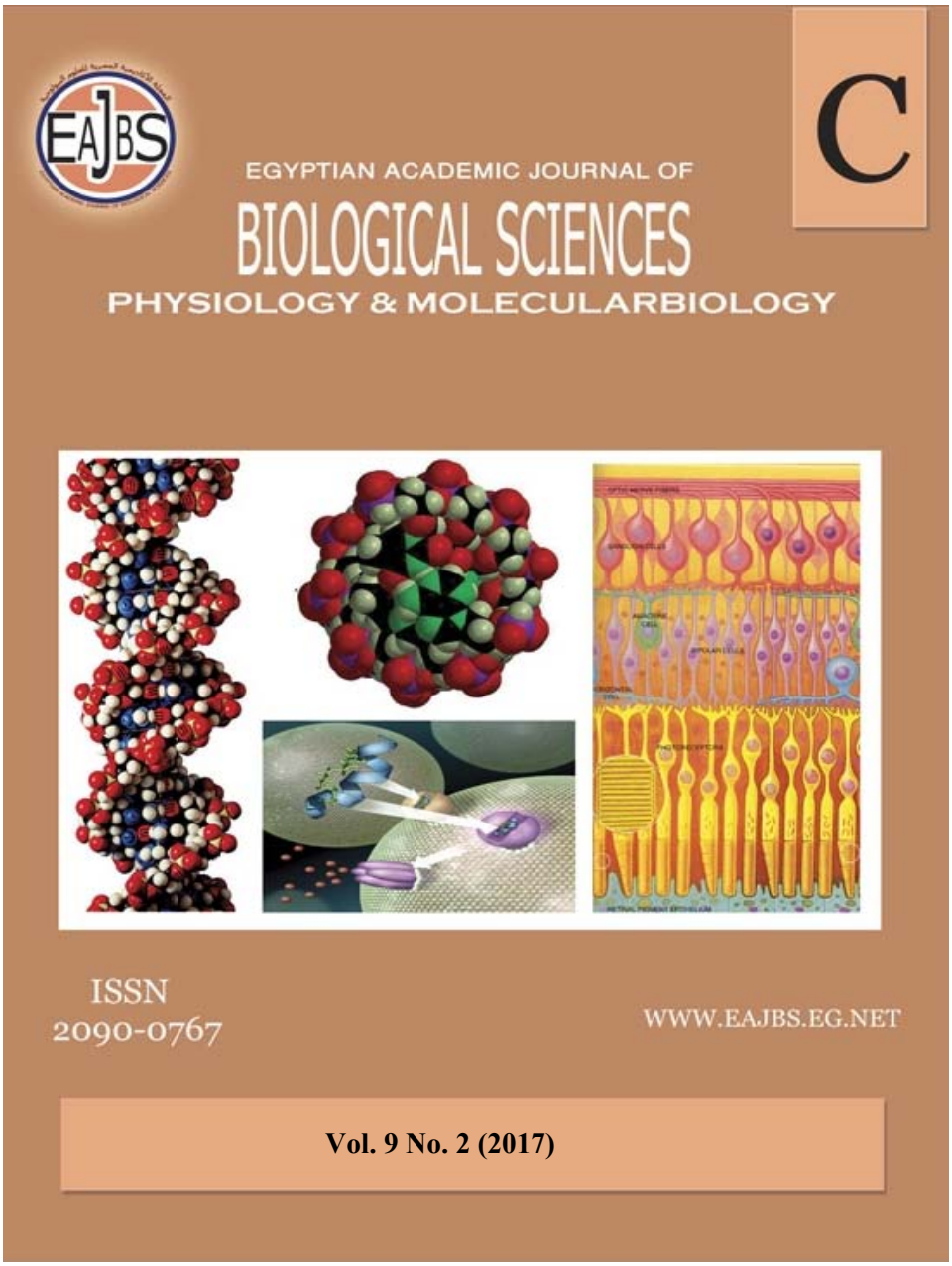

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The Protective Effect of L-carnitine against Gamma Irradiation- Induced Cardiotoxicity in Male Albino Rats.

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ABSTRACT

The aim of this study was focused on the possible protective effect of L-carnitine against gamma radiation induced cardiotoxicity in male albino rats. Forty albino rats were divided into four equal groups as follows: Control group without radiation (placebo), L-carnitine treated group (rats were given orally L-carnitine at a dose of 300 mg/kg/day), irradiated group (animals subjected to whole body gamma irradiation at a dose level of 6Gy) and irradiated group pretreated with L-carnitine (animals were treated orally with L-carnitine at a dose of 300 mg/kg/day before irradiation then exposed to whole body gamma irradiation at a dose of 6Gy). Cardiotoxicity was assessed by measuring the serum levels of CK, CK-MB, LDH, AST, cTnI, TAC, MDA and lipid profile. The obtained results revealed that the administration of L-carnitine to irradiated rats significantly ameliorated the changes occurred in the investigated biochemical parameters. In conclusion, L-carnitine acts as a potent scavenger of free radicals to prevent or ameliorate the toxic effects of gamma irradiation. Also, L-carnitine might provide substantial protection against radiation-induced cardiotoxicity.

INTRODUCTION

Cardiovascular disease and cancer are the two leading causes of morbidity and mortality worldwide (Fuster and Voute, 2005). Over the last half century, radiation therapy (RT) has evolved to become one of the cornerstones of treatment for various types of cancers. It is estimated that more than 50% of patients with cancer are treated with radiotherapy (Yusuf *et al*., 2011).

