大韓獸醫學會誌(2003) 第43卷 第4號
Korea J Vet Res(2003) 43(4) : 633~639

감마선 조사 마우스에서 녹차 및 분획의 방사선 장해 경감 효과

김세라 · 이해준 · 김성호*
전남대학교 수의과대학
(게재승인: 2003년 11월 20일)

The radioprotective effects of green tea and its fractions in Gamma-irradiated mice

Se-ra Kim, Hae-june Lee and Sung-ho Kim*
College of Veterinary Medicine, Chonnam National University, Kwangju 500-757, Korea
(Accepted: November 20, 2003)

Abstract : We investigated the effect of green tea and its fractions of alcohol and polysaccharide on jejunal crypt survival, endogenous spleen colony formation, and apoptosis in jejunal crypt cells of mice irradiated with high and low dose of gamma-irradiation. Jejunal crypts were protected by pretreatment of green tea (i.p.: 50 mg/kg of body weight, at 12 and 36 hours before irradiation., p.o.: 1.25% water extract, for 7days before irradiation, $p<0.01$) and alcohol and polysaccharide fractions showed no significant modifying effects. Green tea and its fractions administration before irradiation (i.p. at 12 and 36hours before irradiation) resulted in an increase of the formation of endogenous spleen colony ($p<0.05$). The frequency of radiation-induced apoptosis in intestinal crypt cells was also reduced by pretreatment of green tea (i.p. at 12 and 36 hours before irradiation, $p<0.05$., p.o. for 7days before irradiation, $p<0.001$) and its fractions ($p<0.001$). These results indicated that green tea might be a useful radioprotector, especially since it is a relatively nontoxic natural product. Further studies are needed to characterize better the promotion nature of green tea and its components.

Key words : Green tea, radiation, crypt survival, endogenous spleen colony, apoptosis

Introduction

Complementary/alternative therapies are increasingly used by the general population. In the US, for instance, it has been suggested that 40% of the public use such therapies [1]. Herbal medicine is among the most prevalent complementary/alternative therapies [1, 2, 20]. This is also confirmed by a recent assessment of the US herbal market [2]. In 1998, total US sales for herbal remedies approached US $4 billion, suggesting as annual growth rate of approximately 25% [24]. In herbal medicine the term *herbs* is used loosely to refer not only to herbaceous plants but also to bark; root; leaves; seeds; flowers and fruit of trees, shrubs, and woody vines; and extracts of the same that are valued for their savory, aromatic, or medicinal qualities. Plants have played a significant role in maintaining human health and improving the quality of human life for thousands of years, and have served humans well as valuable components of seasonings, beverages, cosmetics, dyes, and medicines [5].

As the diversity of radiation used in medicine, agriculture, industry, biochemical research and military operations increases, the risk from exposure including total body or local organs damage will be evaluated. Thus, the protection of individuals against severe radiation damage is an important issue.

After exposure to radiation, the eventual survival

*Corresponding author: Sung-ho Kim
College of Veterinary Medicine, Chonnam National University, Yongbong-dong, Puk-ku, Kwangju 500-757, Korea
[Tel: 82-62-530-2837, Fax: 82-62-530-2841, E-mail: shokim@chonnam.ac.kr]

time and mode of death depend on the magnitude of the dose. At very high doses, death occurs in a matter of hours and appears to result from neurological and cardiovascular breakdown, known as cerebrovascular syndrome. At intermediate dose level, death occurs in a matter of days and is associated with extensive bloody diarrhea and destruction of the gastrointestinal mucosa, known as gastrointestinal syndrome. At low dose level, death occurs in a matter of several weeks and is due to effects on the blood-forming organs, known as hematopoietic syndrome. In the gastrointestinal and hematopoietic syndrome, the death is due to the depletion of the stem cells of a critical self-renewal tissue: that of the epithelium of the gut or that of the circulating blood cells, respectively. Therefore, the enhancements of survival and recovery of blood-forming stem cells and intestine crypts are the fundamental requirements for a radioprotective agent [13, 21].

