays. In this study, we investigate whether the addition of ascorbic acid in combination with a contrast agent, can provide any protective effects against X-ray-induced damage to blood samples. The result shown that the ionized radiation of x-ray acts as oxidative effect on the blood components, and contrast medium enhance the oxidation current peak of the blood medium. But, when using AA with the contrast medium the results have been inhibited the oxidative effect and reduce the oxidation peak into minimum values. Using ascorbic acid (AA) solution is very important to inhibit the oxidative effect of contrast agent with ionizing radiation because AA acts as a good anti-oxidative factor in blood composition. So, it is necessary taking AA solution before exposed to the ionizing radiation by x-ray, so it can be recommended to take AA solution with the contrast medium through scanning x-ray examination.

Keywords: Cyclic Voltammetry, Iodine solution, X-ray, Ascorbic acid, Patient blood sample

1. Introduction

Medical imaging uses ionizing radiation, like X-rays, extensively for diagnostic imaging (Arivalagan *et al.*, 2015; Smith-Bindman *et al.*, 2012; Khan *et al.*, 2023). On the other hand, as Scheme 1 illustrates, exposure to ionizing radiation could result in the generation of reactive oxygen species (ROS), which could cause oxidative stress and possible damage to tissues and cells (Karabulutoglu *et al.*, 2021; O'Neill & Wardman, 2009; Mohamed *et al.*, 2014). According to reports, ascorbic acid possesses antioxidant qualities (Brink & Boice Jr, 2012; Prasad, 2005; Stehli *et al.*, 2014; Radhi *et al.*, 2010), which makes it a viable option for reducing damage from radiation. Furthermore, contrast agents are frequently used in X-ray imaging (Piechowiak *et al.*, 2015; Celik *et al.*, 2016; De La Vega & Häfeli, 2015), and little is known about how they interact with ascorbic acid to affect blood samples exposed to X-rays (Materska *et al.*, 2015; Yamamoto & Kinoshita, 2017; Kayan *et al.*, 2009).

Impact of gamma and X-ray ionizing radiation on the stability of various radio-contrast media employed in diagnostic imaging in terms of their molecular structure. Gamma rays and x-rays have been used for exposing eight distinct kinds of iodinated contrast media (three ionic and five nonionic). The chemical composition regarding contrast media, both nonionic and ionic, did not alter when exposed

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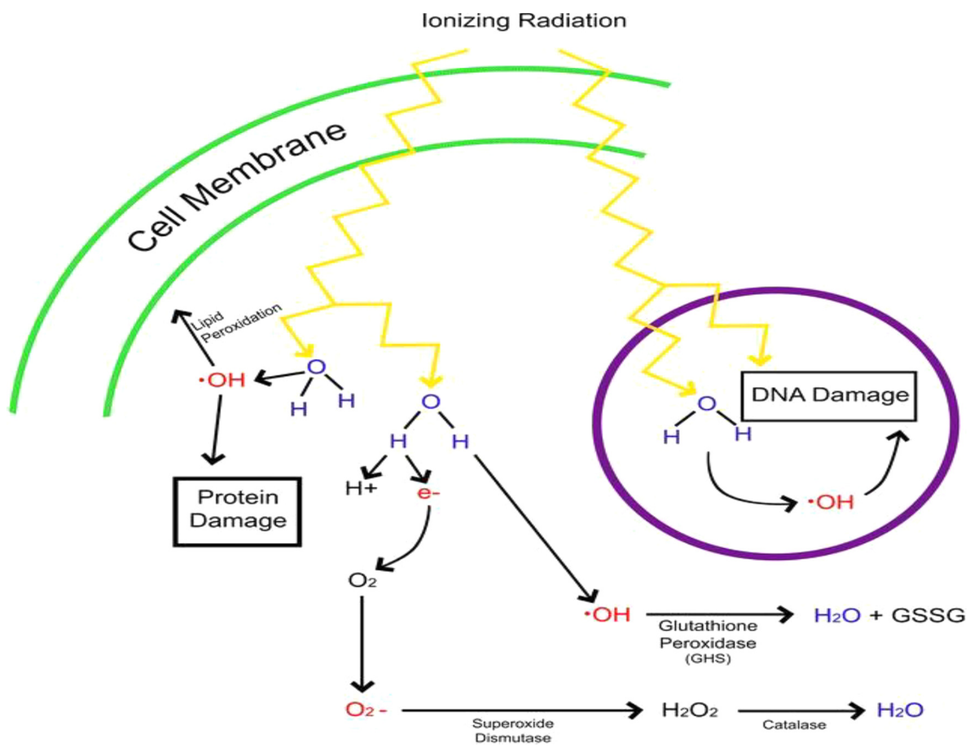

