

## Selenium Sources for Dairy Cattle

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### Abstract

Inorganic selenium (selenite and selenate) and selenium yeast (Se-yeast) are the only approved sources of supplemental selenium (Se) in the U.S. The predominant form of Se in Se-yeast is selenomethionine (Se-met). The mechanism of intestinal absorption is completely different for inorganic and Se-met; therefore, factors that reduce absorption of inorganic Se are unlikely to influence absorption of Se-met. The metabolism of inorganic Se and Se-met within a cell also differs. Inorganic Se is used almost exclusively in the synthesis of seleno-specific enzymes; whereas, Se-met can be used in the synthesis of those enzymes, but it can also be incorporated into any protein that contains methionine. Clinical data comparing health effects of inorganic Se and Se-yeast are lacking, but cattle fed Se-yeast have higher concentrations of Se in whole blood (average = 20% more) and milk (90%) and activity of glutathione peroxidase (16%) than cattle fed inorganic Se. Feeding Se-yeast during late gestation also greatly increases the Se concentration in tissues of the newborn calf. Based on available data, the bioactivity of Se from Se-yeast is probably about 20% higher than inorganic Se, but that difference could be greater when absorption of inorganic Se is reduced because of antagonists.

### Introduction

Almost 50 years ago, Se was shown to be an essential nutrient for mammals (Schwarz and

Folz, 1957) and that a Se deficiency led to white muscle disease in ruminants (Muth et al., 1958). Over time, research identified several beneficial effects when Se intake by domestic animals was increased; however, it was not until 1979 that the U.S. government permitted supplemental Se to be added to diets of domestic animals. Both the concentration (0.1 ppm at that time) and the source (sodium selenite or selenate) of supplemental Se were regulated. The regulation was amended in 1987 and allowed 0.3 ppm of supplemental Se to be added to ruminant diets, but the allowed sources (sodium selenite and selenate) did not change. In September, 2003 (FDA, 2003), the regulation was amended again to allow the use of selenium yeast (Se-yeast) in diets for dairy and beef animals based on data from cattle fed Selplex (Alltech, Inc, Nicholasville, KY). The maximum allowed supplementation rate was maintained at 0.3 ppm of Se. The approval of Se-yeast for dairy cattle greatly expanded the Se supplementation options available to nutritionists, but it also made Se supplementation a more complicated matter.

### Selenium Yeast - What is it?

The definition of Se-Yeast according to FDA (2003) is “a dried, nonviable yeast (*Saccharomyces cerevisiae*) cultivated in fed-batch fermentation which provided incremental amounts of cane molasses and selenium salts... and allows for optimal incorporation of inorganic selenium into cellular organic matter. Residual inorganic selenium

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... must not exceed 2% of the total selenium content in the final selenium yeast product.” During fermentation, the yeast consume Se and incorporate it into various organic compounds. The most prevalent Se endproduct is seleno-methionine (**Se-met**). Although differences are likely among commercial sources of Se-yeast, on average, approximately 90% of the Se is Se-met (Schrauzer, 2003). Seleno-cysteine (**Se-cys**) is produced in much lesser amounts. Those two seleno-amino acids are identical to the regular amino acids, methionine (**met**) and cysteine, except that Se replaces the sulfur atom (Figure 1). The predominant chemical form of Se in Se-yeast makes organic Se different from all other organic trace minerals. All other organic trace minerals are complexes or chelates. The metal is ‘associated’ with an organic compound, but it is not part of the compound’s molecular structure. The Se in Se-met and Se-cys is part of the molecule; the Se cannot be removed without breaking covalent bonds.

Numerous other Se-compounds are produced by yeast, but identifying and quantifying all the different Se compounds found in Se-yeast is extremely difficult and requires very sophisticated techniques and instruments. Although the concentrations of these other Se compounds will be quite low, they may be important biologically. Some of these ‘minor’ selenium compounds have been shown to have potent anti-carcinogenic properties in laboratory animals, and clinical data are accumulating showing similar effects in humans, especially with respect to prostate cancer (Combs et al., 2001). Essentially, nothing is known regarding biological activity of these minor Se compounds in cattle. Therefore, the rest of this paper will consider only the Se provided by Se-met and Se-cys.

