Original Article

Royal jelly modulates oxidative stress and tissue injury in gamma irradiated male Wister Albino rats

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Abstract

Background: Royal jelly is a nutritive secretion produced by the worker bees, rich in proteins, carbohydrates, vitamins and minerals. **Aim**: The present study was designed to determine the possible protective effects of royal jelly against radiation induced oxidative stress, hematological, biochemical and histological alterations in male Wister albino rats. **Materials and Methods**: Male Wister albino rats were exposed to a fractionated dose of gamma radiation (2 Gy every 3 days up to 8 Gy total doses). Royal jelly was administrated (g/Kg/day) by gavages 14 days before exposure to the 1st radiation fraction and the treatment was continued for 15 days after the 1st irradiation fraction till the end of the experiment. The rats were sacrificed 3rd, equivalent to 3rd post 2nd irradiation fraction, and equivalent to 3rd day post last irradiation fraction. **Results**: In the present study, gamma- irradiation induced hematological, biochemical and histological effects in male Wister albino rats. In royal jelly treated irradiated group, there was a noticeable decrease recorded in thiobarbituric reactive substances concentration when compared to γ-irradiated group. Also, the serum nitric oxide concentration was significantly improved. The administration of royal jelly to irradiated rats according to the current experimental design significantly ameliorates the changes induced in serum lipid profile. Moreover, in royal jelly treated irradiated group, there was a noticeable amelioration recorded in all hematological parameters along the three experimental intervals. The microscopic examination of cardiac muscle of royal jelly treated irradiated rats demonstrated structural amelioration, improved nuclei and normal features of capillaries and veins in endomysium when compared to gamma-irradiated rats. **Conclusion**: It was suggested that the biochemical, hematological and histological amelioration observed in royal jelly (g/Kg/day) treated irradiated rats might be due to the antioxidant capacity of royal jelly active constituents.

Keywords: Royal jelly, gamma-irradiation, oxidative stress, hematology, heart.

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Introduction

Exposure to ionizing radiation is characterized by production of reactive oxygen species (ROS) associated with increase in lipid peroxidation [1]. Lipid peroxidation (LP) is one of the main manifestations of oxidative damage and has been found to play an important role in the toxicity and carcinogenesis of many carcinogens. Free radicals are known to attack the highly unsaturated fatty acids of the cell membrane to induce LP which considered a key process in many pathological events and is one of the reactions induced by oxidative stress [2]. The increase in intracellular ROS concentration leads subsequently to oxidative stress [3] and decrease in activity of antioxidant enzymes with possible damage of cellular membranes [4].

Plasma lipids increased by day 6 post irradiation; plasma

cholesterol and triglycerides (TG) were also increased. LDL accumulated in plasma while high-density lipoprotein (HDL) levels decreased [5].

Nitric oxide (NO) is responsible for the control of platelet aggregation and the regulation of cardiac contractility. In addition, NO is produced in large quantities during host defense and immunologic reactions [6].One of the most important reactions under physiological conditions is that of superoxide and nitric oxide radicals resulting in peroxynitrite. The protonated form of peroxynitrite (ONOOH) is a powerful oxidizing agent that might cause depletion of sulfhydryl (-SH) groups and oxidation of many molecules causing damage similar to that observed when hydroxyl radicals (OH^-) is involved. It can also cause DNA damage such as breaks, protein oxidation, and nitration of aromatic amino acid residues in proteins. Under physiological conditions, ONOOH can react with other components present in high concentrations; such as H_2O_2 or CO_2, to form adduct that might be responsible for many of the deleterious effects seen in biological sites [7].

Exposure of animals to ionizing radiation causes a series of physiological changes known as acute radiation syndrome, which is dependent on the exposure dose and may lead to death. The damage to the hematopoietic system is a major factor in the mortality following an acute radiation exposure [8].

Royal jelly (RJ), a food produced by the hypopharyngeal and mandibular glands of the worker honey bees (*Apis mellifera* Linn) contains many important compounds with biological activity, such as free amino acids, proteins, sugars, fatty acids (mainly 10-hydroxy-2-decenoic acid; 10-H DA), minerals (mainly iron and calcium) and vitamins (mainly thiamine, niacin, riboflavin) [9-10]. It has been reported that RJ has several pharmacological activities, including vasodilative and hypotensive activities [11], increase in growth rate of chick embryos [12], disinfectant action [13], antihypertensive activity [14], antifatigue activity [15] and antiallergy activity [16].

