Ionizing radiation (IR) is widely used in the diagnosis and treatment of various cancers. However, IR can cause damage to human health by producing reactive oxygen species. *Lactococcus lactis* is a type of microorganism that is beneficial to human health and has a strong antioxidant capacity. In this study, the protective effect of normal and IR-induced *L. lactis* IL1403 cell-free extracts (CFE and IR-CFE, respectively) against oxidative damage in vitro and the radioprotective effect of IR-CFE in vivo was evaluated using $^{60}$Coγ-induced oxidative damage model in mice. Results showed that IR-CFE exhibited a stronger oxidative damage–protective effect than CFE for *L. lactis* IL1403 under H$_2$O$_2$ in vitro. Moreover, IR-CFE also showed strong radioprotective effect on hepatocyte cells (AML-12) under radiation condition, and the effect was better than that of CFE. Animal experiment indicated that IR-CFE could reduce the IR-induced damage to the hematopoietic system by increasing the number of white blood cells and red blood cells in peripheral blood of irradiated mice. It was also observed that IR-CFE could markedly alleviate the $^{60}$Coγ-induced oxidative stress via increasing the activities of superoxide dismutase and glutathione peroxidase, enhancing the levels of glutathione, and decreasing the contents of malondialdehyde in serum, liver, and spleen. In addition, IR-CFE also could reduce the activities of alanine transaminase and aspartate aminotransferase in serum, thereby reducing radiation damage to the liver. These results suggested that IR-CFE could be considered as potential candidates for natural radioprotective agents. This study provides a theoretical basis for improving the application of lactic acid bacteria.

**Key words:** *Lactococcus lactis* cell-free extract, protective effect, ionizing radiation, oxidant stress, hematopoietic system

**INTRODUCTION**

Ionizing radiation (IR) is widely used in the diagnosis and treatment of various cancers. In addition, people are often exposed to IR from the natural background radiation, electronic equipment, and industrial applications. Studies have shown that IR can directly attack biomacromolecules such as DNA, RNA, and protein in the body and can also produce reactive oxygen species (ROS), thus causing an oxidative stress response (Sinha et al., 2011; Kuo et al., 2019). Overproductive ROS can break the oxidation-reduction (REDOX) levels, leading to dysfunction and pathological changes of tissues and organs in the body (Yamamori et al., 2012; Xia et al., 2014). Radioprotectors have been reported to scavenge IR-induced ROS, and they are effective to alleviate IR-induced damage (Feng et al., 2017). However, chemical radioprotectors are usually synthetic compounds, which have the disadvantages of side effects, short effect time, and high price (Andreassen et al., 2003). Therefore, natural radioprotectors have gained attention in the recent years because they are nontoxic, inexpensive, and have fewer side effects.

Lactic acid bacteria (LAB) have been reported to have a variety of biological activities, such as enhancing immunity, protecting liver function, delaying aging, and inhibiting cancer. These activities are closely related to their antioxidant properties, including reducing power, lipid peroxide inhibition, and some free radical–scavenging capacities (Das and Goyal, 2015; Del Carmen et al., 2017; Zhao et al., 2017; Mu et al., 2018). Among LAB, *Lactococcus lactis* has been used as a model strain and is widely used in the fermentation process of dairy foods. One study shows that probiotic *L. lactis* NK34 can inhibit the proliferation of cancer cells and the production of proinflammatory cytokines (Han et al., 2015). In recent years, the research on LAB has...
increasingly focused on cell-free extract (CFE), with advantages of convenience for storage, transportation, and industrial application. Meanwhile, more and more studies have proven that the CFE of LAB have higher antioxidant activity than fermentation supernatant and intact cells (Tang et al., 2018). Therefore, it can be inferred that CFE plays a significant role in the antioxidant effect. Additionally, during the process of growth, LAB may be exposed to a lot of environmental stresses, such as low and high temperatures, acidity, NaCl, high hydrostatic pressure, and IR. It is well known that IR is a common sterilization method in industrial production. Lactic acid bacteria can activate a series of mechanisms to respond to the new conditions and make them survive when they are in a diverse environment (Bucka-Kolendo and Sokolowska, 2017). It has been proven in our laboratory that the CFE from gradient-freezing L. lactis IL1403 can improve the cell numbers of L. lactis IL1403 after freeze-drying, and the stress-related proteins expression of L. lactis IL1403 change after gradient-freezing (Lin et al., 2017). Based on this, it can be inferred that L. lactis IL1403 CFE induced by IR may have a better antioxidant activity and radioprotective effect. At present, natural compounds that can prevent and alleviate IR-induced damage have become popular to research. However, the radioprotective effect of L. lactis has not been studied yet. Here, we researched the antioxidant activity of L. lactis IL1403 CFE and IR-induced CFE (IR-CFE) in vitro. Then, the radioprotective effect of IR-CFE in vivo was evaluated further by the animal experiment of 60Coγ radiation–induced damage.