Radiotherapy is frequently used as a part of cancer treatment to achieve tumor control. Although, radiotherapy treatment has been widely used as an effective tool to kill tumor cells, it might produce harmful effects to surrounding healthy tissues (Sezen *et al*., 2008 and Ostrau *et al*., 2009). It is well known that ionizing radiations induce oxidative stress on target tissues, mainly through the generation of reactive oxygen species (ROS) resulting in imbalance of the pro-oxidant and antioxidant in the cells, attack diverse cellular macromolecules such as DNA, lipids and proteins, eventually inducing cell death (Boerma and Hauer-Jensen, 2011).

The heart is a vital organ and generates intense oxidative imbalances because of its intense activity. Moreover, the heart presents a less potent antioxidant system when compared to other body tissues. As an example, the catalase (CAT) activity in heart tissue is due prioritarily to erythrocyte catalase (de Freitas *et al*., 2013). All structures of the heart are susceptible to the toxic effects of radiation. The major determinants of cardiotoxicity include the total radiation dose delivered, the dose per treatment and the amount of the heart within the radiation field as well as the delivery technique (Ginat *et al*., 2011).

During radiotherapy (RT) of mediastinal tumors (lymphomas, breast cancer and lung cancer), frequently a part of the heart is included in the treatment field and may receive significant doses of ionizing radiation (Hilbers *et al*., 2012). Clinical reports indicated that a considerable number of patients who receive this therapy develop cardiovascular complications. Radiation damage may affect the pericardium associated with myocardium or coronary vasculature characterised by fibrotic changes or small vessel damage (Rijswijk *et al*., 2008 and Doyen *et al*., 2010).

Ionizing radiation (IR) has attracted a lot of attention due to its beneficial as well as possible harmful effects to human population (Jagetia *et al*., 2003). The deleterious effects of the free radicals are kept under check by a delicate balance between the rate of their production and the rate of their elimination by body's defense systems. When, there is an excessive addition of free radicals from exogenous sources added to the endogenous production, the available tissue defense system becomes overwhelmed resulting in oxidative damage to the tissues (Elkady and Ibrahim, 2014). Radiation exposure attenuates endogenous antioxidant enzymes, which are considered to function as a part of the first line defense mechanism to maintain redox balance and normal biochemical processes. Thus, supplementation of antioxidants to improve the efficacy of radiotherapy is a current proposed strategy as antioxidants are capable to scavenge free radicals from the radiolysis of water and to protect cells from damage (Barker *et al*., 2005).

Antioxidants are chemical or biological agents able to neutralize the potentially damaging action of free radicals such unstable molecules as peroxyl radical, hydroxyl radical and singlet oxygen as well as peroxynitrate radicals. The oxidation process of other macromolecules is avoided or slows down by antioxidants. The destructive effect of free radicals in cells is minimized or terminated by antioxidants. The tissues or cells damage by toxic metabolites are minimized by antioxidants (Piwkowska *et al.*, 2011).

L-carnitine (β-hydroxy-γ-N-trimethy ammonium butyric acid) (Chao *et al*., 2011), that is synthesized from the essential amino acids lysine and methionine (Lee *et al*., 2014). carnitine has two stereoisomeric forms D and L. However, only the L isomer is naturally occurring, known to be essential for human and animal health and possess biological activity, while the other isomer is biologically inactive and does not occur naturally (Sahebkar, 2015). Its name is derived from the Latin carnus or flesh, as the compound was isolated from meat. Carnitine is the generic term for a number of compounds that include L-carnitine, acetyl-L-carnitine and propionyl-L-carnitine (Ismail, 2014).

The main function of carnitine in the body is facilitation lipid oxidation by transporting long-chain acyl groups from fatty acids from cytoplasm to mitochondrial matrix and then be broken down through β oxidation to acetyl CoA

to obtain usable energy *via* the citric acid cycle (Huang *et al*., 2012).

Carnitine is also involved in buffering of the acyl coenzyme-A (CoA)-CoA ratio, branched-chain amino acid metabolism, removal of excess acyl groups and peroxisomal fatty acid oxidation. Fatty acid oxidation is the major energy providing pathway of the myocardium (Khan *et al*., 2014). L-carnitine and its derivatives have antioxidant and anti-inflammatory effects on various pathophysiological conditions (Onem *et al*., 2006). In addition L-carnitine protects cardiac cells against ischaemia, hypoxia and oxidative stress, by decreasing the levels of toxic acyl-CoA derivatives and regulating carbohydrate metabolism (Karanth and Jeevaratnam, 2010).

Thus, the aim of the current study was to investigate the protective effect of L-carnitine in gamma radiation-induced oxidative damages of rat heart by biochemical analysis.

MATERIALS AND METHODS

Animals:

Male albino rats (150-180g) were obtained from Breeding Unit of Nuclear Research Centre, Atomic Energy Authority. Animals were housed in metal cages and kept in a room temperature maintained at 25± 2^{o}C and 50 % relative humidity (R.H.). Rats were kept for 14 days for laboratory adaptation. They fed commercial pellets and provided with tap water.

Chemicals and drugs:

L-Carnitine was purchased from MEPACO-MEDIFOOD Co., Inshas Elraml-Egypt and all chemicals were obtained from Bio Diagnostic Co., Egypt.

Radiation processing:

It was performed by using gamma cell-40 (Ce-sium-137) located at the National Centre for Radiation Research and Technology (NCRRT), Nasr City, Cairo, Egypt. Animals were irradiated with 6Gy as an acute single dose shot.

