Botanical Medicines and Ionizing Radiation

Part I—Radioprotective Herbs

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Abstract

Many medicinal herbs have been assessed for their ability to protect the body against the harmful effects of ionizing radiation. These herbs may be useful both in people exposed to unexpected radiation (e.g., nuclear accidents) or those intentionally exposed to it (e.g., medical imaging). There is little direct human study of radioprotection because of the ethical problems involved in doing controlled trials in this area of research. Mechanisms of protection are multiple but largely focused on redox modulation.

Several members of the Lamiaceae (mint) family have been studied for the effects of their redox-modulating* compounds—such as studies involving occupational radiation exposure in humans—including *Melissa officinalis* (lemonbalm), *Mentha arvensis* (field mint), and *Mentha* x *piperita* (peppermint). Other herbs of interest include *Panax ginseng* (Asian ginseng), *Panax quinquefolius.* (American ginseng), *Angelica sinensis* (dang gui, dong quai), *Eleutherococcus senticosus* (eleuthero), *Aloe vera* (aloe), *Hippophaë rhamnoides* (sea buckthorn), and *Podophyllum hexandrum* (Himalayan mayapple).

Introduction

With the recent disaster in Fukushima, Japan, awareness of the hazards of ionizing radiation have risen. While the damage to the nuclear reactors in Japan from the earthquake and tsunami and resulting radiation leaks have posed a health threat, focusing only on this overlooks a much more prevalent form of serious ionizing radiation exposure: medical imaging. A single computed tomography (CT) scan of the abdomen exposes patients to ~10 mGy of radiation (not all machines are identical).[1] Survivors of the Hiroshima and Nagasaki nuclear bomb detonations are considered to have had low doses at ranges of 5–99 mGy, and high-dose exposures were 100 mGy and above.[2]

Background radiation from natural sources is estimated to be 1–3 mGy/year. See Table 1 for more comparisons. Doses above 5 mGy in the survivors of Hiroshima and Nagasaki are associated with dramatically increased rates of cancer (compared with Japanese people not exposed to atomic bomb radiation), particularly leukemia.[3,4] Because the incidence of multiple CT scans is rising rapidly, more and more people are being exposed to higher and higher levels of lifetime ionizing radiation.[5]

Ionizing radiation has many negative impacts on the body, some of which are cumulative. The increase in cancer risk is well-documented, though, at low-doses, this radiation is more controversial and often inappropriately assumed to have a linear relationship with high-dose exposures.[6] Indirect and lasting effects may occur as a result of induction of genomic and chromosomal instability (clastogenic effects), inflammatory reactions, bystander effects (irradiated cells or plasma traveling in the body damaging other tissues), and transgenerational effects.[7] These results contradict the formerly prevalent belief that ionizing radiation's effects are mediated entirely through damage to structures in cell nuclei.

Research on radioprotective herbs in humans is somewhat restricted by the ethical block against intentionally exposing people to ionizing radiation solely for research purposes. Nevertheless, many occupations involve ionizing radiation exposure. Victims of nuclear accidents, and patients undergoing multiple or high-dose diagnostic procedures involving radiation are potentially appropriate research subjects. A more-controversial area is patients with cancer who are undergoing radiation therapy, given the concern that radioprotective herbs might interfere with the therapy. This is addressed separately below, and herbs that might potentiate the benefits of radiation therapy are also discussed.

*We have moved away from the term antioxidant, because this implies all oxidation is bad or harmful, and that plants act to stop all oxidation. Of course, many healthy biologic processes involve oxidation, and plants do not generally interfere with these processes; instead plants are used to address only harmful oxidative processes. In addition, natural products can, under the right circumstances, act as reducing agents. Thus, the term redox modulator is more correct.

DOI: 10.1089/act.2011.17609 • MARY ANN LIEBERT, INC. • VOL. 17 NO. 6 DECEMBER 2011

Units of Measure of Ionizing Radiation

The modern units of measure of radiation exposure are the Gray (Gy) and Sievert (Sv), which are for clinical approximations functionally equivalent. Older units that are being replaced are:

- *Roentgen (R)*—energy of gamma radiation in one cc of air
- *Radiation absorbed dose (rad)*—amount of energy absorbed by various types of materials; 1 R gamma radiation approximates 1 rad absorbed dose; 1 Gy = 100 rad (and thus mGy is the unit most relevant for discussions of human exposure)
- *Roentgen equivalent man (rem)*—biological effect of a dose of radiation; for γ and β radiation, 1 rad exposure gives 1 rem dose. 1 Sv = 100 rem (and thus, again, mSv are most discussed in human exposures)
- *Becquerel*—the modern unit for measuring radioactive decay and total radioactivity, irrespective of dose exposure.

