Influence of Exposure to Fractionated Dose of Gamma Radiation and Antioxidants Supplementation to Mice on Program Cell Death Induction

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ABSTRACT

The previous studies reported that the tumor suppressor protein (P53) is not functioning correctly in most human cancers, and that it plays a crucial role in the prevention of tumor development. This study was designed to evaluate if exposure to fractionated dose of γ-radiation impair function of P53 by the administration of antioxidants. Group of control mice was used. Another groups treated with 3 mg/mouse/day of Antox drug which contains the three main antioxidant vitamins (A, C, and E) together with trace element selenium for 15 days. Another group subjected to 1 Gy of γ-radiation 5 times every other day either alone or combined with the Antox drug supplementation. Hepatic and renal functions were evaluated. Antioxidant markers (MDA and GSH) levels, histopathological changes and P53 expression were recorded in liver and kidney tissues. Animals treated with Antox showed some increase in liver transaminases, non significant changes in total protein and albumin levels, a non significant change in kidney function profiles, a non significant increase in MDA and a significant increase in GSH levels in liver and kidney tissues. However, the exposure of mice to fractionated dose of γ-radiation led to a significant increase in kidney function profiles, AST and ALT activity, a significant decrease in total protein and albumin level, a significant increase in MDA levels and a significant decrease in GSH levels in liver and kidney were observed. Exposure of experimental animals post treatment with Antox drug to fractionated dose of γ-radiation revealed a significant amelioration in liver and kidney function profiles, a highly significant decrease in MDA levels and a significant increase in GSH level in comparison with irradiated group. Histopathological changes in liver and kidney recorded the same alterations observed with the biochemical parameters. P53 expression negatively expressed in normal liver and kidney tissues. However, the exposure of mice to fractionated dose of γ-radiation showed a highly P53 expression. Antox
supplementation to mice showed some $P53$ expression either alone or combined with fractionated $\gamma$-radiation exposure. The findings suggest that irradiation of mice showed a highly significant increase in MDA and $P53$ expression. The ameliorative effect of Antox against $\gamma$-irradiation induced liver and kidney damage and $P53$ expression recorded in the present work may be attributed to its antioxidant properties.

Key words: $\gamma$-irradiation, Antox, $P53$ expression

INTRODUCTION

Oxidative stress occurs due to excessive free radical production and/or low antioxidant defence, and results in chemical alterations of bio-molecules causing structural and functional modifications $^{(1)}$. These modifications are capable of causing an increase in the generation of various reactive oxygen species, such as $O_2^-$, $H_2O_2$, $OH^-$, and $ROO^-$. These reactive oxygen species in turn are capable of initiating and promoting oxidative damage in the form of lipid peroxidation $^{(2)}$. The generation of the reactive oxygen metabolites plays an important role in the pathogenesis of irradiation-induced tissue injury. Thus, antioxidants that scavenge or inhibit the formation of reactive oxygen metabolites may have relevance to cancer patients by ameliorating the damage to normal tissues exposed to radiotherapy.

Antioxidants have a wide range of biochemical activities. These include inhibiting the generation of reactive oxygen species, directly or indirectly scavenging free radicals, and altering the intracellular redox potential $^{(3)}$. Some antioxidants have been used as inhibitors of apoptosis, because apoptosis was at first thought to be mediated by oxidative stress $^{(4)}$. However, it is clear that reactive oxygen species are not always required to induce apoptosis $^{(5, 6)}$. Pro-oxidant states have been considered to be contributing factors for tumorigenesis $^{(7)}$. Correspondingly, an increasing body of evidence indicates that antioxidants have anticancer activities. Antioxidants can inhibit tumor initiation, tumor promotion, and cell transformation $^{(8, 9)}$.