### Selenium Absorption

The most prevalent forms of Se consumed by dairy cows in the U.S. are selenate and selenite (from inorganic Se supplements), and Se-met and

Se-cys (from Se-yeast and basal feedstuffs). Ruminal metabolism and intestinal absorption of these Se compounds differ. Most of the selenate (**SeO<sub>4</sub>**) consumed by a cow is reduced to selenite (**SeO<sub>3</sub>**) in the rumen, but some of the selenate leaves the rumen and is absorbed as selenate in the small intestine. Based on studies with rats, intestinal absorption of selenate is probably via an active (energy-requiring) transport system. Absorption of selenate by ligated intestinal loops of rats was about 80% (Vendeland et al., 1992). In the rumen, selenite (either that consumed in the diet or produced from selenate) can be converted to low molecular weight insoluble forms of selenium. These compounds have not been chemically identified but most likely are not well-absorbed or utilized by the host. Some of the selenite is used to synthesize seleno-amino acids (predominantly Se-cys) that are incorporated into microbial protein. The remaining selenite leaves the rumen and reaches the small intestine where it is absorbed probably via a passive mechanism. Intestinal absorption of selenite was about 35% using ligated rat intestines (Vendeland, et al., 1992). Because it is so difficult to quantify the various Se compounds, reliable data on distribution of Se in ruminal contents are limited. Reasonable estimates when selenite is fed are 30 to 40% is converted to insoluble forms, 10 to 15% is found in microbial protein and 40 to 60% remains as selenite (Serra et al., 1994). I could not find any information regarding ruminal metabolism of Se from Se-yeast. An *in vitro* experiment found that about 60% of Se-met (not Se-yeast) was incorporated directly into bacterial protein as Se-met (Paulson et al., 1968). Although data are limited, a much higher percentage of Se leaving the rumen is in the form of seleno-amino acids (predominantly Se-met) when cows are fed Se-yeast than when fed selenite or selenate. Seleno-methionine is absorbed from the intestine by the same mechanism as methionine and is quite efficient (>80%). However, because Se-met and met use the same intestinal absorption system, increasing the intestinal flow of met will decrease absorption of Se-met because of competition.

True absorption of Se from diets containing supplemental inorganic Se, calculated from Se balance studies, averages about 50% in dairy cows, goats, and sheep (Harrison and Conrad, 1984; Aspila, 1988; Koenig et al., 1997; Ivancic and Weiss, 1999). True absorption will be lower if the diet contains appreciable quantities of antagonists to Se absorption (discussed below). Data on the true digestibility of Se from Se-met or Se-yeast are very limited and variable. True digestibility of Se from Se-met (measured in goats) was 65% (Aspila, 1988), and the calculated true digestibility of Se from Se-yeast (measured in sheep) averaged about 44% (Koenig, et al., 1997). Because of the method used to produce the Se-yeast in the sheep study, the proportion of Se that was inorganic was probably greater than that found in the currently available Se-yeast products. Even though data are very limited, based on known absorption mechanisms, Se from Se-yeast is probably absorbed with greater efficiency than Se from selenite. Assuming Se-met from Se-yeast has an escape value of 60% (based on in vitro studies with Se-met) and that 90% of the Se in Se-yeast is Se-met, approximately 55% of the Se from Se-yeast that leaves the rumen is in the form of Se-met. Assuming the digestibility of the Se from Se-met is 80% (average digestibility of ruminal microbial protein) and the digestibility of the 45% of total Se that is not Se-met is the same as for selenite (50%), the true digestibility of Se from Se-yeast would be about 66%. This is about 30% higher than the true digestibility of Se from selenite.

### Selenium Metabolism

The reason Se is an essential nutrient for animals is because certain enzymes (selenoenzymes) must contain a Se-cys residue in their active sites. The most familiar selenoenzyme with respect to dairy cattle nutrition is glutathione peroxidase (**GSH-px**), which is an important component in cellular antioxidant systems. Cells have developed a simple, but elegant, method of ensuring that Se-cys is

inserted into the proper location in enzymes (Figure 2). Selenite that is absorbed goes to cells where it is reduced to selenide and then the selenide is used to synthesize Se-met from a serine molecule that is linked to a specific tRNA (UGA codon). The synthesized Se-cys-tRNA<sub>UGA</sub> complex is then put in the right place during protein synthesis. If Se-cys from the diet is absorbed, it cannot be inserted directly into the active site of the enzyme during protein synthesis because it does not have the correct tRNA. Dietary Se-cys must be catabolized and then the Se can be reduced to selenide and a Se-cys-tRNA<sub>UGA</sub> can be synthesized. Absorbed dietary Se-met can be used in place of met in protein synthesis. Cells do not appear to be able to differentiate between regular met and Se-met. Therefore, Se-met can be found in all proteins in the body in direct proportion to the amount of met found in the protein and the relative pool sizes of regular met and Se-met. The Se-met can also be catabolized and its Se be converted to selenide and then put into Se-cys-tRNA<sub>UGA</sub>. The bottom line difference between inorganic (selenite) and organic Se (Se-met) is that inorganic Se is used almost exclusively to produce selenoenzymes, but organic Se can be used to produce selenoenzymes and also result in general labeling of all proteins that contain met. This difference has implications when interpreting Se concentration data.