Scheme 1. Biological effect of ionizing radiation.

to x- or gamma-ray radiation. The radiation levels in x-ray examination rooms are far lower than those utilized in this study since, unlike throughout the testing, the samples have not been directly irradiated. This is an essential point to notice (Pinho *et al.*, 2009). X-rays are frequently used in medicine to identify and cure illnesses. Computed tomography (CT) can be defined as one of the most helpful diagnostic radiology tests when it comes to using X-rays for diagnosis. Furthermore, this examination is now much simpler and more informative thanks to latest advancements in CT technology, which has boosted its use, particularly in Japan. Nevertheless, compared to standard X-ray exams, CT scans have a higher radiation dosage. As a result, although they were the subject of several research, the health risks associated with CT scans remain debatable. Consequently, analysis is being done on the biological as well as cytogenetic consequences of CT (Shi & Tashiro, 2018).

Even at lower doses, prolonged exposure to ionizing radiation (IR) could have detrimental effects on health. Complete blood counts (CBCs) have been the primary focus of earlier biomonitoring research, with varying degrees of success. A radiation worker's personal film badge dosimeter has been used for measuring the amount of radiation that was absorbed. Adjusted multiple linear regression models have been used for measuring and analyzing the specified covariates as well as the biomarkers under study. All radiation workers had exposure levels below dosage limits (overall mean radiation dose = 1.18 mSv). When put to comparison with control group, the mean difference in other vital indicators among radiation workers was not statistically significant. This work shown that even at low doses, prolonged exposure to ionizing radiation is linked to a considerable rise in blood levels of specific biomarkers (eosinophils and Il-6), which could lead to repercussions on health later on, including cancer (Bahrami Asl *et al.*, 2023). With the use of Embase and PubMed, the in vitro, ex vivo, and in vivo radioprotective effects of vitamins were examined, adhering to PRISMA statement. It is possible to utilize vitamins C, A, D, and E alone or in combination with other substances that are both non-food and food. Nutritional supplements or vitamins in their natural form can help lessen the negative effects of radiation on the organs, body, and/or cells. Out of thirteen vitamins, just four (C, A, E, and D) were found to have radiation protective characteristics; vitamin E is the most abundant, followed by A, C, and D (Lledó *et al.*, 2023).

Radiation exposure happens during interventional procedures guided through CT or X-ray, and γ-H2AX foci are recognized as a biomarker of radiation-induced damage because they reflect DNA double-strand breaks (DSBs). Through binding free radicals, antioxidants can lessen the induction regarding γ-H2AX foci. Establishing a dose-effect and time-effect relation for individual antioxidants on DSBs in human blood cells was the goal of the presented work (Brand *et al.*, 2015). In order to guarantee an accurate and timely diagnosis, medical imaging has grown to be a crucial part of patient treatment. Regretfully, ionizing radiation is used in a lot of imaging techniques to produce images. Even at modest levels, ionizing radiation could damage DNA directly and produce free radicals and ROS that harm proteins and lipid membranes. Necrosis, apoptosis, carcinogenesis, or teratogenesis may result from this cell damage. CT exposure alone may be responsible for up to 2% of cancer incidences and the 15,000 deaths that result from them each year. Studies on radioprotective agents were conducted on a variety of models, including animals, humans, and cells. Date indicates that radioprotective agents, via diverse mechanisms, possess the capability to mitigate free radical damage resulting from exposure to ionizing radiation. In order to lower the mortality and morbidity rates of patients exposed to ionizing radiation, radiation protection agents could be a helpful addition to medical imaging. Antioxidant-rich foods contain significant levels of several radiation-protective agents, indicating that a particular diet may be beneficial for radiation prevention (Smith *et al.*, 2017).