The tumor suppressor protein $P53$ is also known to play an important role in inhibiting tumorigenesis. This transcription factor is involved in cell cycle arrest and apoptosis after DNA damage $^{(10, 11)}$. They added that manipulating $P53$-mediated pathways has thus been a major focus for cancer therapy $^{(10, 11)}$. For example, restoring the expression of wild-type $P53$ renders cells more sensitive to spontaneous or chemotherapy-induced apoptosis $^{(12, 13)}$. There is also a good correlation between a tumor's $P53$ functional status and its
response to some chemotherapeutic agents (14, 15, 16). The present work aimed to study the P53 expression in exposed mice to fractionated dose of γ-radiation induced apoptosis in albino mice. In addition, the possible curative effect of the antioxidant drug, Antox, was investigated.

MATERIALS AND METHODS

Animals

Adult male Swiss albino mice weighing 25-30g purchased from the breeding unit of the Egyptian Organization for Biological Products and Vaccines, Cairo, Egypt were used in this study. The animals were maintained on a commercial standard pellet diet and tap water ad libitum. Animal maintenance and treatments were conducted in accordance with the National Institute of Health Guide for Animal, as approved by Institutional Animal Care and Use Committee (IACUC).

Antioxidants

A mixture of antioxidants (Antox) composed of vitamin A (0.554 mg), vitamin C (100 mg), vitamin E (30 mg), and selenium (50 μg), obtained from Arab Company for Pharmaceuticals and Medicinal Plants MEPACO-Egypt, was dissolved in tap water and given orally at a dose of 25 mg/kg bwt, equivalent to the human therapeutic dose according to Paget and Barnes (17).

Exposure of animals to γ-radiation

Mice were whole body gamma irradiation using a Canadian 137Cs Gamma Cell-40 at the National Centre for Radiation Research and Technology (NCRRT), Cairo, Egypt. The dose rate was 0.61 Gy/min.

Fifteen days was the period of the experiment. The experimental animals were divided into the following groups:

G1: group of 6 untreated animals served as control.

G2: group of 6 animals supplemented orally with 3 mg/mouse/day of Antox drug for 5 times, every other day.

G3: group of 6 animals exposed to 1 Gy of γ- irradiation x 5 times every other day.

G4: group of 6 animals orally supplemented with 3 mg/mouse/day of Antox drug x 5 times every other day and exposed to 1 Gy of γ- radiation after two hours of Antox administration.
Twenty four hours after the last exposure to the fractionated $\gamma$-radiation blood was drawn from the vena cava into heparinized syringe and centrifuged at 3000 g for 10 minutes. Immediately after collection of the blood, samples of liver and kidney were removed from the dissected animals and rinsed in saline. Parts of the tissues were stored in the refrigerator till biochemical analysis and the other parts were fixed in neutral formalin for the histopathological and immunohistochemical studies.

**Histopathological studies**

The sacrificed animals were quickly dissected. Sample of 0.5 cm$^3$ of the organs (liver and kidney) were removed and fixed in 10% neutral formalin for 24 hours followed by washing, dehydration in ascending grades of alcohol, clearing in xylene and embedding in hard paraffin. Samples were then serially sectioned at thickness of 5-6 $\mu$m, mounted on albuminized slides and left for 24 hours at 37°C to dry and to avoid detachment of sections during subsequent steps of staining. The tissue sections were stained by Hematoxylin and Eosin stain and then examined under the light microscope.

**Immunohistochemical studies**

For immunohistochemical studies, samples of liver and kidney tissues were fixed in 4% formaldehyde in phosphate-buffered saline (pH 7.4), before dehydration in alcohols and embedding in wax. Tissue sections were cut using a microtome at a thickness of 3 $\mu$m. Immunohistochemistry was performed using P53 Ab-1 (clone PAb 240) mouse monoclonal antibody purchased from Lab Vision Corporation. Immunohistochemistry was performed using anti mouse IgG (H+L) streptavidin peroxidase and diaminobenzidine as the immunodetection substrate.

