

# Modulatory Role of Selenium Nanoparticles and Grape Seed Extract Mixture on Oxidative Stress Biomarkers in Diabetic Irradiated Rats

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## ABSTRACT

**Introduction:** Diabetes is a metabolic disorder of several etiologies, many oral anti-hyperglycemic agents such as sulfonylurea, biguanides are obtainable, but these agents have side effects, thus there is need of a new natural anti-hyperglycemic agent. **Methods:** The present study was performed to evaluate the protective role of selenium nanoparticles-grape seed extract (SeNPs-GSE) mixture in ameliorating the changes in the oxidative stress biomarkers induced by gamma radiation in diabetic rats. Experimental model of diabetic irradiated rats was induced by single intraperitoneal injection of streptozotocin (STZ 45 mg/kg) followed by  $\gamma$ -radiation exposure (4 Gy). Forty eight rats were randomly classified into 6 experimental groups: normal, diabetic, irradiated, diabetic irradiated, diabetic treated with either SeNPs-GSE mixture or glimepiride (1 mg) for (14) days followed by  $\gamma$ -radiation. **Results:** Results of the present study indicated that rats exposed to  $\gamma$ -radiation and, or STZ significantly increase serum glucose & liver MDA levels. This increase was accompanied by a decrease in the levels of serum insulin, total antioxidant (TAC), liver enzyme activities of catalase (CAT), glutathione peroxidase (GPx), superoxide dismutase (SOD), as well as liver tissue contents of vitamin C (Vit.C) and vitamin E (Vit.E). Diabetic rats treated with (SeNPs-GSE) mixture or glimepiride before  $\gamma$ -radiation exert a significant improvement in all tested biochemical parameters. **Conclusion:** The present study showed that a mixture of (SeNPs-GSE) possesses antioxidant and anti-diabetic activities by decreasing oxidative stress biomarkers as well as blood glucose level tested in this study. The tested combination (SeNPs-GSE) mixture is more or less equally active as that of the standard tested anti-diabetic drug glimepiride

**Key words:** Diabetes mellitus, Selenium nanoparticles, Grape seed extract, Oxidative stress, Vitamin C, E.

## INTRODUCTION

Radiotherapy is frequently used as a part of cancer treatment to attain tumor control. It might produce harmful effects to adjacent healthy tissues.<sup>1</sup> Ionizing radiations induce oxidative stress, mainly through the generation of reactive oxygen species (ROS) resulting in imbalance of the pro-oxidant and antioxidant in the cells and attack different cellular macromolecules leading to cell death.<sup>2</sup> Diabetes mellitus (DM) is a pathologic conditions resulting in severe metabolic imbalances in many tissues. It generates ROS through various pathways, such as damage of the redox equilibrium or overproduction of mitochondrial superox-

ides, which leads to oxidative stress in variety of tissues.<sup>3</sup> Glimepiride is a sulfonylurea antidiabetic drug indicated to treat type 2 diabetes mellitus; its mode of action is to increase insulin production by the pancreas.<sup>4</sup> Several radioprotectors have been tested to find out if their administration before or during irradiation diminishes radiation induced damage to the body.<sup>5</sup> Although synthetic radioprotectors such as amino-thiols have yielded the highest protective effects, they are typically more toxic than naturally protectors.<sup>6,7</sup> Herbal medicines with antioxidant resources have attracted great attention as possible radiation protec-