This study was designed to estimate the possible protective effects of RJ against oxidative stress induced by gamma irradiation in male Wister albino rats by measuring certain biochemical parameters (TBARS, NO, triglycerides, cholesterol, HDL, HDL risk ratio and LDL) and hematological parameters as blood elements (Erythrocytes, leukocytes, differential leukocyte count, platelets count, hemoglobin and hematocrite) in addition to monitoring the histological changes in heart tissues.

Materials and Methods

Animal care and handling

All animals' studies were conducted in accordance with criteria of the investigations and Ethics Committee of the Community Laws governing the use of experimental animals. Male Wister albino rats weights (120±5 grams at the beginning of the experiment) were obtained from the Egyptian Holding Company for Biological Products and Vaccines were used as experimental animals. The rats were transferred to the experimental environment one week prior to the initiation of the experiment to ensure their environmental adaptation. The rats were housed in regular designed cages and maintained in conditions of good ventilation, normal temperatures (25 °C) and humidity range (30-50%). Six rats were placed into each cage. Food and water were provided adlibitum to the animals.

Irradiation

Radiation facility were the Canadian Gamma cell–40 (137Cs) housed at the National Center for Radiation Research and Technology (NCRRT), Cairo, Egypt. Rats of irradiated groups were exposed totally to gamma irradiation with a fractionated dose (2 Gy every 3 days up to total dose 8 Gy). The dose rate at the time of experiment was 0.48 Gy /min.

Royal jelly

Royal Jelly (RJ) was supplied by Pharco Pharmaceuticals Alexandria, Egypt. RJ was prepared to supplementation by dissolving 3500 mg RJ (lyophilized) in 50 ml distilled water at a concentration of 70.0 mg/ml just before experimental use. This suspension were given to rats by gavage and every rat was received RJ in a concentration of (1g /kg body weight). The selective doses of RJ were literature based [17].

Animal groups

The patch of animals was distributed into main groups and subgroups according to the treatment and requirements of the experiment. In this study, 72 male albino rats were divided into four groups: Group 1: normal rats (n=18), rats in this group were neither treated nor irradiated. Group 2: irradiated rats (n=18), rats in this group were exposed to whole body gamma radiation with a fractionated dose (2 Gy every 3 days up to 8 Gy total doses). Group 3: royal jelly treated rats (n=18): rats in this group were administrated with freshly prepared RJ at 10:00 am at dose (1g/kg-body weight) in volume of 1-1.5 ml/dose via oral gavages directly into the stomach along the period of the experiment (27 days). Group 4: Royal Jelly treated irradiated rats (n=18): Rats in this group were administrated with freshly prepared RJ at 10:00 am at dose (1g/kg-body weight) in volume of 1-1.5 ml/dose via oral gavage directly into the stomach for 14 consecutive days before exposed to fractionated dose and within the period of fractionated irradiation(13 days) .

Haematological study

Blood was collected from the retro-orbital venous plexus in a vial containing 0.5 M EDTA (Ethylene diamine tetra acetic acid). Total number of erythrocytes, total number of leukocytes, differential leukocyte count, platelets count, hematocrite (Hct) %, and hemoglobin (Hb) concentration were estimated by blood cell counter (Cell dine 1700). Blood smears were prepared as soon as possible after blood collection on glass slide and quickly dried and stained with Leishman's stain for differential blood count.

Biochemical study
After each radiation fraction, the animals were anesthetized on 3rd day after irradiation. Blood samples were collected and put into chilled non heparinized tubes, which were centrifuged at 3000 r.p.m for 10 minutes to prepare serum. The sera were frozen at -20 ºC for the following measurements:

Determination of nitric oxide (NO) is based on measurement of total nitrite levels which is the only stable end product of the autoxidation of NO in aqueous solution (formed by reaction of NO with superoxide or oxyhemoglobin) which provides a reliable and quantitative estimate of NO output in *vivo* [18].

