Protective Effects of Soybean Isoflavone against Gamma-Irradiation Induced Damages in Mice

Li-Hua SONG1,3†, Hong-Li YAN2† and Dong-Lian CAI3* 

Free radicals/Soybean isoflavone/Antioxidant enzyme/Irradiation protection.

In the present work, we investigated the radioprotective efficacy of soybean isoflavone (SI) in mitigating gamma-irradiation-induced oxidative damage to the livers and blood systems of adult Swiss albino mice. We administered various doses of SI (50 mg/kg b.wt, 100 mg/kg b.wt, and 400 mg/kg b.wt) to the mice for seven consecutive days before exposing them to a single dose of 4.56 Gy 60Co-gamma whole-body irradiation. The irradiated mice continued to receive SI for two or seven days before sacrifice. The SI treatments significantly elevated liver catalase (CAT) and glutathione peroxidase (GPx) enzyme activities and mRNA abundances, and decreased the malonaldehyde (MDA) levels. The SI treatments also accelerated the recovery of circulating white blood cells (WBCs) and reticulocytes (RETs) seven days following irradiation. These effects were dose-dependent, and the strongest effect on most biomarkers (but not on histopathology) was seen with an intermediate dose. Our results provide useful information for future investigations, and strongly implicate a clinical application for SI.

INTRODUCTION

Radiotherapy has become a routine treatment for various types of malignancies. Severe adverse side effects commonly arise from radiotherapy, however, including nausea and vomiting, loss of appetite, decreased leukocyte count and weakened immunofunction, which often prevent patients from completing the treatment course.1,2 Protecting normal host tissues from the lethal actions of irradiation is of great clinical importance in radiation medicine. Various compounds have been investigated in experimental animals or in human volunteers as potential radioprotective agents. These include sulfhydryl compounds, such as cysteine, WR2721, antioxidants (vitamins A, C and E) and biological modifiers (γ-interferon).3 However, the inherent toxicity of these agents at radioprotective concentrations prevents their clinical use, and more extensive pursuits for safe and efficacious radioprotectors are underway. Recently, there has been a renewed interest in the search for plant-derived drugs as potential radioprotectors, for example, Brahma Rasayana, which contains Emblica, is reported to have an excellent radio protective activity and non-toxicity in animal models as well as in human volunteers undergoing radiotherapy.4,5

During radiotherapy, ionizing irradiation particles interact with biological systems to induce excessive oxygen free radicals (OFRs) or reactive oxygen species (ROS), which attack various cellular components including DNA, proteins and membrane lipids, thereby leading to significant cellular damage. ROS also negatively impact the antioxidant defense mechanisms, reduce the intracellular concentration of glutathione (GSH), and decrease the activities of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx).6 Thus, scavenging free radicals and inhibiting lipid peroxidation are likely key target activities for developing successful radioprotection strategies.7 Previous in vitro and in vivo studies have demonstrated that soybean isoflavone (SI) is potent antioxidant and free radical scavenger.8-10 Moreover, dietary supplements of purified unconjugated isoflavones administered to humans in single doses exceeding normal dietary intake manyfold resulted in minimal clinical toxicity. Genistein and daidzein were rapidly cleared from plasma and excreted in urine.11,12 Wei et al.13-16 discovered that genistein, one of the active components of SI, could itself protect the skin from oxidative damage induced by ultraviolet (UV) rays. More importantly, ZHOU et al. found that oral administration of genistein stimulates...
hematopoiesis and increases survival in $\gamma^{60}$Co irradiated mice.\textsuperscript{17} The present study investigated SI as a radioprotective agent against $^{60}$Co-gamma radiation on the hepatic antioxidant system in mice, and the mechanisms by which it exerts its protective effects.

**MATERIALS AND METHODS**

**Animals**
Female Swiss albino mice were purchased from the Center of Laboratory Animal of the Second Military Medical University (Shanghai, China). The mice were 10 weeks post-gestational age, and weighed between 23 and 29 g at the time of their irradiation treatment administrations. They were given water ad libitum, were fed with standard mice pellets and were adapted for one week prior to drug administration in the following atmosphere: 25 ± 1°C, 50 ± 5% relative humidity, ventilation at 15 air renewal cycles/h and 24-h light-dark cycle. We obtained permission for performing the research protocols and all animal experiments, and followed the guidelines of the ethics committee of the Second Military Medical University (SMMU).

