

Dietary selenium and selenized yeast

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ABSTRACT: Selenium is an essential trace element in animal nutrition. Human selenium status varies geographically and by diet. While selenium status, as determined by serum selenium levels, of most individuals may be adequate, the role of an individual's genetic makeup with respect to the ability to adequately utilize selenium at the level of the 25 individual selenoproteins is just now being studied. Data clearly show that selenized yeast is an efficient and safe form of dietary selenium. It has been shown to be easily digestible; its selenomethionine is readily incorporated into proteins where it contributes to the body's reservoir of this essential element. This review will briefly discuss the importance of dietary selenium and the role that selenized yeast can play in human nutrition.

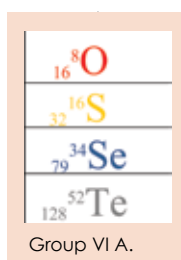
SELENIUM AND HUMAN SELENOPROTEINS

Selenium is a member of Group VIA of the Periodic Table and as such has chemistry closely resembling sulphur. Because their chemistries are so similar, plants and yeasts can substitute selenium for sulphur in the biosynthesis of methionine to produce selenomethionine, (SeMet). SeMet can be metabolized to the Se analogue of cysteine, selenocysteine (SeCys), and its metabolites. While animals can incorporate SeMet into protein, they can't incorporate SeCys. The selenide derived from dietary SeCys either enters into secretory pathways or is incorporated into an estimated 25 selenoproteins via a novel co-translational process. Research over the last 20 years has shown that SeCys so incorporated is critical to the function of these proteins. Selenium, therefore, is an essential trace element required for proper nutrition (1).

In humans, SeCys forms the active centre in important redox enzymes such as five glutathione peroxidases and three thioredoxin reductases. In addition, there are three thyroid hormone iodinases involved in proper thyroid function. Selenoprotein W has been implemented in striated muscle health, and Selenoprotein H is a redox sensing protein involved in the regulation of glutathione synthesis and Phase II detoxification reactions in the liver. Some isoforms of Selenoprotein P contain up to 10 SeCys residues. It constitutes the major source of selenium in blood plasma. Its short half-life (3-4 hrs) and its ability to bind to endothelial cells suggest that it is a major selenium transport protein (2, 3).

Selenoproteins contain SeCys incorporated into nascent proteins via the stop codon UGA. The codon is recognized by a specific transfer RNA carrying acetyl-serine; SeCys is formed *in situ* via the reaction of acetyl-serine with selenophosphate. The recognition of the UGA codon requires the presence of a SeCys insertion sequence (SECIS) present in the 3'-noncoding region of the selenoprotein mRNA. Selenophosphate is derived from dietary selenium (1).

Dietary inorganic selenate (Se VI) or selenite (Se IV) is reduced and enters metabolic pools that either leads to selenoprotein synthesis or to methylated-seleno- and methylated-seleno-glycoside



excretion pathways. SeMet appears to be the predominant selenocompound in cereal grains, meat, and selenized yeast (Se-yeast), while γ -glutamyl-Se-methylselenocysteine (GMSeCys) and Se-methyl-selenocysteine (MSeCys) are characteristic of Se accumulator plant species such as the brassicas (broccoli, radish, cabbage, etc.) and the genus *Allium* (onions and garlic) (4). Ingested SeMet is available for general protein synthesis, where it is non-specifically incorporated into protein in place of

methionine. Here it can accumulate as part of the body's selenium stores and ultimately may become biologically available for other metabolic pathways as a function of protein turn over. SeCys, MSeCys, and GMSeCys do not enter protein synthetic pools where they can be stored; rather they rapidly enter secretory pools. Methylselenol (MSeH) produced in the secretory pathway is considered to be an important *in vivo* anticarcinogenic metabolite. SeMet, via a γ -lyase, can also be converted to MSeH when it enters the secretory pathway either from dietary or protein turn over sources (3, 4). In humans, the whole body half life of SeMet and selenite is 252 and 102 days, respectively. At this time, no human bioavailability or retention data are available for plant compounds such as GMSeCys and MSeCys (4).