Synthetic compounds have been studied for their ability to protect against the adverse effects of ionizing radiation since the original observation of radioprotection by Patt *et al.* [27]. Subsequently, many compounds have been tested for their ability to modify the effect of radiation [30]. Despite some toxic effects, newer compounds are currently under investigation as possible adjuvants in the radiation treatment of cancer [10, 18]. Natural products such as herbal medicines have only recently begun to receive some attention as possible modifiers of the radiation response [11, 15-17, 19, 36].

Green tea has been consumed as a beverage for thousands of years in Asia; it also has been used for its medicinal purposes. Because of the lack of specific scientific methods, scientists have dismissed the notion of green tea for its healing properties. However, in recent years, much attention has focused on the role of green tea for its antimicrobial, immunostimulatory capacities and for its protective effect against cardiovascular diseases [7, 22, 29]. But there is surprisingly little quantitative information in the contemporary literature relating to the modification effect on ionizing radiation-induced response. The present study was performed to determine the effect of green tea and its fractions in irradiated mice.

Materials and Methods

Animals

For jejunal crypt survival and apoptosis assay, seven-week-old female ICR mice, and for the experiment on endogenous spleen colony formation, seven-week-old male ICR mice, obtained from the animal center of Korea Research Institute of Bioscience and Biotechnology, were housed in polycarbonate cages. They were fed on a standard animal diet.

Preparation of extract of green tea and its fractions

Commercially obtained dried green tea leaf (BOSUNGG-REENTEA CO., Korea) was prepared as a 1.25% (1.25% water extract of green tea leaf was prepared by passing 400 ml of hot water through 5 g of tea leaves in a brewing machine) infusion on alternate days using a coffee maker for oral administration. The dry weight of tea solids was measured regularly by drying portions overnight at 60°C. The average solids content over the whole study of the 1.25% infusions was 5.02±0.13 mg/ml. For the i.p. injection, the dried green tea leaf was crushed and left in distilled water at 80°C for 8 hours (100 g of green tea was extracted with 1000 ml of distilled water). The suspensions were spun at 1000 *g* for 30 minute and the supernatants were filtered and dried with a speed vacuum. Fractions (ethyl alcohol fraction and polysaccharide fraction) of green tea were prepared with saline at concentrations that were proportional to the original recoveries in the fraction steps.

Administration of green tea and its fractions

For oral administration, the extract of 1.25% green tea solution was given as drinking water for 7 days before irradiation or for 4 days after irradiation. For i.p. administration, the extract was given as the dose of 50 mg/kg of body weight at 36 and 12 hours before irradiation or at 30 minutes after irradiation. Fractions of green tea (alcohol fraction: 39 mg/kg of body weight, polysaccharide fraction: 7.7 mg/kg of body weight) were given i.p. at 36 and 12 hours before irradiation.

Irradiation

The animals were irradiated with 12 Gy for jejunal crypt survival assay, 6.5 Gy for the experiment on endogenous spleen colony formation, or 2 Gy for the experiment on apoptosis, of ^{60}Co gamma-rays(Gamma-cell Elan 3000, Nordion International, Canada) at a dose-rate of 10.0 Gy per minute.

Jejunal crypt assay

For the determination of jejunal crypt stem cell survival,

the microcolony technique described by Withers and Elkind [34] was used. A total of 60 ICR female mice were divided into 10 groups (6 mice in each group) as untreated control group, an irradiation control group and administration groups with each extract or fraction at pre- or post-irradiation. At 3.5 days after irradiation the animals were killed. Two sections of four different parts of the jejunum were prepared for histological examination in each animal. The regenerating crypts in the jejunal cross-section were counted.

Endogenous spleen colony assay

A total of 72 ICR male mice were divided into 8 groups (9 mice in each group) as an irradiation control group and administration groups with each extract or fraction at pre- or post-irradiation. Nine days after irradiation the mice were killed, and their spleens removed and fixed in Bouins solution. The colonies on the surface of the spleens were counted with the naked eye.

