Assessment of the Effect of Gamma Irradiated Ginger on Testicular and Hepatic Function of Alloxan-Induced Diabetic Rats

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Received: 3/11/2016 Accepted: 20/12/2016

ABSTRACT

This study was conducted to assess the effect of gamma (γ) irradiation on the microbiological quality of dried ginger (DG) and also to determine the effect of raw and γ-irradiated ginger aqueous extract (GAE) on testicular and hepatic function in alloxan-induced diabetic rats. The microbial counts were higher in raw samples (control) than those of irradiated ones (10 kGy) which indicated that the use of irradiation treatment induced a reduction in the microbial load of ginger. The results revealed also that alloxan administration to rats (150 mg/kg B.WT) showed a significant increase in the levels of serum glucose, alkaline phosphatase, γ-glutamyl transferase and transaminases concomitant with a significant decrease in the levels of insulin, testosterone (T), Follicle stimulating hormone (FSH) and leutinizing hormone (LH). Furthermore, alloxan induced a significant oxidative stress in liver and testes tissues notified by an increase of malondialdehyde level concomitant with a decrease in glutathione level and superoxide dismutase and catalase activities. The treatment of diabetic rats with either raw or γ-irradiated ginger aqueous extract (GAE) has significantly ameliorated the alteration in the antioxidant/oxidant status and improved hyperglycemia, hepatic, testicular and endocrine functional abnormalities. In conclusion, this study indicated that ginger, in addition to being hypoglycaemic, is effective in reducing oxidative stress caused by alloxan-induced diabetes and that the γ-irradiation of DG increased its hygienic quality without a significant loss in its quality attributes.

Keywords: Alloxan/ Ginger/ Diabetes/ Antioxidants/ Oxidative stress.

INTRODUCTION

Diabetes mellitus (DM) is a chronic complex metabolic disorder resulting from lack of insulin secretion or insulin action or both characterized by high glucose levels (hyperglycemia) (1, 2, 3). DM has taken place as one of a serious global health problem and considered one of the five leading causes of death in the world. (4, 5). The WHO reported that 5% of total worldwide annual deaths are due to complications of DM. So, the world mortality from this disease is expected to grow in the next 10 years over 50%. (6). Hyperglycemia generated oxygen free radicals which could induce oxidative stress, especially, production of reactive oxygen species (ROS), which results in an imbalance occurs between the antioxidant cellular defense mechanisms and free radicals (7). Biochemical markers of these complexes such as carbohydrate, lipid, protein and electrolyte metabolism, increase through oxidative stress which, affects diabetic patients and associated with accelerated endothelial cell...
dysfunction and trigger the progression of atherosclerosis (8). The DM could induce damages / dysfunctions of various organs, such as, kidneys retina, heart, liver, peripheral, central nervous and sexual dysfunction (9). DM causes disturbance in the male reproductive functions in humans and animals. Glucose metabolism is an important event in spermatogenesis. Previous investigations have confirmed the deleterious effect of DM on sexual functions, associated with levels of testosterone hormone, semen parameters, DNA nuclear fragment, and chromatin quality of humans and animals (10,11).

Ginger (Zingiber officinale R., family: Zingiberaceae) is widely used as tropical safe medicine aromatic herbal plant and used as a spice and as natural food additives for more than 2000 years (12,13). Biochemically, it contains several bioactive compounds including acids, resins, vitamin C compounds, folic acid, inositol, choline, pantothenic acid, gingerol, sesquiterpene, vitamin B1 and B6 volatile oils and bio-trace elements such as Ca, Mg, P and K (14,15,16). Ginger oil was found to protect DNA from oxidative damage induced by Hydrogen peroxidase (H$_2$O$_2$), which induces oxidative stress (17,18). β- carotene, ascorbic acid, terpenoids, alkaloids and polyphenols, such as flavonoids, flavones glycodies and rutin, the main active antioxidants components have been found in ginger (19,20). Furthermore, pharmacological and biological activities, ginger and its constituents are stated to have anti-diabetic, anti-inflammatory, antiemetic, anti-thrombotic, anti-hepatotoxic, hypoglycemic, hypolipidemic and antioxidant effects (17,21).