In the immunohistochemistry, slides were heated to 65°C in an incubator for 60 min. The slides were then directly taken from the incubator and deparaffinized in three changes of xylene for 5 min each, followed by three rinses in absolute ethanol (ETOH) for 2 min each. To eliminate staining due to endogenous peroxidase, sections were treated with an ETOH / $\text{H}_2\text{O}_2$ (45 ml ETOH/3 ml $\text{H}_2\text{O}_2$) block for 10 min at 42°C. Slides were hydrated in decreasing concentrations of ethanol and rinsed in PBS. From this point in the assay, all antibody and complex incubations were carried out in a humidity chamber at 42°C. Slides were pre-incubated for 10 min in 5% NHS diluted in PBS/2% BSA, followed by incubation for 45 min with primary antibody. Slides were then rinsed in PBS and subsequently incubated in the presence of the secondary
antibody for 20 min (Vector). Slides were rinsed in PBS, followed by 20-min incubation in pre-mixed Elite Universal Kit reagents as recommended by the product insert (Vector). The PBS rinse was repeated and sections were developed in the enzyme substrate DAB solution.

\( P53 \) immunoreactivity was recorded according to their intensity in brown colour. Using light microscopy, certain cells exhibited noticeably stronger immunoreactivity than the rest. These cells were classified as strongly stained.

**Liver and kidney functions assay**

Kits for the measurement of plasma creatinine, urea, uric acid, alanine transaminase activity (ALT) and aspartate transaminase (AST) activity were purchased from Biodiagnostic Company Egypt.

**Lipid peroxidation (MDA) and reduced glutathione (GSH) assay**

Tissue samples were homogenized with ice-cold 150 mM KCl for the determination of MDA and GSH levels. The MDA level was assayed for products of lipid peroxidation by monitoring thiobarbituric acid reactive substance formation as described by Yoshioka et al. (18). Lipid peroxidation is expressed in terms of MDA equivalents using an extinction coefficient of 1·56x10\(^5\) M/cm and results are expressed as nmol MDA/g tissue. Reduced glutathione (GSH) measurement was performed using a modification of the Ellman procedure (19). Briefly, after centrifugation at 3000g for 10 min, 0·5 ml supernatant was added to 2 ml 0·3 mol/l Na\(_2\)HPO\(_4\), 2 H\(_2\)O solution. A 0·2 ml solution of dithiobisnitrobenzoate (0·4 mg/ml 1% sodium citrate) was added and the absorbance at 412 nm was immediately measured after mixing. GSH levels was calculated using an extinction coefficient of 1·36 - 105 M/cm. Results are expressed in μmol GSH/g tissue.

**Statistical Analysis**

Statistical analysis of the calculated results was carried out with the aid of the SPSS computer software program.

**RESULTS**

**1-Biochemical studies**

**Effect of Antox supplementation to mice on liver enzymes profile.**

The effect of Antox supplementation on plasma liver function profile is illustrated in Table (1). Gavages of the experimental animals by Antox
represented some increase in liver tensaminases (AST and ALT). Meanwhile, total protein and albumin level showed a non significant change compared to control level. The exposure of animals to fractionated dose of γ-radiation induced a significant increase in AST and ALT activity. However, total protein and albumin level recorded a significant decrease in comparison with control level. Combined treatments of the experimental animals with Antox followed by γ-radiation exposure exhibited a significant amelioration in liver function profiles comparing to those irradiated only.

Table (1): Effect of Antox administration to mice on plasma liver enzyme activity.

<table>
<thead>
<tr>
<th>Groups</th>
<th>AST (U/ml)</th>
<th>ALT (U/L)</th>
<th>Total protein (g/dl)</th>
<th>Albumin (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>34.46 ± 1.08b</td>
<td>41.96 ± 0.14b</td>
<td>6.5±0.21b</td>
<td>3.8 ±0.21b</td>
</tr>
<tr>
<td>G2</td>
<td>36.42±2.03b</td>
<td>42.12±2.15b</td>
<td>6.1±0.31</td>
<td>3.5±0.30</td>
</tr>
<tr>
<td>G3</td>
<td>53.93 ± 1.08a</td>
<td>46.67 ± 3.03a</td>
<td>4.2± 0.19a</td>
<td>2.4±0.19a</td>
</tr>
<tr>
<td>G4</td>
<td>37.67 ± 0.38a</td>
<td>46.22 ± 0.91a</td>
<td>5.3±0.18a5</td>
<td>2.9±0.22a</td>
</tr>
</tbody>
</table>

Each value represents the mean of 6 records ± S.D.
Means with different superscripts are significantly different at the 0.05 level.

a) Significance from control group.  
b) Significance from irradiated group.

