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Efficacy of Carnosine in Modulating Radiation-Induced Oxidative Damage and Neurotransmitter Alterations in Rat Brain.

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ABSTRACT

The present study was designed to investigate the role of carnosine (β-alanyl-L-histidine) in alleviating oxidative damage and alteration of neurotransmitters in the brain of rats exposed to gamma radiation. Male albino rats were whole body exposed to a single dose of γ- rays (5Gy). Carnosine (50mg/Kg/day) was administered via gavages as follows: a) during 28 successive days, b) during 14 successive days before whole body gamma irradiation and administered distilled water for 14 days after irradiation, c) during 14 successive days before whole body gamma irradiation and during 14 days after irradiation with carnosine. The animals were sacrificed at 1, 7 and 14 days post irradiation. (3 hours after the last dose of carnosine). The results revealed that exposure to γ- rays, (5Gy), resulted in significant increases of the levels of thiobarbituric acid reactive substances (TBARS), protein carbonyls (CO), and advanced oxidation protein products (AOPP), associated with significant decreases of superoxide dismutase (SOD) and catalase (CAT) activities, and glutathione (GSH) content which indicate oxidative stress. Gamma rays also, induced significant decrease of the serotonin (5-HT), dopamine (DA), norepinephrine (NE) and epinephrine (EPI) contents as well as significant increase of 5-hydroxy-indole-acetic-acid (5-HIAA) level and monoamine oxidase (MAO) activity which indicated alterations in the metabolism of monoamines. Carnosine has significantly attenuated oxidative stress, and monoamine alterations in the cerebral hemispheres of irradiated rats. Carnosine might preserve the integrity of brain functions.

KEYWORDS

Carnosine, Radiation, Oxidative Stress, Neurotransmitters.

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INTRODUCTION

Radiation-related disorders are one of the challenging current health problems with far reaching medical, social and economic consequences. Human exposure to ionizing radiation has become inevitable with its vast application in diagnosis and industry. For instance, radiation therapy is an essential therapeutic modality in the management of a wide variety of tumors, but its immediate and delayed side effects on the normal tissues limit the effectiveness of the therapy. Moreover, the increased focus on treatment-related side effects in cancer survivors and the need for medical countermeasures against radiologic or nuclear accidents or terrorism have resulted in a resurgence of interest in the mechanisms of, and ways to modify radiation injury. Radiation damage is largely caused by the overproduction of reactive oxygen species (ROS), including superoxide anion ($O_2^{\bullet-}$), hydroxyl radical ($^{\bullet}OH$), and hydrogen peroxide (H_2O_2), that overwhelm the levels of antioxidants, resulting in oxidative stress. The most important consequences of oxidative stress are lipid peroxidation, protein oxidation, and depletion of antioxidant elements. If these damages are irreparable, then injury, mutagenesis, carcinogenesis, accelerated senescence and cell death can occur **(Spitz *et al.*, 2004).**

Increased production of ROS can compromise essential cellular functions, and probably contribute to brain injury (**Starkov *et al.*, 2004**). Experimental evidence revealed that the brain displays numerous biochemical and functional alterations after exposure to ionizing radiations (**Loganovsky and Yuryev, 2004).** Since the monoamines; 5-HT, DA, NE, and EPI play critical roles in consciousness, mood, thought, motivation, cognition, perception, and autonomic responses, alterations in the activity of MAO; enzymes that break down the monoamines, might play an important role in the neurodegenerative disorders. For instance, a decrease in the activity of MAO produces aggressive phenotypes **(Alia-Klein *et al.*, 2008).**

Free radical-mediated lipid peroxidation has been proposed to be critically involved in disease states including brain dysfunction, cardiovascular disease, and cancer as well as in the degenerative processes associated with aging. Efficient defense and repair mechanisms exist in living cells to protect against oxidant species. Enzymatic antioxidants such as superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) protect cell membranes from lipid peroxidation **(Sun *et al.*, 1998).** However, under abnormal conditions such as exposure to ionizing radiation the antioxidant defense system is not full operative.

