

Bioavailability of Selenium from Foods

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Selenium (Se), an essential nutrient, is needed for activity of several important proteins. Additionally, the consumption of Se in amounts that exceed the Recommended Dietary Allowance (RDA) may protect against prostate and colorectal cancer. Supplemental Se may be acquired through the diet, but Se bioavailability depends on the source. Therefore, dietary advice concerning improvement of Se intake depends on characterization of Se bioavailability from Se-containing food sources.

Key words: bioavailability, foods, human, selenium

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doi: 10.1301/nr.2006.mar.146-151

INTRODUCTION

Selenium (Se) is an essential nutrient with diverse physiologic actions that include functioning at the catalytic center of proteins,¹ enhancement of immune function,² and reduction of cancer risk.³ Se deficiency, caused by extremely low dietary intakes, results in severe disease conditions in humans (e.g., Keshan disease) and domestic livestock (e.g., white muscle disease).⁴ Se is required for the catalytic activity of selenoproteins, and many of the signs and symptoms of Se deficiency may be related to reduced selenoprotein activity. In recent years, interest in Se and nutrition has been primarily stimulated

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by reports that the consumption of Se in amounts greater than the Recommended Dietary Allowance (RDA) of 55 $\mu\text{g}/\text{d}^5$ may protect against cancer. This interest was generated by the finding that supplementation of 200 $\mu\text{g}/\text{d}$ of Se to subjects with adequate Se intake decreased total cancer incidence and mortality, and specifically decreased prostate and colorectal cancer (and marginally decreased lung cancer).³ Confirming these results is a high-priority research objective, and to this end, the Selenium and Vitamin E Cancer Prevention Trial (SELECT) has enrolled 32,400 male subjects 50 years or older in the United States, Puerto Rico, and Canada, who will be supplemented daily with a placebo or 200 μg of Se (one of several treatments) as selenomethionine (SeMet) for up to 12 years.

CHEMICAL FORMS OF SELENIUM

Se is covalently bound into multiple compounds; those of biological importance include Se salts, Se derivatives of sulfur amino acids, and methylated derivatives of selenoamino acids. The chemical form of Se partially determines Se metabolism; a simplified metabolic scheme is shown in Figure 1. Inorganic salts of Se (e.g., selenite, selenate) enter a reductive pathway and ultimately form reduced selenide. The amino acid selenomethionine (SeMet) can substitute for methionine in proteins or it can be converted to selenocysteine (SeCys), which subsequently may be cleaved to form selenide. Selenide has two potential metabolic pathways, one of which is sequential methylation and excretion in the urine as the trimethylselenonium ion. Limited evidence suggests that the monomethylated Se intermediate in the excretory pathway is a potent anticancer metabolite.⁶ The other pathway results in the formation of selenoproteins. In this pathway, the selenide may condense with serine bound to tRNA, forming a tRNA^{SeCys} complex that is inserted into selenoproteins by the unique UGA codon sequence. The redox potential of Se allows it to function at the active site of more than a dozen selenoproteins. Thus, ingested Se has three potential fates: 1) in the form of SeMet it may insert into general proteins as a substitute for methionine, an amino acid; 2) in salt form it may be reduced to the selenide and then inserted into

8; eggs: approximately 4; and chemically pure forms of Se: approximately 13. A summary of selected reports is given in Table 1.

Overall, absorption of all forms of Se is relatively high (70% to 95%), but varies according to the source and the Se status of the subject. Wheat and meats (excluding fish) are the dietary sources of Se considered to be the most important.¹¹ Se tends to be present in relatively high concentrations and, compared with Se salts, Se in these foods is highly bioavailable.¹² Fish is unusual in that the Se content is relatively high, but some have reported the bioavailability to be low, especially compared with wheat.¹³