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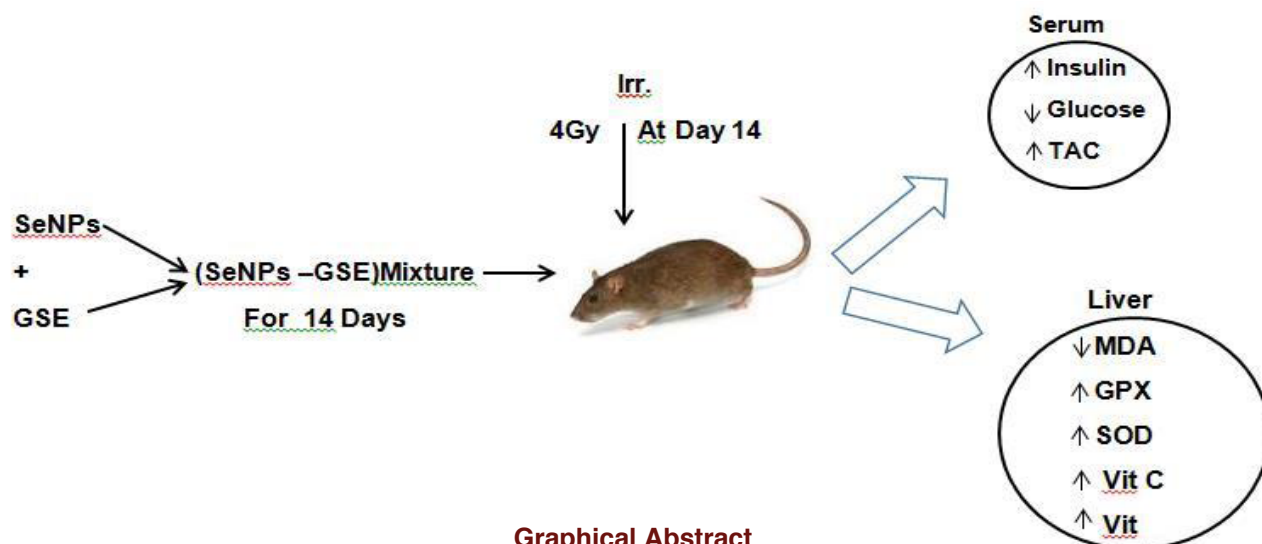
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**Graphical Abstract**

tor.<sup>8</sup> Among the natural products, grape seed extract (GSE) compounds are attracting the interest because of their beneficial effects in human health. GSE contains vit E, flavonoids, linoleic acid, proanthocyanidines.<sup>9</sup> Proanthocyanidins were shown to have a role in lowering cholesterol levels,<sup>10</sup> anti-inflammatory, cardioprotective, anticarcinogenic, and antioxidant activities.<sup>11</sup>

Nanotechnology is the creation of matter on the nanometer length scale (1-100 nm). Materials at the nanometer dimension exhibit novel properties different to those of both isolated atoms and bulk material such as increase bioavailability of drugs, development of new medicines which are more safe, as well as nanoparticles can be administered via different routes like inhalation, through skin, orally, intravenous injection and intraperitoneal injection.<sup>12,13</sup> Development of newer drug delivery systems based on nanotechnology methods is being tried for conditions like cancer, diabetes, fungal infections, and viral infections and in gene therapy. The main advantages of this modality of treatment are targeting of the drug and enhanced safety profile.<sup>14</sup> Previous study reported an association between (DM) and alterations in the metabolism of several trace minerals such as magnesium, selenium, vanadium.<sup>15</sup>

Selenium (Se) is a nutritional trace element with notable antioxidant characteristics. It can inhibit many inflammatory cell mechanisms through antioxidant seleno enzymes.<sup>16</sup> Selenium improved glucose homeostasis in diabetic rats.<sup>17</sup> As a part of glutathione peroxidase, selenium (Se) acts, in performance with vitamin E, to avoid free radical damage to cells.<sup>18</sup> However, Se has a very narrow margin between the thresholds of functionality and toxicity; Se nanoparticles (SeNPs) have excellent bioavailability, high biological activity and low toxicity.<sup>19</sup> Furthermore, SeNPs (5 to 200 nm) were efficient for

free radical scavenging both *in vivo* and *in vitro*.<sup>20</sup> A benefit of using nano scale for medical technologies is that smaller devices are less invasive, faster and more sensitive than typical drug delivery.<sup>21</sup> Moreover, SeNPs has a 7-fold lower acute toxicity than sodium selenite in mice.<sup>22</sup> In view of the previous concepts, this study was performed to investigate the modulatory effects of SeNPs-GSE mixture in restoring the endogenous antioxidant defense capacity as well as glucose homeostasis in STZ-induced diabetes in irradiated rats.