Carnosine, (β-alanyl-L-histidine) is a naturally occurring dipeptide that is highly expressed in the central nervous system and can easily enter the brain from the periphery **(Bakardjiev, 2000).** It has been assigned many putative roles, such as anti-inflammatory, free radical scavenger **(Boldyerv *et al.*, 2004)**. Carnosine protects against acute renal failure induced by ischemia/reperfusion in rats (**Kurata *et al.*, 2006**). In view of these considerations, the objective of the present study is to evaluate the efficacy of carnosine in the modulation of oxidative stress, and alterations in monoamines levels in the cerebral hemispheres of irradiated rats.

MATERIALS AND METHODS

Male albino rats *Rattus rattus* (10 ± 2 weeks old; 120 ± 20 g) were purchased from the Egyptian Holding Company for Biological Products and Vaccines (Cairo, Egypt) and used for the different investigations carried out in the present study. The animals were maintained under standard conditions of light, ventilation, temperature, and humidity and allowed free access to standard pellet diet and tap water. Animals were acclimatized to laboratory conditions before starting the experiment. Biochemical analyses were performed in the morning. All animal procedures were carried out in accordance with the Ethics Committee of the National Research Centre conformed to the "Guide for the care and use of Laboratory Animals" published by the US National Institutes of Health (NIH publication No. 85–23,

1996).

Radiation Facility

Irradiation of rats was carried out with a Canadian Gamma Cell-40 (^{137}Cs) at the National Center for Radiation Research and Technology (NCRRT), Cairo, Egypt. The animal's whole bodies were exposed to gamma rays and received a dose of 5Gy administered at a dose rate of 0.5Gy/minute calculated according to the Dosimeter department in the NCRRT.

Carnosine Treatment

Carnosine was purchased from Sigma Chemical Company, suspended in distilled water and administered via gavages, to rats at doses of 50 mg/Kg body weight/day for 14 or 28 successive days. Carnosine was prepared freshly just before its administration daily.

Animal Groups: Animals were divided into five equal groups (n=18):

Control group: Healthy rats receiving distilled water via gavages for 28 successive days.

Carnosine group*:* Rats received carnosine (50mg/Kg/day) via gavages during 28 successive days.

IR group*:* Rats received distilled water via gavages during 14 successive days before whole body gamma irradiation at 5Gy and continued during 14 successive days after irradiation.

Carnosine + IR group*:* Rats received carnosine (50mg/Kg/day) during 14 successive days via gavages before whole body gamma irradiation at 5Gy and continued during 14 successive days after irradiation with distilled water.

Carnosine + IR + carnosine group*:* Rats received carnosine (50mg/Kg/day) via gavages during 14 successive days before whole body gamma irradiation at 5Gy and during 14 successive days after irradiation.

Animals were sacrificed 1, 7 and 14 days 3hours after the last dose of carnosine. The brain was rapidly excised and cerebral hemispheres separated out and a portion was weighted to prepare 10% weight/volume tissue homogenates in 0.1 M phosphate buffer (pH 7.4) using Teflon homogenizer. The homogenate was centrifugated in refrigerating centrifuge. The supernatant was used for biochemical analysis.

Lipid peroxidation was evaluated by measuring TBARS levels according to **Yoshioka *et al.* (1979)**, and protein oxidation by measuring CO and AOPP levels according to **Levine *et al.* (1990)** and **Witko-Sarsat *et al.* (1996),** respectively. SOD and CAT activities and GSH contents were estimated according to **Minami and Yoshikawa (1979); Aebi (1984**) and **Beutler *et al.*, (1963),** respectively. DA, NE, and EPI contents were determined according to **Ciarlone (1978a).** Estimation of serotonin (5-HT) and its metabolite, 5-hydroxy-indole-acetic-acid (5-HIAA), were determined according to the modified method of **Ciarlone (1978b).** Estimation of MAO activities was evaluated according to **Ozaki *et al.* (1960).**

Statistical analysis:

All the values are expressed as mean ± Standard deviation (SD). Experimental data were analyzed using one way analysis of variance (ANOVA) followed by LSD as a Post Hoc ANOVA test. Differences between means were considered significant at $p \leq 0.05$.