Treatment of food with ionizing radiation (γ- radiation) is a physical method and it has the potential to enhance food safety for both fresh foods that will be consumed raw and for raw foods that will be further processed. This method is considered a simple and effective food decontamination food products (22). Gamma radiation has been used as a tool to destroy harmful pathogenic and spoilage microorganisms (bacteria, molds, and yeasts) (23). Food irradiation is a cold process and one of the latest techniques which has several advantages over conventional methods of food preservation such as salting, cold storage, fumigation and drying, because it does not lead to loss of sensory food quality odor, flavor, and texture or compromising food safety and nutritional properties (24). Therefore, this study was conducted to assess the effect of γ-irradiation on the microbiological quality of dried ginger (DG) and also to determine the effect of raw and γ-irradiated ginger aqueous extract (GAE) in alloxan-induced diabetic rats on testicular and hepatic function.

MATERIAL AND METHODS

Ginger dried roots were obtained from local market of Herbs and Medicinal plants. Chemicals were purchased from Sigma Chemical Co. (St. Louis, MO, USA).

Gamma Irradiation Treatment

Ginger dried roots were transferred into polyethylene bags and treated with 10 kGy of gamma rays, using a Cobalt-60 source (Atomic Energy of Canada Ltd, Ottawa, Ontario, Canada), located at the NCRRT, the Atomic Energy Authority Cairo, Egypt. The dose rate of the irradiation process was 2.50 kGy/hour calculated according to the dosimeter department at the NCRRT.

Assay of Microbial Load

1-Bacterial Load

Ten grams of samples (raw and γ-irradiated ginger) were homogenized for 2 min. in sterile lab blender with 90 ml of saline solution (0.85 % NaCl). Serial dilutions of sample homogenate were prepared in test tubes containing the same saline solution. One ml of three appropriate decimal solution (on duplicate) was plated on plate count agar medium using pour plate technique (25). The inoculated plates were incubated at 30 ºC for 3 days. The developing colonies were counted, and the TBC were expressed as colony forming unit (CFU) per gram of sample. Plate count agar medium
contains (g/L): Agar (15g), Tryptone (5g), yeast extract (2.5g) dextrose as glucose (1g) and sodium chloride (5 g). The pH of the medium was adjusted to 7± 0.1.

2-Totals Mould and Yeast Count

One ml of the selected three appropriate dilutions was plated (on duplicate) on malt extract medium (pH 6.6± 0.1)\(^{26}\) using pour plate technique. Chloramphenicol (100 mg /L) was added to the medium agar just before purity to prevent bacterial growth. The inoculated plates were incubated at 25 °C for 3 -5 days. The developing colonies were counted, and the total moulds and yeasts were expressed as CFU/g. The contents of malt extract agar medium are nutt extract, 30 g mycological peptone, 5g; agar 15g and distilled water 1L.

Preparation of Ginger Aqueous Extracts (GAE)

The water extract was prepared by soaking 100 g of the raw and γ-irradiated ginger in 500 ml hot distilled water at 40–50 °C with daily shaking for 5 days and kept in a refrigerator. The infusions were filtered by a piece of double layer gauze and the filtrate was centrifuged at 3000 rpm for 10 min., then water was evaporated in hot air oven at 50 °C. Known grams of the extract were suspended in distilled water\(^{27}\).

Experimental Design

Animals

Male albino rats Sprague Dawley (170 to 220 g body weight (B.WT)) were purchased from the Egyptian Holding Company for Biological Products and Vaccines (Cairo, Egypt) and used through the different investigations carried out in the present study. Rats were acclimated to controlled laboratory conditions for two weeks. Rats were maintained on stock rodent diet and tap water that were allowed ad libitum. All animals procedures were carried out in accordance with the guidelines of Ethics Committee of the National Research Center and conforme to the Guide for the Care and Use of Laboratory Animals, published by the US National Institutes of Health\(^{28}\).