X-rays, or ionizing radiation, are frequently employed in medicine for both treatment and diagnosis. However, these advantageous applications could put the patient and staff in the cardiac catheterization lab in risky situations. The purpose of the current study was to assess alterations in certain blood cell constituents following radiation exposure throughout cardiac catheterization. Thirty-three individuals were included in a statistical comparison study of blood components taken before radiation (as a control group) and shortly after radiation. Post-irradiation mean RBC counts are $4.47 \pm 0.55 \times 10^{12}$/L and $4.84 \pm 0.59 \times 10^{12}$/L, respectively, substantially lower than pre-irradiation values; similarly, plasma hemoglobin Hb is 11.95 ± 1.55 g/dL and $12.71 \pm 1, 62$ g/dL, and WBC is 6.87 ± 1.581 and 7.58 ± 1.577, respectively (Abdullah *et al.*, 2019). In animal models, chronic and acute radiation exposure was linked to excessive formation of ROS, which could have a number of detrimental and irreversible effects on important organs. Determining the oxidative stress status of radiology unit workers exposed to modest doses of continuous radiation was the goal of this investigation (Malekirad *et al.*, 2005).

2. Patients and methods

2.1. X-ray examination

Fifty patients (25 male and 25 female) with ages range from 16–65 years were prepared to examine the x-ray in different doses.

Sample Collection: blood samples will be collected from 50 patients under the x-ray examination, The fifty patients were divided into five groups as in the following:

Group I: The test was performed on ten patients without exposed the x-ray radiation (control group).

Group II: ten patients were exposed in different doses of x-ray from 150–520 reem without contrast agent.

Group III: ten patients were given contrast medium (50 ml of iodine solution) and exposed with various doses of x-ray from 150–520 reem with contrast agent.

Group IV: ten patients were given contrast medium (50 ml of iodine solution) and exposed with various doses of x-ray from 236–300 reem.

Group V: ten patients were given contrast medium (50 ml of iodine solution) and ascorbic acid (AA) (50 ml of 0.1 Molar) and exposed with various doses of x-ray from 236–300 reem.

The five groups of patients (except group I) were examined in x-ray type Shimadzue HP/Flowro.

2.2. Cyclic voltammetry (CV) examination

Electrochemical analysis with cyclic voltammetry (CV) technique has been used to study the redox reaction of interactions between the hematopoiesis composition and the ionizing radiation (Radhi & Al-Mulla, 2015).

NuVant system Inc. based type potentiometer/galvanic station (USA) was used in-vetro electrochemical.

A 15 ml Pyrex cell and three electrodes have been utilized:

a. glass carbon electrode (GCE) has been utilized as working electrode.
b. Ag/AgCl silver electrode (3M KCL) has been utilized as a reference electrode.
c. a platinum wire (1 mm diameter) has been utilized as a counter electrode.

