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Protective Effects and Its Relative Mechanisms of Low Dose Ionizing Radiation on pancreatic cells of Male Diabetic Rat's

***Hanaa F. Waer, **Seham A. Helmy, *Rabab M. Mahmoud**

*Atomic Energy Authority. National Center For Radiation Research and Technology, Biology Department - (King Khalid University Faculty of Science – University Center for Girls)
**Suez Canal University, Faculty of Veterinary Medicine, Department of Cytology and Histology.

Abstract

Back ground & Aim of the work: Diabetes mellitus (DM) is a chronic metabolic disorder brings great danger to human health. Low-dose-rate radiation modulates various biological responses including carcinogenesis, immunological responses and diabetes. This study examined the effect of low doses of irradiation on the pathological and ultrastructural progression of type I diabetes in rats inducted by Streptozotocin.

Material and Methods: The present study was done on 80 healthy adult albino male rats 9 weeks age, in the weight range from (150–200 gm). Rats were grouped to 4 groups they were cared according to the Guiding Principle in the Care and Use of Animals. Diabetes was induced by a single intraperitoneal injection of freshly prepared Streptozotocin (STZ- 45 mg/kg b.w.).

Whole body gamma irradiation was performed using Caesium -137. Animals were exposed to fractionated dose levels of 0.5 Gy/week of γ-radiation for 3 and 6 weeks. The body weight, blood glucose and insulin levels were measured after 3 and 6 weeks. Small blocks of pancreatic tissues of different groups were removed and prepared for pathological and ultrastructure examination.

Results: An elevated level of glucose and decreased level of insulin in blood were first detected at 3 and 6 weeks of age in the STZ treated rats. There was significant and remarkable tendency of gaining normal levels of both blood glucose and blood insulin by irradiation exposure especially after 6 weeks of irradiation. Both suppression of cell death and cellular injury induced by STZ were also observed by EM examination in 3 week and 6 weeks.

Conclusion: The present results indicated that treatment with 0.5 Gy γ rays suppresses progression of type I diabetes in STZ rats.

Keywords: insulin glucose - electron microscope- pathology –STZ

Introduction:

Streptozotocin (STZ) is a naturally occurring nitrosourea with molecular weight of 265 and empirical formula of C_{14} H_{27} N_5 O_{12} **(Dorr and Fritz, 1980**). It is widely used to induce insulin-dependent diabetes mellitus in experimental animals because of its toxic effects on islet Beta cells **(Punithavathi *et al.*, 2008; Fadillioglu *et al.*, 2008**). The diabetogenic action of STZ is the direct result of irreversible damage to the pancreatic Beta cells resulting in degranulation and loss of capacity to secrete insulin (**Gu *et al.*, 1997).** STZ given intravenously or intraperitoneally to laboratory mice in multiple sub-diabetogenic doses, induces pronounced pancreatic insulitis with eventual destruction of insulin-secreting Beta cells and finally cause

diabetes mellitus. In an experimental study in rats, streptozotocin given intraperitoneally in a dose of 45 mg/kg body weight of animals, effectively produced hyperglycemia (**Zafar *et al.*, 2009 a, b).** Pretreatment with nonlethal low-dose irradiation has been shown to have a protective effect against oxidative injury in animal tissues. At low doses, radiation is generally regarded as safe, and its effect, if any, is considered to be negligible. Induction of hormesis and adaptive response by low-dose radiation (LDR) has been extensively indicated (**Takahashi *et al.*, 2000**). Adaptive response induced by LDR was not only resistant to damage caused by a subsequently high-dose radiation, but also cross-resistant to other non-radiation challenges, such as chemicals. Mechanisms by which LDR induces the preventive effect on radiation- or chemical-induced tissue damage induced by expression of protective proteins, such as heat shock proteins and antioxidants. Since oxidative damage to tissues is a human diseases including diabetes, this review will summarize the available data with an emphasis of the preventive effect of LDR on the development of diabetes and the therapeutic effect of LDR on diabetic cardiovascular complications **(Chi Zhang *et al.*, 2010).** There is some evidence that a little radiation can be effective in stimulating the body's natural defenses against free radical formation that damages cells. Bushing states that "the prevailing explanation is that a little radiation stimulates hormonal and immune responses to other toxic environmental agents (**Antone, 2011**). Few studies indicating LDR prevention of the development of diabetes, many studies have demonstrated LDR, specifically low-intensity or power laser (LIL), therapeutic effectiveness of diabetic wound healing. Diabetes mellitus represents a set of autoimmune, metabolic and genetic disorders that share one major characteristic, hyperglycaemia (**Eisenbarth, 2007**). Diabetes continues to be a major cause of excessive morbidity, severe disability and premature death in Western populations. In developed countries, the cost of diabetes to society may be estimated to be as high as 5% of the total health costs, much of which relates to the chronic vascular complications of this disorder (**Williams *et al.* 1992**). Protective effects of a single low-dose whole body $60^{o}C$ gamma irradiation against alloxan-induced hyperglycemia in rats was previously studied, it had been observed that, the increase in pancreatic lipid peroxide level was prevented by irradiation at a dose of 0.5 or 1.0 Gy; also LDR at 0.5 Gy prevented degranulation observed in diabetic beta cells (**Takehara, 1995**). Prevention of type I diabetes by low-dose gamma irradiation in non-obese diabetic (NOD) mice was detected, it had been stated that treatment with 0.5 Gy γ rays suppresses progression of type I diabetes in NOD mice. The increase in blood glucose and decrease in blood insulin were effectively suppressed by irradiation, also both suppression of cell death by apoptosis and an increase in superoxide dismutase (SOD) activity were observed in the pancreas 1 week after irradiation. **Takahashi *et al.* (2000)** showed that, LDR delayed the onset of type I diabetes in NOD mice by suppressing apoptotic cell death in pancreas probably through enhancing antioxidant defense mechanisms. **Nomura and Sakai (2006)** also declared that, low-dose-rate radiation modulates various biological responses including carcinogenesis, immunological responses and

diabetes (**Wang, 2008**). Clinical application of low-dose-rate γ radiation for diabetes treatment showed that continuous low-dose-rate γ irradiation ameliorates diabetic nephropathy and increases life span in male mice (**Takaharu *et al.*, 2011)** . These preliminary results are really encouraging for us to do further fine structural studies to investigate the effect of repeated low-dose radiation exposure (0.5 Gy X ray/week for 6 weeks) on the ultrastructural change on pancreas of streptozotocin diabetic rats and finally we come to the fact that low dose radiation had a remarkable amelioration on the pathological ultrastructural induced by STZ .

Material and methods:

The present study was done on healthy 9 weeks age adult albino male rats in the weight range of (150–200 gm) housed in specially designed cages and maintained under standard conditions. Rats were consumed standard rodent diet and tap water. Clinical monitoring of the animals was also performed to evaluate body weight, blood glucose, and insulin concentrations weekly.

Chemicals:

Streptozotocin (STZ) was obtained from Sigma Chemical Co. (St. Louis, MO, USA).

Radiation facility:

Whole body gamma irradiation was performed at the National Centre for Radiation Research and Technology, Atomic Energy Authority (NCRRT), Cairo, Egypt, using Caesium -137 in a Gamma cell-40 Irradiator (Atomic Energy of Canada Limited, Canada). Animals were exposed to fractionated dose levels of 0.5 Gy/week of γ-radiation. The γ-radiation delivered at a dose rate of 0.61 Gy min–1 for 3 and 6 weeks.

Induction of diabetes:

STZ provided an animal model of type 1 diabetes. Diabetes was induced by a single intraperitoneally injection of freshly prepared STZ (45 mg/kg B.wt.), dissolved in freshly prepared 0.05M of sodium citrate buffer, pH = 4.6, stored at 4 ^{0}C and protected from environmental extremes **(Mitra *et al.*, 1996).** Normal blood glucose level was measured in fasting rats before STZ injection (zero-time), then measured again 48 hr after STZ injection to be sure that the rats became diabetic, their weight also must determined before and after injection.

STZ-injected groups considered to be diabetic when blood glucose values were above 250 mg/dl. The blood glucose level was determined by glucose oxidase method using a one touch basic plus glucometer (Lifescane Ltd., California, USA).