MATERIALS AND METHODS

Preparation of CFE and IR-CFE

The CFE and IR-CFE were prepared according to the method reported previously with some modifications (Tang et al., 2018). Lactococcus lactis IL1403 was grown at 37°C until mid-exponential phase (16 h). The bacterial cells were collected by centrifugation at 1,800 × g for 10 min at 4°C, washed twice, and resuspended with PBS. Then, the solution containing bacterial cells was crushed with an ultrasonic cell crusher (Ningbo Xinzhi Biotechnology Co., Ltd.) at 300 W for 15 min. Cell debris was removed by centrifugation at 11,000 × g for 10 min at 4°C. The supernatant was filtered with a 0.22-μm filter and freeze-dried to obtain the CFE. In addition, after culturing for 16 h, the strain was treated with radiation at a dose of 500 Gy using a 60Coγ Irradiator at the Institute of Isotope Research, Henan Academy of Sciences (Zhengzhou, China). Then, the bacterial cells were collected, washed, crushed, centrifuged, and freeze-dried to obtain IR-CFE. The CFE and IR-CFE powder were stored at −20°C for subsequent experiments.

In Vitro Experiment

Protective Effect on L. lactis IL1403 Cells from Hydrogen Peroxide (H2O2). Protective effect of CFE and IR-CFE on L. lactis IL1403 cells from H2O2 injury was measured following the previous method with some modifications (Zhang et al., 2020). The survival rate of L. lactis IL1403 was examined to evaluate the protective effect of CFE and IR-CFE. After the L. lactis IL1403 cells were cultured in medium to the mid-exponential phase, 3 mL of fermentation broth was treated with 1 mL of H2O2 (5 mmol/L) and 1 mL of CFE or IR-CFE (2 mg/mL, dissolved in 75 mmol/L PBS) for 1 h at 37°C, and 2 mL of PBS was added as a control group and 1 mL of H2O2 was added as H2O2 group. The viable cell count was determined through a method comprising decimal dilutions followed by plating, where 200 μL of serially diluted samples were prepared.
were spotted in triplicate onto M17 agar plates and incubated at 37°C for 48 h. Plates containing 30 to 300 cfu were counted, and the colony-forming units per milliliter were calculated from the average of 3 times.

**Cell Experiment.** The AML-12 cells were cultured in the Dulbecco’s Modified Eagle Medium/Nutrient Mixture F-12 culture medium with 10% FBS, 1% penicillin-streptomycin, 1% insulin, transferrin, and sodium selenite liquid medium supplement, and 40 ng/mL dexamethasone (Kang et al., 2019). The cells were incubated in a 5% CO₂ incubator (Thermo Fisher Scientific) at 37°C.

The effect of CFE, IR-CFE, and IR on cell viability was measured by MTT assay according to the method reported previously with slight modifications (Rocha et al., 2020). The AML-12 cells (4 × 10³ cells/well) were placed into 96-well plates. After being cultured for 12 h, cells were treated with different concentrations of CFE and IR-CFE (100, 200, 400, 600, and 800 μg/mL) continuously for 12 h. The plates were incubated again at 37°C for 10 min. The substance was removed again and the formazan crystals were diluted with 100 μL of dimethyl sulfoxide per well. Finally, the absorbance at 492 nm was determined using a microplate reader (Molecular Devices). The absorption values represented the cell viability. The EGCG (10 μg/mL) was used as a positive control in vitro (Kang et al., 2019).