Radioprotective Mints

Members of the Lamiaceae or mint family of plants are well-known for containing substantial quantities of redox-modulating compounds. These have the potential for decreasing the damage done by ionizing radiation. Animal and now human studies support that mints of various sorts are radioprotective. Besides redox- and inflammation-modulating actions, mints may work by stimulating DNA repair mechanisms.[8]

Melissa officinalis (lemonbalm) leaf is a pleasant-tasting herb that is much revered as a carminative, nervine, and antiherpetic, and is used to calm an overactive thyroid. Flavonoids in this plant have previously been shown to be redox-modulating.[9] In an open human trial, staff at a radiology clinic with chronic low-dose radiation exposure drank 1.5 g of lemonbalm leaf tea in a 100 mL infusion, twice daily, for 30 days.[10] Levels of various indicators of excessive oxidative stress fell in these subjects, as did markers of DNA damage in the subjects' blood. Routine use of lemonbalm might be indicated in people who have chronic radiation exposure. This study should be replicated in a controlled fashion and in populations with higher levels of unavoidable radiation exposure.

Mentha arvensis (field mint) is a common, weedy mint of Eurasia. At a 10-mg/kg dose, a chloroform extract of field mint leaf was found to protect mice from very high–to-lethal doses of ionizing radiation.[11] Acute radiation sickness symptoms and mortality were significantly reduced by the field mint at this dose. The oil and aqueous extract of *Mentha* x *piperita* (peppermint) also protect mice against radiation sickness and mortality, both by protecting gastrointestinal epithelium and bone marrow.[12–14] Peppermint tea has also been shown to protect spermatogenesis in mice exposed to ionizing radiation.[15] No human studies were located on peppermint or field mint and radiation protection.

Lemonbalm, field mint, and peppermint are all abundant, readily cultivated, safe, flavorful, and inexpensive. If they continue to prove to be effective for protection from radiation, they would represent an important advance in radiation-protection. Given their safety and low cost, there is little reason not to try using them in people exposed to nuclear accidents or occupational ionizing radiation.

Adaptogens

Adaptogens are herbs with multiple effects throughout the body, compensating for harmful effects of stressors of all kinds, including ionizing radiation.[16] *Panax ginseng* (Asian

Table 1. Comparative Approximate Doses of Ionizing Radiation

Source	Amounts
Dental plain film	~ 0.005 mGy
Chest plain film (posterior–anterior)	~ 0.01 mGy
Mammogram, screening	~ 3 mGy
Bone scan	~ 3.5 mGy
Annual background radiation	1–3 mGy
Iitate village, 20 miles NW of Fukushima reactor	2–20 mGy/d (on land), 210–4,600 mGy/d (in the water)
Hiroshima/Nagasaki bomb survivor, low-dose	5–99 mGy
Hiroshima/Nagasaki bomb survivor, high-dose	100+ mGy
Abdominal CT scan	~ 10 mGy
Official UN "low dose" radiation threshold	< 200 mGy
LD_{50} for humans (expected)	5 Gy

Source: United Nations Information Service. UNSCEAR Summary Report of Low Doses of Radiation. May 23, 2011. Online document at: www.unis.unvienna.org/unis/pressrels/2011/unisinf416.html Accessed October 5, 2011.

NW, northwest, CT, computed tomography, UN, United Nations, LD_{50}, half of lethal dose.