Experimental Design:

Animal treatments:

Treatments were initiated soon after establishment of diabetes 3 days after administration of STZ. Soon after diabetes induction is clear low doses γ-radiation were used in this experiments for 3 and 6 weeks.

Animal groups and experimental design:

Rats were divided randomly into four groups ten rats for each:

1- **G1: normal control group**, animals feeding on normal diet (injected i.p. with citrate buffer)

2- **G2: diabetic group**, animals injected with STZ and became diabetic.

3- **G3: irradiated group**, animals exposed to 1/2 Gy/week for 3 weeks and 6 weeks.

4- **G4: diabetic irradiated group**, animals suffer from diabetes and subjected to1/2 Gy/week of γ-radiation for 3 and 6 weeks .

Biochemical measurements

1- **Blood glucose level**

Blood glucose level and body weight of every rat were determined every week. Blood sample was collected from ocular orbit vein by heparinized heamatocrit capillary tubes.

2- Isulin level

Insulin was assayed in the Medical Service Unit of the National center for Radiation Research And Technology Center by ELISA kits according to the method of **Byersdorfer *et al.*, (2005)** and based on the sandwich principle.

Histological preparation:

The sacrificed animals were quickly dissected. Sample of the pancreas was removed and fixed in 10% neutral formalin for 24 hours and thin sections were prepared (5 µ thick) and stained with Hematoxylin and Eosin **(Jamshidzadeh *et al.*, 2008).**

Histochemical preparation

1. Deoxyribonucleic acid (DNA)

DNA was histochemicaly determined by applying Feulgen's technique **(Pearse, 1985).**

Electron Microscope preparation:

Rats were dissected and small blocks of pancreatic tissues of different groups were prepared according to the method of **Reynolds (1963)** and investigated on a JEOL 100CX TEM.

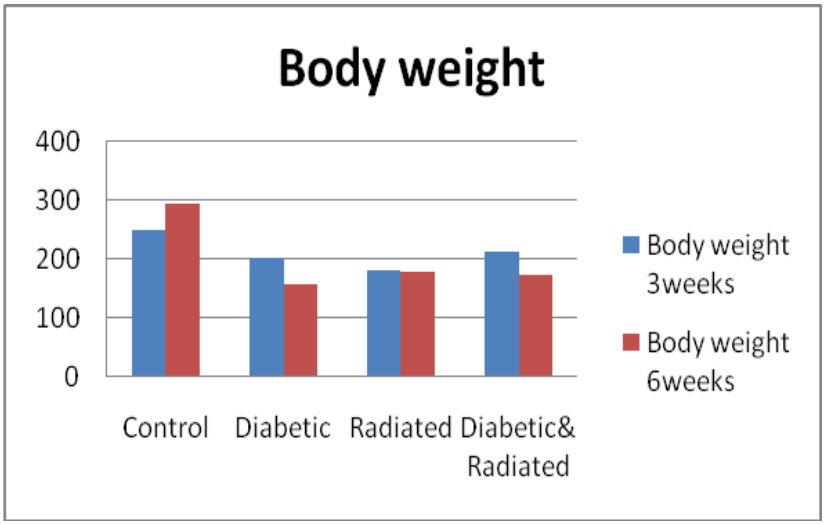
Results: Biochemical detection:

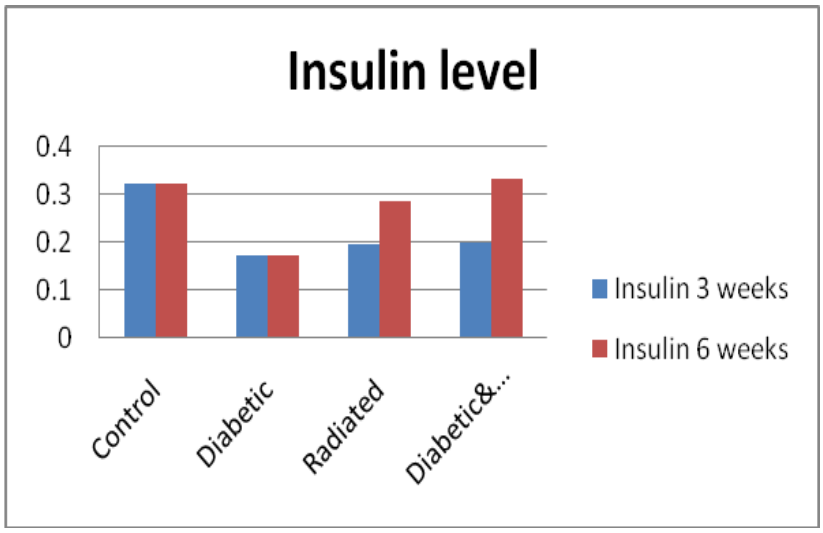
Table 1: Showing the changes in the body weight, blood glucose levels and Insulin blood content in different studied groups:

G1: control untreated rats G2: Diabetic rats G3: irradiated rats G4: diabetic irradiated rats
a: significantly difference from control level. b: significantly difference from diabetic level.

Parameters	Period of time	**G1 Control**	**G2 Diabetic**	**G3 Radiated**	**G4 Diabetic & Radiated**
B.WT (gm)	3Weeks	249.5±8.02^{b}	203±4.12^{a}	180.87±3,55	212±4.16^{a}
	6Weeks	294.5	157±11.14^{a}	179.54±12.03	174.67±8.04^{a}
Insulin ng/ml)	3Weeks	0.322±0.012^{b}	0.173±0.015^{a}	0.198±0.002	0.199±0.018^{a}
	6Weeks			0.287±0.043	0.332±0.015^{b}
Glucose (mg/dl)	3Weeks	86.67±2.19^{b}	300±11.35^{a}	100.22±3.65	107.33±3.29^{ab}
	6Weeks			90.75±1.76	111.50±1.50^{ab}

- Means carrying the same letter [superscript] within the same row are non significantly different from each other's [$P > 0.05$].
- Means carrying different letters [superscripts] within the same row are [significantly or highly significantly] different from each other's [significantly at [$P \leq 0.05$] and highly significantly at [$P \leq 0.01$].





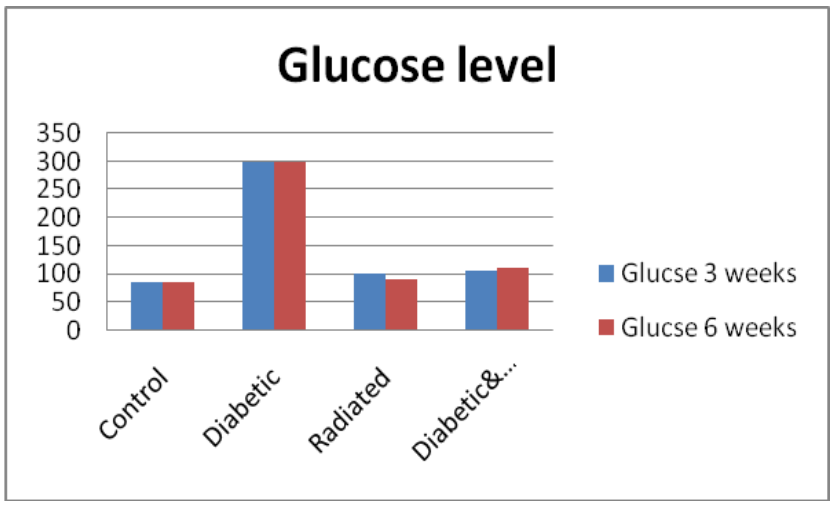


Table 1, showed differences in body weight among the four groups. G1 referred to normal healthy animals body weight in 3 and 6 weeks during the experiment. G 2 showed marked decrease in body weight comparing to control G1. G4 showed significant or slight increase in the body weight than diabetic G2 .

Blood Glucose level of STZ diabetic rat showed significantly increased when compared to normal control, while blood glucose of treated (irradiated) diabetic rat for 3 and 6 weeks were significantly decreased when compared with diabetic group and nearly normal when compared to normal control. The present study revealed that, serum insulin level in diabetic rats showed significantly decrease when compared with normal control. While irradiated diabetic animals showed none significant change in 3 weeks but significant increase noticed after 6 weeks.

Pathological study (Light microscope examination).