**Effect of Antox supplementation to mice on kidney function profile.**

A non significant change in kidney function profile occurred when experimental animals received Antox drug (Table 2). However, the exposure of mice to fractionated dose of γ-radiation caused a significant increase in creatinine, urea and uric acid compared to control level. A significant amelioration in kidney function profiles was observed comparing to irradiated group when the experimental animals treated by Antox followed by γ-radiation exposure.

Table (2): Effect of Antox administration to mice on plasma kidney function profiles.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Creatinine (μg/ml)</th>
<th>Urea (mg/dl)</th>
<th>Uric acid (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>9.4±0.37b</td>
<td>21± 1.25b</td>
<td>6.98±0.52b</td>
</tr>
<tr>
<td>G2</td>
<td>8.61 ±0.02</td>
<td>20±0.81</td>
<td>7.3±0.41</td>
</tr>
<tr>
<td>G3</td>
<td>14.3±0.38a</td>
<td>88±3.56a</td>
<td>8.55±0.46a</td>
</tr>
<tr>
<td>G4</td>
<td>11.2±0.36b</td>
<td>40±4.80b</td>
<td>7.40±0.7b</td>
</tr>
</tbody>
</table>

Legends as in Table (1).
Effect of Antox supplementation to the animals on tissue MDA and GSH levels.

In Table (3) a non significant increase in MDA level was developed in liver and kidney tissues when the experimental animals treated by Antox drug for 15 days in comparison with that of control level. However, the exposure of mice to fractionated dose of γ-radiation showed a highly significant increase compared to the control level. When the experimental animals were orally treated with Antox drug followed by exposure to γ-radiation, a highly significant decrease in MDA level in liver and kidney tissues was manifested compared to the irradiated group.

On the other hand, treatment of the experimental animals with Antox drug revealed a highly significant increase in liver and kidney GSH levels compared to the control level. While, the exposure of the experimental animals to fractionated dose of γ-radiation led to a significant decrease in liver and kidney GSH level compared to control level. Moreover treatment of the experimental animals with Antox combined with the exposure to fractionated dose of γ-radiation showed a highly significant increase compared to that irradiated only.

Table (3): Effect of Antox treatment on the level of MDA and GSH in mice.

<table>
<thead>
<tr>
<th>Organs</th>
<th>Groups</th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>MDA</td>
<td>67.4±2.26</td>
<td>72.9±0.86</td>
<td>175±3.18</td>
<td>114.9±0.54</td>
</tr>
<tr>
<td>Kidney</td>
<td></td>
<td>77.9±1.6</td>
<td>88.5±1.45</td>
<td>207.1±1.63</td>
<td>168.6±2.12</td>
</tr>
<tr>
<td>Liver</td>
<td>GSH</td>
<td>125.6±0.9</td>
<td>162.4±3.6</td>
<td>103.1±3.8</td>
<td>113.0±2.6</td>
</tr>
<tr>
<td>Kidney</td>
<td></td>
<td>155.3±3.0</td>
<td>150.0±2.4</td>
<td>86.7±4.80</td>
<td>171.8±2.0</td>
</tr>
</tbody>
</table>

Legends as in Table (1).

2-Histopathological study

A- Liver.