Experimental design:

Forty rats were divided into four equal groups (10 rats/ group). Group 1 (control group= placebo), included rats received orally of saline solution. Group 2 (L-carnitine treated group); rats of this group received orally L-carnitine at a dose of 300 mg/kg/day for 21 consecutive days by stomach tube. Rats in group 3 (irradiated group) were exposed to 6Gy whole body gamma radiations as a single dose shot and like control group received orally an equivalent volume of saline solution. Group 4 (Irradiated group pretreated with L-carnitine) included rats that were administrated by L-carnitine (300mg/kg/day) by stomach tube for 21 consecutive days before exposure to whole body gamma irradiation of 6Gy as a single dose shot. Rats were sacrificed at the end of experimental period and subjected to serum biochemical analysis.

Samples collection:

At the end of experimental period, the rats were overnight fasted and blood were collected by retro-orbital puncture using blood capillary tubes. Sera were obtained immediately by centrifugation of blood samples at 3000 rpm for 10min.

Estimation of biochemical parameters:

Serum cardiac enzymes were measured creatine phosphokinase (CPK) activity was estimated according to the method of Carl and Edward (1999), creatine kinase-MB (CK-MB) activity was determined according to the methods described by Gerhardt and Waldenström (1979), lactate dehydrogenase (LDH) activity was assayed depending on the method of Zimmerman and Henery (1979) and aspartate amino transferase (AST) acticity was estimated according to IFCC (1986). Serum levels of cardiac troponin I (cTnI) were performed by ELISA technique (Christenson and Azzazy, 1998). Serum level of total antioxidant capacity (TAC) was determined according to Koracevic *et al*. (2001). Serum malondialdehyde (MDA)

level was estimated following the method reported by Satoh (1978). Moreover, serum concentrations of total cholesterol (TC), triglyceride, high density lipoprotein-cholesterol (HDL-C) and low density lipoprotein-cholesterol (LDL-C) were estimated according to Watson (1960), Fossati and Prencipe (1982), Gordon (1977) and Friedwalds *et al.* (1972) respectively.

Statistical analysis:

Data were analyzed using one way analysis of variance (ANOVA< SPSS software ver. 22, IBM Corp., NY). The obtained results were expressed as mean ± standard deviation (SD) of the mean. Differences test were considered significant at $p<0.05$ (Levesque, 2007).

RESULTS

Detecting the cardiac profile (CK, CK-MB, LDH, AST and TnI) obtained data were presented in Table (1). The normal control rats designated similar levels during the study period.

In relation to the normal control rats, a significant ($p<0.05$) increase in the serum activities of CK, CK-MB and AST as well as TnI levels were reported in gamma irradiated animals (6Gy) which induced cardiotoxicity. While, a significant decrease in serum activity of LDH was detected in irradiated rats group compared to control group Table (1).

A considerable correction were occurred in all previous studied parameters when irradiated rats treated with L-carnitine before expose to gamma radiation The obtained data in table (1) showed significant ($p<0.05$) decrease in serum activities of CK, CK-MB, AST and TnI, as compared to irradiated rats group.

From Table (1), irradiated rats group pretreated with L-carnitine where received orally (300 mg/kg of b.wt.) L-carnitine for 21 consecutive days before irradiation, a significant ($p<0.05$) decrease in the serum levels of CK, CK-MB, AST and TnI as compared to irradiated rats group, while noticed a significant increase in serum LDH level was recorded compared to irradiated rats group. It is clear from the data recorded in Table (1), insignificant change in serum level of CK activity in L-carnitine-treated rats group regarding to normal control group, while a marked decrease occurred in serum levels of CK-MB, LDH, AST and TnI.

Table 1: Effect of L-carnitine on the serum levels of cardiac enzymes (CK, CK-MB, LDH, AST and Troponin I TnI (U/L) in the different animal groups.

Groups	**Parameters**				
	CK(U/L)	**CK-MB(U/L)**	**LDH(U/L)**	**AST(U/L)**	**Troponin I (Pg/ml)**
Control group	**1746.6±405.8^{b}**	**369.9±150.5^{b}**	**4306.0±105.1^{a}**	**73.0±9.3^{b}**	**237.9±21.6^{b}**
L-carnitine-treated group %1 of change	1841.7±418.8^{b} **5.45**	204.2±2.7^{c} **-44.79**	2388.8±405.2^{d} **-44.52**	65.9±10.2^{c} **-9.73**	193.9±55.6^{c} **-18.49**
Irradiated group %1 of change	**3400.1±125.2^{a}** **94.67**	**835.5±35.1^{a}** **125.87**	**3305.3±399.6^{c}** **-23.24**	**87.8±6.8^{a}** **20.27**	**324.2±19.01^{a}** **36.28**
Irradiated group pretreated with L-carnitine % 1of change %2 of change	**1095.0±19.9^{d}** **-37.31** **0.00**	**244.1±25.8^{c}** **-34.00** **-70.78**	**3613.5±386.6^{b}** **-16.08** **9.32**	**74.3±3.3^{b}** **1.78** **-15.38**	**136.7±6.6^{d}** **-42.54** **-57.83**

- Data were represented as means ±SD -a, b, c and d: means bearing different superscripts within the same column are significantly different at $p\leq0.05$.
- % 1: Percentage of change of treated group compared to control in the same column.
- % 2 : Percentage of change of treated group compared to irradiated group in the same column.

The effects of gamma radiation on endogenous antioxidant status are shown in Table (2). Gamma-irradiation induced insignificant decrease in the level of total antioxidant capacity (TAC) but caused a significant increase in the level of MDA compared to control group. Administration of L-carnitine prior to gamma irradiation of rats restored the reduced TAC level while it caused a decreased MDA level compared to irradiated group. Animal group treated with L-carnitine showed insignificant changes in the level of TAC, while a significant increase in MDA level was occurred comparing to those of control group.

Table 2: Effect of L-carnitine on the serum levels of total antioxidant capacity (mM/L) and malondialdehyde (mM/L) in the different animal groups.