Lipid peroxidation product, malondialdehyde (MDA), was measured by thiobarbituric acid (TBARS) assay, which is based on the determination of malondialdehyde (MDA), an end product of lipid peroxidation, which can react with thiobarbituric acid to yield a pink colored complex exhibiting a maximum absorption at 532nm [19].

The serum levels of triglycerides, cholesterol and HDL were estimated using kits from bio-diagnostic for Research Kits, Egypt. The concentration of triglycerides was determined using the method of Fassati and Prencipe [20]. The cholesterol is determined after enzymatic hydrolysis and oxidation. The quinonemine is formed from hydrogen peroxide and 4-Aminoantipyrine in the presence of phenol and peroxidase [21]. High density lipoproteins and LDL were separated from serum by precipitating all lipoproteins except the HDL fraction- Cholesterol [22]. Cholesterol of very low-density lipoproteins plus low-density lipoproteins (VLDL+LDL)-C was calculated as the difference between the serum cholesterol value and HDL-C. The HDL risk ratio was calculated as the division of total cholesterol by HDL.

Histological study
Heart samples were excised and fixed in formalin 10% and were hydrated in ascending grades of ethanol, cleaned in xylene and embedded in paraffin. Sections (5 µm thick) were cut and stained with hematoxylin and eosin (H & E) [23].

Statistical analysis
The statistical package for social sciences SPSS/PC computer program was used for statistical analysis of the results. Data were analyzed using one-way analysis of variance (ANOVA) followed by Newman–Keuls post hoc test for multiple comparisons. The data were expressed as mean ±S.E. Differences were considered statistically significant at ($P < 0.05$).

Results

Lipid peroxidation
No significant change observed in serum lipid peroxidation level in RJ treated irradiated group as compared to normal one. Exposure of rats to γ- radiation resulted in significant ($P<0.05$) increase in lipid peroxidation as measured by the formation of TBARS in serum at the 3 time intervals as compared to control (Table1). Daily administration of RJ before and within irradiation period significantly abolished these radiation induced elevation in TBARS level (Table 1).

Lipid profile
No significant change observed in serum triglycerides, cholesterol, HDL, HDL risk ratio and LDL in RJ treated irradiated group when compared to control one. The levels of triglycerides, cholesterol, HDL risk ratio and LDL in serum were significantly higher ($P<0.05$) in irradiated group when compared to control group. Administration of RJ ameliorated the elevation in lipid profile. On the other hand, radiation exposure resulted in significant decrease in HDL in serum of irradiated rats. This effect is significantly prevented by daily administration of RJ (Table 1).

Nitric oxide
There was no significant change in NO concentration in RJ treated irradiated group as compared to normal one. Exposure of rats to gamma - radiation resulted in significant ($P<0.05$) decrease in serum NO concentration at the 3 time intervals as compared to control. In RJ treated irradiated group, there was a significant change in the concentration of NO in comparison with irradiated rats (Table1).

Hematopoietic system
Animals treated with RJ alone didn't show any significant change in various hematological parameters (Erythrocytes, leukocytes, differential leukocyte count, platelets count, hemoglobin and Hematocrite) as compared to control (Tables 2 and 3).

Total erythrocytic count decreased at the 3 time intervals of the experiment with a maximum decrease on the last time interval following γ-irradiation as compared to control values. In RJ treated irradiated group, a significant ($P<0.05$) increase in red cells count was noticed on the 3 time intervals of the experiment when compared to irradiated group (Table 2). Hemoglobin concentration in irradiated group showed significant ($P<0.05$) decrease along the period of the experiment when compared to control group, with a maximum decrease in the last time interval. Irradiated animals treated with RJ exhibited higher hemoglobin concentration when compared to irradiated rats. Hematocrite percentage was found to be significantly lower ($P<0.05$) in irradiated group when compared to control, with a maximum decline on the 15th day post-first irradiation fraction. In RJ treated irradiated group Hematocrite % showed significant change ($P<0.05$) when compared to irradiated group (Table 2).

A marked decline in total leucocytic count was also observed along the period of the experiment, with a maximum decrease on the last time interval in irradiated rats. Animals treated with RJ and irradiated showed significant increase ($P<0.05$) when compared to irradiated rats (Table 2).

