SELENIUM
This Versatile Mineral Bolsters Antioxidant Defenses and Immune Health, and May Help to Prevent Cancer

By Ben Best

Named for the moon goddess Selene, the mineral selenium deserves to be treated with reverence. Perhaps no other mineral can match selenium’s versatility and wide array of health benefits. Selenium is crucial for antioxidant defenses, boosts the immune system, and helps prevent cancer in several distinct ways.

Bolstering Antioxidant Defenses

After antioxidants such as coenzyme Q10 and vitamins E and C neutralize free radicals, they must be regenerated to remain effective as antioxidants. They can be regenerated by the antioxidant peptides glutathione and thioredoxin, which themselves have antioxidant enzymes to regenerate them. Two of these regenerating enzymes are glutathione peroxidase and thioredoxin reductase, both of which contain selenium and depend on selenium activity for their antioxidant functionality. Both the glutathione and thioredoxin systems enhance their own antioxidant activity by inducing the production of other natural antioxidant enzymes, including superoxide dismutase.

In 1989, the United States National Research Council established a recommended dietary allowance (RDA) for selenium based on maximization of plasma glutathione peroxidase activity. Making conservative allowances for body weight and safety, the Council set the RDAs for selenium at 70 mcg per day for adult men and 55 mcg per day for adult women. Despite many discoveries and much research since 1989, the official guidelines for recommended selenium intake have seen little change.

Protecting Against Cancer

In 1996, the Journal of the American Medical Association published the results of a multicenter, randomized, double-blind, placebo-controlled cancer-prevention trial. The 1,312 study participants took either 200 mcg of selenium a day or placebo over a mean period of four and a half years. Subjects who supplemented with selenium had a 37% decrease in total cancer incidence, as well as a 58% reduction in prostate cancer, a 54% reduction in colorectal cancer, and a 30% reduction in lung cancer. This study is a powerful refutation of the contention that dietary supplements offer no measurable health benefit. (After extensive scrutiny of the data, only the evidence for reduction in prostate cancer is now accepted as statistically
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significant (a 52% reduction). The data still show a total cancer mortality reduction of 41%. Selenium has many diverse anticancer benefits, with effects on oxidative stress, DNA methylation and repair, inflammation, cell apoptosis and proliferation, carcinogen detoxification, hormone production, angiogenesis, and immune function.

Cancer sometimes begins with DNA mutation. DNA is normally protected from cancer-causing substances by methyl groups, but selenium deficiency (like folic acid deficiency) can result in decreased DNA methylation and therefore increased DNA damage and mutation. Selenium also promotes the activity of the p53 protein, often called "the guardian of the genome." Well over half of all cancers exhibit evidence of defective p53 protein. When DNA is damaged, p53 either stimulates DNA repair or causes cells to self-destruct (apoptosis) if the DNA damage is irreparable. The thioredoxin reductase system promotes p53 induction of DNA repair enzymes. Cells exposed to selenomethionine have shown a threefold increase in p53 activity.

Healthy wound healing involves a well-coordinated immune/inflammatory response. Neutrophil and macrophage immune system cells enter the wound and fight bacteria by creating toxic free radicals such as hydrogen peroxide, peroxynitrite, and the hydroxyl radical. Antioxidant enzymes like selenium-containing glutathione peroxidase and thioredoxin reductase protect neutrophils, macrophages, and other tissues from the free radicals that are created to destroy pathogens. Macrophages release growth factors to promote tissue re-growth.

With chronic inflammation, however, these natural mechanisms run amok in cycles of tissue regeneration and destruction, creating an environment conducive to cancer development. Continuous exposure to free radicals such as peroxynitrite leads to DNA mutation. Growth factors from macrophages promote proliferation of new cancer cells. An estimated 15% of cancers are attributed to inflammation associated with chronic infections, such as hepatitis, papillomavirus, and the gastric bacterium Helicobacter pylori. Non-infectious causes of chronic inflammation such as tobacco smoke and asbestos also contribute significantly to cancer.

Selenium compounds have been shown to block substances inducing DNA expression of genes that can worsen the inflammatory response. Selenium compounds are likewise very effective in protecting cells from peroxynitrite-induced DNA damage.

Strengthening Immune Response

AIDS patients who are selenium deficient are nearly 20 times more likely to die from HIV-related causes than patients with adequate selenium. Selenium deficiency increases the virulence of viral infection by causing a more pro-inflammatory immune response. Neutrophils with reduced glutathione peroxidase due to selenium deficiency are less able to defend themselves against the free radicals they release on to pathogens.