RESULTS

In the present study, rats fed on a standard pellet diet and treated with carnosine (50mg/Kg body weight/day) via gavages for 28 successive days showed non significant changes in the oxidant/antioxidant status and all biochemical parameters of cerebral hemispheres, compared to control group.

Whole body exposure of male albino rats to gamma radiation (5Gy) provoked oxidative stress demonstrated by significant increase ($p \leq 0.05$) of TBARS, CO and AOPP levels associated with significant decrease ($p \leq 0.05$) of SOD and CAT activities and GSH content, compared to their respective values in the control group (Tables 1 and 2). The results revealed also significant decrease ($p \leq 0.05$) of DA, NE, and EPI on the 1st, 7th and 14th day post

irradiation (Table 3). Whole body exposure of rats to gamma radiations induced decrease ($p \leq 0.05$) in serotonin level parallel to a significant increase in its metabolites 5-hydroxy-indole-acetic acid level and MAO activity ($p \leq 0.05$) on the 7th and 14th day post irradiation (Table 4).

Oral supplementation of carnosine (50mg/Kg body weight/day) to rats, for 14 days before irradiation or 14 successive days before and 14 days after irradiation, via gavages has significantly attenuated the severity of radiation-induced oxidative stress. Significant decrease ($p \leq 0.05$) of oxidative biomarkers levels on the 1st, 7th and 14th day post irradiation (Table 1), and significant increase ($p \leq 0.05$) of antioxidants levels on the 7th and 14th day post irradiation (Table 2), were observed, compared to their respective values in irradiated rats. The supplementation of carnosine has also diminished the increase of MAO activity (Table 4), which was accompanied by significant increase ($p \leq 0.05$) of monoamines level, compared to their respective levels in irradiated rats (Table 3). The results revealed also that carnosine supplementation attenuates serotonin metabolites damage substantiated by a significant improvement ($p \leq 0.05$) in serotonin, 5-hydroxy-indole-acetic acid levels compared to their respective levels in irradiated rats (Table 4).

The modulation of radiation-induced changes was more pronounced by the administration of carnosine before and after irradiation rather than its administration before irradiation only.

Table (1) *Effect of carnosine on thiobarbituric acid reactive substances, protein carbonyl and advanced oxidation protein products levels in brain cerebral hemispheres of different animal groups.*

Animal groups	days post-irradiation		
	1st day	7th day	14th day
Thiobarbituric acid reactive substances (nmol/g)			
Control	157± 3	153± 2.75	150 ±2.75
Carnosine	148 ± 2.5	150 ± 2.5	149 ± 2
IR	188 ± 2 [a]	226 ± 1.75 [a]	235 ± 2.25 [a]
Carnosine + IR	165 ± 1.75 [b]	210 ± 1.5 [ab]	209 ± 1 [ab]
Carnosine + IR+ Carnosine	162 ± 1.5 [b]	191± 2 [abc]	190 ± 0.75 [abc]
Protein carbonyls (CO) (nmol/g tissue)			
Control	39 ± 1.5	38 ± 1.75	42± 1.25
Carnosine	38 ± 1.5	39 ± 1	40 ± 0.75
IR	44 ± 1[a]	56 ± 1 [a]	66 ± 1.5 [a]
Carnosine + IR	41 ± 0.75 [b]	49 ± 0.75 [ab]	57 ± 1 [ab]
Carnosine + IR+ Carnosine	40 ± 0.75 [b]	45 ± 1 [abc]	52 ± 1 [abc]
Advanced oxidation protein products levels (µmol/g)			
Control	0.95 ± 0.012	0.94 ± 0.01	0.96 ± 0.017
Carnosine	0.88 ± 0.012	0.86 ± 0.012	0.87 ± 0.02
IR	1.09 ±0.012 [a]	1.27 ± 0.025 [a]	1.40 ±0.03 [a]
Carnosine + IR	0.98 ± 0.025 [b]	1.15 ± 0.17 [ab]	1.23 ± 0.02 [ab]
Carnosine + IR+ Carnosine	0.97 ± 0.025 [b]	1.04 ± 0.02 [abc]	1.07 ± 0.03 [abc]

Values are expressed as means of 6 animals ± standard deviation.
IR: irradiated group
a: Significant compared to control group.
b: Significant compared to irradiated group.
c: Significant compared to carnosine-pre irradiated group.