Table 1 Serum levels of NO, TBARS, triglycerides, cholesterol, LDL, HDL, HDL risk ratio in different rats

Rat Groups	Experimental times after irradiation fractions		
	3rd day after 2Gy	3rd day after 4 Gy cumulative (2Gyx2)	3rd day after 8 Gy cumulative (2Gyx4)
		NO (μM/l)	
I	46.98±2.04[a]	47.99±2.11[a]	46.98±2.04[a]
II	49.07±0.81[a]	49.76±0.33[a]	50.06±0.42[a]
III	34.18±0.08[b,d]	28.74±0.34[f]	22.35±0.73[g]
IV	42.01±2.14[c]	34.55±0.27[d]	34.71±0.31[d]
LSD = 4.96			
		TBAR I S (nmole/ml)	
I	1.95±0.11[a]	1.85±0.08[a]	1.98±0.03[a]
II	1.93±0.14[a]	1.77±0.14[a]	1.87±0.19[a]
III	4.16± 0.16[b]	4.27±0.29[b]	4.95±0.29[d]
IV	3.01 ±0.44[c]	3.04± 0.28[c]	3.23±0.11[c]
LSD = 4.96			
		Triglycerides (mg/dl)	
I	89.71±2.72[a]	92.34±1.66[a]	91.97±1.73[a]
II	90.65±2.38[a]	90.65±2.38[a]	91.51±2.55[a]
III	144.0±2.78[b, f]	174.38±7.47[d]	266.85±12.81[e]
IV	112.78±1.65[c]	121.28±4.23[c]	144.99±2.65[f]
LSD = 20.44			
		Cholesterol (mg/dl)	
I	125.18±3.9[a]	124.82±3.17[a]	124.58±3.32[a]
II	124.95±2.50[a]	124.23±3.32[a]	121.53±4.6[a]
III	183.35±5.51[b]	188.59±1.9[b]	266.87±12.81[d]
IV	142.04±1.59[c]	161.69±2.22[f]	202.62±2.15[e]
LSD = 14.03			
		LDL (mg/dl)	
I	51.79±6.96[a]	52.63±4.62[a]	52.28±2.29[a]
II	48.79±3.42[a]	51.37±5.21[a]	50.67±3.43[a]
III	120.55±5.53[b]	142.18±2.11[f]	230.18±13.05[g]
IV	75.53±1.32[c]	107.03±3.57[d,]	157.02±2.09[e, f]
LSD = 21.63			
		HDL (mg/dl)	
I	76.07±0.95[a]	74.25±0.7[3a]	74.18±0.71[a]
II	76.45±0.77[a]	76.23±0.52[a]	74.55±1.41[a]
III	62.81±0.46[b]	46.41±0.71[f]	36.45±0.58[g]
IV	67.17±0.76[c]	54.67±1.9[d]	45.6±0.51[e, f]
LSD = 4.37			
		HDL risk ratio (%)	
I	1.62±0.09[a]	1.57±0.05[a]	1.60±0.0[3a]
II	1.58±0.048[a]	1.55±0.043[a]	1.58±0.04[a]
III	2.87±0.09[b]	4.02±0.08[f]	7.30±0.42[g]
IV	2.03±0.02[c]	2.93±0.142[d, b]	4.38±0.06[e, f]
LSD =0.41			

Group I = Control; Group II = RJ treated; Group III = irradiated; Group IV = RJ treated + irradiation. Each value represents mean of 6 records ± S.E. Means with dissimilar superscript letter are significantly different at ($P < 0.05$).