The three electrodes have been immersed in the blood samples being studied, coupled to a potential terminal, and connected to a computer to analyze the oxidation-reduction reaction-based blood sample

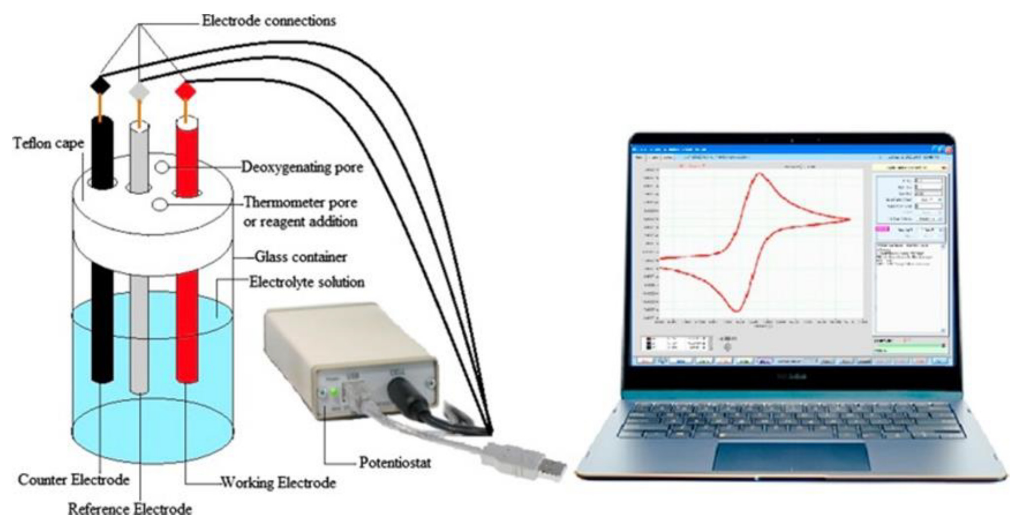

Fig. 1. Cyclic voltammetry set up.

characteristics. As seen in Fig. 1, all tests employed GCE cleaning following alumina polishing and sonicating for ten to fifteen minutes (Abdul-Amir *et al.*, 2017; Radhi *et al.*, 2013).

10 ml of blood samples were received from each patients to be examined in the cyclic voltammetry. The patient blood samples were examined in cyclic voltammetry as in the following:

a. Control Group: blood samples without any treatment exposed to X-ray.
b. Group I: blood samples without contrast medium and exposed to X-ray from 150–520 reem.
c. Group II: blood samples treated with a contrast agent and exposed to X-ray from 150–520 reem.
d. Group III: blood samples treated with contrast agent, exposed to X-ray from 236–300 reem.
e. Group IV: blood samples treated with contrast agent and AA, exposed to X-ray from 236–300 reem.

Blood Sample Analysis: After exposure, blood samples will be analyzed for various parameters, including oxidative stress markers.

3. Results and discussion

The results of this study will provide insights into the potential protective effects of the contrast agent, and in combination with ascorbic acid, on blood samples exposed to different X-ray doses. The data will be presented in a comprehensive manner, including graphical representations, to illustrate any significant differences between the experimental groups. The discussion section will interpret the study's findings, considering the potential implications for patient care and the underlying mechanisms responsible for the observed effects (Radhi *et al.*, 2017).

3.1. Effect x-ray in patient blood samples with and without contrast agent

The results showed that patient blood samples who were subjected to x-ray showed different doses of ionizing radiation that enhanced oxidative stress by increasing the radiation dose from 150 to 520 reem. Fig. 2 show the effect of the ionized radiation by x-ray compare to control samples that enhanced the oxidation peak (ΔIp) in cyclic voltammography against doses of 150, 175, 205, 329, 352, 401, 406, 410, 475, and 520 reem. Therefore oxidative stress was found in exposed patient blood samples and gradually increases against radiation doses as shown in Fig. 3.