**In Vivo Experiment**

**Animals and Treatments.** Male Kunming mice (6-8 wk old, 18–20 g) of specific pathogen-free were housed at the animal facility of the Laboratory Animal Center of Zhengzhou University according to institutional guidelines. Animal use protocols were reviewed and approved by the Zhengzhou University Institutional Laboratory Animal Care and Use Committee (No. SYXK-2019-0002). Animal room was kept in standard housing conditions (temperature, 22 ± 2°C; humidity, 50 ± 10%) with a 12-h light, 12-h dark cycle. After an adaptation period of 1 wk, 70 mice were randomly divided into 7 groups with 10 mice per group. For the normal control group (NC), mice received saline by gavage once daily for 30 d; for the IR group, mice were exposed to a dose of 6 Gy radiation at 2 Gy/min using a 60Coγ irradiator; for the positive control group, mice were administered with leucogen (12 mg/kg of BW) for 30 d and then exposed to the same IR (Li et al., 2013); one group of mice was administered with CFE (200 mg/kg of BW; CFE-H) for 30 d and then exposed to the same IR; the remaining mice were administered with IR-CFE at 50 (IR-CFE-L), 100 (IR-CFE-M), and 200 (IR-CFE-H) mg/kg of BW for 30 d and then exposed to the same IR. On the basis of in vitro experiments, the radioprotective effect of IR-CFE was focused in the animal experiment. Therefore, 3 concentration gradients of IR-CFE were designed and further studied. Meanwhile, to reduce the experimental work and the use of animals, only CFE-H group was used as a comparison in the animal experiment.

The BW of each mouse was recorded before gavage every day. After radiation, mice were deprived of food and water for 24 h. The blood samples were collected from the eyeball and maintained at 4°C for 3 h, followed by centrifugation at 1,800 × g for 10 min at 4°C to obtain the serum (Zhao et al., 2017). Meanwhile, the liver, spleen, kidney, and heart were taken, washed, and stored at −80°C for subsequent experiments.

**Peripheral Blood Cell Counts.** Peripheral blood cell counts were determined using the previous method with minor modifications (Han et al., 2019). We added EDTA (5 μL) and the blood (30 μL) into an Eppendorf tube (0.5 mL). The mixture was then supplemented to 240 μL with buffer. The diluted blood sample was used to determine peripheral blood cell counts using an automatic blood cell analyzer (Siemens).

**Antioxidant Status Assessment.** The liver and spleen were homogenized with 0.9% saline (wt/vol = 1/9) in tissue lapping apparatus (Servicebio). Then the mixture was centrifuged at 1,800 × g for 10 min at 4°C and the supernatant was collected and stored at −80°C (Sinha et al., 2011). The protein concentrations of collected liver and spleen were measured with the bicinchoninic acid assay kit. The activities of SOD and GSH-Px and the levels of MDA and GSH in the serum, liver tissue, and spleen tissue were evaluated according to the protocols of the commercial assay kits.

**Determination of AST and ALT Activities in Serum.** The activities of AST and ALT in the serum of mice were determined according to the instructions of the commercial assay kits (Abdel-Magied et al., 2019). Aspartate and alanine were used as substrates to measure the activities of AST and ALT, respectively. First, 0.1 mL of serum was mixed with 0.5 mL of the corresponding matrix liquid. The mixture was reacted at 37°C for 10 min. The reaction was terminated with 2,4-dinitrophenyl hydrazine, and the mixture was incubated again at 37°C for 10 min. The substance appeared reddish-brown in alkaline solution. Finally, the absorbance was evaluated at 505 nm using UV-spectrophotometry (Beijing General Analysis General Instrument Co. LTD).
Histopathological Analysis

The isolated liver and spleen tissue were fixed in tissue-fixing liquid at 4°C for 24 h, then washed and dehydrated. The dehydrated liver and spleen tissue were appropriately trimmed off, embedded in paraffin block, and cut into 3- to 5-μm sections. The sections were deparaffinized, rehydrated, and stained by hematoxylin and eosin. Finally, the stained sections were determined by optical microscopy for histopathological examination (Sayed et al., 2019).