Table 2 Variation in hematological parameters in different animal groups

Rat Groups	Experimental times after irradiation fractions		
	3rd day after 2Gy	3rd day after 4 Gy cumulative (2Gyx2)	3rd day after 8 Gy cumulative (2Gyx4)
	Erythrocytes (10^6/mm^3)		
I	6.56± 0.26[a]	6.44±0.49[a]	6.29 ± 0.31[a]
II	6.58± 0.50[a]	6.71± 0.27[a]	6.74±0.28[a]
III	4.97±0.16[b,c]	4.29±0.14[b,e]	2.75±0.44[d]
IV	6.02±0.26[a,c]	5.33±0.16[c]	5.11±0.12[c,e]
LSD = 0.92			
	Leukocyte count (10^3/mm^3)		
I	8.55±0.85[a]	8.55 ±0.85[a]	7.97±0.58[a]
II	8.58±0.43[a]	8.80± 0.88[a]	8.88±0.87[a]
III	4.43±0.13[b]	2.54± 0.28[d]	0.26±0.02[e]
IV	6.30±0.35[c]	4.28±0.26[f,b]	3.2±0.24[f,b,d]
LSD = 1.67			
	Platelets count (10^3/mm^3)		
I	317.67± 28.35[a]	302.17±40.65[a]	314.0±53.05[a]
II	325.67± 36.92[a]	339.83±33.23[a]	347.0±31.04[a]
III	177.83±16.76[b,c]	130.83±5.28[b,f]	49.50±10.53[e]
IV	298.50±17.02[a]	214.50±6.87[c]	179.17±17.19[c,f]
LSD =83.66667			
	Hemoglobin concentration (g/dl)		
I	13.13±0.31[a]	12.8±0.34[a]	12.78±0.39[a]
II	13.23±0.59[a]	13.2±0.61[a]	13.25±0.8[a]
III	9.82± 0.43[b]	9.42± 0.35[b]	8.07± 0.13[d]
IV	11.42±0.36[c]	11.2±0.54[c]	11.23±0.28[c]
LSD = 1.35			
	Hematocrite %		
I	44. 95± 0.98[a]	45.57±0.96[a]	44.38±1.27[a]
II	43.38± 0.6[a]	43.88±0.61[a]	44.52±0.95[a]
III	33.68±0.75[b]	26.5±0.87[d]	22.03±2.52[e]
IV	42.47± 0.66[a]	31.57±1.11[c,b]	34.78±1.54[c,b]
LSD = 4.46			

Group I = Control; Group II = RJ treated; Group III = irradiated; Group IV = RJ treated + irradiation. Each value represents mean of 6 records ± S.E. Means with dissimilar superscript letter are significantly different at ($P < 0.05$).

Table 3 Variation in differential leukocyte count in different animal groups

Rat Groups	Experimental times after irradiation fractions		
	3rd day after 2Gy	3rd day after 4 Gy (cumulative 2Gyx2)	3rd day after 8 Gy (cumulative 2Gyx4)
	Lymphocytes %		
I	77.33±0.76[a]	77.17±0.65[a]	76.33±0.71[a]
II	78.5±2.03[a]	79.17±2.09[a]	78.33± 1.69[a]
III	46.0± 1.90[b]	33.33±1.31[d]	very low Count 50.0±4.48[e]
IV	60.83±3.26[c]	57.83±3.37[c]	
LSD = 7.83			
	Monocytes %		
I	6.83±0.40[a]	7.00±0.40[a]	7.00±0.40[a]
II	7.17±0.31[a]	7.33±0.42[a]	7.50±0.34[a]
III	3.0±0.37[b]	2.16±0.31[b]	very low count
IV	4.83±0.48[c]	4.67±0.33[c]	5.83±0.26[c]
LSD = 1.33			
	Neutrophil %		
I	31.33±1.33[a]	31.5±1.52[a]	31.00±1.11[a]
II	32.00±1.39[a]	32.5±1.75[a]	33.00±1.51[a]
III	16.30±0.51[b]	12.67± 0.8[b]	very low count
IV	24.67±2.011[c]	23.33±1.63[c]	25.0±2.58[c]
LSD =6.00			

Group I = Control; Group 2 = RJ treated; Group III = irradiated; Group IV = RJ treated + irradiation. Each value represents mean of 6 records ± S.E. Means with dissimilar superscript letter are significantly different at ($P < 0.05$).