Fig. 3 shows the results of good correlation with the linearity of the following equation with the sensitivity of the oxidation peak current for patient blood samples exposed to ionizing radiation of x-ray:

$$Y = 0.1617\,X - 26.546\ldots \text{ with a good sensitivity}$$

$$R^2 = 0.9274$$

3.2. Effect x-ray on patient blood samples with contrast and contrast with ascorbic acid

The results showed that patient blood samples contained contrast agent (Iodine solution) which were exposed to ionizing radiation at different doses using x-ray technique. It is enhanced at the peak of the oxidation current depending on the increase in the

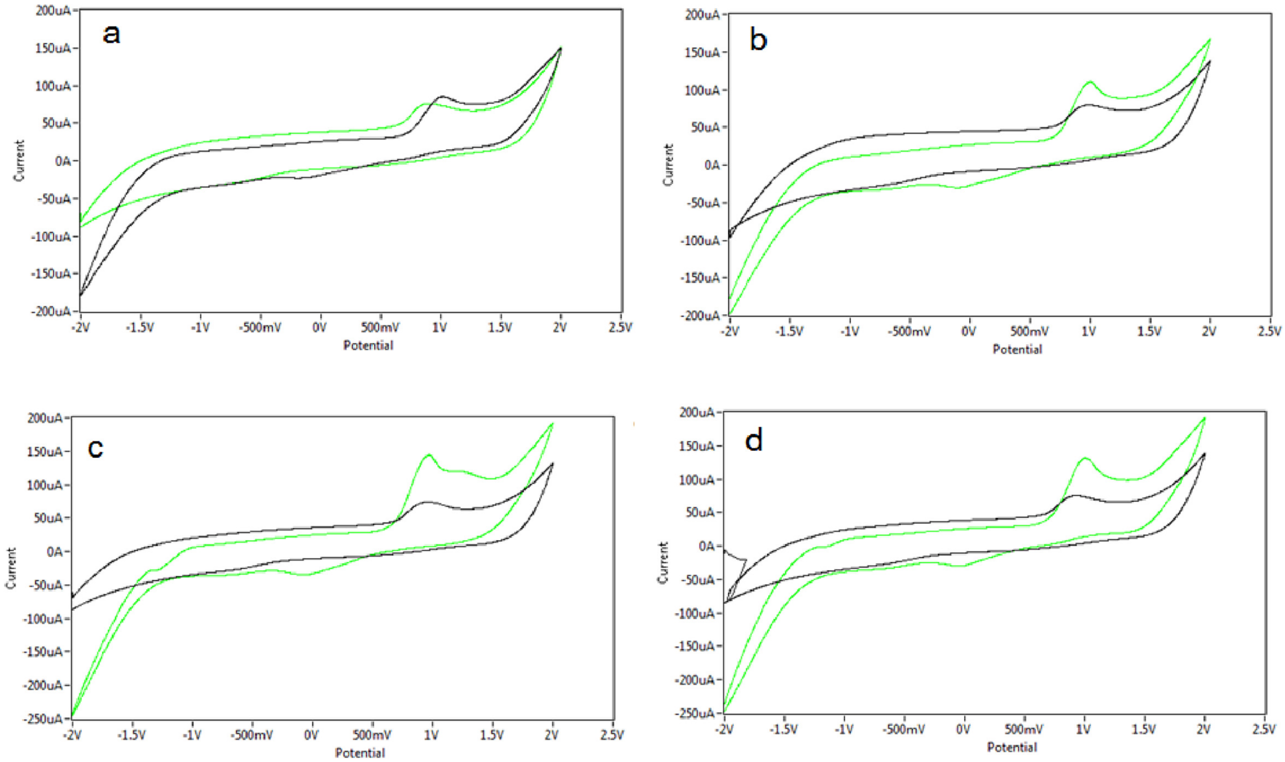

Fig. 2. Cyclic voltammogram of patient blood sample with and without contrast medium exposed with different X ray Dose (a) 150 Reem (b) 350 Reem (c) 400 Reem (d) 520 Reem (green line of blood with contrast and black line of the blood without contrast).