## MATERIALS AND METHODS

### Chemicals and Drugs

All chemicals were from Sigma-Aldrich (USA). Grape seed extract was obtained from (AL-Debeiky Pharma, Egypt). Glimperide was purchased from (Sanofi Aventis, Egypt). Kits used in the experiment were purchased from (Biodiagnostic, Egypt). All other chemicals were of the highest commercially available grade.

### Animals

Adult male albino rats, weighing 140-160 gm were purchased from the Animal House Colony of the Veterinary Serum and Vaccine Research Institute, Cairo, Egypt. Rats were housed under conventional laboratory conditions throughout the period of experimentation and fed standard rat pellet diet and allowed free access to water. The animal's treatment protocol has been approved by the Animal Care committee of the National Center for Radiation Research and Technology (NCRRT), Cairo, Egypt.

### Irradiation

Whole body  $\gamma$ -irradiation of animals were performed using gamma cell 40 which is cesium-137 irradiated unit

belonging to National Center of Radiation and Technology (NCRRT) Cairo, Egypt. The dose rate was 0.996 rad / sec at the time of exposure.

### Preparation and characterization of SeNPs–GSE Mixture

SeNPs were formed by adding 0.04 mM selenious acid and 0.2 mM GSH solution (1:4 ratio v/v) containing bovine serum albumin to 100 ml deionized water with stirring to initiate the reaction. The pH of the mixture was adjusted to 7.2. The reaction lasted 1 hour under sonication and Centrifuged at 20000 rpm (Hettich cooling centrifuge; type Werk Nr. Made in Germany). Red elemental Se and oxidized glutathione (GSSG) were formed and characterized by measured average particle size and size distribution by Dynamic light scattering (DLS). The particle size and shape were observed by Transmission Electron Microscopy (TEM).

The pellets were mixed with the powders of Grape seed extract under sonication conditions for 1 hour to form mixture.<sup>20,23</sup>

### Induction and assessment of diabetes

Overnight fasted animals were rendered diabetic by a single intraperitoneal (i.p) injection of STZ (45 mg/kg b.wt) in freshly prepared citrate buffer (0.1 M, pH 4.5).<sup>24</sup> STZ injected animals were given 5% glucose solution for 48 h to prevent initial drug-induced hypoglycemic mortality as a result of enormous pancreatic insulin release. After one week of administration, blood glucose level was measured from tail vein using one touch select glucose meter (LifeScan Europe, Switzerland) rats exhibiting blood glucose levels 200 mg/ dl or more were included in the study.<sup>25</sup>

### Treatment schedule

Forty eight male albino rats were divided randomly into six groups, each contain eight animals. The dose of (SeNPs–GSE) mixture was chosen after preliminary experimental trials.

Group 1: Control group: Animals treated orally with saline for 14 days.

Group 2 :(Diabetic group): Rats were made diabetic by a single i.p injection of STZ (45 mg/kg b.wt).

Group 3: Irradiated group (Irr): Rats were received the same dose of saline as group (1) and on day14 rats were submitted to a single dose of whole-body  $\gamma$ -radiation (4 Gy).

Group 4: (Diabetic + Irr): Rats were received the same dose of STZ as group (2) and on day14 rats were submitted to a single dose of whole-body  $\gamma$ - radiation (4 Gy).