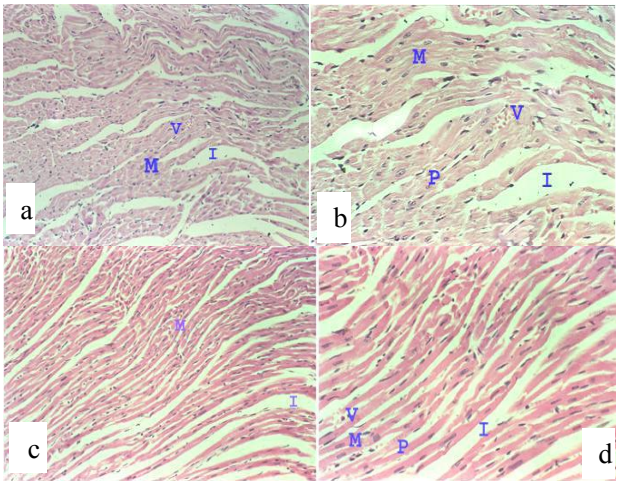

Fig. 1 Transverse section in the cardiac muscles of rats: (a)Control: normal architecture of branched anastomose cardiac muscle fibres with nucleus (M) and interstitial connective tissue (I), (H&E X: 250) (b)Control: vein with erythrocytes (V); Capillary (P), (H&E X: 500) (c) RJ: normal architecture of branched anastomose cardiac muscle fibres with nucleus (M) and interstitial connective tissue (I), (H&E X: 250) (d) RJ: vein with erythrocytes (V); Capillary (P), (H&E X: 500).

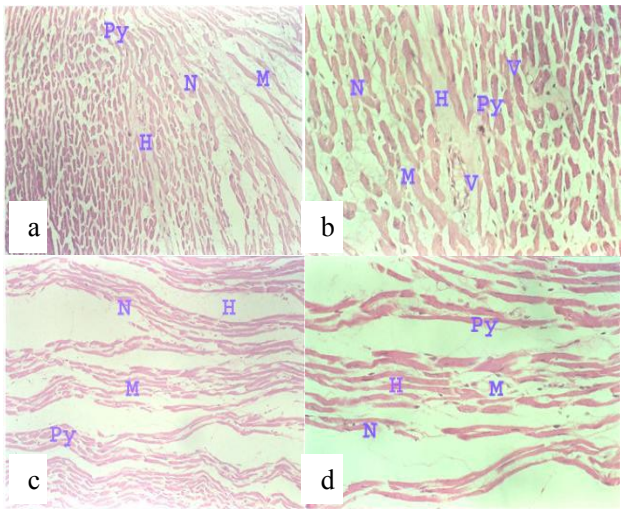

Fig.2 Transverse section in the cardiac muscles of rats: (a) Irradiated (2 Gy):sticky , ill-defined shape and moderately damaged cardiac muscle fibres (M); sever hyaline degeneration(H), (H&E X: 250) (b) Irradiated (2 Gy): necrosis (N); pyknosis (Py) and congested blood vein (V), (H&E X: 500) (c) Irradiated (2 Gy)+ RJ: slight damage of cardiac muscle fibres, mild hyaline degeneration (H) (H&E X: 250) (d) Irradiated (2 Gy)+ RJ: improved nuclei and reduction in necrosis (N), (H&E X: 500).

In differential leucocytic count, a significant decrease ($P < 0.05$) of monocytes, lymphocyte and Neutrophil was observed at the 3 time intervals in irradiated group as compared to control values. In γ- irradiated rats treated with RJ, this decrease was less pronounced in comparison with irradiated rats (Table3).

The histological study on control and RJ treated rats display normal cardiac muscle fibers branch which anatomized with other fibers to form a network, each cardiac muscle cell own nucleus located centrally as well as normal veins with erythrocytes and blood capillaries (Figure 1).

In the present work, clear histopathological changes were observed after the whole body γ-irradiation in cardiac muscles. Abnormal structures of cardiac muscles were found as ill-defined shape, necrotic, pyknotic nuclei, sever dilated, widened and inflammated capillaries in endomysium (Figures 2-4).