SELENIUM AND HUMAN HEALTH

While the functions of some of the selenoproteins in the proteome remain unknown, some, such as the glutathione peroxidases and thioredoxin reductases are redox enzymes with roles in preventing oxidative and free radical damage. They contribute to the body's defence mechanisms against damage by reactive oxygen species (ROS). Accumulation of

redox damage is thought to play a role in many disease processes including cardiovascular disease, cancer, muscle disorders and aging (5, 6). As an example, Keshan Disease is a cardiomyopathy endemic to regions of selenium deficient soils in the People's Republic of China. This disease may be associated with Coxsackie virus B infection and low selenium status, but it responds well to dietary selenite supplementation (2, 7).



SEM Yeast 4000X.

The current United States Recommended Daily Allowance (RDA) for selenium requirements of 55 µg/day for men and women were derived from Chinese studies that determined the levels of selenite supplementation in the diet required to maximize plasma glutathione peroxidase (GPx) levels in Chinese men. The requirement for RDAs to be this high has been questioned because of the absence of selenium deficient pathologies in the New Zealand population which consumes less than 30 µg Se/day (8, 9). At issue is the fact that maximal GPx activity may not be necessary for optimum human health and that there may be other indicators of sufficient selenium nutritional status, such as plasma Selenoprotein P levels (10).

Se-yeast was used in the Nutritional Prevention of Cancer Trial (NPC), one of the first human interventional trials (11). The endpoint for these trials was recurrent nonmelanoma skin cancer. This endpoint was null, but secondary endpoints revealed lower mortalities and incidences for prostate, colorectal, and lung cancer. Another study reported a higher incidence of lung cancer was associated with low selenium status, especially in subjects with low intakes of vitamin C and β-carotene (12). Extension and further analysis of lung cancer data from this trial suggested that selenium supplementation most benefited individuals with low selenium baseline levels or former smokers (13).

A major follow up trial, Selenium and Vitamin E Cancer Prevention Trial (SELECT), found no correlation between selenium, as SeMet, and/or vitamin E supplementation and reduced rates of prostate cancer (14). Other authors have noted that the form of selenium in the SELECT study differed from the form of the selenium in the NPC study and that other forms organic selenium present in Se-yeast may be important. As the major form of selenium in Se-yeast is SeMet with minor levels of other selenium species, this may not be relevant. Also, it was noted that the SELECT study used participants with higher plasma selenium baseline levels (15, 16).

While epidemiological and supplementation studies suggest benefits in reducing prostate, colorectal, and lung cancers rates (11-13, 17), the benefits of supplementation on the incidence of putative ROS related diseases such as cardiovascular diseases are less apparent (18). The relationship of selenium status to the ageing process has been stimulated by reports that mortality rates were higher in elderly populations with low plasma selenium levels as compared to individuals in the study group with higher plasma selenium levels (19). The potential role of selenium in proper immune function has been suggested by data demonstrating lymphocyte stimulation by elevated plasma selenium levels (20).

SELENIZED YEAST

Selenium yeast can be produced by one of two techniques. In one, sodium selenite is added to a yeast suspension and the mixture is dried. Selenite can, to some extent, be bound to the cell surface by ionic forces, but the selenium remains as Se IV and is considered inorganic selenium. This product is a selenium yeast product, but not a "selenized yeast" product. The second form of selenium yeast is manufactured by slowly adding sodium selenite to yeast production fermentations during growth of the organism. In this case, the yeast's metabolism reduces selenite to selenide and incorporates it into cellular constituents in place of sulphur. In this selenized yeast (Se-yeast) 50-80 percent of the selenium is "organically bound selenium" as SeMet (21, 22), which can replace about 30 percent of the methionine in the yeast proteome (23). Unlike mammals, *Saccharomyces* yeasts do not contain specific selenoproteins, but selenium is incorporated non-specifically into protein as SeMet (23). In addition to SeMet, SeCys and lesser amounts of

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