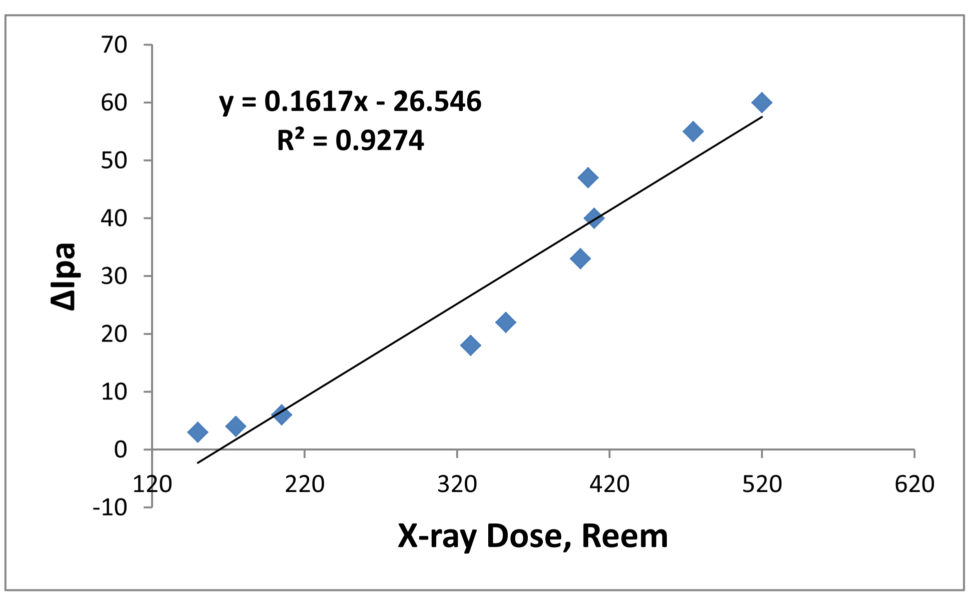

Fig. 3. Relationship between the oxidative difference (ΔIpa) of patient blood samples without contrast agent (Iodine solution) and with contrast against to the different doses of x-ray (150-520 reem).

radiation dose 150 to 520 reem. It has been found that contrast medium affects oxidation current peak of the patient blood samples (with contrast medium) enhanced the oxidation reaction, while adding ascorbic acid (AA) solution to patients that work to reduce oxidative stress compared to patient blood sample exposed with x-ray with contrast medium with different doses of 236, 240, 245, 250, 255, 260, 270, 275, 280, and