Statistical Analysis

All the values were carried out in triplicates, and the data are presented as the means ± standard deviations. Statistical analysis was performed by t-test using GraphPad Prism 5.0. A value of \( P < 0.05 \) was considered significant.

RESULTS

Protective Effect on L. lactis IL1403 Cells from \( \text{H}_2\text{O}_2 \)

The protective effect of IR-CFE on \( L. \text{lactis} \) IL1403 cells from \( \text{H}_2\text{O}_2 \) was shown in Figure 1. The number of bacteria in the \( \text{H}_2\text{O}_2 \) group was lower than that in the control group (\( P < 0.001 \)), which indicated that \( \text{H}_2\text{O}_2 \) had an apparent lethal effect on \( L. \text{lactis} \) IL1403. However, the addition of CFE and IR-CFE both could significantly improve the survival rate of \( L. \text{lactis} \) IL1403 under \( \text{H}_2\text{O}_2 \) stress, and the survival rate of IR-CFE group was higher than that of the CFE group (\( P < 0.05 \)). These results showed that both CFE and IR-CFE had protective effects against \( L. \text{lactis} \) IL1403 under \( \text{H}_2\text{O}_2 \) oxidative stress, and IR-CFE had better protective effects than CFE.

Effects of CFE and IR-CFE on AML-12 Cell Viability Under Radiation

Hepatic cells (AML-12) of mice were used to investigate the radiation protection effect of IR-CFE. In our previous study, EGCG could effectively inhibit IR-induced damage to AML-12, and thus EGCG was chosen as the positive control (Kang et al., 2019). As shown in Figure 2, the AML-12 cell viability was significantly decreased after \( ^{60}\text{Co}\gamma \) radiation (\( P < 0.01 \)), which showed that IR could inhibit cell proliferation and damage cells. However, the cell viability was all greatly increased after treatment with CFE and IR-CFE at different concentrations (\( P < 0.01 \)). When the concentration of CFE and IR-CFE was 600 µg/mL, the cell viability reached its maximum (0.64 ± 0.02 and 0.79 ± 0.01, respectively). Interestingly, the cell viability treated with IR-CFE was higher than that with CFE at the same concentration after \( ^{60}\text{Co}\gamma \) radiation (Figure 2C). These results indicated that IR-CFE had a stronger protective effect on cells under radiation conditions than CFE.

In Vivo Experiment

Effect of IR-CFE on BW. Before the radiation, the mice were administered with different doses of IR-CFE for 30 consecutive days. The effect of IR-CFE on the BW of mice is shown in Figure 3. The BW of mice presented a slow upward trend with the increase of days, which indicated that the mice were in a normal state of growth. In addition, there was no significant difference in the average daily BW of mice administered IR-CFE compared with the NC group (\( P > 0.05 \)), suggesting that IR-CFE did not produce acute toxicity in mice at the maximum concentration of 200 mg/kg.

Effect of IR-CFE on Peripheral Blood. To investigate the effect of IR-CFE on hematopoietic system after ionizing irradiation in mice, the number of white blood cells (WBC), red blood cells (RBC), and platelets (PLT) and the content of hemoglobin (HGB) were measured. As shown in Figure 4A, the number of WBC (\( 1.06 ± 0.19 \times 10^9/L \)) was dramatically decreased after radiation compared with the NC group (\( 5.31 ± 0.41 \times 10^9/L, P < 0.01 \)). The CFE treatment had no effect on WBC (\( P > 0.05 \)), but IR-CFE treatment could increase the WBC number in irradiated mice in a concentration-dependent manner. Meanwhile, a significant (\( P < 0.05 \))
reduction in the count of RBC (9.39 ± 0.27 × 1,012/L) was detected compared with the NC group (10.34 ± 0.64 × 1,012/L; Figure 4B). Although the RBC counts of all the CFE-H group, IR-CFE-M group, and IR-CFE-H group were significantly increased compared with the IR group, the effect was most pronounced in the IR-CFE-H (200 mg/kg of BW) group (10.64 ± 0.43 × 1,012/L). However, it can be seen from Figure 4C and Figure 4D that IR and IR-CFE had no great effect on the count of PLT and the content of HGB in the blood of mice. In summary, IR-CFE pretreatment can reduce radiation damage to hematopoietic system.