Figure (1), represents sections in liver of adult male mice fed on the control diet. The normal liver section is composed of lobules separated from each other by portal spaces. Each lobule contains the vein and parenchyma cells. There are branching cords that radiate from the middle of the lobule to the periphery of the lobule, their cytoplasm is stained approximately violet with some darker granules. Most of the cells contain a central rounded nucleus while some had two. The blood sinusoids are present between the cords. The
sinusoidal endothelium is formed of endothelial lining cells and the phagocytic kupffer cells (Figure 1A). Treatment of the mice with Antox drug showed many of the hypertrophied hepatocytes (↑) with pink cytoplasm which contained few minutes to large vacuoles (Figure 1B). In addition to hypertrophy of some nuclei the central vein showed some dilatation (↓). The blood sinusoids are narrower and the kupffers cells appeared larger than normal, prominent and bulging (curved arrow). Exposure of experimental animals to fractionated γ–radiation at dose level 1 Gy /day x5 times every other day represents hydropic degeneration (↓) in numerous hepatocytes. Some nuclei of hepatocytes lost their shape and other contain enlarged nuclei (▼). Also haemolysed blood cells inside the central vein (↓), enlarged kupffer cells, pyknotic (curved arrow) and karyolysis nuclei (blocked arrow) were observed (Figure 1C). Liver section of mice treated with Antox drug and exposed of fractionated dose of γ-radiation showed approximately normal architecture of liver tissue (Figure 1D).

![Liver micrographs of control (A), Antox (B), γ-irradiation (C) and Antox plus γ-irradiation treated mice (D). Original magnification X400.](image)

**B- Kidney.**

Figure (2), reveals kidney sections from control and treated mice. The normal kidney section showed two main parts, the outer cortex and the inner medulla, the main structures of the cortex is the renal corpuscles, proximal and
distal convoluted tubules. Each Malpighian corpuscle consists of Bowman’s capsule surrounds a glomerulus of blood capillaries. The glomerular tuft consists of a network of endothelial-lined capillaries with a thin basement membrane. The tubules, mainly proximal convoluted are lined by a single layer of cuboidal or low columner epithelium (Figure 2 E). Oral treatment of experimental mice with Antox drug showed nearly normal architecture of the kidney tissue of mice treated with the drug with the exception of the thickening the inner surface of convoluted tubules (star) and shrunken of Malpeghian corpuscle (↑) in kidney tissue (Figure 2F). Exposure of the experimental animals to fractionated dose of γ-radiation showed many of pathologic changes in the kidney tissue. Some nuclei of the cuboidal cells of the distal convoluted tubules are free from their cytoplasm (↑) with small and haemorrhagic areas (Figure 2 G). Meanwhile, the nuclei of the proximal convoluted tubules recorded bizarre distribution and karolysis (curved arrow). Gastric intubations of the experimental mice with Antox drug accompanied with γ-ray exposure showed normal appearance of kidney tissue. However, hypertrophied and lobulated glomerulus was recorded (curved arrow) (Figure 2 H).

Fig. 2: Kidney micrographs of control (E), Antox (F), γ-irradiation (G) and Antox plus γ-irradiation treated mice (H). Original magnification X400.
3-Immunohistochemical studies.

A- Liver.

Figure (3) demonstrates section in liver of adult male mice stained with P53 mouse monoclonal antibody. Normal tissue section recorded a negatively P53 expression in most of the hepatocytes (Figure 3 I). When experimental mice treated with Antox, P53 mostly expressed in kupffer cells nuclei (↓) and hepatocytes covering membrane (Figure 3 J). However exposure of the experimental animals to fractionated dose of γ-radiation mostly of P53 expression occurred in the hepatocytes (↓) and the interstitial stroma (Figure 3 K). On the other hand, when experimental mice treated with Antox and exposed to fractionated dose of γ-radiation some hepatocytes (↓) represented P53 expression (Figure 3 L).

Fig. 3: Liver micrographs stained with P53 mouse monoclonal antibody of control (I), Antox (J), γ-irradiation (K) and Antox plus γ-irradiation treated mice (L). Original magnification X400.