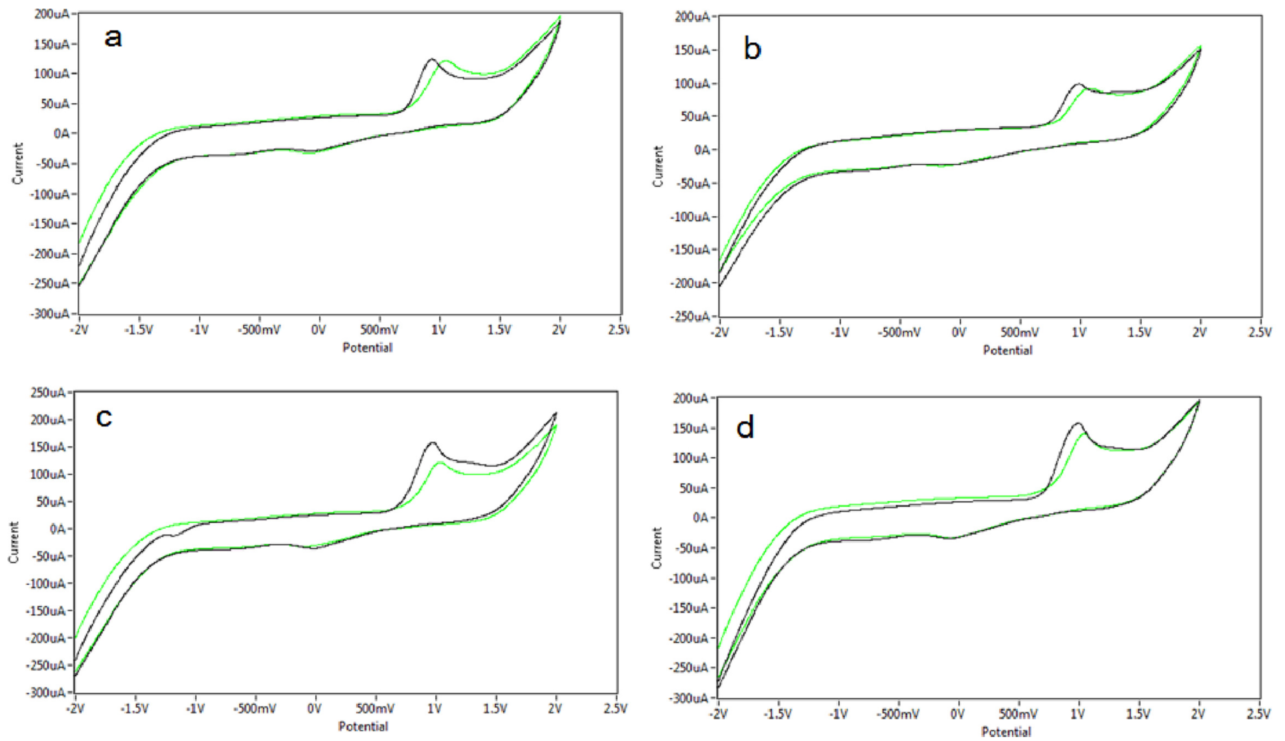

Fig. 4. Cyclic voltammogram of patient sample exposed with X-ray dosed (a) 236 Reem (b) 250 Reem (c) 275 Reem (d) 300 Reem (black line with contrast and green line with contrast and with AA).

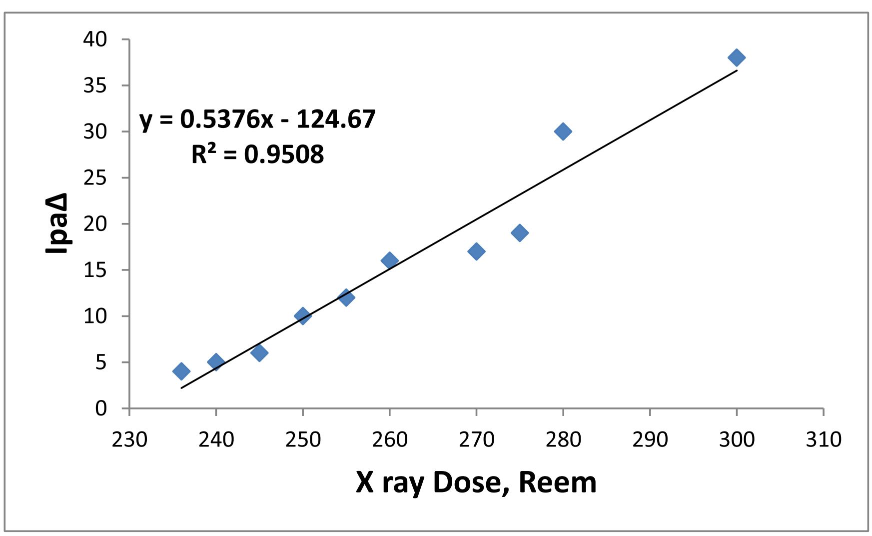

Fig. 5. Relationship between the oxidative difference (ΔIpa) of patient blood samples with contrast agent (Iodine solution) and with AA against to the different doses of x-ray (236-300 reem).

300 reem, as shown in Fig. 4. So, the contrast medium acts as oxidizing stressor in patient blood samples interfering with the x-ray ionizing radiation. But by using AA solution with contrast medium in blood acts as an inhibitor of the oxidation reaction carried out by AA (Radhi *et al.*, 2015).