Table (2) *Effect of carnosine on superoxide dismutase and catalase activities and glutathione content in brain cerebral hemispheres of different animal groups.*

Animal groups	days post-irradiation		
	1st day	7th day	14th day
Superoxide Dismutase (U/g)			
Control	133 ± 1.75	132 ± 1.5	134 ± 2.75
Carnosine	135 ± 2.25	137 ± 3.5	136 ± 2.25
IR	155 ± 2.5 [a]	88 ± 1.5[a]	74 ± 2 [a]
Carnosine + IR	139 ± 1 [b]	103 ± 2 [ab]	92 ± 2.25 [ab]
Carnosine + IR+ Carnosine	137 ± 4 [b]	118 ± 3.5 [abc]	107 ± 4.5 [abc]
Catalase (U/g)			
Control	80 ± 3.25	82 ± 4.75	81 ± 2
Carnosine	82 ± 1.5	84 ± 3.75	85 ± 2.75
IR	95 ± 2 [a]	51 ± 2.75 [a]	43 ± 1.5 [a]
Carnosine + IR	76 ± 2.5 [b]	63 ± 2.5 [ab]	57 ± 2 [ab]
Carnosine + IR+ Carnosine	77 ± 3.5 [b]	72 ± 4 [abc]	66 ± 2 [abc]
Glutathione contents (mg/g)			
Control	8.2 ± 0.25	8.5± 0.35	8.3 ± 0.175
Carnosine	8.6 ± 0.4	8.8 ± 0.42	8.7 ± 0.4
IR	9.4 ± 0.27 [a]	5.5 ± 0.125 [a]	4.5 ± 0.175 [a]
Carnosine + IR	9.2 ± 0.25 [a]	6.5 ± 0.25 [ab]	5.6 ± 0.37 [ab]
Carnosine + IR+ Carnosine	9.1 ± 0.57 [a]	7.4 ± 1.75 [abc]	6.6 ± 0.2 [abc]

Values are expressed as means of 6 animals ± standard deviation.
IR: irradiated group
a: Significant compared to control group.
b: Significant compared to irradiated group.
c: Significant compared to carnosine-pre irradiated group.

Table (3) *Effect of carnosine on dopamine, norepinephrine and epinephrine levels in brain cerebral hemispheres of different animal grouups.*

Animal groups	days post-irradiation		
	1st day	7th day	14th day
Dopamine (ng/g)			
Control	315 ± 3.75	330 ± 1.75	327 ± 1.75
Carnosine	321 ± 1.75	338 ± 2	325 ± 2.5
IR	243 ± 1 [a]	158 ± 1.5 [a]	141 ± 1.5 [a]
Carnosine + IR	290 ± 2 [b]	246 ± 1.75 [ab]	203 ± 1.5 [ab]
Carnosine + IR+ Carnosine	287 ± 2.25 [b]	284 ± 1.5 [abc]	262 ± 1.5 [abc]
Norepinephrine (ng/g)			
Control	314 ± 3.75	300 ± 1.25	319 ± 2.5
Carnosine	303 ± 1	307 ± 2.25	315 ± 3
IR	219 ± 2.25 [a]	165 ± 2 [a]	160 ± 1.75 [a]
Carnosine + IR	248 ± 2.5 [ab]	216 ± 3.75 [ab]	208 ± 2.25 [ab]
Carnosine + IR+ Carnosine	286 ± 1.75 [bc]	261 ±1.75 [abc]	253 ± 1.5 [abc]
Epinephrine (ng/g)			
Control	161 ± 1.5	159 ± 3	164 ± 2
Carnosine	155 ± 2	154 ± 1.5	157 ± 2.5
IR	114 ± 3 [a]	71 ± 1.75 [a]	62 ± 1.75 [a]
Carnosine + IR	136 ± 3 [ab]	123 ± 2.25 [ab]	102 ± 4 [ab]
Carnosine + IR+ Carnosine	153 ± 4 [bc]	140 ± 3.5 [abc]	122 ± 1.25 [abc]