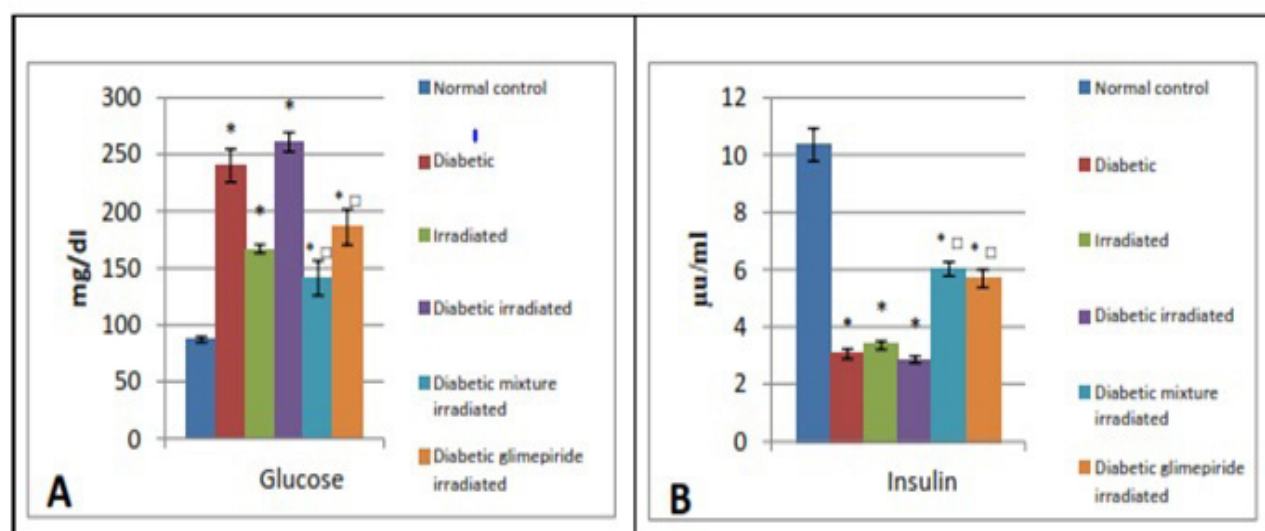
Group 5: Rats were received the same dose of STZ as group (2) followed by oral administration of SeNPs–GSE mixture (Se 6.7  $\mu$ g/kg + GSE 110.7 mg/kg) for 14 consecutive days then on day 14, rats were exposed to  $\gamma$ -radiation (4 Gy).

Group 6: Rats were made diabetic as in group 2 then injected orally with glimepiride (1 mg/kg)<sup>26</sup> as a reference drug for 14 consecutive days, on day 14 rats were irradiated (4 Gy).

The animals were carefully monitored every day.

### Biochemical Studies

At the end of the experimental period, animals were fasted overnight. Twenty-four hours after  $\gamma$ -irradiation, animals were anesthetized by (i.p) injection of urethane (1.5 g/kg b.wt).<sup>27</sup> Blood samples were withdrawn from the retro-orbital venous plexus using non heparinized



**Figure 1: Effect of SeNPs – GSE mixture or glimepiride on glucose [A] & insulin [B] levels in diabetic irradiated rats**

Rats were rendered hyperglycemic by a single i.p. injection of STZ (45 mg/kg). SeNPs–GSE mixture (Se 6.7  $\mu$ g/kg + GSE 110.7 mg/kg) or glimepiride (1 mg/kg) were administered orally for 14 consecutive days then exposed to whole body  $\gamma$ -radiation (4 Gy). Results are expressed as means  $\pm$  SEM (n=8). \*, <sup>†</sup>Significantly different from control group and diabetic irradiated group at P<0.05.

capillary tubes. Blood samples were centrifuged at 3000 rpm for 10 min using universal 16 R, Germany centrifuge. The clear sera were obtained for the determination of serum glucose, insulin and total antioxidant capacity levels. Liver was excised from the rats and homogenization was carried out using a homogenizer (Tri-R STIR-R model K41). The homogenates were centrifuged at 4000 rpm for 10 min at 4°C using centrifuge (Hettich, MIKRO 22, Germany) and was used to estimate MDA, SOD, CAT, GPx, Vit.C and Vit. E. Serum insulin level was estimated using immunoradiometric assay (IRMA) kit according to the method of Mullner.<sup>28</sup> Serum glucose level was done using kit according to the method of Trinder.<sup>29</sup> Serum TAC level was determined by the method of Koracevic<sup>30</sup> using TAC kit, MDA content as an indication of Lipid peroxidation in liver tissue was measured according to the method of Yoshioka and his colleagues,<sup>31</sup> GPx was assayed according to Gross,<sup>32-34</sup> CAT enzyme activity was evaluated by the method of (Bergmeyer,<sup>33-35</sup> SOD enzyme activity assayed by the