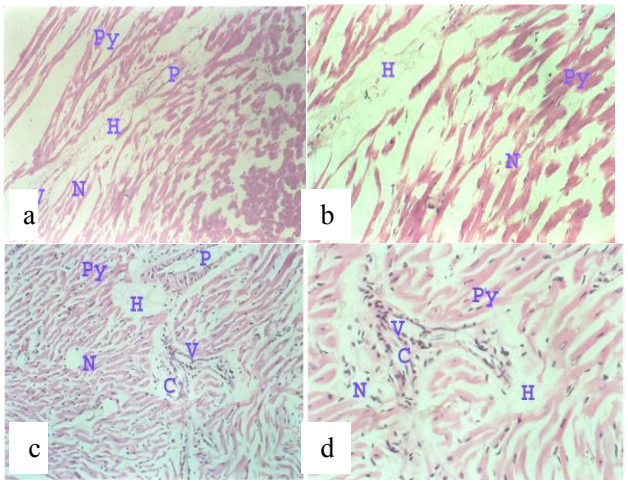

Fig.3 Transverse section in the cardiac muscles of rats: (a) Irradiated (2×2 Gy): sticky, ill-defined shape and severely damaged cardiac muscle fibres (M); sever hyaline degeneration (H); dilated congested vein (V); congested blood capillary (P),(H&E X: 250) (b) Irradiated (2×2 Gy): necrosis (N); pyknosis (Py), (H&E X: 500) (C) Irradiated (2×2 Gy)+ RJ: moderately damaged cardiac muscle fibres (M); moderate hyaline degeneration (H); congested blood capillary (P),(H&E X: 250) (d)Irradiated (2×2 Gy)+ RJ: mild dilated congested vein (V); cellular infiltration (C); mild necrosis (N); mild pyknosis (Py),(H&E X: 500).

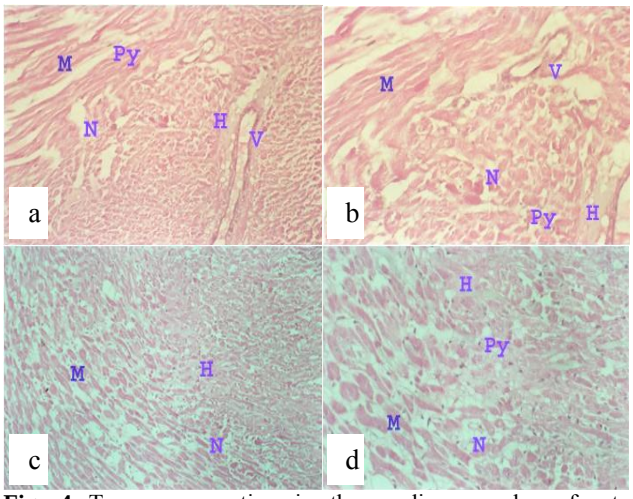

Fig. 4 Transverse section in the cardiac muscles of rats. (a)Irradiated (2×4 Gy): sticky, ill-defined shape and severely damaged cardiac muscle fibres (M); sever hyaline degeneration (H); sever congested vein (V), (H&E X: 250). (b)Irradiated (2×4 Gy); severely ruptured congested vein (V); sever necrosis (N); pyknosis (Py), (H&E X: 500). (c) Irradiated (2×4 Gy) + RJ: moderately damaged cardiac muscle fibres (M); moderate hyaline degeneration (H) (H& E X: 250) (d) Irradiated (2×4 Gy) +RJ: reduction in necrosis (N) and pyknosis (Py), (H&E X: 500).

The supplementation of RJ to rats before the exposure to the first dose of radiation and within the period of radiation exposure ameliorate the structure of cardiac muscles, improve nuclei and ameliorating features of capillaries and veins in endomysium were noticed (Figures 2-4).

Discussion

The exposure to ionizing radiation is known to induce oxidative stress through generation of reactive oxygen species (ROS) resulting in imbalance of the pro-oxidant and antioxidant activities ultimately resulting in cell death [24]. The major forms of cellular damage induced by radiation are DNA damage, lipid peroxidation and protein oxidation. The results of the present study demonstrate increased concentration of TBARS; one of the lipid peroxide indices (Table1). The increase in TBARS level may be attributed to the overproduction of ROS [1]. Radiation exposure induced radiolysis of water in the aqueous media of the cells which leads to production of hydroxyl radicals (•OH). Hydroxyl radical interact with the polyunsaturated fatty acids in the lipid portion of biological membranes initiating the lipid peroxidation and finally damaged the cell membranes [25].