Plate (1): Light microscopic investigation can be illustrated as: (Figure a) of **G1** showed regular structure of pancreatic cells and islets of Langerhans, while examined sections from **G2** (Figure b) showed presence of the lymphocytic infiltrations by numerous lymphocytes in the islet of Langerhans. (Figure c) of G2 showed diffusely atrophied pancreatic tissues which characterized by reduced size and decreased amounts of zymogen granules in each cell along with severe atrophy or loss of islets as a direct effect of STZ treatment. The atrophy of pancreatic acini seemed less severe around the residual islets. Examined sections from those irradiated groups with low-dose gamma radiation of **G3** (Figure d) showed no remarkable changes seen neither in 3 or 6 weeks. While (Figures e,f) from diabetic irradiated groups (**G4**) for 3 and 6 weeks showed amelioration for the pathological changes of the cells. Also normal appearance of islets of Langerhans can be detected in (Figure g).

Histochemical observation Plate (2): In this experiment. DNA content were studied, showing that STZ resulting diabetes 1 and cause a detectable decrease in DNA content in G2 comparing with normal control group (Figs a,b).

On the other hand radiation alone has no remarkable effect. Exposure of diabetic groups to low dose of gamma radiation showed a remarkable restoration in DNA contents, this elevation seem to be time dependent (Figs c,d).

Electron Microscopic Findings:

Control group:

Plate (3): Figures (a,b) of **G1** showed normal structure of exocrine and endocrine cells, basally located nucleus and zymogene granules, rays of rough endoplasmic reticulum, healthy mitochondria were recognized, also the Beta cell granules appeared clear with normal chromatin distribution (Figure c).

Diabetic group:

Plate (4): On the other hand, diabetic animals of G2 showed great difference in the structure of pancreatic cells. Cytoplasm as well as nuclei of islet Beta cells of diabetic control animals showed typical signs of degeneration, border of cells was not clear and nuclear chromatin was irregularly condensed, Lymphocytic infiltration was found frequently among islet cells in diabetic control animals (Figure a). Reduced secretory granules, margination of granules toward cell periphery, nuclear pyknosis and cytoplasmic vacuolization was found in the cytoplasm of Beta cells of diabetic control animals (Figure b).

Plate (5): The cells of the pancreatic acini of G2 illustrated apoptotic nuclei and destructive granules (Figure a). (Figure b) revealed deformed structure of rough endoplasmic reticulum. But (Figure c) showed increase in the amount of

autophagositic granules with vacuolated disorganized cytoplasm.

Irradiated group

Plates (6 and 7): Irradiated group by low dose of gamma radiation for 3 and 6 weeks (**G3**) showed nearly normal structure of the pancreatic tissue, in which the acinar cells appeared rounded with healthy nucleus, regular pattern of rough endoplasmic reticulum and zymogenic granules (plates 6 and 7), but had slight difference than control group in the shape of mitochondria that lost some of their cristea and matrix as showed in (plate 7b).

Diabetic irradiated group

Plate (8): (Figure a) showed a remarkable recovery of the destructive organelles and the pancreatic acinar cells retain its normal structure which seem as to be time and dose dependant in rats which were treated with fractionated 3 Gy of gamma rays of G4 (diabetic irradiated 3weeks). (Figure b) of the same plate showed a recognized amelioration in the cell structure, the endoplasmic reticulum retain its organization and ribosomes, also the granules gain its normality. On the other hand, the mitochondria still fail to retain its normality.

Plate (9): In diabetic irradiated 6 weeks animals (Fig. a,b), the size of β cells were smaller than normal but their granules within the cytoplasm, especially the immature granules were increased when compared with the normal islet β cells. Well developed endoplasmic reticulum were found in the cytoplasm of the diabetic irradiated animals. Also the nucleus and the chromatin did not show any obvious changes when compared to normal control group.

Plate (10): G4 of diabetic irradiated 6weeks showed highly recovery in the structure of the different organoids of the pancreatic acini such as, the nucleus was healthy and activated the endoplasmic reticulum looks well organized but the mitochondria still vacuolated and lost its matrix (Figures a,b).

Discussion

Streptozotocin (STZ) is an antibiotic that can cause pancreatic β-cell destruction, so it is widely used experimentally as an agent capable of inducing insulin-dependent diabetes mellitus (IDDM), known as type 1 diabetes mellitus (T1DM). STZ is a nitrosourea compound which generally shares similar fate of disposition with other nitrosoureas and is a drug of choice in islet cell carcinoma and malignant carcinoid tumors. It is diabetogenic, hepatotoxic, nephrotoxic and also causes gastric ulceration **(Piyachaturawat *et al.*, 1988; Piyachaturawat *et al.*, 1991).** In the present investigation on the type 1 diabetes induced by STZ, a marked decrease in body weight was detected. Blood glucose level showed significantly increased while serum insulin level showed significantly decrease, these results were confirmed by **Ichinose *et al.* (2006) and Muhammad and Syed** (**2010)** who stated that, studies have shown an association between hyperglycemia, hypoinsulinemia and decreased body weight of diabetic animals. Also It could be attributed to increased triglyceride accumulation leading to enlarged liver which could be due to the increased influx of fatty acids into the liver induced by hypoinsulinemia and the low capacity of excretion of lipoprotein secretion from liver resulting from a deficiency of apolipoprotein B

synthesis **(Merzouk *et al.*, 2000; Ohno *et al.*, 2000; Habibuddin *et al.*, 2008; Lee *et al.*, 2008).**

Results obtained in the present work showed that, many histological changes appeared as for necrosis and infiltration found in diabetic group. It may be concluded that the streptozotocin through its direct alkylating action can cause cellular necrosis and selective destruction of the Beta-cells producing hyperglycaemia at a dose of 45 mg/kg body weight **(Panchatcharam *et al.*, 2006; Kanitkar *et al.*, 2008).**

Histochemical investigation in the present study revealed that, there was a remarkable decrease in DNA content, this is in line with previous studies on STZ-diabetic rats **(Vats *et al.*, 2003)**. On the other hand, electron microscopic investigations of STZ treated animal in this study showed great changes in the structure of pancreatic cells, vacuolation and disorganized cytoplasm, apoptotic nuclei, destructive granules, inflammatory infiltration, deformed structure of rough endoplasmic reticulum, increased amount of autophagocytic granules were also recognized. In coincidence, previous study contributed decreased granules in the cytoplasm usually encountered in insulin dependent diabetes due to the decrease in insulin production or depletion of secretory stores of insulin in damaged cells. Moreover, the observed vacuoles may be due to increased cellular damage. Variable changes in nuclei of islets of diabetic pancreas, some appeared vesicular, others pyknotic where the euchromatin predominates over the heterochromatin. These changes were in agreement with previous study that suggested this may be due to condensation and shrinkage of the nuclear material (**Arulselvan and Subramanian, 2007).** These results were in line also with **Yasuda *et al.* (1982)** who stated that, light and electron microscopic studies on exocrine pancreas of diabetic dogs with duration of diabetes up to a year induced by streptozotocin were performed. In the pancreatic acinar cells of the long-term diabetic dogs, atrophy, hyperplastic nodules, and interacinar and interlobular fibrosis were exclusively observed by light microscopy and autophagocytic vacuoles, lipid droplets, fragmentation of rough endoplasmic reticulum, and decrease or varying size of zymogenic granules were much more frequently found by electron microscopy compared with the control group.