method of Minami,<sup>34</sup> Vit C content was estimated by the method of Roe and Kuether.<sup>35</sup> whereas, Vit. E content was evaluated by fluorometric method of Duve.<sup>36</sup>

### Statistical Analysis

Data are expressed as means ± SEM of eight animals. Statistical significance was taken as P<0.05 for all experiments, using one way analysis of variance (ANOVA) followed by Tukey-Kramer test multiple comparison- using Graph pad software prism (version 3).

## RESULTS

### Biochemical evaluations

#### Serum glucose and Insulin Levels

Whole body exposure of rats to a single dose of γ- radiation (4 Gy) or induction of diabetes by STZ (45 mg/kg i.p) showed a significant increase in serum glucose level by 91.4% and 175, 52% respectively as compared to nor-

**Table 1: Effect of SeNPs–GSE mixture or glimepiride on TAC and MDA levels in diabetic irradiated rats**

Group	Serum TAC (mM/L)	Liver MDA (nmol/g tissue)
Normal control	1.145 ± 0.01	80.17 ± 3.4
Diabetic	0.77 ± 0.03*	198.3 ± 3.6*
Irr	0.768 ± 0.01*	135.2 ± 3.1*
Diabetic+irr	0.768 ± 0.01*	292.2 ± 1.6*
Diabetic+ SeNPs-GSE+Irr	0.908 ± 0.007*	119.2 ± 3 <sup>□</sup>
Diabetic+ glimepiride+Irr	1.057 ± 0.02 <sup>□</sup>	119.5 ± 3.2 <sup>□</sup>

Rats were rendered hyperglycemic by single i.p. injection of (STZ; 45 mg/kg); SeNPs–GSE mixture (Se6.7 µg/kg +GSE 110.7 mg/kg) or glimepiride (1 mg/kg) were administered orally for 14 consecutive days then exposed to whole body gamma radiation (4 Gy). Results are expressed as means ± SEM (n=8).\*, <sup>□</sup>Significantly different from control group and diabetic irradiated group at P<0.05.

**Table 2: Effect of SeNPs– GSE mixture or glimepiride on some liver antioxidant enzymes activity in diabetic irradiated rats**

Parameter	CAT (U/g tissue)	SOD (µg/g tissue)	GPx (nmol/min/g tissue)
Normal control	57.26 ± 1.2	78.8 ± 1.4	2.84 ± 0.05
Diabetic	22.5 ± .53*	63.2 ± 0.9*	1.64 ± 0.12*
Irr	20.17 ± 1.2*	61.7 ± 0.5*	1.72 ± 0.04*
Diabetic+ irr	19.07 ± 0.9*	54.5 ± 1.3*	1.34 ± 0.09*
Diabetic+ SeNPs-GSE+Irr	29.8 ± 2.1 <sup>□</sup>	61 ± 0.4 <sup>□</sup>	2.056 ± 0.07 <sup>□</sup>
Diabetic + Glimepiride+Irr	31.68 ± 1.6 <sup>□</sup>	60.6 ± 0.9 <sup>□</sup>	2.61 ± 0.14 <sup>□</sup>

Rats were rendered hyperglycemic by single i.p. injection of (STZ; 45 mg/kg); SeNPs–GSE mixture (Se6.7 µg/kg +GSE 110.7 mg/kg) or glimepiride (1 mg/kg) were administered orally for 14 consecutive days then exposed to whole body gamma radiation (4 Gy). Results are expressed as means ± SEM (n=8).\*, <sup>□</sup>Significantly different from control group and diabetic irradiated group at P<0.05.