Values are expressed as means of 6 animals ± standard deviation.
IR: irradiated group
a: Significant compared to control group.
b: Significant compared to irradiated group.
c: Significant compared to carnosine-pre irradiated group.

Table (4) *Effect of carnosine on serotonin, monoamine oxidase activities and 5-hydroxyindole acetic acid levels in brain cerebral hemispheres of different animal groups.*

Animal groups	days post-irradiation		
	1st day	7th day	14th day
Serotonin Levels (ng/g)			
Control	300 ± 1.75	330 ± 3	340 ± 2.5
Carnosine	306 ± 2.5	333 ± 1.5	332 ±2.75
IR	288 ± 2.25	192 ± 3 [a]	140 ± 3 [a]
Carnosine + IR	292 ± 1.25	248 ± 2.5 [ab]	220 ± 2 [ab]
Carnosine + IR+ Carnosine	296 ± 1.75	288 ± 2.25 [abc]	276 ± 1.5 [abc]
Monoamine oxidase (MAO) (mg 5-HT consumed/g tissue /hr)			
Control	0.40 ± 0.018	0.42 ±0.018	0.44 ± 0.018
Carnosine	0.42 ± 0.017	0.41 ± 0.018	0.43 ± 0.017
IR	0.44 ± 0.015	0.65 ± 0.018 [a]	0.71 ± 0.007 [a]
Carnosine + IR	0.43 ± 0.012	0.54± 0.016 [ab]	0.57± 0.017 [ab]
Carnosine + IR+ Carnosine	0.41 ± 0.012	0.47 ±0.012 [abc]	0.50 ±0.013 [abc]
5-hydroxyindole acetic acid (ng/g)			
Control	580 ± 2	550 ± 1.25	570 ± 3
Carnosine	570 ± 3.25	540 ± 4	554 ± 3.25
IR	595 ± 2.5	808 ± 4.5 [a]	929 ± 4 [a]
Carnosine + IR	597 ± 2	732 ± 2.5 [ab]	803 ± 3 [ab]
Carnosine + IR+ Carnosine	591 ± 3.25	643± 1.75 [abc]	718 ± 4.5 [abc]

Values are expressed as means of 6 animals ± standard deviation.
IR: irradiated group
a: Significant compared to control group.
b: Significant compared to irradiated group.
c: Significant compared to carnosine-pre irradiated group.

DISCUSSION

Exposure of mammals to ionizing radiations, leads to the development of a complex, dose-dependent series of changes, including injury to different organs, which causes changes in the structure and function of cellular components. Oxidative stress with the subsequent production of ROS was postulated as one of the mechanisms of radiation toxicity (**Finkel and Holbrook, 2000).**

Experimental evidence has considered the brain a radiosensitive organ because of its high O_2 utilization rate, its high content of polyunsaturated fatty acids, which are prone to lipid peroxidation, and its high content of iron which through the Fenton reactions increases the formation of free radicals (**Halliwell, 2001**). In addition, relative to other organs brain tissues are poor in antioxidants (**Sherki *et al.*, 2001**).

Reactive oxygen species are widely implicated in the pathogenesis of secondary neuronal damage and apoptotic/necrotic cell death after traumatic or ischemic brain injury (**Hall *et al.*, 2010).** Free oxygen radicals either disrupt the blood–brain barrier or cause brain edema by affecting the neurons (**Santos *et al.*, 2005**). These radical species can also cause extensive damage to biological macromolecules, including peroxidation of membrane polyunsaturated fatty acids (PUFA). PUFA peroxidation ultimately leads to loss of both structural and functional integrity of the cell with generation of toxic aldehydic by-products which may further contribute to neuronal cell death by protein and DNA modifications (**Hall *et al.*, 2010**).