Radiation is known to have significant effects on living organisms dependent on the dose received. At high doses, radiation destroys the cells in the tissue. At low doses, on the other hand, radiation is no longer considered to be as harmful as once though. Hormesis and adaptive response of cells or tissues in response to LDR were extensively documented (**Luckey, 1982; Cai, 1999; Cai *et al.*, 1999; Calabrese, 2002; Calabrese and Baldwin, 2002).** However, debates for the induction and importance of hormetic effect and adaptive response still exist, in particularly for the risk of LDR in genetic instability and carcinogenesis (**Johansson, 2003; Poumadere, 2003; Calabrese, 2004)**. Low-dose radiation significantly increases endogenous antioxidants in different tissues including liver, spleen, brain and testes**;** (**Yamaoka *et al.*, 1991; Zhang *et al.*, 1998; Kojima *et al.*, 1999**). The activation and/or induction of antioxidants in these tissues, the increased antioxidants by LDR significantly prevents tissue damage from various oxidative stresses, for instance, cardon

tetrachloride-induced liver damage, **(Yamaoka *et al.*, 2004)** and 1-methyl-4- phenyl-1,2,3,6-tetrahydropyrine- or Fe-NTA-induced brain damage, **(Yamaoka *et al.*, 2002)**. In studies by **Takehara *et al.* (1995) and Takhashi *et al.* (2000),** LDR (0.5Gy) indeed also significantly increases the superoxide dismutase (SOD) activity in the pancreas of non-diabetic mice. The activity of pancreatic SOD in ALX-induced or NOD diabetic mice was significantly decreased, but this decrease could be prevented by LDR. In addition, in STZ-induced diabetic mice, plasma and pancreatic lipid peroxide levels were also significantly increased, but were not in LDR-irradiated diabetic mice **(Takehara *et al.*, 1995).** These results suggested that, the increased antioxidant capacity of pancreases by LDR is one of the major mechanisms to prevent ALX-induced or spontaneously developed diabetes .

The mechanisms discussed above are predominantly for results and findings of the present study which shows that, LDR (fractionated dose levels of 0.5 Gy/week of γ-radiation). The γ-radiation delivered at a dose rate of 0.61 Gy min–1 for 3 and 6 weeks can more or less ameliorates the cellular damage effects seen in both light and electron microscopic studies. Also it had been found that glucose and insulin levels retain its normal levels .

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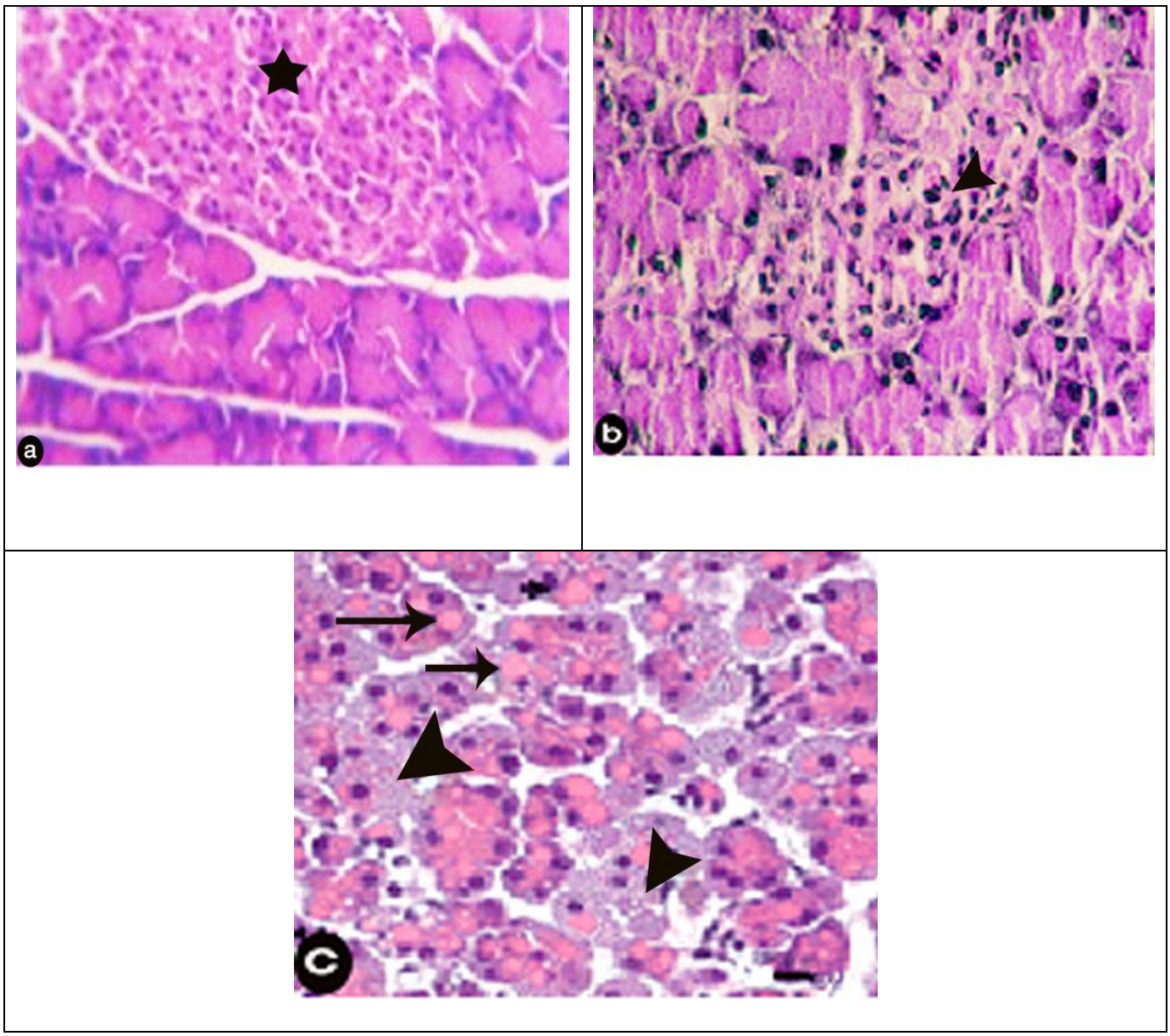


Plate (1):Photomicrographs of sections in pancreas of albino rats represent Figure [aG1]: control rat showing: Normal architecture of pancreatic cells and islets of Langerhans (star). (X 400). Figures [b G2]: diabetic rat showing: lymphocytic infiltration in the islets of langerhans (arrow head). (X 600). Figures [c G2]: diabetic rat showing: atrophied pancreatic acini (arrow) except around the residual islets (arrow head). (X 200). (H&E stain).