Fig. 5 shows the relationship between the difference of the peak oxidation current in patient blood samples exposed to ionizing radiation in the presence of the contrast medium and the oxidation current in the presence of contrast medium with AA (ΔIpa) versus the different doses of ionizing radiation in x-ray that explains the linearity of the equation:

$$Y = 0.1306\, X - 21.612 \ldots \text{ with accepted sensitivity}$$

$R^2 = 0.9761$

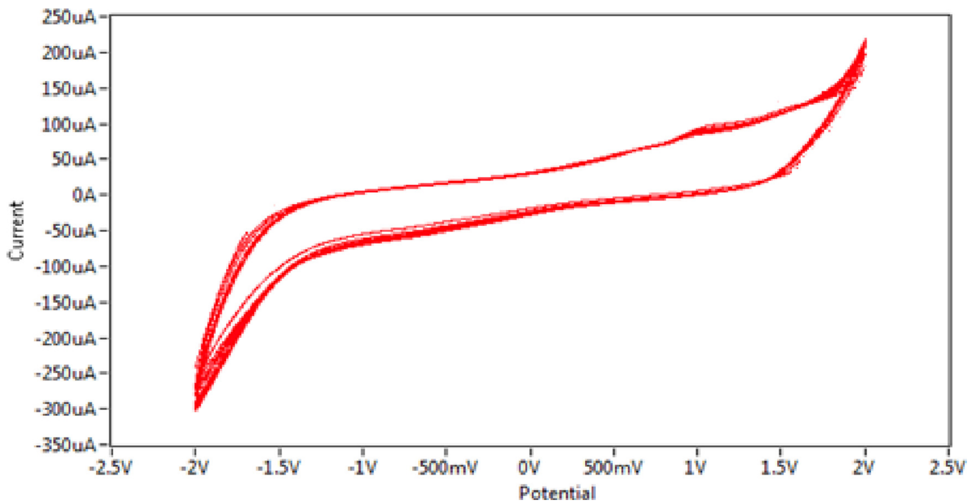

Fig. 6. Cyclic voltammogram of patient blood sample with contrast agent and AA exposed in X-ray at ten times scanning on GCE as working electrode against Ag/AgCL as reference electrode.

It has been found that contrast medium has an effect on oxidative stress while AA solution inhibits the oxidative effect and is induced by x-ray detector irradiation which reduces oxidation by increasing the x-ray doses.

3.3. *Reliability and stability study*

In electrochemical analysis using cyclic voltammetric method can be obtain the reliability of the results that appear by cyclic voltammogram scanning for ten times, and find the extent matching by calculate the accuracy with the stability of working electrode using relative standard deviation (RSD) of the oxidation current peak of patient blood samples with contrast medium and AA exposed with ionized radiation (x-ray). The results of RSD for Fig. 6 that shows the cyclic voltammogram for ten times scanning which has value of 0.95 $\pm$ 0.5, its good reliability for the results in all experiments of the study (Radhi *et al.*, 2016; Radhi & El-Bermani, 1990).

4. Conclusion

This study aims to assess the effect of using ascorbic acid, with and without a contrast agent, on blood samples exposed to different X-ray. The results will contribute to understand of the potential protective properties of ascorbic acid against X-ray-induced damage. This research may have implications for the development of strategies to minimize radiation-induced harm in patients undergoing diagnostic imaging procedures. So, it can be concluded as in the following:

1. The ionizing radiation of x-ray causes oxidation effect to the blood compositions of the patients that exposed with x-ray.
2. Using the contrast agent causes enhancing the oxidative effect of the patient blood through exposed with ionizing radiation of x-ray.
3. Using ascorbic acid (AA) solution is very important to inhibit the oxidative effect of contrast agent with ionizing radiation because AA acts as a good anti-oxidative factor in blood composition. So, it is necessary taking AA solution before exposed to the ionizing radiation by x-ray.

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