**Irradiation**
The animals were treated with a single dose of $^{60}$Co-gamma irradiation of 4.56 Gy at an exposure rate of 0.57 Gy/min. The source of irradiation was from $^{60}$Co-gamma rays in the Radiotherapy Department of Changhai Hospital, Shanghai. Each mouse was restrained in a specially designed, well-ventilated and perspex-covered cage, and was exposed without anesthesia to whole-body irradiation in a field size of $25 \times 25$ cm$^2$ and at a distance of 75 cm from the source.

**Intervention method**
A 41.56% SI extract solution (containing 16.42% isoflavone daidzin, 1.03% daidzein, 22.63% genistin and 1.48% genistein) was purchased from LuFeng Bio-Products Co., Ltd. (Dalian, China). The SI suspensions used in the intervention experiments (50 mg/kg bw, 100 mg/kg bw, 400 mg/kg bw) were prepared with corn oil, and mixed vigorously prior to use.

The body weight (bw) of each animal was measured prior to experimentation. In all, we randomized 80 mice equally into five experimental groups: 1) the non-irradiated controls, treated with corn oil (N group), 2) the irradiated controls, treated with corn oil (IR group), 3) the irradiated animals, treated with SI 50 mg/kg bw p.o. (SI\textsubscript{l} group), 4) the irradiated animals, treated with SI 100 mg/kg bw p.o. (SI\textsubscript{M} group), and 5) the irradiated animals treated with SI 400 mg/kg bw p.o. (SI\textsubscript{H} group).

Animals in the SI\textsubscript{l}, SI\textsubscript{M} and SI\textsubscript{H} groups were treated with their respective SI doses for seven consecutive days before being exposed to the whole-body irradiations, and after irradiation, the SI treatments were continued for another two or seven days. Then two groups of eight mice from each experimental cohort were sacrificed two or seven days following the irradiation treatments. The livers were dissected, washed with ice-cold saline, transferred immediately into liquid nitrogen and stored at −80°C until needed.

**Determination of WBC, RET and RBC**
The body weights of all animals were measured, and the blood was collected from the caudal veins into heparinized tubes before sacrifice. The following parameters were recorded: (a) total white blood cell (WBC) count; (b) reticulocyte (RET) count; and (c) red blood cell (RBC) count. RBCs and WBCs were counted microscopically with the blood cell counting chamber. In specifically colored smears, the RET number was estimated per 10$^5$ RBCs, and was then calculated for different blood cell counts per liter.

**Evaluation of lipid peroxidation and antioxidant enzyme activity**
On the day of analysis, a 10% liver tissue homogenate was prepared in 0.9% ice-cold saline, and the crude homogenized tissues were centrifuged at 6000 g and 4°C for 20 min. The supernatant was collected to analyze the antioxidant enzyme activities, and the malonaldehyde (MDA) levels.

The CAT activity was estimated following methods

<p>| Table 1. Effects of SI on body weight, WBC, RET and RBC of mice after irradiation (Mean ± SD n = 6) |
|---------------------------------------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|</p>
<table>
<thead>
<tr>
<th>group</th>
<th>Body weight</th>
<th>WBC($\times 10^5$/L)</th>
<th>RET($\times 10^5$/L)</th>
<th>RBC($\times 10^{12}$/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>25.81 ± 2.15</td>
<td>28.84 ± 2.79</td>
<td>3.96 ± 0.55</td>
<td>4.10 ± 1.13</td>
</tr>
<tr>
<td>IR</td>
<td>26.25 ± 1.92</td>
<td>27.82 ± 3.04$^*$</td>
<td>0.75 ± 0.24$^*$</td>
<td>0.80 ± 0.45$^*$</td>
</tr>
<tr>
<td>SI\textsubscript{l}</td>
<td>26.29 ± 1.80</td>
<td>27.36 ± 2.18$^*$</td>
<td>0.78 ± 0.39$^*$</td>
<td>0.95 ± 0.21$^*$</td>
</tr>
<tr>
<td>SI\textsubscript{M}</td>
<td>26.61 ± 2.22</td>
<td>29.02 ± 2.23</td>
<td>0.68 ± 0.26$^*$</td>
<td>2.22 ± 1.06$^*$</td>
</tr>
<tr>
<td>SI\textsubscript{H}</td>
<td>26.37 ± 1.95</td>
<td>29.59 ± 2.36</td>
<td>0.90 ± 0.32$^*$</td>
<td>1.30 ± 0.50$^*$</td>
</tr>
</tbody>
</table>