Apoptosis assay

A total of 36 ICR female mice were divided into 9 groups (4 mice in each group) as an untreated control, an irradiation control group and administration groups with each extract or fraction at pre- or post-irradiation. The mice were decapitated at 6 hours after irradiation. Irradiations were performed between 9 and 10 a.m. The small intestines were fixed in Carnoys fixative for a minimum of 30 minutes. The blocks were then embedded in paraplast wax and 4 um sections were cut, and stained with hematoxylin-eosin and in situ DNA end-labeling (ISEL) technique. Apoptosis was detected by using a nonisotopic ISEL technique (APOPTAG™, Oncor, Gaithersburg, MD, U.S.A.) applied to paraffin sections. With the ISEL technique, residues of digoxigenin-nucleotides are catalytically added to the fragmented DNA (3-OH ends) by adding terminal deoxynucleotidyl transferase to the slides. The added residues were subsequently immunostained by an anti -digoxigenin-peroxidase antibody. The localized peroxidase enzyme was then revealed by routine diaminobenzidine (Sigma Chemical Co.) staining. In good longitudinal crypt sections (showing a large portion of crypt base, lumen, and at least 17 cells along the crypt column), apoptotic cells were counted under the light microscope. When several apoptotic fragments were believed, on the base of their size and clustering, to represent the remains of a single cell, they were recorded as a single cell. Details of such scoring techniques can be found elsewhere [12, 14]. Forty crypt sections were scored for each mouse.

Results

The results of the jejunal crypt survival assay are summarized in Table 1. Unirradiated controls show the density of crypts at the bases of the villi. There is an average of about 160 crypts per complete circumference. Pre-treatment with green tea extracts ($p<0.01$) resulted in a significant increase in the number of surviving crypts compared with those in the irradiation control. Alcohol and polysaccharide fractions showed no significant modifying effects on the crypt survival.

The effect of the extract on the radioresponse of hematopoietic cells that form endogenous spleen colonies are presented in Table 2. The numbers of

Table 1. Effect of green tea and its fraction on intestinal crypt survival in irradiated mice (M±SD)

Groups	Crypts per circumference
Untreated control	159.2±8.1
Irradiation control (12 Gy)	9.2±4.5
Green tea (p.o.)[a] + irradiation	30.1±13.9*
Green tea (i.p.)[b] + irradiation	33.2±16.5*
Irradiation + green tea (p.o.)[c]	21.2±12.7
Irradiation + green tea (i.p.)[d]	31.8±28.1
Untreated control	161.4±11.2
Irradiation control (12 Gy)	8.9±7.6
Alcohol fraction of green tea (i.p.)[e] + irradiation	25.3±18.5
Polysaccharide fraction of green tea (i.p.)[e] + irradiation	22.8±20.0

[a]1.25% water extract of green tea leaf was prepared by passing 400 ml of hot water through 5 g of tea leaves in a brewing machine. The extract was given for 7days before irradiation.
[b]Extract of green tea (50 mg/kg of body weight) was given i.p. at 36 and 12 hours before irradiation.
[c]1.25% water extract of green tea leaf was given for 4 days after irradiation.
[d]Extract of green tea (50 mg/kg of body weight) was given i.p. at 30 minutes and 24 hours after irradiation.
[e]Fractions of green tea were prepared with saline at concentrations that were proportional to the original recoveries in the fraction steps. They (alcohol fraction: 39 mg/kg of body weight, polysaccharide fraction: 7.7 mg/kg of body weight) were given i.p. at 36 and 12 hours before irradiation.
*$p<0.01$ as compared with irradiation control group.