Effect of IR-CFE on Antioxidant Status in Irradiation Mice. In this study, the enzyme activities of SOD and GSH-Px and the contents of MDA and GSH in serum, liver, and spleen were determined and shown in Figure 5. In the IR group, the activities of SOD and GSH-Px were all greatly decreased in serum ($P < 0.01$), liver ($P < 0.001$), and spleen ($P < 0.01$), which suggested that 6 Gy of $^{60}$Co radiation could damage antioxidant systems. Meanwhile, the levels of GSH in the IR group were all greatly decreased in serum ($P < 0.01$), liver ($P < 0.001$), and spleen ($P < 0.01$), which suggested that 6 Gy of $^{60}$Co radiation could damage antioxidant systems. In contrast, the contents of MDA were significantly increased after treatment with IR, indicating that IR

**Figure 2.** The effects of ionizing radiation (IR)-induced cell-free extract (CFE) on AML-12 cell viability. (A) CFE; (B) IR-CFE; (C) comparison of CFE and IR-CFE. These results were expressed as mean ± SD ($n = 5$). **$P < 0.01$ and ***$P < 0.001$ compared with the control group of IR; ##$P < 0.01$ compared with the control group of sample. EGCG = epigallocatechin gallate; OD = optical density.

**Figure 3.** The effect of ionizing radiation (IR)-induced cell-free extract (CFE) on the BW of mice. These results were expressed as mean ± SD ($n = 10$). CFE-H groups = mice administered CFE (200 mg/kg of BW) for 30 d and then exposed to IR; IR-CFE-L, IR-CFE-M, and IR-CFE-H groups = mice administered IR-CFE (50, 100, and 200 mg/kg of BW, respectively) for 30 d and then exposed to IR. NC = normal control; PC = positive control.
could trigger lipid peroxidation and cause imbalance of REDOX system. With the treatment of IR-CFE, the activities of SOD and the contents of MDA in serum, liver, and spleen were reversed to a certain extent in a concentration-dependent manner (Figure 5A and B). Meanwhile, the GSH-Px of all the IR-CFE-treated in serum and spleen were significantly increased compared with the IR group ($P < 0.05$). Additionally, the GSH-Px of IR-CFE-H group reached $980.65 \pm 49.73$ U/L, $444.72 \pm 38.63$ U/L, and $187.32 \pm 10.25$ U/L in serum, liver, and spleen, respectively (Figure 5C). In addition, the trend of GSH were similar to that of SOD activity, and the IR-CFE-H group represented the strongest radiation protection effect ($P < 0.001$, Figure 5D).

**Effect of IR-CFE on AST and ALT in Serum.** As shown in Figure 6, IR caused a significant increase of AST and ALT levels ($P < 0.001$), which suggested that IR could cause toxicity to the liver of mice. However, pretreatment of IR-CFE inhibited IR-induced AST and ALT activities. In addition, IR-CFE could alleviate the AST and ALT levels in a dose-dependent manner.