Furthermore, the oxidative stress is possibly involved in the pathology of some diseases and other errors of lipid and protein metabolism [26].Alterations in lipid metabolism are probably due to radiation induced liver injury [25]. In the present study, significant changes in serum lipid profile post- irradiation were observed when compared to control values (Table1).The ionizing radiation induced oxidative stress that might alter hepatic lipid metabolism and serum lipoproteins [27]. Onody et al [26] reported that radiation exposure is associated with induction of oxidative stress and elevated levels of lipid fractions and LDL. The hyperlipidemic state observed on the serum of irradiated rats might result from increased fat mobilization from adipose tissues due to radiation induced cellular biomembranes injury. In addition, the decrease in lipoprotein lipase activity (clearing factor) reduces the uptake of lipids by adipose cells. Furthermore, the elevated level of total cholesterol could be resulted from increased synthesis as an early reaction necessary for the restoration of biomembranes [28].

Meanwhile, Nitric oxide is a small diffusible highly reactive molecule, can generate oxidative stress. However, the decrease in NO content recorded in serum after exposure to gamma radiation (Table 1) might be due to its interaction with superoxide anion to form the peroxynitrite which is a potent oxidant that can react with cellular lipids, proteins and DNA and accelerate cell toxicity [29-30]. It was reported that NO concentration showed significant decreases in liver, intestine and plasma of irradiated rats [31]. Furthermore, the depletion in NO level could be attributed to a decrease in its synthesis. The radiation exposure induced decrease in NO synthase expression [32].

In addition, there was a considerable decrease in hematological values (erythrocytes, leukocytes, differential leukocyte count, platelets count, hemoglobin and hematocrite) post-irradiation as compared to control values (Tables 2 and 3). The decrease in platelets count is accompanied with decrease in erythrocyte count. Whole-body gamma-irradiation induced direct destruction of mature circulating cells, loss of cells from the circulation by hemorrhage, or leakage through capillary walls and reduced cell production [8]. The decrease in the values of hematological parameters following radiation exposure may be assigned to direct damage caused by a lethal dose of radiation [33]. The cellular elements of the blood are particularly sensitive to oxidative stress because their plasma membranes contain a high percentage of polyunsaturated fatty acids (PUFA) [34]. Therefore the decrease in white blood cells differential count recorded in the irradiated rats might be the consequence of radiation-induced lipid peroxidation and damage of their cell membranes. The decrease in hemoglobin content could be attributed to the decline in the number of red blood cells. Also, the decrease in hematocrite might be the consequence of erythropoiesis failure, destruction of mature cells, or increased plasma volume [35]. Also, the depletion of peripheral blood elements may be a bone marrow syndrome [36].

Reduction of oxidative stress after radiation exposure was one of the basic mechanisms used in to reduce radiation hazards. Many of chemicals that protect cells against the effects of radiation are especially effective when they act as radical scavengers. In addition, antioxidants do not act only as scavengers of reactive oxygen species, but they affect gene expression in cultured cells, in laboratory animals, and in humans [37].

The RJ administration to irradiated rats decreased the serum TBARS level when compared to irradiated rats (Table 1). The increase in TBARS levels were claimed as an important determinant of altered lipid metabolism due to radiation exposure. El-Nekeety et al [38] reported that, the RJ administration resulted in significant improvement in serum MDA levels of irradiated albino rats. In current study, RJ administration according to the experimental design reduced serum cholesterol, triglycerides and LDL in serum. Moreover, significant amelioration were observed in HDL level of RJ treated irradiated rats. It is reported that antioxidants reduce oxidative susceptibility to HDL [39] and control hyperlipidemia [40].That might potentiate antiatherogenic effects of antioxidants including RJ. Therefore, the present data suggest that daily administration of RJ might have a beneficial effect in treatment of the hyperlipidemic cases.

The experimental data revealed that, rats treated with RJ before whole body gamma -irradiation and during the period of radiation exposure significantly reduced structural changes induced in cardiac muscles (Figures 1-4).

Conclusively, the prolonged administration of RJ provides

a considerable ameliorative effect against oxidative stress, biochemical impairments and histological changes observed after irradiation. It protects hematopoietic system and exhibited antihyperlipidemic properties that reduce the risk of atheroma.

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