Table 2. Effect of green tea on endogenous spleen colonies in irradiated mice at ninth day after irradiation (M±SD)

Groups	Number of colonies
Irradiation control (6.5 Gy)	4.44±3.32
Green tea (p.o.)[a] + irradiation	10.10±9.28
Green tea (i.p.)[b] + irradiation	16.90±13.43*
Irradiation + green tea (p.o.)[c]	1.17±1.94
Irradiation + green tea (i.p.)[d]	7.90±7.44
Irradiation control (6.5 Gy)	5.29±1.89
Alcohol fraction of green tea (i.p.)[e] + irradiation	19.86±14.02*
Polysaccharide fraction of green tea (i.p.)[e] + irradiation	17.63±10.90*

[a]1.25% water extract of green tea leaf was prepared by passing 400 ml of hot water through 5 g of tea leaves in a brewing machine. The extract was given for 7 days before irradiation.
[b]Extract of green tea (50 mg/kg of body weight) was given i.p. at 36 and 12 hours before irradiation.
[c]1.25% water extract of green tea leaf was given for 9 days after irradiation.
[d]Extract of green tea (50 mg/kg of body weight) was given i.p. at 30 minutes and 24 hours after irradiation.
[e]Fractions of green tea were prepared with saline at concentrations that were proportional to the original recoveries in the fraction steps. They (alcohol fraction: 39 mg/kg of body weight, polysaccharide fraction: 7.7 mg/kg of body weight) were given i.p. at 36 and 12 hours before irradiation.
*$p<0.05$ as compared with irradiated control group.

Table 3. Effect of green tea on incidence of cell death by apoptosis in crypt of intestine following irradiation (M±SD)

Groups	Apoptotic cells per crypt	
	Base	Total
Untreated control	0.071±0.035	0.091±0.031
Irradiation control (2 Gy)	3.750±0.331	4.125±0.378
Green tea (p.o.)[a]+irradiation	2.314±0.374*	2.509±0.382*
Green tea (i.p.)[b]+irradiation	1.975±0.808*	2.313±1.103**
Irradiation+green tea (i.p.)[c]	2.925±0.704	3.481±0.848
Untreated control	0.068±0.024	0.089±0.041
Irradiation control (2 Gy)	3.175±0.102	3.675±0.155
Alcohol fraction of green tea (i.p.)[d]+irradiation	1.806±0.085*	2.181±0.145*
Polysaccharide fraction of green tea (i.p.)[d]+irradiation	2.031±0.140*	2.338±0.078*

[a]1.25% water extract of green tea leaf was prepared by passing 400 ml of hot water through 5 g of tea leaves in a brewing machine. The extract was given for 7 days before irradiation.
[b]Extract of green tea (50 mg/kg of body weight) was given i.p. at 36 and 12 hours before irradiation.
[c]Extract of green tea (50 mg/kg of body weight) was given i.p. at 30 minutes and 24 hours after irradiation.
[d]Fractions of green tea were prepared with saline at concentrations that were proportional to the original recoveries in the fraction steps. They (alcohol fraction: 38.5 mg/kg of body weight, polysaccharide fraction: 7.7 mg/kg of body weight) were given i.p. at 36 and 12 hours before irradiation.
*$p<0.01$, **$p<0.05$ as compared with irradiated control group.

spleen colonies were higher in the mice that received green tea extract, its fractions ($p<0.05$) and radiation than in mice exposed to radiation only.

Table 3 show how the number of apoptotic cells varied with the administration of extracts 6 hours after irradiation. Apoptotic cells, which occur predominantly in the lower third of crypt, are easily recognized from the condensation of their cytoplasm and nuclear fragments. Not all the fragments necessarily contain fragments of the cell nucleus. These cytoplasmic fragments nevertheless usually can be recognized by their eosinophilic staining properties in hematoxylin-eosin stain. Apoptosis was easily recognized by the presence of peroxidase-stained entire apoptotic bodies. In ISEL-positive cells or bodies, the stained products correlated exactly with the typical morphologic characteristics of apoptosis as seen at the light microscopic level. Pretreatment of extracts or fractions were associated with decreases of 39.2% (green tea, p.o.), 43.9% (green tea, i.p.), 40.6% (alcohol fraction) and 36.4% (polysaccharide fraction) decrease in the number of cells with nuclei positively stained for apoptosis compared with the irradiation control group.

Discussion

We investigated the effect of green tea and its fractions on jejunal crypt survival, endogenous spleen colony formation, and apoptosis in jejunal crypt cells of irradiated mice with high and low doses of gamma-irradiation.