Groups	**Parameters**	
	Total anti-oxidants (mM/L)	**Malondialdehyde (nM/ml)**
Control group	**0.33±0.095^{a}**	**21.02±1.06^{d}**
L-carnitine-treated group **%1 of change**	**0.29±0.074^{a}** **-12.12**	**24.22±2.36^{c}** **15.22**
Irradiated group **%1 of change**	**0.28±0.079^{a}** **-15.15**	**32.61±3.09^{a}** **55.14**
Irradiated group pretreated with L-carnitine **%1 of change** **%2 of change**	**0.33±0.095^{a}** **0.00** **17.86**	**29.13±0.84^{b}** **38.58** **-10.67**

- Data were represented as means ±SD - a, b, c and d: means bearing different superscripts within the same column are significantly different at $p \leq 0.05$.
- %1: Percentage of change of treated group compared to control in the same column.
- % 2: Percentage of change of treated group compared to irradiated group in the same column.

As presented in Table (3), whole body gamma-irradiation induced a significant increase in the levels of cholesterol, Triglyceride and LDL-C while a significant decrease in HDL-C concentration was noticed compared to control group. Pretreatment with L-carnitine prior to gamma irradiation was found to significantly abolish these radiation-induced elevation in the levels of cholesterol, triglyceride and LDL-C and also maintained the level of HDL-C near to the normal level.

Table 3: Effect of L-carnitine on lipid profile (cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol mg/dl in the different animal groups.

Groups	**Parameters**			
	Cholesterol (mg/dl)	**T.G. (mg/dl)**	**HDL (mg/dl)**	**LDL (mg/dl)**
Control group	84.5±1.90^{b}	129.3±1.49^{c}	32.6±1.51^{ab}	26.04±1.28^{b}
L-carnitine-treated group %1 of change	78.4±2.63^{c} -7.22	100.7±2.71^{d} -22.12	34.5±3.66^{a} 5.83	23.76±5.28^{b} -8.76
Irradiated group %1 of change	100.8±6.23^{a} 19.29	158.3±4.72^{a} 22.43	24.0±1.89^{c} -26.38	45.14±6.31^{a} 73.35
Irradiated group pretreated with L-carnitine %1 of change %2 of change	85.1±4.04^{b} 0.71 -15.58	142.9±4.89^{b} 10.52 -9.73	32.3±1.89^{ab} -0.92 34.58	24.22±3.91^{b} -6.99 -46.34

Data were represented as means ±SD a, b, c and d: means bearing different superscripts within the same column are significantly different at $p \leq 0.05$.
%1: Percentage of change of treated group compared to control in the same column.
% 2: Percentage of change of treated group compared to irradiated group in the same column.

DISCUSSION

The exposure to ionizing radiation is known to induce oxidative stress. Oxidative modification of DNA, proteins, lipids and small cellular molecules by reactive oxygen species (ROS) which plays a role in a wide range of common diseases and age-related degenerative conditions including cardiovascular disease (Elkady and Ibrahim, 2014).

A single dose 6Gy of whole body gamma irradiation induced a marked acute cardiotoxicity in rats characterized by disorders in cardiac enzymes in gamma irradiated group compared to normal control group. Serum indicators widely used in the determination of myocardial injury are cardiac troponin I (cTnI), creatine kinase (CK) and creatine kinase myokard band (CK-MB). Troponin is a preventive protein located in the actine fiber of all striated muscles (Con *et al*., 2015). Heart sourced troponin I (cTn I) is only present in the heart and used as the sensitive and specific indicator of heart muscle injury (Caliskan *et al*., 2010).

Total CPK and CPK-MB enzymes that catalyse the conversion of creatine to phosphocreatine. In tissues that consume ATP rapidly, especially muscle, phosphocreatine serves as an energy reservoir for the rapid regeneration of ATP. LDH, on its turn, converts pyruvate, the final product of glycolysis to lactate when oxygen is absent or in short supply as happens in heart tissue physiology. Because of this, measuring stress from oxygen-poor environments under radiation allow one to infer some conclusions about the major aspects of damage in well oxygenated tissues (de Freitas *et al*., 2013).

The increase in CK, CK-MB, AST and troponin I in irradiated group may be attributed to the fact that excessive production of free radicals and lipid peroxides might cause the leakage of cytosolic enzymes including the aminotransferase, creatine kinase and phosphatases enzymes; ionizing radiation instigates the alterations in the dynamics permeability of membranes allowing leakage of biologically active materials out of the injured cells (Fahim, 2008 and Abd El Kader *et al*., 2015). Moreover, the increase in CK-MB activity after irradiation may be related to the muscular injury (Brodie *et al*., 2003).

The mechanism of radiation-induced cardiotoxicity has been also reported to be through the formation of superoxide anions and their derivatives, particularly highly reactive and damaging hydroxyl radicals, which induces peroxidation of cell membrane lipid (Mohamed *et al*., 2016).

A single dose of 6Gy caused insignificant decrease in the level of total antioxidant as compared to normal control rats. These results are in accordance to some experiment with the previous study of Akpolat *et al*. (2011), they reported that total body irradiation is known to cause a marked decrease in antioxidant capacity. Bhatia and Jain (2004) found a significant depletion in the antioxidant system accompanied by enhancement of lipid peroxides after whole body gamma-irradiation. This could be due to an enhanced utilization of the antioxidant system as an attempt to detoxify the free radicals generated by radiation exposure.