**Table 3: Effect of SeNPs –GSE mixture or glimepiride on Vitamin C&E content in diabetic irradiated Rats**

Parameter Group	Vitamin C (Liver) (µg/mg tissue)	Vitamin E (Liver) (µg/mg tissue)
Normal control	2.26 ± 0.06	0.414 ± 0.007
Diabetic	1.11 ± 0.04*	0.123 ± 0.004*
Irr	1.07 ± 0.04*	0.188 ± 0.01*
Diabetic+ Irr	1.009 ± 0.04*	0.139 ± 0.01*
Diabetic+ SeNPs-GSE + Irr	1.616 ± 0.07 <sup>□</sup>	0.275 ± 0.003 <sup>□</sup>
Diabetic+ glimepiride+ Irr	1.783 ± 0.04 <sup>□</sup>	0.235 ± 0.008 <sup>□</sup>

Rats were rendered hyperglycemic by single i.p. injection of (STZ; 45 mg/kg); SeNPs–GSE mixture (Se 6.7 µg/kg + GSE 110.7 mg/kg) or glimepiride (1 mg/kg) were administered orally for 4 consecutive days then exposed to whole body gamma radiation (4 Gy). Results are expressed as means ± SEM (n=8). \*, <sup>□</sup>Significantly different from control group and diabetic irradiated group at P<0.05.

mal group Figure 1(A). This elevation in glucose level was accompanied by a significant decrease in serum insulin level by 67.5% in irradiated group and 70.5% in diabetic group as compared to normal control group (Figure 1B). The combined STZ treatment and  $\gamma$ - radiation exposure intensified the damaging effect induced by either STZ or irradiation alone, as it recorded 199.2 % for serum glucose and 72.46% for serum insulin comparing to control values (Figure 1 A, B). Administration of SeNPs–GSE mixture or glimepiride after induction of diabetes exerts significant amelioration on the tested parameters (Figure 1 A, B).

### Serum TAC and Liver tissue MDA Levels

As shown in Table 1 serum TAC significantly decreased in diabetic, irradiated and diabetic- irradiated groups by 32.4%, 32.6% and 32.6% respectively as compared to normal control group. This decrease in TAC was accompanied by increase in liver MDA level by 147.3%, 68.6% and 264.47%. Administration of SeNPs-GSE mixture or glimepiride before  $\gamma$ -irradiation exerts significant enhancement on serum TAC with reduction on liver MDA level.

### Liver Enzyme antioxidants activities

The result of the present study, have demonstrated that rats treated with STZ or exposed to irradiation (4 Gy) or double treatment of STZ and Irradiation showed a significant decrease in liver enzyme activities of CAT (60.7%, 64.7%, 66.7%), SOD (19.8%, 21.7% and 30.8%) and GPx (42.2%, 39.4% and 52.8%) respectively as compared to normal values (Table 2). Diabetic rats treated with SeNPs–GSE mixture or glimepiride before  $\gamma$ -irradiation exert significant improvement on these enzymatic antioxidants as compared to diabetic irradiated group (Table 2).

### Liver Tissue content of VitC and VitE

Data in Table 3 shows that exposing animals to STZ alone or  $\gamma$ -radiation (4 Gy) as a single dose caused a significant

decrease in both liver tissue vit.C and Vit.E contents. The percentage of these decreases recorded by 50.8% and 70% for STZ and 52.6% and 56.1% for  $\gamma$ -radiation respectively as compared to the normal control group. Whole body exposure of rats to  $\gamma$ -radiation (4Gy) following STZ injection showed a significant decline in the levels of liver Vit C and Vit E by 55.35% and 66.09% respectively, as compared to control group. Treatment by SeNPs-GSE mixture or glimepiride after induction of diabetes restore liver Vit. C and Vit. E levels.

### Characterization of SeNPs

Application of DLS technique revealed that the SeNPs size were distributed in nano scale and the main particle diameter was 81.4 nm ± 8.7 (SD). TEM examination of the solution containing Se nanoparticles demonstrated particles within nano range and main particle diameter of 73.1 nm.