* $P < 0.05$ compared with N group; $^\Delta P < 0.05$ compared with SI\textsubscript{l} and IR group; $^\Delta^\Delta P < 0.01$ compared with IR group; $^\Delta^\Delta^\Delta P < 0.01$ compared with day 2 after irradiation.
described previously, by measuring the rate of hydrogen peroxide (H$_2$O$_2$) decomposition at 240nm. The GPx activity was determined at room temperature following methods described previously, by measuring the rate of NADPH oxidation at 340 nm. The MDA levels were measured by the thiobarbituric acid (TBA) method described by Devasa-gayam et al. The results are expressed as the relative enzyme activity and MDA level per mg of protein, respectively.

**Real-time quantitative RT-PCR analysis of CAT and GPx mRNA expression**

Real-time quantitative RT-PCR was used to assess the hepatic expression levels of CAT and GPx mRNA in irradiated mouse livers. In brief, we extracted the total RNA from the liver samples using Trizol Reagent (Life Technologies Inc., Rockville, MD), according to the manufacturer’s protocol. Two micrograms of total RNA was subjected to an RT reaction using Superscript II Reverse Transcriptase in 25 µl of reaction mixture (Invitrogen). Real-time quantitative PCR was performed in a Light Cycler System using the Fast Start DNA master SYBR green I kit as recommended by the manufacturer (Roche, Mannheim, Germany). In a total volume of

![Fig. 1](image1.png)

**Fig. 1.** Effects of SI on CAT activity (A) and GPx activity (B) in hepatic tissue at day 2 and 7 after irradiation. SI treatment is described in the “Materials and Methods” section. At day seven post-irradiation, the CAT activities of the three SI groups were significantly higher than those exhibited by the IR group; the GPx activities of the SI group were significantly elevated above those of the IR mice. Data represents the mean ± SD of three independent experiments. ($^*P < 0.05$ vs. IR group, $^{a}P < 0.05$ vs. the 2nd day).

![Fig. 2](image2.png)

**Fig. 2.** CAT mRNA expression levels of the N, SI and IR groups at days 2 and 7 post-irradiation (measured by real-time quantitative RT-PCR). A: the corresponding dissociation curves of the real-time PCR products. Dissociation curve analysis shows that the melting temperature for the CAT genes was more than 75°C, indicating no primer-dimer formation. B: The mRNA expression of CAT relative to GAPDH in each group. Data were expressed as mean ± SD of three separate analyses performed on six independent samples ($^*P < 0.05$, vs. IR group). 1. IR2 Irradiation alone group; 2. SI group; 3. SI group at day 2; 4. IR7 Irradiation alone group; 5. SI group at day 7 after irradiation.
20 µl, each reaction contained 2 µl SYBR green I reaction mix (consisting of Taq DNA polymerase reaction buffer, dNTP mix, SYBR green I, MgCl₂ and Taq DNA polymerase), 0.4 µM of each primer, 3–4 mM MgCl₂ and 2 µl cDNA, nuclease-free water as a negative control. The following primer sets were used: GAPDH: forward 5'-AACGACCCTTCTATTGAC-3', reverse 5'-TCCACGACATACTCAGCAC-3', product size is 191 bp; CAT: forward 5'-AACGCTGGATGGATTCTCCC-3'; reverse 5'-GCCCTAACCTTCTATTTCCTTCAG-3'; product size is 135 bp; GPx: forward 5'-TTGGCTTTGATTACTGGC-3'; reverse 5'-CATTTAGGTGAAAGGCATCG-3'; product size is 150 bp; Quantification of the targets was performed using a relative quantification method with external standards. The target concentration is expressed relative to the concentration of a reference housekeeping gene, GAPDH. After each run, melting curve analysis was performed to verify the specificity of the PCR reaction. Each sample was run and analyzed in triplicate.

**Histological evaluation**

Seven days post-irradiation, the 0.5 cm³ pieces taken from the left liver lobes were fixed in 10% neutralized formalin, paraffin-embedded and sectioned to a mean thickness of 3 micrometers. The sections were stained with hematoxylin-eosin (HE), and observed by two pathologists independently. The tissues were examined in a random order and without knowledge of animal or group.