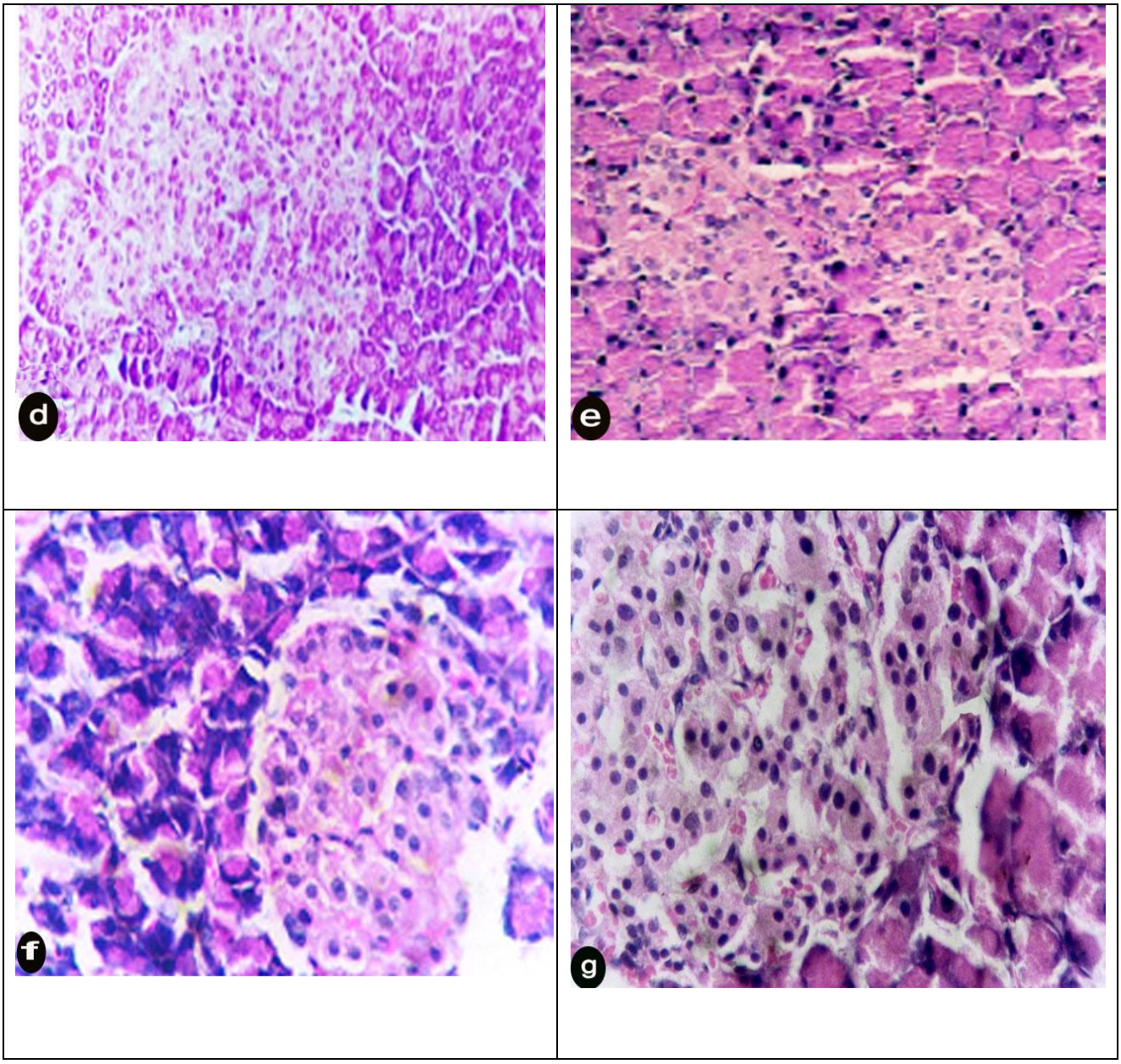
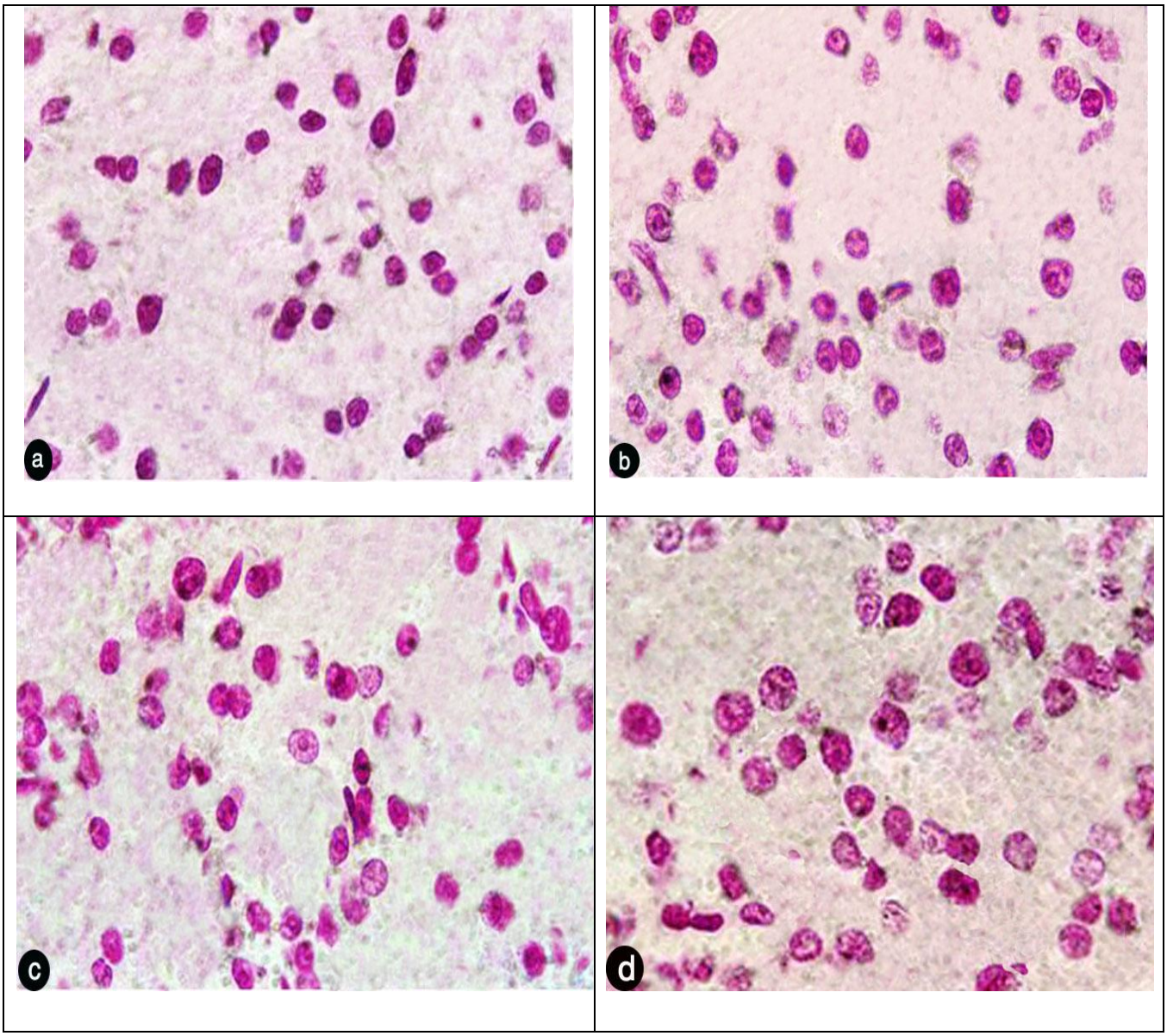
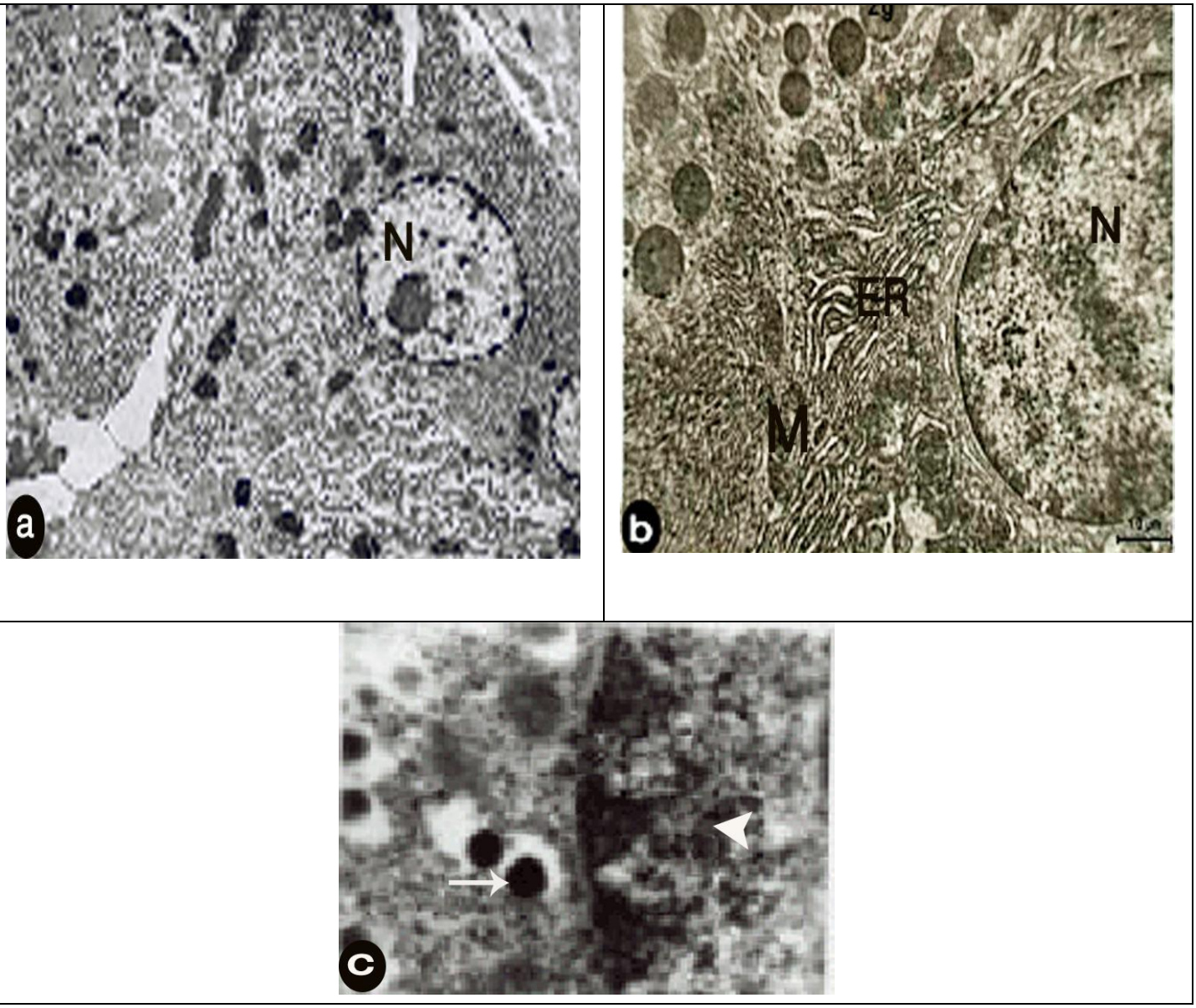