Selenized yeast has been the primary form of Se available for use as a dietary supplement. Reports of the bioavailability of Se from yeast are mixed; one group reported that Se from yeast was effective for increasing the concentration of Se in red blood cells, but compared with selenite and selenate, was ineffective for increasing GPx activity.¹⁴ However, another group reported Se from yeast was almost twice as bioavailable as Se from selenite and selenate for restoration of depleted GPx activity.¹⁵ These discrepancies may reflect differences in the study populations as well as a difference in the chemical speciation of Se in yeast. Some have reported Se in yeast to be primarily (>70%) SeMet,¹⁶ whereas at least one report found less than 30% of the Se as SeMet.¹⁷

Studies of the bioavailability of selenized vegetables provide an example of another complication in determining Se bioavailability: laboratory methods to determine bioavailability may not assess some of the other important physiologic actions of Se. While restoration of tissue Se concentrations or GPx activities in Se-depleted humans or animals is a common measure of bioavailability, it may give no indication of the anti-carcinogenic potential of Se. However, reduction of cancer is one of the primary reasons people seek to increase their Se intake. Se from selenized garlic^{18,19} or broccoli²⁰ has been found to be equally or less bioavailable than Se from selenite and selenate when bioavailability was based on repletion of tissue Se concentrations or GPx activity, but were superior to selenite or selenate alone for the reduction of colon²¹ or mammary cancer.²²

Some researchers suggest that it is Se in the excretory pathway, and not in the selenoprotein pathway, that is most active for reducing cancer.²³ Thus, the bioavailability of Se must be discussed within the context of the desired physiologic activity. If repletion of GPx activity is the desired physiologic outcome, then foods that contain salts of Se, SeCys, or SeMet (e.g., wheat²⁴ and meat⁸) are the most effective. However, if the person is already in adequate Se status and desires to consume "supranutritional" levels of Se for protection against

carcinogenesis, then foods containing methylated forms of Se may be best (e.g., garlic¹⁶ and broccoli²⁵).

The largest intervention that measured selenium bioavailability from foods was conducted in Finland. Because of extremely low dietary Se intakes, Finland adopted a national policy in the mid-1980s of adding Se as sodium selenate to all agricultural fertilizers.²⁶ By 1989, the supplementation regimen had increased the human dietary intake of Se by Finnish people from 20 to 30 $\mu\text{g}/\text{d}$ (in 1986) to 80 to 90 $\mu\text{g}/\text{d}$ (in 1989), with the primary increases being in wheat flour and, to a lesser extent, milk and eggs. Within 2 years of beginning fertilization, markers of Se status in Finnish people were similar to people in the United States. Arthur²⁷ reviewed the evidence for increasing the content of Se in foods by the addition of selenized fertilizer to the soil, and concluded that fertilization is safe and effective for increasing Se status in humans and animals.

Parts of the central United States and Canada have soils with high concentrations of Se, and crops grown on these soils are naturally enriched in Se. For example, the average concentration of Se in US wheat and beef is approximately 0.3 and 0.2 mg Se/kg, respectively. However, wheat produced in some areas of central South Dakota is consistently between 5 and 15 mg Se/kg, and beef from the same area can be as high as 2.5 mg Se/kg (wet weight basis).^{28,29} Work is in progress by multiple research groups to characterize the bioavailability and sensory characteristics of Se from foods with enhanced concentrations of Se.³⁰⁻³²

Recently, Fox et al.³³ used stable ⁷⁷Se and ⁸²Se to estimate Se bioavailability to men. ⁷⁷Se was intrinsically incorporated into yeast and then the labeled yeast was fed to trout. Subjects were fed a test meal of a labeled trout or yeast, and 24 h later all subjects were also given a reference dose of ⁸²Se-labeled selenate. For each subject, stable isotope retention from food sources was compared with that from selenate. Se absorption (total Se minus fecal Se) was similar for trout, salted trout, and selenate, and Se retention (total Se minus fecal and urinary Se) was approximately 20% greater for trout and salted trout than for selenate; however, Se absorption and retention from yeast was less than that from selenate.