An experiment with aged mice showed that supplementation with above-normal levels of selenium could restore immune cell multiplication caused by antigens to the levels seen in young adult mice. Previously, the same researchers had shown that increasing selenium above normal levels in young adult mice increased the bacteria-killing activity of spleen lymphocytes by 22.3%. Humans who supplemented with 200 mcg per day of selenium for eight weeks showed a 118% increase in lymphocyte-mediated tumor cytotoxicity and an 82% increase in natural killer-cell activity.
The selenium-containing iodothyronine deiodinase enzyme converts thyroid hormone from its inactive (T4) form to its active (T3) form. Thyroid problems have been linked to selenium deficiency. T3 normally controls the rate of metabolism and the activity of many other hormones. Although most T3 production occurs in the liver, the thymus gland (which produces T-cells) has a local form of iodothyronine deiodinase, which indicates selenium's importance for the development and function of thymic cells.

The major non-cardiac cause of death in American hospitals is sepsis due to infection, resulting in more than 100,000 deaths per year in the US. Two thirds of those cases occur in patients who have been hospitalized for other conditions. Selenium not only protects against sepsis by boosting the immune system, but also acts directly against bacterial lipopolysaccharide, a large molecule that contributes significantly to death due to bacterial toxins. Elderly people worried about the risk of hospital infections should also consider selenium supplementation as part of their protection against influenza.

Effects on Aging and Disease

Natural selenium-containing antioxidant enzymes such as glutathione peroxidase and thioredoxin reductase have the potential to reduce the effects of free radicals on the aging process. Sulfur atoms in amino acids can cross-link proteins, decreasing enzyme function and increasing the toughness of aging collagen. Thioredoxin reductase is particularly effective in reducing bonds between sulfur atoms.

Methionine sulfoxide reductase is an unusual enzyme that directly repairs oxidative damage to the methionine residues in proteins. There are two forms of methionine sulfoxide reductase, one of which contains selenium at its active site. Both forms depend on the thioredoxin system for regeneration. Selenium deficiency has been shown to increase protein oxidation in mice. Transgenic fruit flies that over-express methionine sulfoxide reductase have shown a 70% increase in life span.

Selenium deficiency can contribute to osteoarthritis, cardiovascular disease, and infertility. Selenium protects against toxic metals such as mercury and arsenic. Selenium deficiency also can lead to epileptic seizures and may even contribute to Parkinson's disease. Thioredoxin is particularly protective against ischemia-reperfusion injury in the brain.

Dietary Sources and Safety

Dietary selenium is primarily inorganic selenite or organic selenomethionine. Dietary selenite is more than 80% bioavailable, while dietary selenomethionine is more than 90% bioavailable. Selenomethionine is the major seleno-compound in cereal grains, legumes, soybeans, and yeast. Brazil nuts may be the richest food source of selenium, and meats and fish are also good sources. The amount of selenium in fruits and vegetables is typically low, though garlic, onions, leeks, and broccoli florets are sources of the selenium-containing compound Se-methylselenocysteine.

Selenium has greater capacity than selenomethionine to cause DNA damage, but is more effective in preventing cancer. Se-methylselenocysteine, however, not only has less capacity for toxicity, but also may be the most effective of the selenium compounds for cancer prevention. All selenium compounds must be metabolized in the body to selenocysteine before they are incorporated in selenoproteins (including selenium-containing enzymes).

The selenium content of foods depends greatly on the selenium content of the soil in which they are grown.
grovm. The Great Plains of the US and Canada are rich sources of selenium, whereas the soils of the northeast, northwest, and Florida have lower selenium content. The selenium content of soil in Europe and the selenium blood levels of Europeans are generally much lower than in North America. Selenium is particularly low in the soils of Finland, New Zealand, and central parts of China.

Selenium can be dangerously toxic in higher doses, so a "more is better" attitude is especially hazardous with this mineral. Selenium poisoning is associated with liver cirrhosis, neurological damage, and skin lesions. A 1989 study in China estimated 800 mcg per day to be the safe upper limit and reduced that amount to 400 mcg per day to ensure a large margin of safety. This recommendation was adopted by the World Health Organization. People who take multiple supplements should pay careful attention to ensuring that their total selenium intake does not exceed 400 mcg per day.

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