Many chemical compounds that exert the effect of radiation protection in mice have been investigated. Washburn *et al.* [32] and Cairnie [3] suggested that these compounds such as WR2721, which include the thiol group in their molecular structure, have some effects on radiation protection. However, most of these chemicals have to be administered by injection immediately before irradiation, as they provide little or no protection when given orally or after irradiation. In addition, they produce severe toxicity to normal cells.

As a result, it is difficult to use these chemicals in patients who receive high doses of radiation without additional side effects.

The nutraceutical natural products, including simple herbs and compounded prescriptions, are known to be effective in accelerating recovery from disease or injury and do not appear to have obvious side effects. Therefore, it may be practical and valuable to develop herbs for eliminating radiation damage. It has been reported that many kinds of crude drugs such as ginseng [15, 17, 35], *Cnidium officinale* [25], *Angelica sinensis* [31], *Acanthopanax senticosus* [23], *Astragalus menbranaceous* [28], and *Ganoderma lucidium* [11] have some effects on promoting recovery of radiation damage. The National Institutes of Health opened its Office of Alternative Medicine in 1993 to provide support to qualified investigators wanting to systematically study unconventional therapies. According to survey published by Eisenberg *et al.* [8] in 1993, 1 of 3 Americans used at least one unconventional therapy per year, and most of those used the unconventional therapy for chronic rather than life-threatening medical conditions. People seek solutions without side effects for problems such as arthritis, allergies, insomnia, headaches, anxiety, and depression [8].

Green tea has been reported to possess antimicrobial, immunostimulatory, anticarcinogenic, and anti-inflammatory capacities and for its protective effect against cardiovascular disease [7, 22, 29]. In this experiment, green tea administration before irradiation protected the jejunal crypt, increased the formation of endogenous spleen colony and reduced the frequency of radiation-induced apoptosis.

Although after *in vitro* and *in vivo* models have suggested that a few herbs might be a useful radioprotector, it is unknown whether the herbs are also capable of protecting radiation damage by preventing apoptosis and enhancing crypt survival in the intestine. In this study, we demonstrated for the first time the green tea can reduce the extent of radiation-induced apoptosis and protect the jejunal crypt. Since the survival and recovery of blood forming stem cells [13], the survival of intestine crypts [21] and the reduction of radiation-induced apoptosis [26] is the fundamental requirement for a radioprotective agent, the result of this study confirms the efficacy of green tea as a radioprotective agent.

Green tea contains polyphenols such as epigallocatechin gallate, epicatechin gallate, epigallocatechin, and epicatechin, which have antioxidant properties [4, 6, 9]. Despite the growing body of research demonstrating tea polyphenols to be powerful antioxidants, understanding of the mechanisms involved in the biological effects of green tea is far from complete. Initial studies focused on: (1) antioxident and free-radical scavenging activity which may play a role in lowering LDL-cholesterol, with a consequent decreased risk of cardiovascular disease; (2) stimulation of detoxification systems, specifically selective induction or modification of phase I and phase II metabolic enzymes which increase the formation and excretion of detoxified metabolites of carcinogens; (3) inhibition of biochemical markers of tumor initiation and promotion, including lowering the rate of cell replication and thus the growth and development of neoplasms; and (4) prevention of mutagenicity and genotoxicity [33, 37]. Whole body irradiation under the proper conditions is highly lethal and the effect is mediated largely through the generation of free radicals. The mechanism (s) of the inhibitory effects of green tea on radiation-induced damages is unknown but may be related to the antioxidant and free radical-scavenging activities of the tea. More research is needed to identify the active constituents in the green tea and to determine the possibility of synergistic or antagonistic effects of the multiple constituents in tea.

Because green tea is safe (it is sterilized with boiling) and relatively cheap, drinking green tea can be recommended without risk for people suffering from radiation-induced damages.

Acknowledgements

This project has been carried out under the Nuclear R&D Program by MOST of Korea.

