

## Selenium and human health

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### Abstract

*Selenium is of fundamental importance to human health. It is an essential component of several major metabolic pathways, including thyroid hormone metabolism, antioxidant defence systems, and immune function. The decline in blood selenium concentration has several potential public health implications, particularly in relation to the chronic disease such as cancer and cardiovascular disease. Selenium is incorporated as selenocysteine at the active site of a wide range of selenoproteins. The four glutathione peroxidase enzymes (classical GPx1, gastrointestinal GPx2, plasma GPx3, phospholipids hydro peroxide GPx4) which represent a major class of functionally important selenoproteins, were the first to be characterised. Thioredoxin reductase (TR) is a recently identified seleno-cysteine containing enzyme which catalyzes the NADPH dependent reduction of thioredoxin and therefore plays a regulatory role in its metabolic activity. Selenium is present in soil and enters the food chain through plants. We obtain most of our dietary Se from bread, cereal, meat and poultry.*

### Introduction

Selenium was identified as essential to human nutrition 42 years ago (1). The importance of selenium in human nutrition was documented in 1979 when Chinese scientists reported that selenium supplementation prevented the development of a cardiomyopathy (2).

### Selenoproteins

Selenium is an essential micronutrient of major metabolic significance. It is incorporated as selenocysteine at the active site of a wide range of proteins(1), Selenoproteins with known functions play a critical role in a variety of biological processes, and several of them are involved in antioxidant defense(3).

- Selenoprotein P has been associated with the oxidant defense properties of selenium. Selenoprotein P is an extracellular glycoprotein found in plasma and also associated with endothelial cells. One function of selenoprotein P is to supply selenium to the brain to maintain normal neurologic function and to the testis for spermatogenesis (2).
- The selenoenzymes that are found to have strong antioxidant activity include six groups of the GPx (catabolize hydroperoxides) that play a significant role in protecting cells against oxidative damage from reactive oxygen species (ROS) and reactive nitrogen species (RNS). The other essential antioxidant selenoenzymes are the TrxR where they use thioredoxin (Trx) as a substrate to maintain a Trx/TrxR system in a reduced state for removal of harmful hydrogen peroxide . Increasing evidence suggests that selenoprotein P may also play a significant role in antioxidant defense system in preventing attack from harmful ROS and RNS (4).

- **Selenoprotein W**

This selenoprotein was originally identified in muscle and was postulated to play a role in the development of white muscle disease(2). In animal studies, Se intake effects tissue concentrations of selenoprotein W which is reported to be necessary for muscle metabolism(1).

- **Selenophosphate Synthetase**

Two selenophosphate synthetases have been identified in animals. One contains a selenocysteine residue in its primary structure, and the other contains a cysteine residue at the same position (2).

The iodothyronine deiodinases (I to III) have all been shown to be selenoproteins. These enzymes catalyze the deiodination of thyroxine, triiodothyronine, and reverse triiodothyronine and thereby regulate the concentration of the active hormone triiodothyronine(2)

### **Selenium and human health:**

- **Cancer prevention**

Even though Se is reported to play a significant role in cancer development, its exact anticancer mechanism of action at molecular levels is not fully understood. However, it has been hypothesized that the most possible mechanistic action of Se as chemoprevention is its role in

the antioxidant defense systems to reduce oxidative stress and limit DNA damage(1).The protection from excess ROS involved in cancer development involves glutathione peroxidases, thioredoxin reductases and possibly other selenoproteins (e.g. SeP) containing Se in the form of selenocysteine. The effect of Se on modulating the activity of these proteins is one possible means by which Se might suppress carcinogenesis(3). Battin et al found that selenocysteine inhibited DNA damage more strongly than the selenomethionine. Other possible anticancer mechanisms of Se include the induction of apoptosis, cell-cycle arrest and DNA-repair genes, inhibition of protein kinase C activity and cell growth and effect on estrogen- and androgen-receptor expression( 4).

- **Immune function**

Dietary selenium is important for a healthy immune response. The effects of Se deficiency can include reduced T-cell counts, impaired lymphocyte proliferation and responsiveness. Thioredoxin reductase has recently been identified and purified from human T-cells, and may be important in reducing thioredoxin enhanced tumour cell growth(1). The importance of Se in improving the immune system has also a beneficial effect on the reduction of antibody load in autoimmune thyroiditis, a condition associated with euthyroidism or hypothyroidism . Selenium supplementation has resulted in the improvement of inflammatory activity in patients with autoimmune thyroiditis . Severe nutritional Se deficiency could result in an increased rate of thyroid cell necrosis and the invasion of macrophages(4).

- **heart disease**

The increased production of ROS can exert oxidative stress in the physiological system, and if excess ROS are not properly regulated they can cause damage to cellular lipids, proteins and

DNA. The damage caused by ROS has been linked to various human diseases, including heart diseases(4).

Low blood Se concentrations have been associated with increased cardiovascular disease mortality. This may be a reflection of sub-optimal GPx4 activity in the prevention of LDL oxidation, with subsequent uptake by endothelial cells and macrophages in arterial blood vessels(1).

- **Asthma**

GPx 4 may have a regulatory role in the inflammatory response through suppression of lipoxygenase catalysed leukotriene biosynthesis from arachidonic acid. Moreover, it has been hypothesised that vitamin E may have a regulatory influence over leukotriene biosynthesis as a substrate for both n-6 and n-3 unsaturated fatty acid desaturase enzymes. This indication that functional selenium and vitamin E status may influence leukotriene metabolism has important implications in relation to chronic inflammatory disease, particularly asthma which is now the most prevalent chronic inflammatory condition in childhood(1).

### **Se deficiency**

Inadequate supply of the essential trace element selenium (Se) has been associated with predisposition for, or manifestation of, various human diseases such as Keshan and Kashin-Beck disease, cancer, impaired immune function, neurodegenerative and age-related disorders and disturbances of the thyroid hormone axis. Se deficiency in combination with inadequate iodine contributes to the pathogenesis of myxedematous cretinism(5).

Kashin-Beck disease is a preadolescent or adolescent osteoarthritis. Necrotic degeneration of the chondrocytes is the most striking pathologic feature of this disease. Dwarfism and joint deformation result from these cartilage abnormalities. Aside from selenium deficiency, numerous other etiologic factors have been suggested for this condition (e.g., mycotoxins in grain, mineral imbalance, organic contaminants in drinking water). Attempts to improve the clinical condition of subjects with Kashin-Beck disease by administering selenium have not been successful, however, it is still possible that selenium deficiency permits the development of the illness(2).

### **Dietary Reference intake**

The RDA for selenium 55µg/day for women, men, and adolescents( ages14 to 18), whereas the RDAs for children range from 20 to 30 µg/day. The AIs for infants is 15 to 20 µg/day. The RDA during pregnancy is 60µg, and the RDA during lactation is 70 µg/day. Requirements for selenium may increase with a high consumption of SFAs because of the need for the antioxidant activity of selenium.

### **Food Sources of selenium**

The selenium concentration in foods depends on the selenium content of the soil and water where the food was grown. The major food source of selenium is animal flesh foods. Grains vary in selenium content, depending on where they are grown.

Selenium content and GSH-Px activity in human breast milk are influenced directly by maternal selenium intake and by the form of selenium consumed. Plasma selenium

concentrations of infants fed unsupplemented formula are lower than those of infants fed supplemented formula or human milk(6).

### **Toxicity**

Indicators of selenium toxicity have been reported in China and Australia. Signs of toxicity, referred to as selenosis, include skin and nail changes, tooth decay, and nonspecific GI and neurologic abnormalities(6).

### **References**

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