**Statistical Analyses**

We analyzed the statistical differences among each experimental group on the 2nd and 7th days following irradiation, and between the N group, IR group and the three SI groups, using Student’s t tests, and analysis of variance (ANOVA), respectively. The results were expressed as mean ± standard deviation (mean ± SD), and all data were analyzed with the SPSS statistical software package (SPSS for Windows, version 10.0). The test differences were considered statistically significant at a P value less than 0.05 or 0.01 (P < 0.05, or P < 0.01).

**Fig. 3.** GPx mRNA expression levels of N, SI₂ and IR groups at day 2 and 7 after irradiation (measured by real-time quantitative RT-PCR). A: the corresponding dissociation curves of the real-time PCR products. Dissociation curve analysis shows that the melting temperature for the GPx genes was more than 75°C, indicating no primer-dimer formation. B: The mRNA expression of GPx relative to GAPDH in each group. Data were expressed as mean ± SD of three separate analyses performed on six independent samples (*P < 0.05, vs. IR group). 1. IR2 Irradiation alone group; 2. SI₂ intermediate SI group; 3. N2 normal group at day 2 after irradiation; 4. IR7 Irradiation alone group; 5. SI₇ intermediate SI group; 6. N7 normal group at day 7 after irradiation.

**Fig. 4.** Effects of SI on MDA levels in hepatic tissues at days 2 and 7 after irradiation. The SI treatment procedure is described in the “Materials and Methods” section. The mean SI₂ group MDA level was significantly reduced below that of the IR group at day 7 after irradiation. Superscript letters indicate statistically significant difference in the three SI groups, between days 2 and 7 after irradiation. These data represent the mean ± SD of three independent experiments. (*P < 0.05 vs. IR group, a P < 0.05, bP < 0.01 vs. the 2nd day).
Fig. 5. Light microscopic photomicrography of the hepatic histological structure at day 7 after irradiation. A: SI$_L$ group. The capillaries, central and collecting veins are slightly engorged, the liver cells are swollen and the liver trabeculae are irregular. B: SI$_M$ group. The capillaries, central and collecting veins are engorged, the liver cells are swollen. C: SI$_H$ group. The capillaries, central and collecting veins are appreciably engorged, and the liver cells appear normal. D: irradiated control group. The capillaries, central and collecting veins are engorged, and accompanied by degenerative and necrotic changes in the parenchyma. Liver trabeculae are irregular, the normal liver structure is distorted and the liver cells appear to be acutely swollen and alienated. In addition, there are large liver cells with two or more nuclei. The arrow indicates the vacuole cells, or the cells with two nuclei. E: non-irradiated control group (H.E. × 50).
RESULTS

The irradiation-exposed mice were alive throughout the experimental period. Two weeks after treatment administration, the body weights of the SI_M, SI_H and N mice increased non-significantly by 9.05%, 12.21% and 11.74% ($P > 0.05$), respectively, from their initial weights. The incremental increases in the body weights of the SI_L and IR groups were significantly smaller than those experienced by the SI_M, SI_H and N groups ($P < 0.05$; Table 1).

Effects of SI on recovery of WBC, RET and RBC after irradiation

Compared with those of the normal controls, the total WBC and RET counts decreased significantly among the three SI groups and the IR group ($P < 0.05$) two days after irradiation. Seven days after irradiation, the WBC and RET counts of the three SI groups were elevated to varying extents. In particular, the SI treatments elevated the RET counts significantly ($P < 0.01$) as compared to those measured the 2nd day post-irradiation. However, the elevation of the RET counts in the IR group was much slower than that of three SI groups. In addition, the SI_M WBC counts were significantly higher than those of the SI_L and IR groups ($P < 0.05$), but the RBC alteration in the SI groups and the IR group were not significantly distinct ($P > 0.05$).

Effects of SI on hepatic CAT and GPx activities after irradiation

The GPx and CAT activities represent two major enzymatic events in the antioxidant defense mechanism. Continuous administration of SI_M and SI_H significantly increased ($P < 0.05$) CAT activities as compared to those of the IR group two days post-irradiation. On the seventh day following the irradiation treatments, the CAT activities of all three SI intervention groups were significantly higher than those measured for the IR group ($P < 0.05$) (Fig. 1A). Moreover, the activity change of GPx was slightly different from that of CAT in three SI group and IR group. As shown in Fig. 1B, the SI_M groups GPx activity was significantly higher than that of the IR mice seven days following the irradiation treatments ($P < 0.05$).