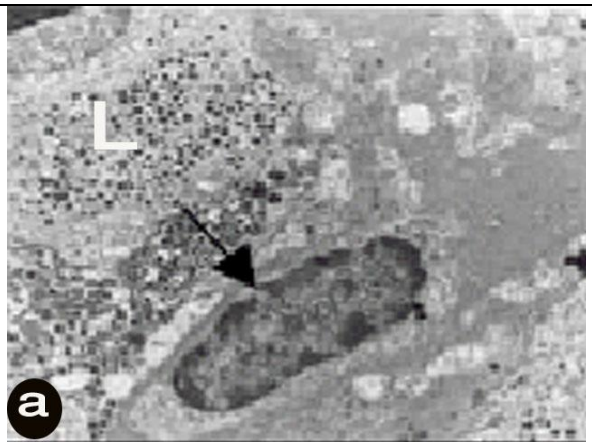
Plate (1):Photomicrographs of sections in pancreas of albino rats represent Figure [d G 3] irradiated group for 3weeks showing: Normal appearance of pancreatic cells and islets of Langerhans. (X 400). Figure [e G4] diabetic irradiated group for 3weeks showing: disappearance of the inflammatory infiltration and regeneration of the cells of the islets of Langerhans. (x 600). Figure [f G4] diabetic irradiated group for 6 weeks showing: normal appearance of pancreatic acini and the cells of islets of Langerhans. (X 400). Figure [gG4]: section from group [4] diabetic irradiated group for 6 weeks showing: a higher magnification of figure f. (X 600). (H&E stain).



Plat (2): Photomicrographs of sections in pancreas of albino rats represent Figure [aG1]: section in control rat showing: normal DNA content. Figures [b G2]: section in diabetic rat showing: decrease in DNA content. Figure [c G 3] section from group [4] diabetic irradiated group for 3 weeks showing: obvious restoration of DNA content and increase in the mitotic division than control group. Figure [d G4] section from group [4] diabetic irradiated group for 6 weeks showing: nearly normal appearance of DNA content and increase in the mitotic division than control group. (All the figures Feulgen reaction X1000).



Plat (3): Thin sections of pancreas in control rats represent Figure (a): showing normal endocrine cell with healthy nucleus (N), (X4000). Figure (b): showing exocrine cell with healthy nucleus (N), well designed endoplasmic reticulum (ER) with ribosomes, well defined mitochondria (m) and zymogenic granules (zg) (X8000). Figure (c): showing islet Beta cells with clear Beta cell granules (arrow) and normal chromatin distribution (arrow head) (X 30000).



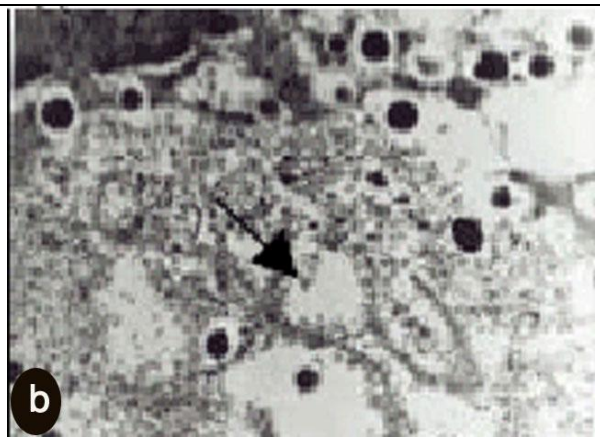
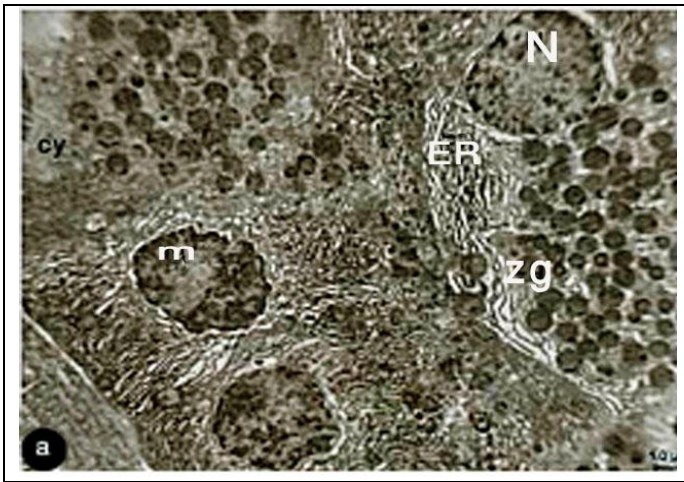
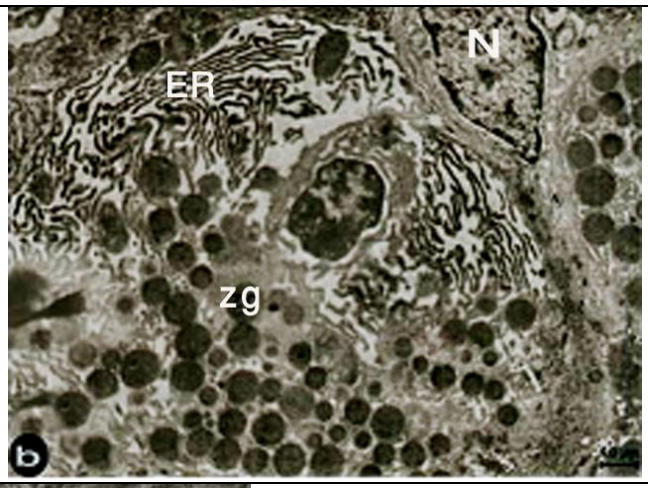


Plate (4): Thin sections of pancreatic islets Beta cells in diabetic rats represent Figure (a): showing chromatin condensation and marginalization toward the priphery of the nucleus (arrow), lymocytic infilteration (L) (X 10000). Figure (b): showing vacuolation of cytoplasm (arrow) (X20000).





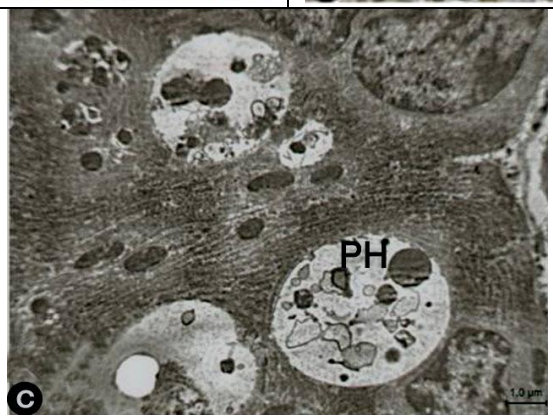


Plate (5): Thin sections of pancreatic acini in diabetic rats represent Figure (a):showing shrinked nucleus (N) with damaged structure, injured granules (zg) and disorganized endoplasmic reticulum (ER) (X4000). Figure (b): showing apoptotic nucleus (N), disorganized rough endoplasmic reticulum (ER), lost its ribosomes and irregular zymogene granules (zg) (X4000). Figure (c): showing increased amount of phagocytic granules (PH) as a sign of cell death (X4000).