References

1. **Astin, J. A.** Why patients use alternative medicine: results of a national study. J. A. M. A. 1998, **279**, 1548-1553.
2. **Brevoort, P.** The booming US botanical market - a new over view. Herbalgram. 1998, **44**, 33-46.
3. **Cairnie, A. B.** Adverse effect of radioprotector WR2721. Radiat. Res. 1983, **94**, 221-226.
4. **Cotelle, N., Bernier, J. L., Henichart, J. P., Catteau, J. P., Gaydou, E. and Wallet, J. C.** Scavenger and

antioxidant properties of ten synthetic flavones. Free Radic. Biol. Med. 1992, **13**, 211-219.

5. **Craig, W. J.** Health-promoting properties of common herbs. Am. J. Clin. Nutr. 1999, **70**, 491S-499S.
6. **Dreosti, I. E.** Bioactive ingredients: antioxidants and polyphenols in tea. Nutr. Rev. 1996, **54**, S51-58.
7. **Dufresne, C. J. and Farnworth, E. R.** A review of latest research findings on the health promotion properties of tea. J. Nutr. Biochem. 2001, **12**, 404-421.
8. **Eisenberg, D. M., Kessler, R. C., Fodter, C., Norlock, F. E., Calkins, D. R. and Delbanco, T. L.** Unconventional medicine in the United States. Preference, costs and patterns of use. N. Engl. J. Med. 1993, **328**, 246-252.
9. **Guo, Q., Zhao, B., Li, M., Shen, S. and Xin, W.** Studies on protective mechanisms of four components of green tea polyphenols against lipid peroxidation in synaptosomes. Biochim. Biophys. Acta. 1996, **1304**, 210-222.
10. **Hospers, G. A., Eisenhauer, E. A. and de Vries, E. G.** The sulfhydryl containing compounds WR-2721 and glutathione as radio- and chemoprotective agents. A review, indications for use and prospects. Br. J. Cancer. 1999, **80**, 629-638.
11. **Hsu, H. Y., Lian, S. L. and Lin, C. C.** Radioprotective effect *Ganoderma lucidum* (Leyss. ex. Fr.) Karst after X-ray irradiation in mice. Am. J. Chin. Med. 1990, **18**, 61-69.
12. **Ijiri, K. and Potten, C. S.** Further studies on the response of intestinal crypt cells of different hierarchical status to eighteen different cytotoxic agents. Br. J. Cancer. 1987, **55**, 113-123.
13. **Ijiri, K. and Potten, C. S.** Radiation-hypersensitive cells in small intestine crypts; their relationship to clonogenic cells. Br. J. Cancer. 1986, **53**, 20-22.
14. **Ijiri, K. and Potten, C. S.** The re-establishment of hypersensitive cells in the crypt of the mouse intestine. Int. J. Radiat. Biol. 1984, **46**, 609-623.
15. **Kim, S. H., Jeong, K. S., Ryu, S. Y. and Kim, T. H.** *Panax ginseng* prevents apoptosis in hair follicles and accelerates recovery of hair medullary cell in irradiated mice. *In Vivo*. 1998, **12**, 219-222.
16. **Kim, S. H., Lee, S. E., Oh, H., Kim, S. R., Yee, S. T., Yu, Y. B., Byun, M. W. and Jo, S. K.,** The radioprotective effects of Bu-Zhong-Yi-Qi-Tang: a prescription of traditional Chinese medicine. Am. J. Chin. Med. 2002, **30**, 127-137.
17. **Kim, S. H., Son, C. H., Nah, S. Y., Jo, S. K., Jang, J. S. and Shin, D. H.** Modification of radiation response in mice by *Panax ginseng* and diethyldithiocarbamate. In Vivo. 2001, **15**, 407-412.
18. **Kligerman, M. M., Shaw, M. T., Slavid, M. and Yudas, J. M.** Phase I clinical studies with WR2721. Cancer Clin. Trials. 1980, **3**, 217-221.
19. **Lee, S. E., Oh, H., Yang, J. A., Jo, S. K., Byun, M. W., Yee, S. T. and Kim, S. H.** Radioprotective effects of two traditional Chinese medicine prescriptions: Si-Wu-Tang and Si-Jun-Zi-Tang. Am. J. Chin. Med. 1999, **27**, 387-396.
20. **MacLennan, A. H., Wilson, D. H. and Taylor, A. W.** Prevalence and cost of alternative medicine in Australia. Lancet. 1996, **347**, 569-573.
21. **Milas, L., Hunter, N., Ito, H. and Peter, L. J.** *In vivo* radioprotective activities of diethydithiocarbamite. Int. J. Radiat. Oncol. Biol. Phys. 1984, **10**, 2335-2343.
22. **Mitscher, L. A., Jung, M., Shankel, D., Dou, J. H., Steele, L. and Pillai, S. P.** Chemoprotection: a review of the potential therapeutic antioxident properties of green tea (*Camellia sinensis*) and certain its constituents. Med. Res. Rev. 1997, **17**, 327-365.
23. **Miyanomae, T. and Frindel, E.** Radioprotection of hemopoiesis conferred by *Acanthopanax senticosus* Harms (Shigoka) administered before or after irradiation. Exp. Hematol. 1988, **16**, 801-806.
24. **Muller, J. L. and Clauson, K. A.** Pharmaceutical considerations of common herbal medicine. Am. J. Manage. Care. 1997, **3**, 1753-1770.
25. **Ohta, S., Sakurai, N., Sato, Y., Inoue, T. and Shinoda, M.** Studies on chemical protectors against radiation. XXX. Radioprotective substances of cnidii rhizoma. Yakugaku Zasshi. 1990, **110**, 746-754.
26. **Orazi, A., Du, X., Yang, Z., Kashai, M. and Williams, D. A.** Interleukin-11 prevents apoptosis and accelerates recovery of small intestine mucosa in mice treated with combined chemotherapy and radiation. Lab. Invest. 1996, **75**, 33-42.
27. **Patt, H., Tyree, M. and Straube, R. L.** Cystein protects against x-irradiation. Science. 1949, **110**, 213-214.
28. **Quan, H. X. and Li, H. S.** Effect of *radix Astragali* on hemopoiesis in irradiated mice. Chung Kuo Chung Yao Tsa Chin. 1994, **19**, 741-743.
29. **Sato, T. and Miyata, G.** The nutraceutical benefit, part I: green tea. Nutrition. 2000, **16**, 315-317.
30. **Sweeney, T. R.** A survey of compounds from the