Administration of Alloxan

Male albino rats were made diabetic by injecting them with alloxan monohydrate dissolved in saline intraperitoneally with dosage of 150 mg/kg B.WT\(^{29}\). Alloxan can induce fatal hypoglycemia as a result of massive pancreatic insulin release; therefore, rats were treated with 30 % glucose solution orally at different time intervals after 6 h of alloxan induction, and 5% glucose solution was kept in bottles in their cages for the next 24 h. After one week, blood was extracted from the tail vein for glucose analysis by the method described by P Trinder\(^{30}\). Experimental animals exhibited fasting blood glucose levels in the range of 200 to 250 mg/dl.

Grouping of Animals

The animal were randomly divided into 4 groups, each consisted of 7 rats.

**Group C:** rats fed on balanced diet and served as control.

**Group D:** Diabetic group.

**Group D + RGAE:** diabetic rats received raw ginger aqueous extract (RGAE) orally (500mg/kg B. Wt) three times per week\(^{27}\).

**Group D + γ-Irr. GAE:** diabetic rats received oral γ-irradiated ginger aqueous extract (Irr. GAE) (500mg/kg B. Wt) three times a week for 8 weeks.

At the end of the experiment, animals from each group were sacrificed 24 h. post the last dose of treatment. Blood samples were withdrawn by cardiac puncture after slight anthesation of rats using diethyl ether and allowed to coagulate and centrifuged to get serum for biochemical analysis.
Biochemical Analysis

Serum samples were analyzed for glucose \(^{(30)}\) and insulin hormone was determined by radioimmunoassay kit supplied by Diasari, Italy. The activity of serum aspartate transaminase (AST) and alanine transaminase (ALT) were estimated according to Reitman et al. \(^{(31)}\), serum γ-glutamyl transferase (GGT) was assessed according to S.B.Rosalki\(^{(32)}\) and serum alkaline phosphatase activities (ALP) was assessed according to Kind & King \(^{(33)}\). Estimation of testosterone hormone was performed according to the method of Wilson et al \(^{(34)}\), Follicle stimulating hormone (FSH) and leutinizing hormone (LH) were estimated according to Garrett\(^{(35)}\).

Liver and testes were dissected, thoroughly washed with ice-cold 0.9% NaCl, weighed, minced and homogenized (10% w/v) using 66 mmol/L chilled phosphate buffer (pH 7.0). The tissue homogenates were centrifuged at 6000 rpm for 15 min and the supernatants were used to estimate MDA\(^{(36)}\), GSH \(^{(37)}\), superoxide dismutase activity (SOD) \(^{(38)}\) and Catalase activity (CAT) \(^{(39)}\).

Statistical Analysis

Data were presented as mean ± SE (n = 7). Experimental data were analyzed using one way analysis of variance (ANOVA). Duncan’s multiple range test was used to determine significant differences between means. The statistical analyses were performed using computer program Statistical Packages for Social Science (SPSS) \(^{(40)}\). Differences between means were considered significant at P < 0.05.

RESULTS

Table (1) indicated that raw ginger samples had high total aerobic bacterial count and relatively low total mold and yeast counts. Irradiation at 10 kGy greatly reduced the content of total aerobic bacterial count namely about 4 log counts (99.9 %). This irradiation dose greatly reduced the total mold and yeast counts to non-detectable level (> 10 CFU/g).