**Effect of IR-CFE on Liver Histopathological Alterations.** The changes of liver tissue morphology induced by IR and IR-CFE in mice were shown in Figure 7. In the NC group, uniform distribution of liver cells and clearly visible nuclei were observed, and the liver cells were arranged neatly and stained evenly, suggesting that the liver was in a normal state without lesions. However, there were obvious pathological changes in the IR group, including cellular swelling of liver, disorder of hepatic cord, and heterogeneous hepatocytes. Compared with the IR group, hepatocyte cords were neatly arranged and hepatocytes were mildly swollen in IR-CFE groups, which indicated that

![Figure 4](image-url)
Figure 5. The effect of ionizing radiation (IR)-induced cell-free extract (CFE) on antioxidant status in irradiation mice. (A) The activity of superoxide dismutase (SOD), (B) the content of malondialdehyde (MDA), (C) the activity of glutathione peroxidase (GSH-Px), and (D) the level of glutathione (GSH) in the serum, liver, and spleen of radiation mice. These results were expressed as mean ± SD (n = 7). ### *P < 0.001 compared with the normal control (NC) group, *P < 0.05, **P < 0.01, and ### *P < 0.001 compared with the IR group. CFE-H groups = mice administered CFE (200 mg/kg of BW) for 30 d and then exposed to IR; IR-CFE-L, IR-CFE-M, and IR-CFE-H groups = mice administered IR-CFE (50, 100, and 200 mg/kg of BW, respectively) for 30 d and then exposed to IR. PC = positive control; mgprot = mg of protein.
IR-CFE could improve the pathological changes of mice liver after radiation.

**Effect of IR-CFE on Spleen Histopathological Alterations.** The effects of IR-CFE and IR on spleen tissues of mice were shown in Figure 8. Clear distribution of red and white pulps and intact splenic corpuscles and lymphocytes were observed in the NC group. In the IR group, lymphocytes in spleen tissues were reduced and scattered. Meanwhile, red and white pulps were not clearly distributed, and spleen corpuscle volume was reduced. With the pretreatment of IR-CFE, the part of the red pulps was damaged and the number of lymphocytes was increased. Additionally, the structure of the spleen body was restored. The results indicated that IR-CFE could reduce radiation damage to the spleen and then protect the immune system.

**DISCUSSION**

When an organism is stressed by its external environment, it will initiate a variety of resistance mechanisms to resist the stimulation of the adverse environment, and
LAB is no exception (Wang et al., 2018). Salt stress can induce a series of oxidative stress genes and antioxidant enzymes in *Bacillus cereus* ATCC 14579, which leads to the improvement of the antioxidant capacity of this strain (den Besten et al., 2009). *Lactococcus lactis* ssp. *cremoris* and *Lactobacillus acidophilus* NCFM grown in 10 mM Ca\(^{2+}\) medium increased the survival rate after spray drying (Wang et al., 2020). As an oxidant closely related to oxidative stress, H\(_2\)O\(_2\) can cause nonspecific damage to nucleic acids, proteins, lipids, and other cellular macromolecules (Sayed et al., 2019). Therefore, H\(_2\)O\(_2\) is widely used to evaluate the antioxidant activity of LAB. In our study, IR-CFE had better protective effect on *L. lactis* IL1403 under H\(_2\)O\(_2\) condition (Figure 1). Based on this, it can be inferred that IR stress can enhance the expression of antioxidant enzymes and proteins in bacteria to adapt to changes in the external environment. Therefore, the antioxidant capacity of *L. lactis* IL1403 induced by radiation was improved. Meanwhile, IR-CFE also showed stronger radiation protection at the cellular level (Figure 2). The adaptation of bacteria to one type of stress may produce cross-protection effects to the other kind of stress, mainly through protein expression and metabolic pathway.

It is well known that IR is widely used in the radiotherapy of various cancers. However, IR can cause certain damage to the normal tissues and systems of body, especially the hematopoietic system, immune system, and liver tissue (Piryani et al., 2019; Sayed et al., 2019). Therefore, we further investigated the radioprotection of IR-CFE on the hematopoietic system and oxidative stress in the mice model. The results suggested that IR-CFE pretreatment could protect mice from radiation-induced damage. The effects of these protections were mainly expressed as an obvious increase in WBC and RBC; an increase in SOD, GSH, and GSH-Px levels; a decrease in MDA content; a decrease in AST and ALT levels in serum; and mitigation of pathological changes in liver and spleen.

