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Radioprotective Effect of American Ginseng on Human Lymphocytes at 90 Minutes Post-irradiation: A Study of 40 Cases

Tung-Kwang Lee, MD,[1*] Kevin F. O'Brien, PhD,[2] Weidong Wang, MD, PhD,[1,3] Roberta M. Johnke, PhD,[1] Chao Sheng, PhD,[1] Sidi M. Benhabib,[1] Tao Wang, MD, PhD,[4] and Ron R. Allison, MD[1]

[1]Department of Radiation Oncology, Leo W. Jenkins Cancer Center, Brody School of Medicine at East Carolina University, Greenville, NC 27834, USA
[2]Department of Biostatistics, School of Allied Health, East Carolina University, Greenville, NC 27834, USA
[3]Department of Oncology, Xinqiao Hospital, Third Military Medical University, Chongqing 400037, China
[4]Department of Anatomy and Cell Biology, Brody School of Medicine at East Carolina University, Greenville, NC 27834, USA
*To whom correspondence should be addressed. Tel: 1-252-744-3768, FAX: 1-252-744-3775, Email: leet@ecu.edu

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Summary

It is well known that exposure of normal tissue cells to ionizing radiation (IR) activates genetic cascades of signaling events, generating free radicals collectively known as reactive oxygen species (ROS), which attack DNA, ultimately leading to cell death. Due to the increased utilization of IR in human life and the growing threats of global terrorism, IR-induced normal tissue morbidities are of further importance to both civilians and military populations, since they are potentially subject to accidental or intentional nuclear mishaps. Hence, the development of efficacious radioprotector would be a contribution to radiation oncology, public health, national defense, and environmental remediation,

The term "radioprotector" primarily refers to free radical scavengers that avert the initial radiochemical events in cells following IR exposure. Currently, the majority of potential radioprotective chemical compounds under investigation are designed to scavenge IR-induced free radicals. Nevertheless, their efficacy is linked to high-drug dosages that will evoke unacceptable side effects, and none of these agents is available for human use outside the clinic. Thus, the search for less- or nontoxic agents to counter the effects of IR remains an area of intense focus. Natural products such as herbal medicines with an abundance of antioxidant resources have received attention as possible radiation modifiers. Herbal medicine, or phytomedicine, is generally considered a well-established form of complementary medicine. **Ginseng** is one of the most frequently purchased herbs in the US marketplace and is frequently taken orally as a traditional herbal medicine. The term **ginseng** refers to the dried root of several species in the plant genus Panax, which belongs to the Araliaceae family; it comprises two commonly used ginseng species, i.e., Panax ginseng C.A. Meyer (Asian ginseng) and Panax quinquefolius L. (**North American ginseng**). These two forms of **ginseng** have drawn worldwide attention for their broad medicinal potential, such as antiaging, antidiabetic, anticarcinogenic, antihypertension, antipyretic, antistress, analgesic, and antifatigue effects, as well as their enhancement of immune response to polyclonal stimulation and promotion of DNA, RNA, and protein synthesis. Recently, in a 18.8 years cohort study based on 6282 human subjects, Yi et al found that ginseng intake significantly decreased all-cause martality in older Korean males. The predominant bioactive components of **ginseng** are a diverse group of triterpenoid saponins with steroidal structures, labeled ginsenosides. Although the mechanisms are still largely unknown, the medicinal properties of **ginseng** have been closely related to the effects of ginsenosides against free radical attack.

After the exposure of mammalian cells to ionizing radiation (IR), an unregulated production of ROS, associated with a shift in the intracellular oxidant-antioxidant balance towards a pro-oxidant state, triggers damage to cellular membranes and DNA, leading to a state of oxidative stress. However, because effective antioxidants are free radical scavengers that interfere with radical chain reactions, it is possible to protect cellular DNA from oxidative stress by supplementation with antioxidants.

Studies of the radioprotective effect of **ginseng** have been performed primarily with the application of Asian **ginseng** in rodent models. Micronuclei (MN) in interphase mammalian cells are reliable biomarkers for evaluating IR-induced chromosome damage. We recently found that incubation with Asian **ginseng** dried root crude water extract 24 h before 137Cs exposure significantly reduced radiation-induced (MN) yield in peripheral blood lymphocytes (PBL) obtained from four human subjects. However, although **North American ginseng** (NAG) is one of the best-selling herbs on the market, relative few studies have involved NAG. The purpose of this study was to investigate whether radioprotective effect of a standardized **North American ginseng** extract (NAGE) could also be achieved in human PBL when applied postradiation. The hypotheses behind this study are (1) that IR-induced oxidative injury in PBL is preventable by the administration of exogenous antioxidants; and (2) that the radioprotective effect of NAGE on human PBL is a result of modulation of the activity of the intracellular antioxidant defense systems. To test these hypotheses, we investigated the impact of NAGE when applied 90 min after 137Cs exposure on MN yield in PBL obtained from 40 healthy individuals. The MN results in PBL obtained from NAGE application were compared with similar experiments using WR-1065, the biologically active aminothiol form of amifostine (WR-2721), which is currently the only "gold standard " of radioprotectors approved by the US Food and Drug Administration. In addition, in ten of these individuals, we also evaluated the correlation between the effect of NAGE on intracellular total antioxidant capacity (TAC), levels of ROS production, and MN yield in PBL before and after 137Cs exposure. Although preliminary, we believe that the information generated from these in vitro studies will provide the foundation for in vivo trials to assess the potential of NAGE as a natural dietary radiation countermeasure.