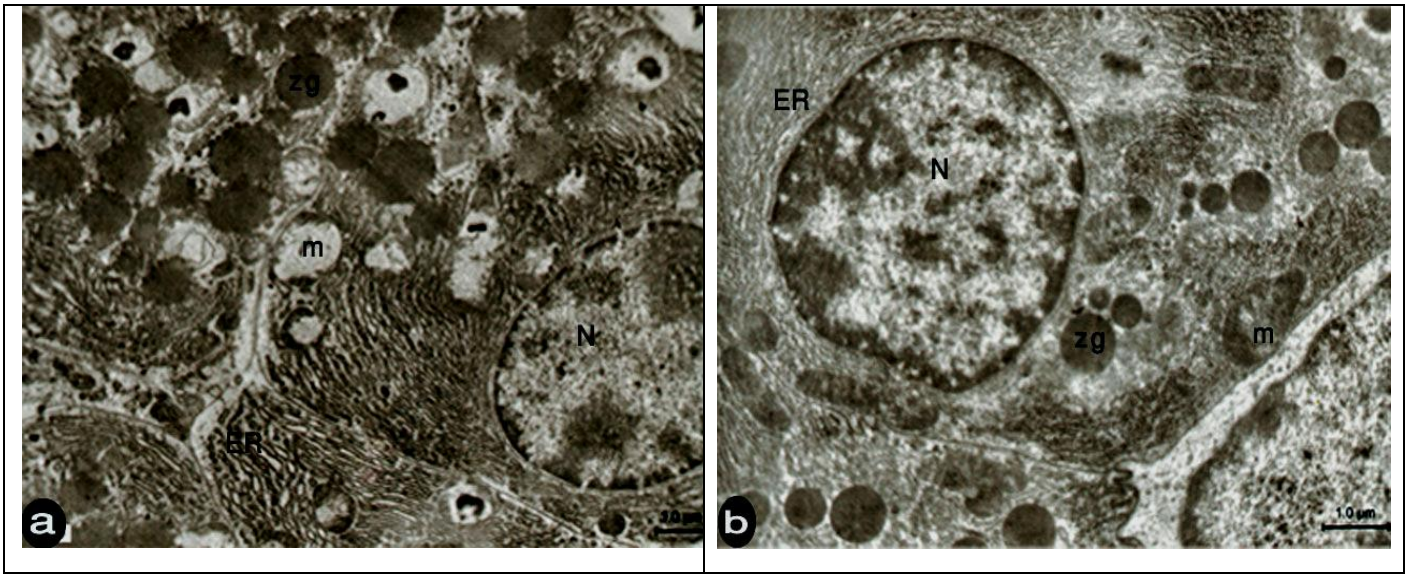


Plate 6: Thin sections of pancreatic acini in 3 weeks radiated rats represent Figure (a): showing nearly regular structure of the nucleus (N), normal structure of endoplasmic reticulum (ER), some mitochondria (m) showed reduction in its cristae (vacuolated and lost their matrix) (X6000). Figure (b): showing nearly regular structure of the nucleus (N), endoplasmic reticulum (ER) and zymogene granules (zg). (X6000).

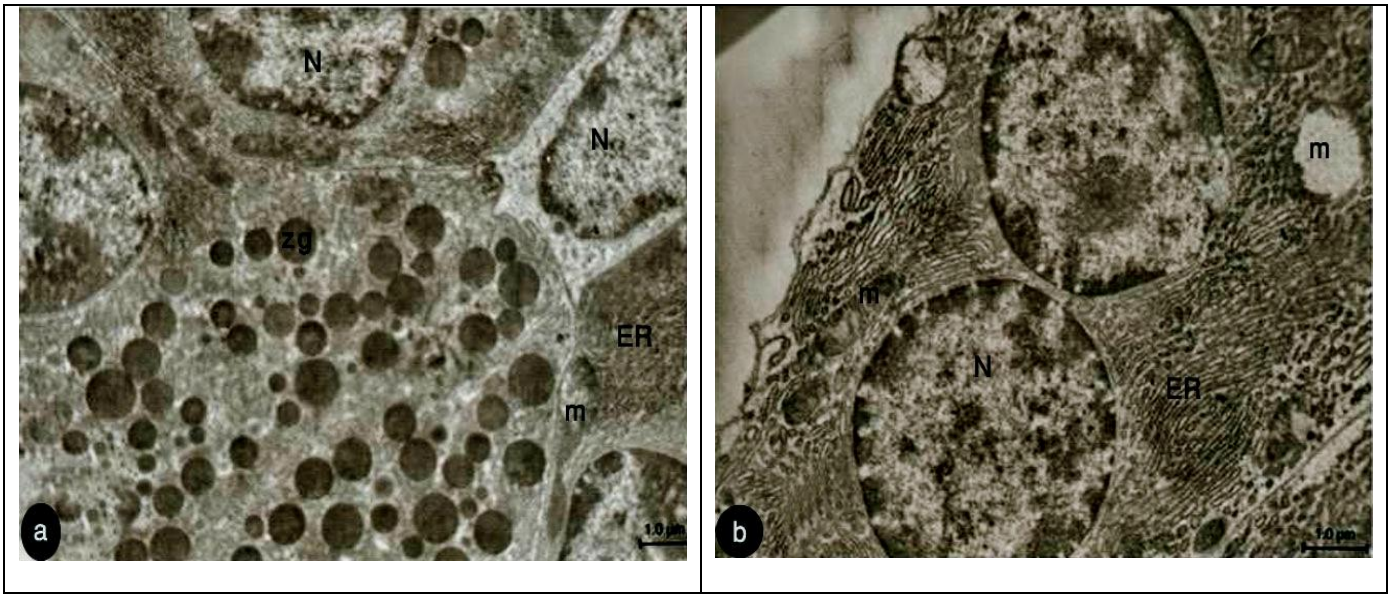


Plate 7: Thin sections of pancreatic acini in 6 weeks radiated rats represent Figure (a): showing considerable number of zymogene granules (zg), healthy mitochondria (m) (X4000). Figure (b): showing regular structure of the nucleus (N), endoplasmic reticulum (ER), some mitochondria lost their matrix (m). (X6000).

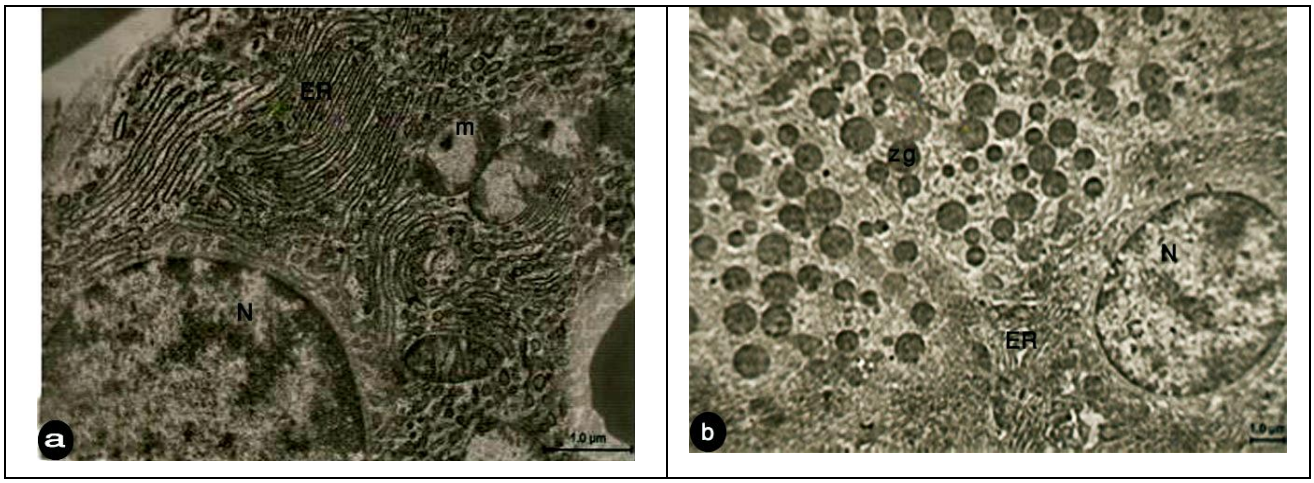


Plate 8: Thin sections of pancreatic acini in 3 weeks diabetic and radiated rats represent Figure (a): showing healthy nucleus (N) and endoplasmic reticulum (ER), some mitochondria still lost their matrix (m) (X6000). Figure (b): showing restoration of the zymogenic granules to its normal appearance (zg), regular structure of the nucleus (N) and the endoplasmic reticulum (ER) (X4000).