<table>
<thead>
<tr>
<th>Item</th>
<th>Sample</th>
<th>Raw ginger</th>
<th>γ-irradiated ginger (10 kGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total aerobic bacterial count (TAB)</td>
<td>2.8 × 10(^6)</td>
<td>1.5 × 10(^2)</td>
<td></td>
</tr>
<tr>
<td>Total yeast and mold count</td>
<td>5.8× 10</td>
<td>&lt; 10</td>
<td></td>
</tr>
</tbody>
</table>

The data presented in Table (2) reveal a significant increase in glucose and a remarkable decline in insulin level in diabetic rats compared to normal rats. In contrast, administration of RGAE and γ-Irr. RGAE to diabetic rats significantly decreased the level of glucose and significantly increased the level of insulin compared to diabetic group.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Diabetic</th>
<th>D+ RGAE</th>
<th>D + γ-Irr. GAE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose(mg/dl)</td>
<td>87.72(^{c}) ±5.88</td>
<td>233.45(^{a}) ±8.12</td>
<td>157.47(^{b}) ±6.85</td>
<td>131.25(^{b}) ±6.74</td>
</tr>
<tr>
<td>Insulin(μU/ml)</td>
<td>30.84(^{a}) ±3.28</td>
<td>18.51(^{c}) ±2.77</td>
<td>25.62(^{b}) ±3.81</td>
<td>28.88(^{ab}) ±3.54</td>
</tr>
</tbody>
</table>

Values are expressed as means ± S.E. (n=7).
Values in the same row with different superscripts are differing significantly at P<0.05.
Alloxan administration to rats significantly produced adverse effects on the liver function and increased the activity of ALT, AST, ALP and γGT enzymes as compared with normal animal group (Table 3). Moreover, treatment of diabetic rats with either RGAE or Irr. GAE exhibited the improvement in these liver enzymes levels compared to those of the diabetic rats.

The results demonstrated in Table (4) reveal that the group of rats injected with alloxan exhibited a high level of hepatic and testicular MDA and a low level of GSH with a reduction of SOD and GSH activity when compared to the control group. Whereas, a significant reduction in lipid peroxidation and significant improvement of the antioxidant status was observed in the liver and testes tissues of diabetic rats received RGAE or γ-Irr. GAE.

**Table (3):** Effect of administration of RGAE and γ-Irr. GAE to diabetic rats on liver enzymes levels

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Diabetic</th>
<th>D+ RGAE</th>
<th>D+ γ-Irr. GAE</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST (U/ml)</td>
<td>34.47 ± 1.57</td>
<td>57.75 ± 3.85</td>
<td>39.51 ± 2.68</td>
<td>36.15 ± 1.86</td>
</tr>
<tr>
<td>ALT (U/ml)</td>
<td>25.66 ± 1.67</td>
<td>45.64 ± 2.95</td>
<td>29.18 ± 2.19</td>
<td>28.57 ± 2.11</td>
</tr>
<tr>
<td>ALP (U/100ml)</td>
<td>8.58 ± 0.78</td>
<td>14.28 ± 0.78</td>
<td>10.23 ± 0.92</td>
<td>9.42 ± 0.68</td>
</tr>
<tr>
<td>γGT (U/ml)</td>
<td>4.61 ± 0.37</td>
<td>6.28 ± 0.52</td>
<td>5.56 ± 0.47</td>
<td>5.50 ± 0.50</td>
</tr>
</tbody>
</table>

Values are expressed as means ± S.E. (n=7).
Values in the same raw with different superscripts are differing significantly at P<0.05.