### DISCUSSION

STZ is a toxin that selectively destroys the beta cells of islets of Langerhans irreversibly, causing reduction of insulin secretion and increase in blood glucose level.<sup>37</sup> This is in accordance with our study, rats injected with STZ exerted significant increase in serum glucose concentration with a decrease in serum insulin level. STZ resulted as well, in a marked decrease in liver enzyme activities of SOD, CAT, GPx, and serum TAC levels. These decreases in the oxidative stress parameters were accompanied by an elevation in liver lipid peroxidation level. Previous investigators<sup>38</sup> accounted comparable data. They noted a decrease in the antioxidant enzyme activities. They stated that the augmentation in the oxidative stress could be attributed to the depletion of GSH during diabetes,<sup>39</sup> as well as, the reduced activity of GPx resulting from radical induced inactivation and

glycation of the enzyme in addition to excess ROS that is responsible for glucose and lipid auto oxidation.<sup>38</sup>

Vit C and E are endogenous non enzymatic antioxidants, they detoxify free radicals directly. Vit C particularly sequester the singlet oxygen radical, alleviate the hydroxyl radical while Vit E transfers its phenolic hydrogen to a peroxy free radical of peroxidized polyunsaturated fatty acids, thereby breaking the radical chain reaction and preventing the peroxidation of membrane lipids.<sup>40</sup> In diabetic rats there were significant decreases in the levels of liver tissue Vit C and Vit E contents. The decreased level of VitC may be due to either increased utilization as an antioxidant defense against increased ROS or to a decrease in glutathione level, since glutathione is required for the recycling of ascorbic acid.<sup>41</sup>

Ionizing radiation is known to induce oxidative stress through generation of ROS which is an imbalance in pro-oxidant, antioxidant status in the cell.<sup>42</sup> In the present study,  $\gamma$ -irradiation caused a noticeable increase in serum level of glucose concentration with a decrease in serum insulin level. These data agree with that reported in previous study of Kafafy,<sup>43</sup> who reported a significant increase in blood glucose concentration after exposure to whole body  $\gamma$ -irradiation and this might be related to endocrine abnormalities induced by irradiation that promote the secretion of biologically active peptide which has relation with carbohydrate metabolism by increasing gluconeogenesis in liver. SOD, CAT and GPx constitute the major enzymatic antioxidant defenses which convert active oxygen molecules into nontoxic compounds. Our results revealed that exposure to  $\gamma$ -radiation decreased the activities of these antioxidant enzymes in the liver tissues, indicating oxidative stress in the liver. The obtained results were in agreement with Kalpana,<sup>44</sup> who reported that exposure to 4 Gy  $\gamma$ -radiations decreased the activities of these antioxidant enzymes in the liver.

Lipid peroxidation refers to the oxidative stress degradation of lipid in which malondialdehyde (MDA) is one of its end products.<sup>45</sup> It mostly affects polyunsaturated fatty acids causing tissue damage.<sup>46</sup> Our results observed an elevation in MDA levels in liver of irradiated rats which may be due to the free radicals attack on cell membrane phospholipids and circulating lipids.<sup>47</sup> Furthermore, in the present study there were significant decreases in Vit. C and Vit. E levels in irradiated group which may be due to increased ROS by irradiation. Result of the current study showed that double treatment of STZ induced diabetes in rats and  $\gamma$ -irradiation resulted in marked alterations in all the tested parameters which were more pronounced than that observed in each model alone.

Our result further indicated that diabetic rats orally treated with SeNPs-GSE mixture before  $\gamma$ -irradiation significantly ameliorated the double treatment effect of STZ and gamma irradiation. Consequently, it increases the levels of liver enzymes activities of SOD, CAT, GPx as well as Vit. C, Vit. E contents. Such treatment caused augmentation in serum insulin, serum TAC levels accompanied by a decrease in the level of serum glucose and liver MDA.