The study by Fox et al.³³ is notable for the use of foods intrinsically labeled with stable isotopes, as well as for the double-label method that allowed each individual to serve as their own control. However, because the chemical form of Se dictates potential metabolic transformations, it must be recognized that the chemical form of Se in the trout depended on the form in the yeast, and the form in the yeast may have depended on the form that was synthesized from the isotope. Presentation of the isotope to living organisms certainly allowed the Se isotope to be transformed into naturally occurring com-

Table 1. Selected Selenium (Se) Bioavailability Studies in Humans and Rats

Food	Subjects	Method	Bioavailability	Reference
Human Studies				
Wheat, natural Se enrichment	Dutch men and women	Plasma Se	Good compared with low-Se diet	van der Torre et al., 1991 ¹²
Undefined meat	Finnish men	Platelet GPx		
Yeast, selenized		Plasma Se	Good for increasing Se, poor for increasing GPx	Alfthan et al., 1991 ¹⁴
		Platelet GPx		
All agricultural food products fertilized with selenate	Population of Finland	Blood Se and GPx	Good compared with previous low-Se status	Varo et al., 1988, ²⁶ Arthur 2003 ²⁷
Wheat, foliar application of Se	Yugoslavian men and women	Plasma Se	Good compared with low-Se diets	Djujic et al., 2000 ³¹
Fish	British men	Blood GPx		
Yeast, selenized		Retention of stable Se isotopes	Fish Se highly bioavailable, yeast less bioavailable compared with selenate	Fox et al., 2004 ³³
Animal Studies				
Tuna	Rats	Tissue Se and GPx	Tuna low compared with wheat	Alexander et al., 1983 ¹³
Wheat				
Yeast, selenized	Rats	Tissue Se and GPx	Very good compared with selenite	Yoshida et al., 1999 ¹⁵
Broccoli, selenized	Rats	Tissue Se and GPx	Poor compared with Se salts and selenomethionine	Finley, 1998 ²⁰
Garlic, selenized	Rats	Liver GPx and deiodinase	Equal to selenite	Ip and Lisk, 1993 ¹⁹
Se-enriched beef, broccoli	Rats	Retention of radioactive Se	Good for beef, poor for broccoli	Finley et al., 2004 ³⁰
Broccoli, selenized	Rats	Reduction of colon cancer	Superior to Se salts	Finley et al., 2000 ²¹
Garlic, selenized	Rats	Reduction of mammary cancer	Superior to Se salts	Ip and Lisk, 1994 ¹⁸

GPx = glutathione peroxidase.

pounds, but without direct speciation of the labeled selenocompounds in each food, it is impossible to make broad statements about bioavailability. Instead, conclusions about bioavailability are limited to the exact experimental conditions; for example, isotope converted by an identical process, yeast grown by an identical process, and trout raised by an identical process.

Se bioavailability studies must also assess whether the particular Se source is metabolically active. Fox et al.³³ concentrated on measures of absorption and retention and therefore did not have measures directly related to functionality, such as incorporation of isotopic Se into a selenoprotein. However, the Se methylation pathway may be an important marker for both potential anticancer metabolites and for Se that is not available for protein synthesis. Therefore, while an indirect assessment, appearance of isotope in the urine, is indicative of metabolic transformations, future studies would be greatly strengthened by a more direct assessment of metabolic activation.

SUMMARY

Increasing evidence of the health benefits of supplemental Se is resulting in a greater interest in Se-containing foods. However, before nutritionists can recommend a particular Se-containing food, there must be information regarding the bioavailability of Se from that food. Measures of Se bioavailability must take into account metabolic transformations, as some forms of Se may be well absorbed but not transformed into biologically active metabolites. Measures also must define the biological action that is considered to be a criterion of bioavailability, as some forms of Se may be efficacious for one action (e.g., selenoprotein synthesis) but may not be as efficacious for another action (e.g., reduction of cancer). Finally, one of the most important factors affecting bioavailability of Se from foods is the chemical speciation of the Se in the food. Thus, future Se bioavailability studies will be increasingly tied to chemical analysis of the specific forms of Se in the foods.

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