On the other hand, the significant increase in serum level of malondialdehyde (MDA) a major biomarker in irradiated group, which is the end product of lipid peroxidation pointed to the impairment of the antioxidant defense mechanism. This result is in accordance with the previous study of Yilmaz and Yilmaz (2006). The increase in MDA could be explained on the basis that ionizing radiation induces lipid peroxidation through the radiolysis of water in the aqueous media of the cells

which leads to production of hydroxyl radicals ($^{\bullet}OH$). Hydroxyl radicals interact with the polyunsaturated fatty acids in the lipid portion of biological membranes initiating the lipid peroxidation and finally damage the cell membranes which causing cell death and apoptosis (Azab *et al*., 2011 and de Freitas *et al*., 2013).

Lipid profile is always acquiring the most attention for its close association with chronic heart diseases and brain stroke. Moreover, TC, TG, LDL and free radicals are also risk factors that tend to damage arteries leading to heart disease (Howard-Alpe *et al*., 2006). Since, lipids are major target of oxidative damage. The dramatic rise of cholesterol, TG and LDL with the decrease of HDL in irradiated rats was expected. These data are in accordance with previous results of Ragab and Ashry (2004); Abou-Safi *et al*. (2005) and Osman *et al*. (2009) who observed that the elevation in serum lipid fractions might result from ionizing radiation ability to accelerate other pathways of cholesterol formation like increasing its rate of biosynthesis in the liver and other tissues, or destruction of cell membrane by radiation and also to disturbance of LDL cholesterol receptors, leading to hypercholesterolemia. Makhlouf and Makhlouf (2012) suggested that oxidative stress might be an important determinant of altered lipid metabolism due to radiation exposure.

Beside the release of cholesterol and cholesterol fractions from tissues, destruction of cell membrane and increase rate of cholesterol biosynthesis in the liver and other tissues. The increase of activation of HMG CoA reductase enzyme, the key regulatory enzyme in the reduction of the overall process of cholesterol synthesis (Abdel-Magied and Ahmed, 2011). The increase in plasma triglycerides in rats exposed to γ -irradiation may be attributed to inhibition of the activity of lipoprotein lipase (Abd El-Azime and Ossman, 2013). The elevation of serum triglycerides after exposure of rats to gamma irradiation comes in accordance with Ahmed (2006) and Abdel Magied (2007).

Radiation therapy (RT) is an important component of the therapeutic arsenal for the treatment of breast cancer, Hodgkin's disease, lung cancer and other tumors involving the cervical and thoracic regions and is linked to increased cardiovascular morbidity and mortality (Moreira *et al*., 2016). Which is proportional to the dose of radiation and the site exposed in the cardiovascular system (Daher *et al*., 2012) The cardiac effects of RT in the long term are heterogeneous and include coronary artery disease, valve disease; diseases of pericardium; myocardial diseases, with systolic and diastolic dysfunction in particular; and conduction system disturbances (Wu *et al*., 2013). Thus, supplementation of antioxidants to improve the efficacy of radiotherapy is a current proposed strategy as antioxidants are capable to scavenge free radicals from the radiolysis of water and to protect cells from damage (Barker *et al*., 2005). Carnitines are essential factors of several enzymes necessary for the transformation of long chain fatty acids, and act also as scavengers of oxygen free radicals in mammalian tissues (Mansour, 2006). Morever the efficacy of L-carnitine supplementation in cardiovascular diseases and/or atherosclerosis (Keskin *et al*., 2015).

Ferrari *et al*. (2004) reported that carnitine is an essential cofactor which can reduce ischemia-reperfusion injury in the myocardium, its effectiveness in the recovery of post-ischemic cardiac function and carnitine could significantly reverse mechanical dysfunction during both myocardial ischemia and reperfusion, carnitine in the myocardium avoids fatty acid gathering and lactic acid production, led to in the enhancement of myocardial function.

The significant decrease of CK-MB, AST, LDH and troponin in L-carnitine group compared to control reflect improvement of myocardial function especially that Con *et al*. (2015) has showed that L- carnitine has a positive effect on troponin I due to its effect in increasing mitochondrial Ca^{+2} secretions and reported that troponin is presented

Although L-carnitine is a free radical scavenger (Kolodziejczyk *et al*., 2011). This is not evident in the current study as L-carnitine cause significant increase of MDA compared to control this may due to the fact that MDA is a part of prooxidant and not all the oxidants. Dokmeci *et al*. (2006) they showed that protective role of L-carnitine against lipid peroxidation by improvement in the levels of MDA in the plasma of hamsters pretreated with L-carnitine before irradiation. Mohamed and Farghaly (2009) showed that L-carnitine suppressed hydroxyl radical production in the fenton reaction, probably by chelating the iron required for the generation of hydroxyl radicals.

CONCLUSION

This study demonstrated that L-carnitine through its marked antioxidant activity led to reduction of the hazardous effects of radiation induced cardiotoxicity, oxidant-antioxidant equilibrium and distributed lipid profile and most probably through enhancing antioxidant activities and decreasing lipid peroxidation protecting cellular membrane from oxidative damage. The radioprotective effect of L-carnitine was obviously demonstrated as an effective agent on cardiotoxicity as radioprotector. On the basis of the pervious investigations and the present data in this work, the use of antioxidant L-carnitine prior and followed to radiation therapy can paractically help to encourage the clinical use of this antioxidant (L-carnitine) as a treatment against exposure to gamma radiation. However, we believe that L-carnitine should be further evaluated for it's radioprotective potential in a clinical setting.

REFERENCES

Abd El-Azime, A. Sh. and Ossman, N. N. (2013): Protective Effect of Hawthorn (Crataegus Linn) against Radiation-Induced Damage in Rats. Arab J. Nuclear Sci and Appl., 46(1): 304-312.