**Table (4):** Effect of administration of RGAE and γ-Irr. GAE to the diabetic rats on the hepatic and testicular antioxidant status.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Diabetic</th>
<th>D+ RGAE</th>
<th>D+ γ-Irr. GAE</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDA (n mol/g tissue)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>181.52 ± 6.57</td>
<td>358.25 ± 7.52</td>
<td>241.14 ± 6.72</td>
<td>233.57 ± 5.93</td>
</tr>
<tr>
<td>Testes</td>
<td>132.82 ± 4.25</td>
<td>219.97 ± 5.34</td>
<td>172.58 ± 4.16</td>
<td>169.64 ± 3.96</td>
</tr>
<tr>
<td>GSH (mg/g tissue)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>27.10 ± 2.37</td>
<td>17.28 ± 1.66</td>
<td>22.82 ± 1.44</td>
<td>23.13 ± 1.68</td>
</tr>
<tr>
<td>Testes</td>
<td>22.15 ± 1.68</td>
<td>12.27 ± 1.56</td>
<td>17.24 ± 1.23</td>
<td>18.17 ± 1.57</td>
</tr>
<tr>
<td>SOD (U/mg protein)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>46.09 ± 3.35</td>
<td>34.98 ± 3.22</td>
<td>41.28 ± 3.55</td>
<td>43.92 ± 3.72</td>
</tr>
<tr>
<td>Testes</td>
<td>21.06 ± 1.25</td>
<td>13.27 ± 0.46</td>
<td>16.82 ± 0.81</td>
<td>19.02 ± 0.71</td>
</tr>
<tr>
<td>CAT (U/g protein)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>3.68 ± 0.12</td>
<td>1.75 ± 0.08</td>
<td>2.98 ± 0.07</td>
<td>3.32 ± 0.11</td>
</tr>
<tr>
<td>Testes</td>
<td>3.41 ± 0.12</td>
<td>1.62 ± 0.11</td>
<td>2.67 ± 0.21</td>
<td>2.87 ± 0.12</td>
</tr>
</tbody>
</table>

Values are expressed as means ± S.E. (n=7).
Values in the same raw with different superscripts are differing significantly at P<0.05.

In this work, induction of diabetes by alloxan administration resulted in a remarkable reduction in the level of testosterone, LH and FSH compared to the control rats. On the other hand, treatment of diabetic rats by RGAE or γ-Irr. GAE induced a significant increase in the level of these hormones compared with diabetic group (Table 5).

**Table (5):** Effect of administration of RGAE and γ-Irr. GAE to diabetic rats on the level of T, LH and FSH

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Diabetic</th>
<th>D+ RGAE</th>
<th>D+ γ-Irr. GAE</th>
</tr>
</thead>
<tbody>
<tr>
<td>T (n mol/L)</td>
<td>4.88 ± 0.16</td>
<td>2.47 ± 0.13</td>
<td>4.62 ± 0.17</td>
<td>4.78 ± 0.13</td>
</tr>
<tr>
<td>LH (IU/L)</td>
<td>0.82 ± 0.08</td>
<td>0.58 ± 0.06</td>
<td>0.73 ± 0.05</td>
<td>0.76 ± 0.07</td>
</tr>
<tr>
<td>FSH (IU/L)</td>
<td>0.76 ± 0.04</td>
<td>0.60 ± 0.05</td>
<td>0.69 ± 0.05</td>
<td>0.70 ± 0.04</td>
</tr>
</tbody>
</table>

Values are expressed as means ± S.E. (n=7).
Values in the same raw with different superscripts are differing significantly at P<0.05.
DISCUSSION

DM is a global chronic common health diseases associated with carbohydrate metabolism. It is also an indication of co-morbidities such as hypertension, obesity, and hyperlipidemia which are metabolic complications of both clinical and experimental diabetes. Alloxan, a beta cytototoxin induces chemical diabetes (Alloxan diabetes) in a wide variety of animal species by damaging the insulin the secreting pancreatic β-cell, resulting in a diminish in endogenous insulin release, which paves way for the decreased utilization of glucose by the tissues. In view of the medicinal properties of ginger, the present study was conducted to investigate the anti-diabetic, anti-hyperlipidaemic and anti-oxidant activities of raw and γ-irradiated ginger aqueous extract (GAE) in alloxan-induced diabetic rats.