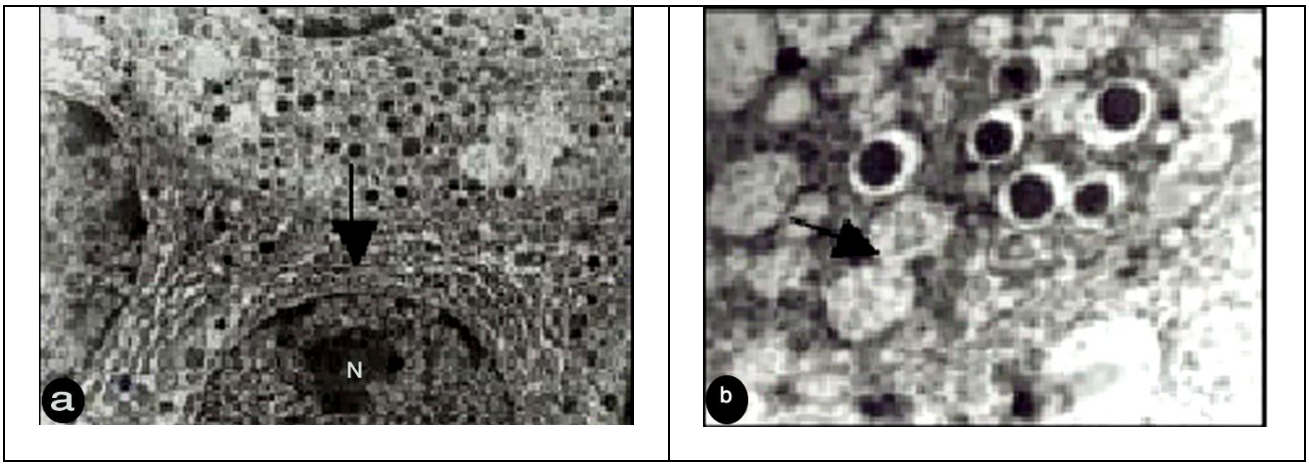


Plate 9: Thin sections of pancreatic islet Beta cells in 6 weeks diabetic and radiated rats represent Figure (a): showing normal nucleus (N) and well developed endoplasmic reticulum (arrow) (X1000). Figure (b): showing immature granules in the cytoplasm of the Beta cells (arrow) (X3000).

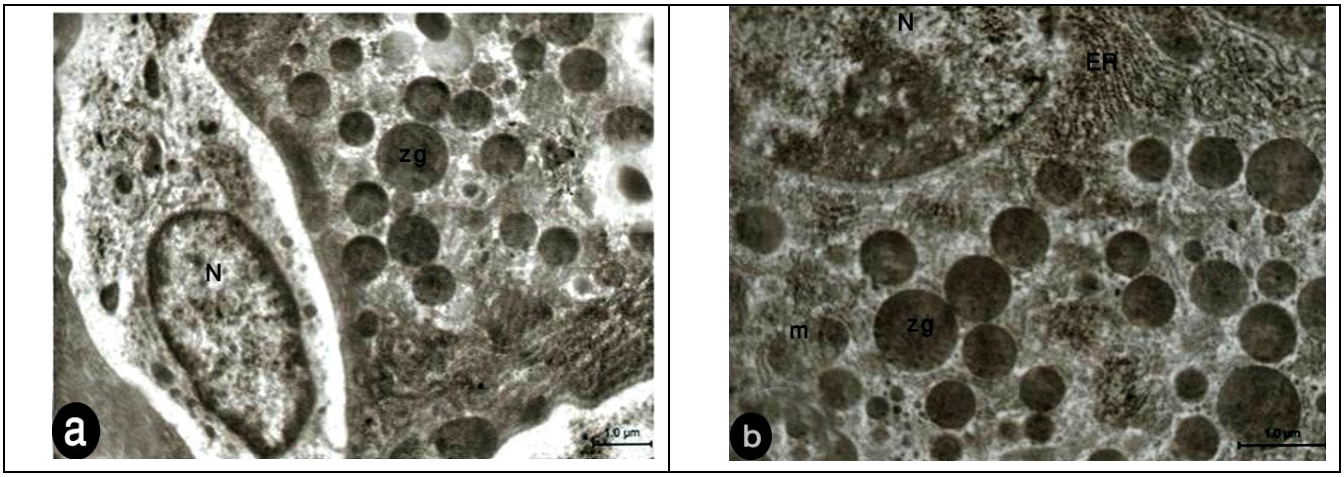


Plate 10: Thin sections of pancreatic acini in 6 weeks diabetic and radiated rats represent Figure (a): showing normal nucleus (N) and normal polymorphic zymogenic granules (zg) (X6000). Figure (b): showing healthy nucleus (N), well designed endoplasmic reticulum (ER), zymogenic granules retain their density (zg), some vacuolated mitochondria losing their matrix were still observed (m**)** (X8000).

الملخص العربي

التأثير الوقائي للجرعات الضئيلة من الإشعاع علي خلايا البنكرياس لذكور الجرذان المصابة بداء السكري

1-هناء فتحي واعر –2- سهام عباس حلمي 1- رباب محمود

1-هيئة الطاقة الذرية- المركز القومي للبحوث وتكنولوجيا الإشعاع – معمل بيولوجيا الخلية
2 -قسم الخلية والأنسجة - كلية الطب البيطري – جامعة قناة السويس

الخلفية:

داء السكري هو اضطراب مزمن في عملية الأيض وينتج عنها خطرا كبيرا على صحة الإنسان. استخدام جرعات منخفضة من الإشعاع ينظم استجابة الجسم البيولوجية لبعض الأمراض بما في ذلك التقليل من حدة السرطان وكذلك داء السكري. تناولت هذه الدراسة تأثير جرعات منخفضة من الإشعاع علي التغيرات الباثولوجية وكذلك التركيب الدقيق لخلايا البنكرياس في الجرذان المصابة بداء السكري (النوع الأول) والتي استحثت بالستربتوزوتوسين.

المواد والأساليب:

أجريت هذه الدراسة على 80 من ذكور الجرذان و التى تظهر عليها علامات الصحة والبالغين من العمر سن 9 أسابيع، ويتراوح وزن الواحد منهم (150-200 جم). تم تقسيم الجرذان إلى 4 مجموعات مع العناية بهم وفقا لمبدأ التوجيهية في رعاية واستخدام الحيوانات. تم استحداث داء السكري عن طريق الحقن البريتوني بجرعة واحدة من الستربتوزوتوسين حديثة التحضير (الستربتوزوتوسين 45مجم/ كجم من وزن الجسم). تم استخدام السيزيوم - 137 كمصدر لأشعة جاما. تعرضت الحيوانات إلى جرعات مجزأة من أشعة جاما (0,5 جراى / الأسبوع) لمدة 3 و 6 أسابيع. تم وزن الجرذان، وقياس السكر والأنسولين في الدم بعد 3 اسابيع ثم 6 أسابيع. وتم اخذ عينات صغيرة من أنسجة البنكرياس من مختلف المجموعات والتي أعدت للفحص الباثولوجي والتركيب الدقيق.

النتائج :

تم اكتشاف ارتفاع مستوى الجلوكوز وانخفاض مستوى الأنسولين بالدم بعد 3 و 6 أسابيع من عمر الجرذان المعالجة بالستربتوزوتوسين. وكان هناك ميل كبير وملحوظ لعودة مستويات السكر والأنسولين في الدم إلي طبيعتها عقب التعرض للإشعاع وخصوصا بعد مرور 6 أسابيع. وقد لوحظ أيضا التقليل من موت الخلايا والإصابة الخلوية التي يسببها المعالجة بالستربتوزوتوسين وذلك بواسطة الفحص الالكتروني بعد 3 و 6 أسابيع.

والخلاصة:

إن النتائج الحالية تشير إلى أن العلاج بواسطة 0,5 جراى من أشعة جاما يمنع تطور داء السكري (النوع الأول) في الفئران المستحثة بالستربتوزوتوسين.