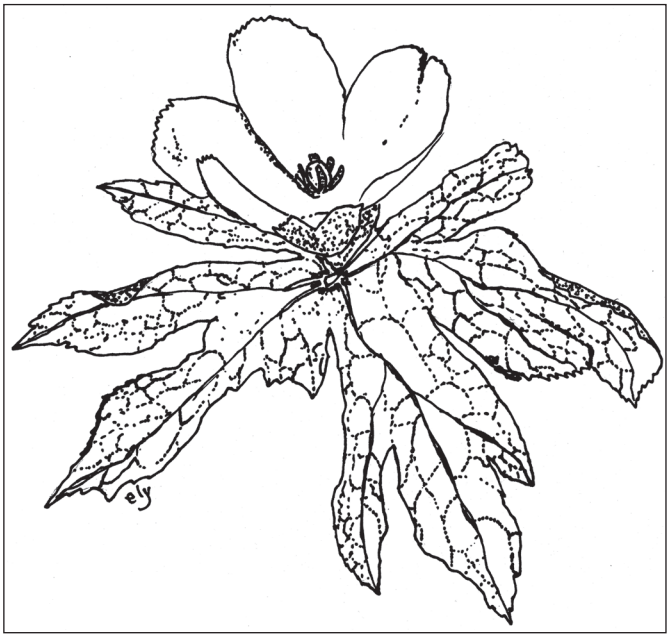
ginseng) root is one of the most revered herbs in Asian traditional medicine, where the herb is known as a *qi* tonic, but, in the West, it is considered a quintessential adaptogen and radioprotective agent.[17,18] In one clinical trial in China, patients with nasopharyngeal carcinoma were all treated with radiation therapy and half of the subjects were also given injections of Asian ginseng polysaccharides.[19] The two groups had similar, excellent survival rates at 1 year (100% in the combined-treatment group, 96.6% in the radiation-only group), though natural-killer (NK) cell activity rates were significantly higher in the ginseng-treated group. The full report was not available in English to determine if the toxicity of radiation was lower in the ginseng group. One trial in Korea found that adverse effects of radiation therapy for cervical cancer were reduced, particularly bone-marrow function, after treatment with a partially purified extract of Asian ginseng.[20]

A relatively large body of in vitro and animal research supports the radioprotective effects of Asian ginseng.[21] An aqueous extract has been shown specifically to decrease hair loss after radiation exposure in mice and to speed its return if lost.[22] Although saponin glycosides (ginsenosides) in Asian ginseng are frequently considered the major active compounds in this plant, its polysaccharides are just as important if not more so.

Adverse effects of radiation therapy for cancer were reduced after treatment with a partially purified extract of Asian ginseng.

They protect the small intestines from radiation damage in mice.[23] Bone marrow is also protected from ionizing radiation by ginseng polysaccharides in vitro.[24] They protect mice from the overall lethality of radiation.[25] *Panax quinquefolius* (American ginseng) root has also been shown to have experimental radioprotective effects.[26]

Angelica sinensis (dang gui, dong quai) root is less-often recognized as an adaptogen, though clinically and experimentally it shares many properties with this class of agents. In a study similar to the trial conducted with Asian ginseng in nasopharyngeal carcinoma cited above, a combination of dang gui and toad skin (containing antineoplastic glycosides) was shown to improve the efficacy of radiation while offsetting its immunotoxicity.[27] Prior studies confirm the radioprotective effect of dang gui and its polysaccharides in various experimental models.[28–30] An herbal formula combining dang gui with another established adaptogen, *Astragalus membranaceus* (astragalus) root, along with some other herbs has been shown to promote recovery of bone marrow in irradiated mice.[31] The combination of dang gui and astragalus has previously been shown to stimulate bone marrow in other mouse models not involving radiation.[32]



Podophyllum hexandrum (Himalayan mayapple).
Drawing © 2011 by Eric Yarnell, ND.

Eleutherococcus senticosus (eleuthero) root is another well-established adaptogen found across Siberia and northern China. It was mildly radioprotective in one in vitro model; Asian ginseng was more active in this assay.[33] Mice exposed to radiation appeared to have less bone-marrow suppression when they were pretreated with eleuthero.[34] In one randomized trial in patients with breast cancer who were undergoing chemo- and radiotherapy, eleuthero apparently reduced immunotoxicity in a treatment group of subjects, compared to what occurred in controls.[35] The study, available only in Russian, could not be analyzed in depth. This and the other studies cited above provide better human-based evidence for the potential to use radioprotective agents in patients exposed to iatrogenic radiation.