Antioxidant enzymes are influenced by oxidation status, and changes in their activity can serve as a biomarker for oxidative stress (**Voss and Siems 2006)**. In the present study, whole body exposure of male albino rats to gamma radiation (5Gy) has provoked an imbalance between oxidant and antioxidant species in the cerebral hemispheres of rats. Significant increase in the levels of TBARS, CO and AOPP accompanied by significant decrease of SOD and CAT activities and GSH content were recorded.

The increase of TBARS level is probably due to the interaction of •OH resulting as a byproduct of water radiolysis, upon exposure to ionizing radiation, with the polyunsaturated fatty acids present in the phospholipids portion of cellular membranes (**Spitz *et al.*, 2004**). In the same way, the increase of CO and AOPP levels might be attributed to the interaction of proteins with ROS (**Meaney *et al.*, 2008**). The decrease of SOD and CAT activities and GSH content is probably the consequence of cellular membrane damages. In favor of this postulation, **Saada *et al.* (2003)** reported that radiation induced oxidative damage to cell membrane and alterations in dynamic permeability followed by the release of intracellular molecules to the blood stream. In addition, proteins oxidation may contribute to the partial inactivation of enzymes **(Kregel and Zhang, 2007).** One must consider, also, that the decrease of antioxidants might result from their increased utilization to neutralize the excess of free radicals generated in the body after exposure to ionizing radiations.

It is well documented, that antioxidants play an important role in mitigating the damaging effects of oxidative stress on cells. Carnosine could readily pass through the blood brain barrier (BBB) and concentrates in the brain, which consequently protects against protein and lipid oxidation (**Yuneva *et al.*, 1999**). In the present study, carnosine (50mg/Kg / day) administered to rats via gavages 14 days pre- and 14 days post-irradiation, has significantly attenuated radiation-induced oxidative stress in the cerebral hemispheres. The decrease of TBARS, CO and AOPP, suggests its free radical scavenging activity. Furthermore, the amelioration of SOD and CAT activities and the significant recovery of GSH content suggest its potential effect in enhancing antioxidant defense. The results corroborate the findings of **Kalpana *et al.* (2011)** that carnosine possesses antioxidant activity and radical scavenging properties.

The modulatory role of carnosine might be the consequence of its ability to consume superoxide, singlet oxygen and hydroxyl radicals (**Pradeep *et al.*, 2008**), thereby contributing significantly to the intracellular antioxidant defense system (**Gandhi *et***

***al.,* 2009**). In addition, carnosine acts as metal chelating agents and inhibits the superoxide-derived Fenton reaction (**Lanza *et al.,* 2011**). Carnosine stabilizes proteins against oxidation (**Yen *et al.,* 2002**) and inhibits the formation of protein carbonylation products which occurs due to oxidative stress on proteins (**Aldini *et al.,* 2005**). In addition, carnosinase enzymes convert carnosine into β-alanine and histidine; both of these amino acids can be used for protein synthesis (**Bertinaria *et al.,* 2011**). Moreover, histidine is able to quench 49.1 to 94.9 % of hydroxyl radicals produced by Fe_2^+ and H_2O_2 (**Chan *et al.,* 1994**).

The decrease of monoamines level observed in the cerebral hemispheres of irradiated rats could be attributed to radiation-induced oxidative stress and oxidation of monoamines. However, the decrease of monoamines might be attributed to decreased synthesis resulting from radiation-induced damage to the ileal mucosa and reduction in net ilea absorption **(Herrera *et al.,* 1995**), where a decrease in the absorption of tryptophan would reduce the synthesis of serotonin, while a decrease in absorption of L-tyrosine may diminish the production of DA, NE and EPI.