Literature survey revealed that GSE exhibit insulinomimetic properties<sup>48</sup> and anti-hyperglycemic effects<sup>49</sup> in addition to its antioxidant activity.<sup>50</sup>

These effects may be due to antidiabetic activity of the natural plant phenolic compounds.<sup>51</sup> The antioxidant activity of GSE may be due to the inhibition of the oxidation of plasma lipids. Moreover, it is able to scavenge hydroxyl radicals, peroxy radicals, superoxide anion radicals.<sup>52</sup>

On the other hand, previous studies showed that selenium plays important roles in the enhancement of the antioxidant defense system,<sup>53</sup> protective function against ionizing radiation<sup>54</sup> and decrease blood glucose level.<sup>55</sup> Se acts by scavenging the free radicals and ROS.<sup>56</sup> This indicates that Se moderates oxidative stress-mediated complication. Moreover; Nanoparticles are designed to carry drugs and bring that medication all the way to the diseased cells in a body without harming the healthy cells. Nano-Se possesses equal efficacy of selenium with much lower toxicity.<sup>57</sup> Therefore, in the present study the tested combination of both SeNPs and GSE may reflect the sum of efficiency of either compound alone. Thus, acting with more than one mechanism of action including, reduction of ROS and scavenging of free radicals as well as an improvement of the tissue enzymatic and non-enzymatic antioxidant activities.

In the present study, glimepiride significantly elevated serum insulin and significantly decrease serum glucose levels in STZ-diabetic rats. This result is in agreement with other authors<sup>58</sup> Furthermore, it lowered serum TBARS level. Hence, restoring the endogenous antioxidant defense capacity; our results were in accordance with the work of Kakadiya and Shah.<sup>59</sup> The present data suggest that glimepiride may possess antioxidant activity against oxidative stress. This postulation runs in parallel with other work.<sup>60</sup> This antioxidant effect of glimepiride may be attributed to its activation of antioxidant enzymes such as SOD.<sup>61</sup> In spite of glimepiride is an important oral hypoglycemic agent of the sulfonylurea group it exerts severe side effects such as gastrointestinal disorders, hypersensitivity reactions<sup>62</sup> and severe hypoglycemia which may be life-threatening.<sup>63</sup> Therefore; there is a need to look for natural, newer and alternative therapy for DM to be more effective and less toxic.

In the present study there were no significant differences between glimepiride and SeNPs-GSE mixture in all the tested parameters. As a result, it may be fulfilled that SeNPs-GSE mixture possess antioxidant and anti-diabetic activity. The tested combination (SeNPs-GSE) mixture is more or less equally active as that of the standard tested ant-diabetic drug glimepiride.

## CONCLUSION

SeNPs-GSE mixture should be considered as an excellent subject for potential studies as natural anti-diabetic as well as radio protector comparable to synthetic hypoglycemic drug. The obtained data appreciate the usage of such combination for treating diabetic patients undergoing radiotherapy.

## ACKNOWLEDGEMENT

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## CONFLICT OF INTEREST

The authors declared that there is no conflict of interest.

## ABBREVIATION

Se	: Selenium
SeNPs	: Se nanoparticles
GSE	: grape seed extract
SeNPs-GSE	: selenium nanoparticles-grape seed extract
STZ	: streptozotocin
Irr	: Irradiated
ROS	: reactive oxygen speices
MDA	: malondaldehyde
TAC	: total antioxidant capacity
CAT	: catalase
GPx	: glutathione peroxidase
SOD	: superoxide dismutase
Vit.C	: vitamin C
Vit.E	: vitamin E
NCRRT	: National Center for Radiation Research and Technology.

## SUMMARY

- Gamma irradiation intensify the toxic effect of STZ induce diabetes.
- SeNPs-GSE mixture showed protection against gamma irradiation.
- SeNPs-GSE mixture possesses anti diabetic activity.
- The tested combination (SeNPs-GSE) mixture is more or less equally active as that of the reference anti-diabetic drug glimepiride.

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