Aloe and Radiation Dermatitis

Aloe spp. (aloe) is native to Africa but is extensively cultivated in many other parts of the world because of this herb's medicinal benefits. Aloe gel contains polysaccharides with immunomodulating and vulnerary properties. Much work has gone into assessing whether aloe can prevent dermatitis induced by radiation therapy for cancer. Trials have largely failed to support the efficacy of aloe in various types of patients with different degrees of radiation dermatitis; however, there has been poor reporting on the exact products used, making comparison difficult.

One double-blinded randomized trial of 194 women with breast cancer found that aloe gel was no better than placebo for preventing radiation-induced dermatitis.[36] An aqueous cream was superior to aloe gel for treatment of radiation-induced dermatitis in patients who had received breast radiation in a different randomized clinical trial.[37] Another trial involving 172 women with

breast cancer compared aloe gel or petroleum jelly with the product Biafine, and found they were equally effective for preventing radiation-induced dermatitis.[38] A phospholipid cream was superior to aloe gel at preventing radiation-induced dermatitis in 45 children undergoing radiation therapy in another double-blinded randomized trial.[39] At this point, there is little indication for using aloe gel to prevent or treat radiation-induced dermatitis.

However, systemic aloe gel may still be relevant, based on studies in rodents. These have shown that aloe gel ingestion reduces oxidation caused by ionizing radiation while delaying and reducing severity of radiation sickness.[40,41] Further research is warranted.

Sea Buckthorn to the Rescue

Hippophaë rhamnoides (sea buckthorn) is a dioecious, nitrogen-fixing shrub native to a wide area of Eurasia. The fruit contains flavonoids and seeds that are rich in a beneficial oil. An extract of the fruit has been shown to protect cells from ionizing radiation in vitro.[42] This appears to be partially the result of stabilization of chromatin, redox modulation, and topoisomerase I inhibition.[43,44]

Intraperitoneal administration of this extract to mice exposed to lethal doses of radiation at a 30-mg/kg dose led to an 82% survival rate, compared with 0% survival in untreated controls.[45] Clearly, injection of sea buckthorn into the peritoneum is not suitable for human application, but this brutal experimental method provided support for the concept of sea buckthorn as a radioprotective agent. Protection of spermatogenesis and immune function have also been reported in irradiated mice pretreated with sea buckthorn fruit.[46,47]

No human research was identified on sea buckthorn and ionizing radiation. Flavonoids from this medicine are definitely absorbed by humans and are enhanced by combination with sea buckthorn oil.[48] This safe medicinal food should be considered as part of a radioprotective diet for patients with ongoing occupational or iatrogenic exposures and in patients who are exposed unintentionally to large doses of ionizing radiation.

A Surprise from the Himalayas

Podophyllum hexandrum = *P. emodi* (Himalayan mayapple) is known as bantrapushi or giriparpat in Hindi. It grows in the foothills of the Himalayas. Its roots are most well-known as a source of the cathartic laxative and anticancer podophyllotoxins originally identified in its more famous cousin *P. peltatum* (American mayapple). However, numerous studies have shown that this plant is also radioprotective. Rodents exposed to normally lethal doses of ionizing

Table 2. Miscellaneous Effective Redox-Modulating Herbs for Protecting Mice from γ-Radiation

Herbs, common names, and parts used	References & dates
Aegle marmelos (bael) fruit	Baliga, et al., 2010[a]
Brassica rapa (field mustard) leaf	Tiku, et al., 2008[b]
Camellia sinensis (green tea) leaf	Guo, et al., 2010[c]
Centella asiatica (gotu kola) whole plant	Joy & Nair, 2009[d]
Curcuma longa (turmeric) rhizome; curcumin*	Akpolat, et al. 2009[e] Dange, et al. 2007[f]
Echinacea purpurea herb	Abouelella, et al. 2007[g]
Phyllanthus emblica (amla), *Terminalia bellirica* (beleric myrobalan), and *Terminalia chebula* (chebulic myrobalan) fruits (*Triphala*, "three fruits" formula)	Jagetia, et al., 2002[h]
Phyllanthus emblica (amla) fruit	Singh, et al., 2005[i]
Prunus avium (sweet cherry) fruit	Sisodia, et al. 2009[j]
Rhus coriaria (sumach) leaf	Chakraborty, et al. 2009[k]
Zingiber officinale (ginger) rhizome	Jagetia, et al. 2003[l]

*As will be addressed in Part II of this series, curcumin can also act as a radiosensitizer.