Abd-El Kader, M.A.; El kafrawy M.H.; Tolba, A.M.; Ali, M.M. and Mohamed, A.S. (2015): Evaluation of Taurine Role on Some Biochemical and Histological Alterations in γ-Irradiated Rats. Int. J. Pharm. Sci. Rev. Res., 30(1): 263-271.

Abd-El-Azime, A.Sh. and Ossman, N.N. (2013): Protective Effect of Hawthorn (Crataegus Linn) against Radiation-Induced Damage in Rats. Arab Journal of Nuclear Science and Applications, 1:304-312.

Abdel-Magied, N. (2007): Experimental studies on the protective role of onion oil (Allium cepa Linn) against radiation induced biological hazards in mammalian tissues. Ph.D. thesis, Faculty of Science, Tanta Univ., Egypt.

Abdel-Magied, N. and Ahmed, A.G. (2011): The Protective Role of Lettuce oil (Lactuca sativa) against Radiation induced Biological Hazards in Male Rats The Protective Role of Lettuce oil (Lactuca sativa) against Radiation induced Biological Hazards in Male Rats. J. Rad. Res. Appl. Sci., 4: 923 – 938.

Abou-Safi, H.M.; Ashry, O.M. and Kafafy, Y. A. (2005): Effect of N-acetyl-l-cysteine and alpha-Tocopherol administration on endogenous antioxidant protection of liver DNA and RNA and plasma lipid profile in gamma-irradiated

rats. Egyp. J. Radiat. Sci. Appl., 18(1): 81-96.

Ahmed, G.A. (2006): The prospective role of natural product application in diminished some physiological disorders causeby gamma radiation in rats. Ph.D. Thesis Faculty of Science Ain shams University Egypt.

Akpolat, M.; Topcu-Tarladacalisir, Y.; Dokmeci, D.; Turan, F.N. and Uzal, M.C. (2011): Protective effects of ibuprofen and L-carnitine against whole body gamma irradiation-induced duodenal mucosal injury. Balkan Med. J., 28: 80-85.

Azab, K.S.; Bashandy, M.; Salem, M.; Ahmed, O.; Tawfik, Z. and Helal, H. (2011): Royal jelly modulates oxidative stress and tissue injury in gamma irradiated male Wister Albino rats. N. Am. J. Med. Sci., 6: 268- 276.

Barker, S.; Weinfeld, M.; Zheng, J.; Li, l. and Murray, D. (2005): Identification of mammalian proteins cross-linked to DNA by ionizing radiation. J. Biol. Chem., 280(40): 33826-33838.

Basavaraj R.D., Biyani C.S., Browning A.J., and Cartledge J.J. (2007): The role of urinary kidney stone inhibitors and promoters in the pathogenesis of calcium containing renal stones. Eau-Ebu update series J., 5: 126–136.

Bhatia, A.L. and Jain, M. (2004): Spinacia oleracea L. protects against gamma radiations: a study on glutathione and lipid peroxidation in mouse liver. Phytomed., 11(7): 607-615.

Boerma, M. and Hauer-Jensen, M. (2011): Preclinical research into basic mechanisms of radiation-induced heart disease. Cardiol. Res. Pract., 2011:1-8.

Brodie, D.; Liu, X. and Jackson, M. (2003): Changes in serum biochemical responses during cardiac rehabilitation. Med. Sci. Sports. Exer., 35 (5):741.

Caliskan, E.; Kilic, T.; Doger, E.; Cakiroglu, Y.; Turker, G. and Duman, C. (2010): Neonate gender and gestational age are independent determinants of cord blood troponin I. Turkiye Klinikleri J. Med. Sci., 3: 1025-1031.

Carl, A. and Edward, R.A. (1999): Tietz textbook of clinical chem-istry. Philadelphia: WB Sunders, 776(840): 1244.

Chao, H.; Liu, j.; Hong H.; Lin J.; Chen C. and Cheng, T. (2011): L-carnitine reduces doxorubicin induced apoptosis through a prostacyclin-mediated pathway in neonatal rat cardiomyocytes. Int. J. Cardiol., 146 (2): 145-152.

Christenson, R.H. and Azzazy, H.M.E. (1998): Biochemical markers of the acute coronary syndromes. Clin. Chem., 44:1855-1864.

Con, M.; Tasmektepligil, M.Y.; Cankaya, S.; Agaoglu, S.A.; Dogan, E.; Cenesiz, S., and Cenesiz, M. (2015): Effects of L-Carnitine on Obese Rats Exposed to Swimming Exercise. Anthropolog., 19(2):407-412.

Daher, I.N.; Daigle, T.R.; Bhatia, N. and Durand, J.B. (2012): The prevention of cardiovascular disease in cancer survivors. Tex. Heart Inst. J.; 2:190-198.

de Freitas, R.B.; Boligon, A.A.; Rovani, B.T.; Piana, M.; de Brum, T.F.; da Silva Jesus, R., Rother, F.C.; Alves, N.M.; Teixeira da Rocha, J.B.; Athayde, M.L. and Barrio, J.P. (2013):Effect of black grape juice against heart damage from acute gamma TBI inrats. Molecules, 18(10):12154-12167.

Dokmeci, D.; Akpolat, M.; Aydogdu, N.; Uzal, C.; Doganay, L. and Turan, F.N. (2006): The Protective Effect of L-carnitine on Ionizing

Radiation-induced Free Oxygen Radicals. Scand. J. Lab. Anim. Sci., 33: 1-9.

Doyen, J.; Giraud, P. and Belkacemi, Y. (2010): Normal tissue tolerance to external beam radiation therapy: cardiac structures. Cancer Rad., 14(4-5): 319-326.