Effect of SI on CAT and GPx mRNA levels

The above data indicated that an intermediate dose of SI had a significant effect on the CAT and GPx enzyme activities. Thus, we compared the CAT and GPx mRNA levels to observe any gene expression pattern differences among the N, IR and SI_M groups. We used SYBR Green real-time PCR to measure the mRNA levels. Dissociation curve analysis showed that melting temperature for the genes was more than 75°C, indicating no primer-dimer formation (Fig. 2A and 3A). The specificity of the amplification was also examined by running the product in 3% agarose gel, which revealed a single band consistent with the predicted size of GPx and CAT. (data not shown) As shown in Figs 2B, the CAT mRNA levels were significantly increased on the 2nd and the 7th days following irradiation ($P < 0.05$, vs. IR group). Although the GPx mRNA values also increased two days following irradiation treatments, a significant enhancement was only observed on the 7th post-irradiation day ($P < 0.05$, vs. IR group) (Fig. 3B).

Effect of SI on the Prevention of Lipid Peroxidation

MDA is an aldehyde end product of polyunsaturated fatty

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose</th>
<th>Lesion degree</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>0.5 ml (corn oil)</td>
<td>– – – – – – – –</td>
</tr>
<tr>
<td>IR</td>
<td>0.5 ml (corn oil)</td>
<td>++ ++ ~ +++ +++ +++ +++ +++</td>
</tr>
<tr>
<td>SI_L</td>
<td>50 mg/kg (SI)</td>
<td>± ± ± ± + ~ ++ ++ ++ +++</td>
</tr>
<tr>
<td>SI_M</td>
<td>100 mg/kg (SI)</td>
<td>+ + ~ + + ~ ++ ++ ++ ~ +++ +++</td>
</tr>
<tr>
<td>SI_H</td>
<td>400 mg/kg (SI)</td>
<td>– ~ ± + + ~ ++ + ~ ++ +++</td>
</tr>
</tbody>
</table>

++ The capillaries, central and collecting veins are congestive, accompanied with degenerative and necrotic changes in the parenchyma. The liver trabeculae become irregular; the normal structure of the organ becomes indistinct, and the liver cells appear to be acutely swollen and separate from each other. In addition, multinucleated giant cells appear.

++ The capillaries, central and collecting veins are slightly congestive, and liver cells appear to be swollen.

+ The capillaries, central and collecting veins are slightly congestive; liver cells appear to be swollen and liver trabeculae become irregular.

± The capillaries, central and collecting veins are appreciably congestive; while the swelling of liver cells is unconspicuous.

– No lesion is observed

~ In an intermediate degree or in between two different lesion degree.
acids and related esters that is used to assess lipid peroxidation. On the seventh day post-irradiation, the hepatic MDA levels in the three SI intervention groups subsided significantly \((P < 0.05)\) compared with the 2nd day post-irradiation; the MDA level in the SI_{M} group was significantly decreased compared with that in the IR group \((P < 0.05)\) (Fig. 4).

**Histopathologic Observations**

The pathological examinations of the IR group mouse livers revealed obvious hyperaemia of the capillaries, central and collecting veins. The circulatory disturbances were accompanied by degenerative and necrotic changes in the parenchyma (Fig. 5D). In addition, the liver trabeculae were irregular, the normal organ structure was distorted, swollen liver cells were visible and alienated from each other and multinucleated giant cells appeared. As shown in Table 2, the degree and number of lesions that appeared among the three SI-treated groups were lower than those observed in the IR group in general. Although some of these pathologic changes did occur in the presence of SI, the degree of pathological changes observed among the SI_{M} mice was more severe than that observed in the SI_{H} and SI_{L} groups (Fig. 5 A, B, C).

**DISCUSSION**

In present study, we observed hepatic alterations of the CAT and GPx enzymatic activities and mRNA levels in irradiation-exposed mice, following treatments with \(^{60}\)Co-gamma rays and varying doses of SI. The results showed that SI significantly increased the CAT and GPx activities at different stages after irradiation exposure. Because the intermediate dose (SI_{M}; 100 mg/kg body weight) of SI elevated the antioxidant enzyme activities and reduced the lipid peroxide (LPO) content of the liver tissue sufficiently, we chose the SI_{M} mice to represent the influence of SI on antioxidant enzyme mRNA abundance. Our results showed that SI also increased the gene expression levels of the CAT and GPx antioxidant enzymes after the mice were subjected to irradiation.