[a]Baliga MS, Bhat HP, Pereira MM, et al. Radioprotective effects of *Aegle marmelos* (L) Correa (Bael): A concise review. J Altern Complement Med 2010;16:1109–1116; [b]Tiku AB, Abraham SK, Kale RK. Protective effect of the cruciferous vegetable mustard leaf (*Brassica campestris*) against in vivo chromosomal damage and oxidative stress induced by gamma-radiation and genotoxic chemicals. Environ Mol Mutagen 2008;49:335–342; [c]Guo S, Hu Y, Liu P, et al. Protective activity of different concentration of tea polyphenols and its major compound EGCG against whole body irradiation-induced injury in mice [in Chinese]. Zhongguo Zhong Yao Za Zhi 2010;35:1328–1331; [d]Joy J, Nair CK. Protection of DNA and membranes from gamma–radiation induced damages by *Centella asiatica*. J Pharm Pharmacol 2009;61:941–947; [e]Akpolat M, Kanter M, Uzal MC. Protective effects of curcumin against gamma radiation–induced ileal mucosal damage. Arch Toxicol 2009;83:609–617; [f]Dange P, Sarma H, Pandey BN, Mishra KP. Radiation-induced incidence of thymic lymphoma in mice and its prevention by antioxidants. J Environ Pathol Toxicol Oncol 2007;26:273–279; [g]Abouelella AM, Shahein YE, Tawfik SS, Zahran AM. Phytotherapeutic effects of *Echinacea purpurea* in gamma-irradiated mice. J Vet Sci 2007;8:341–351; [h]Jagetia GC, Baliga MS, Malagi KJ, et al. The evaluation of the radioprotective effect of *Triphala* (an Ayurvedic rejuvenating drug) in the mice exposed to gamma-radiation. Phytomedicine 2002;9:99–108; [i]Singh I, Sharma A, Nunia V, Goyal PK. Radioprotection of Swiss albino mice by *Emblica officinalis*. Phytother Res 2005;19:444–446; [j]Sisodia R, Sharma K, Singh S. Acute toxicity effects of *Prunus avium* fruit extract and selection of optimum dose against radiation exposure. J Environ Pathol Toxicol Oncol 2009;28:303–309; [k]Chakraborty A, Ferk F, Simic T, et al. DNA-protective effects of sumach (*Rhus coriaria* L), a common spice: Results of human and animal studies. Mutat Res 2009;661(1–2):10–17; [l]Jagetia GC, Baliga MS, Venkatesh P, Ulloor JN. Influence of ginger rhizome (*Zingiber officinale* Rosc) on survival, glutathione and lipid peroxidation in mice after whole-body exposure to gamma radiation. Radiat Res 2003;160:584–592.

radiation had much higher (48%) survival rates, which were increased a little further (to 55%) with the addition of the herb *Picrorhiza kurroa* (kutki).[49] These results were repeated in further studies that also found that reduction in podophyllotoxin levels improved the safety of the extract without reducing its efficacy.[50]

Himalayan mayapple appears to be radioprotective, in part and, as usual, because of redox modulation.[51] However, in this study this herb also inhibited immunosuppression in irradiated mice. Presence of p53, a protein commonly mutated in carcinogenesis, enhances the radioprotective properties of Himalayan mayapple.[52] No human research was located on Himalayan mayapple for radioprotection.

Conclusion

Herbal medicines offer great promise as protective agents against ionizing radiation's adverse effects. Ample in vitro and animal studies support that a range of herbs may be protective. Some of these studies have been followed with human research that seems to, at least in part, agree with the preclinical research. Optimal doses, dose forms, and timing of dosing related to ionizing radiation exposure remain unknown.

It is recommended that patients who have been or expect to be exposed to ionizing radiation should be treated with at least one redox-modulating herb and an adaptogen. It is possible redox modulators may interfere with the benefits of radiation therapy for cancer, though this remains highly controversial. The issue of radiation sensitizers (herbs that augment the benefits of radiation therapy while offsetting its toxicity) will be discussed in a future article in more depth. ■

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