The results obtained in the present study, however, showed a significant increase of MAO activity, which suggests the possibility that radiation provokes the degradation of monoamines. The increase of MAO activity might result from depletion in the absorption of sodium (**Sarobe *et al.,* 2005**). According to the results obtained in the current study, administration of carnosine induced a significant decrease of MAO activity, which was associated with a significant increase of monoamines levels, compared to their respective levels in the IR group. The results support the role of carnosine in scavenging free radicals. Carnosine can compensate for the pathogenic effects of catecholamines and may limite the synthesis of tyrosine hydroxylase, which is excitotoxic compounds and protecting pathways of their oxidative conversion **(Antonini *et al.,* 2002)**. Carnosine could readily pass through the blood brain barrier (BBB), and acts as the precursor of transmitter of histaminergic neuron system and effectively regulate brain histamine level. However, histamine cannot cross BBB and may be involved in brain inflammation **(Silverman *et al.,* 2000)**.

Carnosine has protective, antioxidant, and antiapoptotic properties. This endogenous dipeptide is important for nervous cell defense against brain injury. Carnosine increased the resistance of neuronal membranes to the *in-vitro* induced oxidation and also suppressed the glutamate receptor hyper- activation (**Min *et al.,* 2008**). The antioxidant potential of carnosine depends on the presence of imidazole ring in carnosine chemical structure. The hydrogen on the methylene carbon next to imidazole ring is likely to be a proton donor which retards oxidation **(Kohen *et al.,* 1988)**.

In conclusion, the present data suggest the ability of carnosine to protect brain against radiation injury through maintaining brain homeostasis via modulating and restoring the brain antioxidant defense system.

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مجلة
التقنيات النووية
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فاعلية الكارنوزين في تخفيف الضرر التأكسدي وإضطرابات مستوى الناقلات العصبية في مخ الجرذان المعرضة لأشعة جاما

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يتناول هذا البحث تقييم فاعلية المركب الطبيعي الكارنوزين (ثنائي الببتيد) في الحد من الضرر التأكسدى وإضطراب مستوى الناقلات العصبية في مخ الجرذان البيضاء المعرضة كلياً للأشعة جاما بجرعة واحدة قدرها ٥ جراي. ولقد تم إعطاء الكارنوزين عن طريق الفم بجرعة قدرها ٥٠ ملجم / كجم يومياً لمده ١٤ أو ٢٨ يوماً .

أوضحت النتائج أن تعرض جسم الجرذان الكلي لأشعة جاما أدي إلى حدوث نقص معنوي فى مستوى السيروتنين والدوبامين والإبينفرين والنورإبينفرين كما لوحظ وجود زيادة معنوية في مستوى خماسي هيدروكسي إيندول حمض الخليك ونشاط إنزيم أكسيديز أحادي الأمين فى خلايا المخ. و أوضحت النتائج أيضا حدوث نقص في مستوى الجلوتاثيون وبعض إنزيمات مضادات الأكسدة مثل (السوبر أكسيد ديسميوتيز والكتاليز) وهذا النقص يكون مصحوبا بزيادة نسبة الدهون فوق المؤكسدة وزيادة مستوى النواتج المتطورة لأكسدة البروتين وذلك فى أنسجة مخ الجرذان المشعة في اليوم الأول والسابع والرابع عشر بعد التعرض للجرعة الإشعاعية . أما في مجموعة الجرذان التي أعطيت الكارنوزين يوميا قبل التعرض لأشعة جاما لمده ١٤ يوما أو ١٤ يوما قبل و ١٤ يوما بعد التعرض لأشعة جاما فقد حدث تحسن ملحوظ في جميع الدلالات الكيميائية الحيوية المقاسة فى معظم أوقات التجربة. دلت النتائج علي أن الكارنوزين بما يحتويه من مواد طبيعية يلعب دورا هاما في الحد من الضرر التأكسدي وإضطرابات مستوى الناقلات العصبية في مخ الجرذان المعرضة لأشعة جاما. ولقد إتضح أن إعطاء الكارنوزين للجرذان قبل وبعد التعرض للإشعاع الجامي أعطى نتائج أفضل .

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