antiradiation drug development program of the U.S. army medical research development command. Walter Reed Army Institute of Research. Washington, DC, 1979.

31. **Wang, Y. and Zhu, B.** The effect of angelica polisaccharide on proliferation and differentiation of hematopoietic progenitor cell. Chung Hua I Hsueh Tsa Chin. 1996, **76**, 363-366.
32. **Washburn, L. C., Carlton, J. E. and Hayes, R. L.** Distribution of WR-2721 in normal and malignant tissue of mice and rats bearing solid tumors: dependence on tumor type, drug dose and species. Radiat Res. 1974, **59**, 483-575.
33. **Weisburger, J. H.** Tea and health: the underlying mechanism. Proc. Soc. Exp. Biol. Med. 1999, **220**, 271-275.
34. **Wither, H. R. and Elkind, M. M.** Microcolony survival assay for cells of mouse intestinal mucosa exposed to radiation. Int. J. Radiat. Biol. 1970, **17**, 261-267.
35. **Zhang, J. S., Sidgdestad, C. P., Gemmell, M. A. and Grdina, D. J.** Modification of radiation response in mice by fractionated extracts of *Panax ginseng*. Radiat. Res. 1987, **112**, 156-163.
36. **Zhang, R. J., Quin, J. K., Yang, G. H., Wang, B. Z. and Wen, X. L.** Medicinal protection with Chinese herb-compound against radiation damage. Aviat. Space Environ. Med. 1990, **61**, 729-731.
37. **Zloch, Z.** The role of dietary plant polyphenols in health maintenance. Cas. Lek. Cesk. 1996, **135**, 84-88.