It was noticed that γ-irradiation caused a great reduction in the tested microorganisms of raw samples. The reduction in total aerobic bacterial counts of γ-irradiated ginger samples might be due to the direct effect of radiation as well as the indirect effect resulting from water radiolysis which is greater in fresh samples than irradiated one. Al-Kuraieef and Al-shawi (2014) showed that γ-radiation (5.0, 10.0 and 15.0 kGy) processing had led to a significant reduction in total number of bacteria, yeast and fungi.

Diabetic rats in the current study, showed a significant elevating in blood glucose level associated with a significant decrease in the level of insulin, compared to their respective values in the control group. Alloxan induced diabetic models by destroying/ damage the insulin secreting cells of the pancreas resulting in hypoinsulinaemia and hyperglycemia. Alloxan generated hyperglycemia by specific cytotoxic impact on pancreatic β-cells. One of the intracellular phenomena for its cytotoxicity occurs through the generation of free radical exhibited both in- vivo and in- vitro. The sensitivity of β-cells to oxidative stress has been attributed to their low levels of antioxidants compared with other tissues. β- cells dysfunction eventually culminates in reduction in insulin release leading to hyperglycemia. The alloxan induced sustained hyperglycemia aggravates the oxidative stress status by auto-oxidation of glucose and its primary and secondary adducts. Whereas, there was a significant reduction in the glucose level with a significant increase in insulin level of diabetic rats treated with either RGAE or Irr. GAE when compared to diabetic rats. Therefore, it could be concluded that ginger has anti-hyperglycemic action in the experimentally induced diabetic rats. The results comply with the previously reported work of Akhani et al. who reported that ginger treatment inhibited the induced hypoinsulinaemia and hyperglycemia, other authors also found the hypoglycemic effects of ginger in their experiments on rats. They found that post treatment and pre-treatment of streptozotocin induced diabetic rats with ginger extract significantly decreased the glucose level and increased the insulin level.

Many studies reported that compounds of ginger such as, polyphenolic compounds, tannins, flavonoids, and triterpenoids possess hypoglycemiac and other pharmacological properties. Rani et al. (2014) suggested that ginger, via its major component, gingerol, by inhibition of key enzymes relevant to type 2 diabetes, α-glucosidase and α-amylase, are known to improve diabetes. Ginger promotes glucose clearances in insulin responsive peripheral tissues, which is crucial in maintaining blood glucose homeostasis. Also, Sekiya et al. reported that 6-gingerol elevated the glucose uptake at insulin responsive adipocytes.

In this work, diabetic rats showed a significant increase in blood serum activity of ALT, AST, ALP and γGT. Supporting these findings, it has been found that the liver was necrotized in diabetic rats. Therefore, the increased liver enzymes activity in serum is mainly due to the leakage of these enzymes from the liver into the blood stream, which gives an indication of hepatotoxic effect of alloxan. Mallikarjuna et al. attributed the possibility of prevention and treatment of chronic hepatitis (liver inflammation) to the active compounds present naturally in ginger. Sekiya et al. sustained that novel glucosides related to gingerdiol from ginger has an anti-oxidative activity. Thus, the anti-oxidative action of ginger might play an important role in the anti-hepatotoxic activity.
As for the hepatic and testicular anti-oxidant status, the current study revealed oxidative stress increased due to alloxan-induced diabetes which was evidenced by increasing tissue concentration of MDA level and depletion of GSH concentration and anti-oxidant enzymes activity (SOD and CAT). The increase in MDA level resulted from hypoinsulinemia that increases the activity of fatty acyl coenzymes A oxidase, which initiates β-oxidation of fatty acids, resulting in lipid peroxidation. Also, protein glycation and glucose auto-oxidation can lead to the formation of free radicals, and this can equally induce lipid peroxidation (56). Increased lipid peroxidation impairs membrane functions by decreasing membrane fluidity and changing the activity of membrane-bound enzymes and receptors (56). Also, it was observed that the decrease in antioxidant enzymes activity under diabetic conditions could be due to glycation of these enzymes, which occurred at persistently elevated blood glucose levels (57). Glycation of SOD reduces its activity, leading to the insufficient dismutation of superoxide anions (O2-) (58, 59). Studies by Young et al. (60) demonstrated a correlation between the improved glycaemic control and the inhibition of protein glycation, and hence an increase in SOD activity. The oxidative stress is the result of a redox imbalance between the generation of reactive oxygen species (ROS) and the compensatory response from the endogenous antioxidant network.