The hematopoietic system is one of the systems most sensitive to IR, and it is vulnerable to radiation (Kim et al., 2019). Hematopoietic stem cells are very sensitive to radiation, and they are sharply decreased after radiation, which makes the source of mature blood cells in peripheral blood deficient. Therefore, the number of WBC in peripheral blood will decrease after radiation, which leads to hematopoietic dysfunction, resulting in anemia, bleeding, and other complications (Peng et al., 2020). The number of WBC in peripheral blood will decrease after radiation, which leads to hematopoietic dysfunction, resulting in anemia, bleeding, and other complications (Peng et al., 2020).

Many studies have shown that the damage of tissues and physiological systems caused by radiation are closely related to oxidative stress (Cho et al., 2019; Thimmaiah et al., 2019). The imbalance between the production of ROS and the antioxidant system can lead to an increase in oxidative stress. Superoxide dismutase is an important antioxidant enzyme in organisms and a key substance for scavenging free radicals (Feng et al., 2017). On the contrary, ROS produced by the damaged body triggers a series of lipid peroxidation reactions to...
produce MDA (Gokul et al., 2010). Therefore, the determination of SOD and MDA is often used to evaluate the ability of the body to scavenge free radicals and the severity of free radical attack, respectively. Also, GSH-Px is an important enzyme that catalyzes the decomposition of hydrogen peroxide. It can specifically catalyze the reduction reaction of GSH to H2O2 and reduce the harm of H2O2 to the body (Spanou et al., 2010). Our research found that 60Coγ radiation of 6 Gy could cause imbalance of the REDOX system of serum and tissue. However, the administration of IR-CFE could increase the reduction of antioxidant capacity caused by radiation, including an increase in SOD, GSH, and GSH-Px levels and a decrease in MDA content in the serum, liver, and spleen of irradiated mice. These results were consistent with the previous report that showed that pretreatment with EGCG increased antioxidant levels in mice liver after radiation (Yi et al., 2020). When liver tissue is damaged, AST and ALT escape from the liver cells and enter the blood, resulting in a significant increase in AST and ALT activities in the blood (Duan et al., 2018). Therefore, the AST and ALT activities are the most important indicators of liver injury. Our results showed that AST and ALT levels increased in the serum after 60Coγ radiation. Histopathological examination of the liver demonstrated significant pathological changes in the irradiated mice. However, this situation was restored with IR-CFE treatment, which indicated that IR-CFE played an important role in protecting the liver from radiation damage. All the data showed that IR-CFE can alleviate IR-induced injury including the hematopoietic system, REDOX system, liver, and spleen, suggesting that IR-CFE is a potential natural radiation protection agent. The components of the CFE of L. lactis IL1403 may include some antioxidant enzymes, such as SOD and GSH (Zhang et al., 2020). Our research showed that IR-CFE had a radioprotective effect against 60Coγ injury in mice, but the component that is responsible for the radioprotective effect is worthy of further exploration in the future.

CONCLUSIONS

In the present research, the oxidative damage–protective effects of CFE and IR-CFE in vitro were evaluated. We found that IR-CFE had a stronger oxidative damage–protective effect than CFE. Therefore, the radioprotection of IR-CFE based on the hematopoietic system and oxidative stress level against IR-induced damage in mice were further explored. Our research also proved that IR induction can increase the antioxidant activity of IR-CFE and can promote the development of new methods to improve the antioxidant capacity of strains. Meanwhile, our study provided evidence that the radioprotection of IR-CFE is mainly achieved by protecting the hematopoietic system and improving oxidative stress level. Therefore, IR-CFE can counteract the damage caused by radiation as a novel and natural radioprotector. However, the radioprotective effect of IR-CFE was preliminarily researched in this study. It only proved that IR-CFE has a good radioprotective function, but its specific mechanism of radiation protection still needs to be further studied.

ACKNOWLEDGMENTS

This study was supported by the National Natural Science Foundation of China (81870093; Beijing, China), the Research Project of People’s Liberation Army (BXP20C006, BX115C007; Beijing, China), the Special Subject Funding of Zhengzhou University (Zhengzhou, China), and the Natural Science Foundation of Henan Province for Outstanding Youth (202300410365; Zhengzhou, China). The authors declare they have no competing interests.

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