B-Kidney

In Figure (4), kidney tissue of adult male mouse fed on the control diet stained with stained with P53 mouse monoclonal antibody showed a negatively P53 expression (Figure 4 M). When experimental animals received orally Antox drug, pre tubular convoluted tubules membranes some interstitial cells represents some P53 expression (Figure 4 N). Exposure of experimental animals to fractionated dose of γ-radiation manifested a highly cytoplasmic P53
expression in all cells of the kidney tissue section (Figure 4 O). However, when experimental mice treated with Antox drug and exposed to fractioned dose of $\gamma$-radiation, a negatively $P53$ expression was observed in most of the kidney tissue (Figure 4 P).

**Fig. 4: Kidney micrographs stained with P53 mouse monoclonal antibody of control (M), Antox (N), $\gamma$-irradiation (O) and Antox plus $\gamma$-irradiation treated mice (P). Original magnification X400.**

**DISCUSSION**

Radiation is known to induce oxidative stress through generation of ROS, resulting in imbalance of pro-oxidants and antioxidants in the cells, which is suggested to culminate in cell death $^{(20, 21)}$. One of the basic mechanisms of radiation damage is the production of free radicals, leading to the formation of peroxides and oxidative reactive species. These peroxides, via lipid peroxidation, damage the cell membrane and other cell components. Free radicals such as superoxide anion ($O_2^-$), the hydroxyl radical ($OH^-$), and hydrogen peroxide ($H_2O_2$) are typically triggered by the exposure of living tissue to ionizing radiation. Membrane damage caused by these reactive oxygen species may allow the entry of excess calcium into cells with sequential biochemical and micro anatomical cellular degranulation and necrosis $^{(22, 23)}$.

The exposure to fractionated dose of $\gamma$-radiation leads to a significant increase in plasma creatinine, urea, uric acid, AST and ALT activity due to the
production of ROS and oxidative stress \(^{(24)}\). However, total protein and albumin level recorded a significant decrease in comparison with control level. This conclusion may be due to the decrease in plasma volume as a result of water loss by \(\gamma\)-irradiation and the alteration in the exchange of individual polypeptides \(^{(25)}\). A highly significant increase in MDA level and a significant decrease in GSH level compared to control level were take place in liver and kidney tissues due to generation of ROS, resulting in imbalance of pro-oxidants and antioxidants in the cells, which is suggested to culminate in cell death \(^{(20)}\).

Also, experimental animals exposed to fractionated \(\gamma\)–radiation suffered from oxidative stress \(^{(26)}\) represents hydropic degeneration in many of the hepatocytes. Many nuclei of them becomes larger in size due to the accumulation of post mitotic hepatocytes \(^{(27)}\), suggesting a radiation induced cell cycle block. The findings of Robbins et al., \(^{(1)}\) indicated that kidney irradiation clearly leads to a progressive reduction in function associated with concomitant glomerulosclerosis and/or tubulointerstitial fibrosis with many of pathologic changes.