On the other side, in this study, the treatment of diabetic rats with RGAE and γ-Irr RGAE resulted in a remarkable reduction in the level of MDA with an obvious enhancement in GSH concentration and antioxidant enzymes activity (SOD and CAT) in the hepatic and testicular tissues compared to those of alloxan-induced diabetic rats. Ginger has been reported to have a lowering effect on lipid peroxidation by influencing the enzymatic level of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPX). It has been also shown that ginger reduces cellular oxidation and scavenges superoxide anion and hydroxyl radicals (64). Madkor et al. (62) indicated that addition of ginger (1%) to a normal diet prevented the formation of free radicals and maintained the integrity of rat erythrocytes. The antioxidant potency of ginger has been attributed to gingerols as a bioactive substances that prevents reactive oxygen species (ROS) production.

Mallikarjuna et al (54) showed that concomitant dietary feeding of ginger (1% w/w) for 4 weeks induce a significant decrease in MDA levels and significant increases in activities of SOD, CAT and GSH content. The levels of MDA formed in liver of rats fed with ginger at different concentrations, namely 0.5%, 1% and 5% were reduced significantly as compared to the control group that was not received ginger. The percentage of inhibition was 35%, 56% and 59% respectively (63). Khanom et al. (64) indicated that the occurrence of phenolic compounds such as, flavonoids and ferulic acid in ginger rhizome may be responsible for scavenging the superoxide anion radicals and thereby maintains the high activity of SOD even in alcohols. This beneficial result indicates further evidence for the hepatoprotective effect of dietary ginger. Ahmed et al. (2000) (65) showed the anti-oxidant property of ginger in Wistar rats with a comparative study of well-known antioxidant ascorbic acid.

The administration of alloxan to male rats induces decrease in the sex hormones (testosterone, LH and FSH) concentrations compared to the control rats. This finding is parallel to that of the previous investigations (66, 67). The diminished in testosterone levels may be the result of alloxan-induced decrease in the total number of Leydig cells causing strong decrease in the expression of testosterone (68). Also the increases in glucose level induces changes in leydig cells, including decrease in androgen synthesis (69) and changes in the pituitary-testicular axis with subsequent decrease in LH level. LH itself is responsible for normal leydig cell function (70) and plays an important role in testosterone production (71). Onah et al. (72) reported that the effect of diabetes on testicular hormones may be as a result of high oxidative stress generated in diabetic patients that affect the normal functioning of the pituitary gland and hypothalamus.

In the present study, the beneficial effect of RGAE and γ-Irr.GAE on the level of sex hormones (testosterone, LH and FSH) has been well documented in treated diabetic rats when compared to the non-treated diabetic group. These findings are in line with those of Border et al. (73) who confirmed that ginger stimulates male reproductive system and significantly increased testosterone level in...
busulfan- induce infertility in rats. Also, these results were supported by finding of Arash et al.\textsuperscript{(74)} who reported that administration of ginger for twenty days significantly increased testosterone. Morakinyo \textit{et al.}\textsuperscript{(75)} revealed that the positive effects of ginger on reproductive functions might be a consequence of both its potent anti-oxidant properties and androgenic activities.

**CONCLUSION**

Gamma-radiation processing of ginger has an effective role in reducing the microbial load of ginger without a significant loss in its quality attributes. Also, the present study indicated that ginger possesses an anti-diabetic and strong anti-oxidant activity and has useful effects on reducing endocrine abnormalities caused by alloxan-induced diabetes.

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