Elkady, A.A. and Ibrahim, R.M. (2014): Royal jelly attenuates ionizing radiation induced cardiac toxicity in male albino rats. Med. J. Cairo Univ., 82(1): 13-18.

Fahim, T. h. (2008): Possible radio-protective efficiency of Bee-pollen against radiation induced cardiotoxicity in male rats. Egypt. J. Rad. Sci. Applic., 21: 547-563.

Ferrari, R.; Merli, E.; Cicchitelli, G.; Mele, D.; Fucili, A. and Ceconi, C. (2004): Therapeutic effects of L-Carnitine and Propionyl-L carnitine on cardiovascular diseases: a review. Ann. NY Acad. Sci., 1033:79-91.

Fossati, P. and Prencipe, L. (1982): Serum triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide. Clin. Chem., 28(10): 2077-2080.

Friedwald W.T.; Levy, R.I. and Fredickson, D. S. (1972): Estim-ation of concentration of LDL cholesterol in plasma without using preparative ultracentrifuge. Clin. Chem. Acta., 18:499-502.

Fuster, V. and Voˆ ute, J. (2005): "MDGs: chronic diseases are not on the agenda." The Lancet., 366 (9496): 1512–1514.

Gerhardt, W. and Waldenström, J. (1979): Creatine kinase B-subunit activity in serum after immunoinhibition of M-subunit activity. Clin. chemist., 25(7):1274-1280.

Ginat, D.T.; Fong, M.W.; Tuttle, D.J.;Hobbs, S.K. and Vyas, R.C. (2011): Cardiac imaging: Part 1, MR pulse sequences, imaging planes, and basic anatomy. AJR Am. J. Roentgenol, 197(4):808–815.

Gordon, T. (1977): Colorimetric method for HDL-choleserol determination. AM. J. Med., 26: 707-711.

Hilbers, F.S.; Boekel, N.B.; Van Den Broek, A.J.; Van Hien, R.; Cornelissen, S.; Aleman, B.M.; Van 'T veer, L.J.; Van Leeuwen, F.E. and Schmidt, M.K. (2012): Genetic variants in TGFβ-1 and PAI-1 as possible risk factors for cardiovascular disease after radiotherapy for breast cancer. Radiother. Oncol., 102(1): 115-121.

Howard-Alpe, G.M.; Sear, J.W. and Foex, P. (2006): Methods of detecting atherosclerosis in non-cardiac surgical patients; the role of biochemical markers. Br. J. Anaesth., 97:758-769.

Huang, H.; Liu, N.; Guo, H.; Liao, S.; Li X, Yang C.; Liu, S. and Song, W. (2012): L-carnitine is an endogenous hdac inhibitor selectively inhibiting cancer cell growth in vivo and in vitro. PLoS., 7(11):1-10.

IFCC expert panel on enzymes part 3. (1986): J. Clin. Chem. Clin Biochem., 24:481-495.

Ismail, S.H. (2014): Effect of L-carnitine supplementation on the blood profile in healthy iraqi subjects. Int. j. compr. pharm., 5(2): 1-3.

Jagetia, G.C.; Shirwaikar, A.; Rao, S.K. and Bhi-Legaonkar, P.M. (2003): Evaluation of the radioprotective effect of Ageratum conyzoides Linn. Extract in mice exposed to different dose of gamma radiation. J. Pharm. Pharmacol., 55(8): 1151-1158.

Karanth, J., and Jeevaratnam, K. (2010): Effect of carnitine supplementation on mitochondrial enzymes in liver and skeletal muscle of rat after dietary lipid manipulation and

physical activity. Indian J. Exp. Biol., 48:503-510.

Keskin, E.; Uluisik, D. and Altin, M. (2015): Antioxidant Effect of L-carnitine in Rats Fed Cholesterol Rich Diet. Sci., 3(4): 113-116.

Khan, H.A.; Alhomida, A.S.; Habib, S.S.; Khan, A.A.; Ola, M.S.; Siddiqui, N.J. and Al Madani, H. (2014): Blood carnitine as a biomarker for acute myocardial infarction. Biomed. Res., 25(1): 63-66.

Kolodziejczyk, J.; Saluk-Juszczak, J. and Wachowicz, B. (2011): L-Carnitine protects plasma components against oxidative alterations. Nutr. J., 27(6): 693-699.

Koracevic, D.; Koracevic, G.; Djordjevic, V.; Andrejevic, S. and Cosic, V. (2001): Method for the measurement of antioxidant activity in human fluids. J. clin. Pathol., 54(5): 356-361.

Lee, B.J.; Lin, J.S.; Lin, Y.C. and Lin, P.T. (2014): Effects of L-carnitine supplementation on oxidative stress and antioxidant enzymes activities in patients with coronary artery disease: a randomized, placebo-controlled trial. Nutr. J., 13(1): 1-7.

Levesque R. SpSS., (2007): Programming and Data Management: A Guide for SPSS and SAS Users , Fourth Edition , SPSS Inc., Chicago.

Makhlouf, R. and Makhlouf, I. (2012): Evaluation of the effect of Spirulina against Gamma irradiation induced oxidative stress and tissue injury in rats. Int. J. Appl. Sci Engr.Res., 1: 152-164.

Mansour, H. H. (2006): Protective role of carnitine ester against radiation-induced oxidative stress in rats. Pharmac. Res., 54(3): 165-171.

Mohamed, E.T.; Elkady, A.A.; El Kiki, S. and El, S. M. (2016): Protective Effect of Symplocos racemosa Roxb Against Gamma Radiation Induced Cardiotoxicity in Male Albino Rats. Pakisan J. Zool., 48(6): 1831-1837.