In the current study, exposure of the experimental animals to whole body fractionated dose of \(\gamma\)-radiation led to \(P53\) expression in hepatocytes and their interstitial stroma and a highly cytoplasmic \(P53\) expression in all cells of the kidney tissue sections. \(P53\) function is essential for a major component of the normal response to gamma-irradiation induced DNA damage in tissue cells, and suggests that \(P53\) deficiency permits a population of cells bearing DNA damage to escape the normal process of deletion \(^{(28)}\). There is a link between oxidative stress and apoptosis \(^{(29)}\). Besides oxidative damage directly inflicted on DNA by free radical, there are other indirect mechanisms by which radicals can cause destruction of the genome. As already reported, lipid peroxides enter the nucleus where they react with Fe+2 to generate the aloxyl radical which attacks DNA \(^{(30)}\). Also, intracellular calcium levels increase as a result of oxidation damage to membranes, calcium then enters the nucleus where it can activate nucleases which lead to DNA strand breaks \(^{(31)}\). Marked reduction in antioxidant enzymes activities and tissue glutathione contents resulted in oxidative damage of tissues \(^{(32)}\). The depletion of glutathione is sufficient for the onset of apoptosis in cellular systems, especially, in hepatocytes \(^{(33)}\). Christine et al., \(^{(34)}\) reported that the \(P53\) tumor suppressor protein is activated and phosphorylated in response to various DNA damaging agents like ionizing radiation through the production of mutated ataxia telangiectasia (ATM).
The potential role of antioxidants to reduce the activity of free radical-induced reactions has drawn increasing attention. Treating animals with Antox revealed an improvement in histopathological alterations induced by exposure to fractionated dose of γ-radiation. Moreover, Antox treatment led to a decrease in P53 expression either in liver or kidney tissues. Antox is an antioxidant drug composed of selenium, vitamin A acetate, ascorbic acid and vitamin E. Antox was used in therapy of different liver diseases \(^{(35, 36, 37, 38)}\). Antox succeeded in minimize cadmium induced toxicity in albino rats and increase the activity of endogenous antioxidants including glutathione, superoxide dismutase and catalase \(^{(36)}\). Watson et al. \(^{(35)}\) reported that bio-Antox have protective effect against primary biliary cirrhosis. A significant reduction in oxidative stress parameters in blood and hepatic 8-oxodeoxyguanisone phosphate were recorded after giving Antox to Schistosoma-infected and chronic lead exposed hamsters \(^{(39)}\). Antox was found to maintain blood glutathione, plasma vitamin C and serum selenium levels towards the normal range \(^{(40)}\). Antox is a multivitamin compound (e.g. vitamins A, B, C). Many investigators reported that vitamins may act as antiapoptotic agents \(^{(41, 42, 43)}\). The effect of Antox components (vitamines A, B, C) rests with strong antioxidants, free radical scavenging activity and inhibition of lipid peroxidation \(^{(44)}\). Also, Sakr and Abel-Samie \(^{(45)}\) reported that Antox can reduced histological alterations and reduce apoptosis in liver of metalaxyl fungicide –treated mice. Thus, the preventive effect of Antox against γ-irradiation induced liver and kidney damage and P53 expression recorded in the present work may be attributed to its antioxidant properties.

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تأثير تعرض الفئران لجرعات مقسمة من أشعة جاما وتناول مضادات الأكسدة

في إحداث الموت المبرمج للخلايا

نعمات جنفي أحمد

قسم بحوث بيوتكولوجيا الإشعاع - المركز القومي لبحث وتقنية الإشعاع - هيئة الطاقة الذرية - القاهرة

يفيد هذا البحث إلى معرفة تأثير تعرض الفئران لجرعات مقسمة من أشعة جاما وتناول مضادات الأكسدة على التجربين divider بـ53 وقد استخدم في هذه الدراسة عقار الأنتوكس المحتوي على فيتامين ج، هـ، والسيليتين كمضادات للأكسدة. ولإجراء البحث تم اتباع عدد 24 فأر صغير أبيض وقسمت إلى 4 مجموعات. مجموعة الضابطة. مجموعة عولجت بعقار الأنتوكس، مجموعة عولجت لجرعات مقسمة من أشعة جاما و مجموعة عولجت بعقار الأنتوكس وجرعات عرضت لجرعات مقسمة من أشعة جاما و مجموعة عولجت بعقار الأنتوكس و مجموعة عولجت بعقار الأنتوكس و مجموعة عولجت بعقار الأنتوكس و مجموعة عولجت بعقار الأنتوكس و مجموعة عولجت بعقار الأنتوكس و مجموعة عولجت بعقار الأنتوكس و مجموعة عولجت بعقار الأنتوكس و مجموعة عولجت بعقار الأنتوكس و مجموعة عولجت بعقار الأنتوكس و مجموعة عولجت بعقار الأنتوكس و مجموعة عولجت بعقار الأنتوكس و مجموعة عولجت بعقار الأنتوكس و مجموعة عولجت بعقار الأنتوكس و مجموعة عولجت بعقار الأنتوكس و مجموعة عولجت بعقار الأنتوكس و مجموعة عولجت بعقار الأنتوكس و مجموعة عولجت بعقار الأنتوكس و مجموعة عولجت بعقا...