Besides the alteration of antioxidant enzymes in irradiation, excessive ROS produced during irradiation exposure can cause tissue injury through lipid peroxidation. Malondialdehyde is an end product derived from the breakdown of polyunsaturated fatty acids and related esters. The measurement of this aldehyde provides a convenient index of lipid peroxidation. Our results showed that the MDA levels significantly decreased in the SI intervention groups at the later stages following irradiation, this may ascribe to the induction of antioxidant enzyme activities by SI, which consequently mitigate the cell membrane lipid peroxidation damage. Above data suggested that SI possesses potential antioxidative activity in mitigating oxidative stress resulting from irradiation in vivo.

As the oxidative stress, in particular lipid peroxidation, induces collagen synthesis and liver fibrosis,\(^{21}\) antioxidants have been proposed as therapeutic agents, as well as drug coadjuvants, to counteract liver damage.\(^{22}\) Theismania et al. determined that ellagic acid, an antioxidant, plays a role in inhibiting the fibrotic process induced during liver cell damage.\(^{23}\) Our results also provide encouraging clues that SI can serve as a potential radioprotective agent on the cellular level. Moreover, we discovered that SI might ameliorate liver morphology as well, because the SI treatments mitigated the degree of liver damage resulting from irradiation treatments, compared to that acquired by the non-SI-treated IR mice. Interestingly, our histopathological findings showed that the low and high SI doses exhibited higher protective effects than the intermediate SI dose, even though the strongest protective effects on most of the molecular biomarkers occurred with SI_{M}. One reasonable explanation is that the biological activities of SI are highly correlated with its concentration. Messina et al.\(^{24}\) found that genistein could inhibit the growth of both hormone-dependent and hormone-independent breast cancer cells in vitro, but at low concentrations (< 10 \(\mu\)mol/L) proliferation of at least one breast cancer line is stimulated. Yamagihara\(^{25}\) reported that genistein were cytostatic for the gastrointestinal originated cancer cell lines at low concentration (< 10 mg/ml), but were cytotoxic at high concentration (> 40 mg/ml). In addition, Cai et al.\(^{26}\) reported that feeding a 250 ppm genistein diet to SENCAR mice significantly increased the activities of CAT in the small intestine, liver, kidneys, the activities of SOD and GPx in the skin and the activities of GSH in the skin and small intestine. However, feeding 50 ppm genistein to SENCAR mice resulted in elevation of CAT activity in the small intestine and increased the GST (glutathione-S-transferase) activities in the skin, small intestine, liver, kidneys and lungs. This biphasic effect is attributed to genistein exerting estrogen-like effects at lower and what may be considered physiologic concentrations but at higher concentrations exerting other non-estrogen receptor-mediated effects, for example, inhibition of the activity of one or more cellular molecules that control cell signaling, growth and death. Present studies also showed that SI is a substance with numerous biological activities, such as tyrosine kinase inhibitor, estrogen activity and antioxidant activity. Thus, SI might exert its effects on numerous targets, in addition to adjusting the oxidative stress state of cells at different concentrations. The pathological results we observed herein were likely the comprehensive effects of the multifarious biological activities of SI.

Furthermore, chemotherapy- and/or radiotherapy-induced damage to the blood circulatory system of cancer patients persist as a difficult clinical problem. Rapidly dividing cells of the blood system, especially leukocytes and erythrocytes, are highly prone to irradiation-induced damage, because ROS impacts the blood system and decreases its cellular components, including reticulocytes, considerably. Reticulo-
cyte decline following irradiation reflects the early damage of the bone marrow hematopoietic function, to some extent. We studied the protective effect of different SI doses on the blood system against 60Co-gamma irradiation at two time points. The results showed that SI stimulated the elevation of WBC and RET levels after irradiation, suggesting that SI can attenuate irradiation-induced damage to the blood system. In summary, we present evidence supporting the radioprotective effects of soybean isoflavone in irradiated mouse livers and blood systems. Protection was observed at the molecular and cellular levels, as evidenced by enhanced antioxidant enzyme activities and mRNA levels and decreased liver lipid peroxide levels. SI also protected against liver lesion damage at the tissue level. Although the exact mechanism of the SI dose-dependency remains unclear, our results suggest a clinical application for SI in radiotherapy. Further investigation is warranted to determine the molecular SI targets of therapeutic action, unravel its potent antioxidant activity and its protective mechanism in the blood system.

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