Mohamed, N.E. and Farghaly A.A. (2009): Evaluation of the Protective Effect of L-Carnitine on Radiation Induced Free Oxygen Radicals and Genotoxicity in Male Mice. Researcher, 6: 7-15.

Moreira, L.A.R.; Silva, E.N.; Ribeiro, M.L. and Martins, W.D.A. (2016): Cardiovascular effects of radiotherapy on the patient with cancer. Rev. Assoc. Med. Bras., 62(2): 192-196.

Onem, G.; Aral, E.; Enli, Y.; Oguz, E.O.; Coskun, E.; Aybek, H. and Baycu, C. (2006): Neuroprotective effects of L-carnitine and vitamin E alone or in combination against ischemia-reperfusion injury in rats. J. Surg. Res., 131(1): 124-130.

Osman, N.N.; Hussien, E.M. and Farag, M.F.S. (2009): Black tea role in modulating antioxidant enzymes and biochemical changes in gamma irradiated rats. Egypt. J. Rad. Sci. and Applic., 1:265-282.

Ostrau, C.; Hülsen beck J.; Herzog, M.; Schad, A.; Torzewski, M. and Lackner, K. J. (2009): Lovastatin attenuates ionizing radiation-induced normal tissue damage in *vivo*. Radiother Oncol., 92:492–499.

Piwkowska, A.; Rogacka, D.; Audzeyenka, I.; Jankowski, M. and Angielski, S. (2011): High glucose concentration affects the oxidant-antioxidant balance in cultured mouse podocytes. J. cell. Biochem., 112(6): 1661-1672.

Ragab, E.A. and Ashry, O.M. (2004): Natural products garlic oil and vitamin E, control radiation induced disorders of lipid and carbohydrate metabolism in rats. Egy. J. Radiat.. Appl., 17(2): 403-412.

Rijswijk, V.S.; Huijbregts, M.A.; Lust, E. and Strack van Schijndel, R.J. (2008): Mini-review on cardiac complications after mediastinal irradiation for Hodgkin lymphoma. Neth. J. Med., 66(6): 234-237.

Sahebkar, A. (2015): Effect of L-Carnitine Supplementation on Circulating C-Reactive Protein Levels: A Systematic Review and Meta-Analysis. J. Med. Biochem., 34(2): 151-159.

Satoh, K. (1978): Serum lipid peroxide in cerebrovascular disorders determined by a new colorimetric method. Clin. Chim. Acta., 90: 37-43.

Sezen, O.; Ertekin, M. V.; Demircan, B.; Karslıoğlu, İ.; Erdoğan, F.; Koçer, İ. and Gepdiremen, A. (2008): Vitamin E and L-carnitine, separately or in combination, in the prevention of radiation-induced brain and retinal damages. Neurosurg. Rev., 31(2): 205-213.

Watson, D. (1960): A simple method for the determination of serum cholesterol. Clin. Chim. Acta., 5: 637-643.

Wu, W., Masri, A.; Popovic, Z.B.; Smedira, N.G.; Lytle, B.W. and Marwick, T.H. (2013): Long-term survival of patients with radiation heart disease undergoing cardiac surgery: a cohort study. Circulatio., 14:1476-1485.

Yilmaz, S. and Yilmaz, E. (2006): Effects of melatonin and vitamin E on oxidative -antioxidative status in rats exposed to irradiation. Toxicol., 222:1-5.

Yusuf, S. W.; Sami, S. and Daher, I. N. (2011): Radiation-Induced Heart Disease: A Clinical Update. Cardiol. Res. and Pract., 2011:1- 9.

Zimmerman, H.J. and Henery, J.B. (1979): Clinical enzymology. In: Clinical diagnosis and management by laboratory methods, 16 th., JB Henery, editor, saunders, philadelphia, 365-368.

ARABIC SUMMARY

تأثير ل- كارنتين الوقائى ضد التسمم القلبى المحدث بأشعة جاما فى ذكور الجرذان البيضاء.

نفيسة حسين مكى[1]-امل محمود حجاج[2]-امال محمد كمال[2]-زينب على احمد[2]

1-قسم علم الحيوان كلية العلوم جامعة عين شمس

2-قسم التطبيقات البيولوجية مركز البحوث النووية هيئة الطاقة الذرية

يستخدم العلاج بالاشعاع كجزء من علاج السرطان لتحقيق السيطرةعلى الورم.وان 50% من المصابون بالسرطان يتم علاجهم بالاشعاع وعلى الرغم من أن العلاج الإشعاعي قد استخدم على نطاق واسع كأداة فعالة لقتل الخلايا السرطانية ولكن قد تحدث آثارا ضارة على الأنسجة المحيطة بها فاثناء العلاج بالاشعاع لمرضى سرطان الرئة ، الثدى ،او اى ورم فى منطقة الصدر فعند تلقى الجرعات المخصصة للعلاج فقد يحدث مضاعفات للقلب سواء عضلة القلب او الصمامات او غشاء التامور ولان كل تراكيب القلب عرضة للتأثيرات الضارة للاشعاع لانه اقل قوة فى مضادات الاكسده له بالمقارنة بانسجة الجسم الاخرى نظرا لنشاطه المكثف ولذلك لابد من وقاية القلب من التأثير الضار للاشعاع المؤين اثناء التعرض للاشعاع مما يؤثر سلبا على وظيفة القلب.وتعتبر مادة ل-كارنتين من اقوى مضادات الاكسدة التى حيث انها تستطيع معادلة الشوارد الحرة الناتجة من الاشعاع وتدعيم مضادات الاكسدة الخاصة بالقلب كما اوضحت النتائج انها تحسن من وظيفة القلب والانزيمات.