### Se-yeast versus Selenite: The Data

When comparing sources of nutrients, the most important question is, "Which source will result in the greatest net return?" To answer this question, you need to know the cost of the supplement (per unit of nutrient) and the value of the response. For Se, the response is usually health-related. Numerous studies have shown that supplemental Se (usually from inorganic sources) improve immune function and mammary gland health and reduce the prevalence of retained fetal membranes (Weiss, 2003; Weiss and Spears, 2005). Therefore, the best method to compare Se sources is with clinical

trials that measure prevalence and severity of certain diseases when cows are fed different sources of Se. I could find only one study (Malbe et al., 1995) in which selenite and Se-yeast were fed and clinical measures were taken, and because of the experimental design, the effects of Se source could not be statistically compared. Cows were fed diets with 0.2 ppm Se from selenite or Se-yeast and milk somatic cell count (SCC) and prevalence of infected quarters were measured. Following 8 weeks of supplementation, infected quarters decreased 60% for cows fed selenite and 43% in cows fed Se-yeast compared with day 0 values. The SCC decreased 37% and 30%, and NAGase activity in milk (a measure of inflammation) decreased 21 and 45%, respectively, for cows fed selenite and Se-yeast. All measures of mammary gland health were improved in Se supplemented cows, whereas no changes occurred in cows not fed supplemental Se. Based on these data, source of Se did not appear to have a large effect.

The effects of Se source (inorganic vs. Se-yeast) on concentrations of Se in blood and milk and activity of GSH-px have been compared in numerous experiments (Table 1; Figures 3, 4, and 5). The median increase in whole blood Se when Se-yeast was fed was 20% (Figure 3). Whole blood GSH-px activity was numerically higher in all studies when Se-yeast was fed, but only two studies reported statistically higher values (Figure 4). The median increase in activity was 16%. The relative response in GSH-px activity when Se-yeast is compared with selenite might be a function of Se intake. The two studies with the greatest difference between Se-yeast and selenite in GSH-px activity fed the lowest concentration of supplemental Se (approximately 0.1 ppm Se). Knowles et al. (1999) reported no difference in GSH-px activity between cows fed selenite and Se-yeast when cows consumed 4 mg/day of supplemental Se (approximately 0.2 ppm), but when cows were fed 2 mg/day of Se (approximately 0.1 ppm), GSH-px activity was about 50% higher when Se-yeast provided the supplemental Se (Figure 4).

The median increase in milk Se was 90% when Se-yeast was fed (Figure 5). The vast majority of the Se in milk when Se-yeast is fed is in the form of Se-met. Milk Se concentrations increase linearly as intake of Se from Se-yeast or from feeds that are high in Se increase, but milk Se does not change greatly as intake of selenite increases (Figure 6). One factor considered by FDA during the Se-yeast approval process was the concentration of Se in milk and meat. Based on human health concerns, FDA set the maximum allowable concentration of Se in milk at 0.14 mg/L. Based on the equation in Figure 6, an intake of approximately 25 mg/day of Se from Se-yeast and basal ingredients will produce milk that exceeds the legal limit in Se concentrations (approximately 3.5 times the legal dietary limit for lactating cows).

Selenium is transferred to the fetus in utero. The concentration of Se in plasma of newborn Holstein calves was 42% higher when cows were fed Se-yeast during the last 60 days of gestation compared with cows fed selenite (Weiss, unpublished). In studies with beef cows, whole blood from newborn (or very young) calves was 35% (Pehrson et al., 1999) and 42% (Gunter et al., 2003) higher in Se concentration, and activity of GSH-px activity in the calves was 32 and 75% higher, respectively, when dams were fed Se-yeast. Awadeh et al. (1998) reported only an 18% increase in whole blood Se and no effect on GSH-px in newborn beef calves when dams were fed Se-yeast.

Based on blood concentrations and GSH-px, Se-yeast is about 1.2 times 'better' than selenite, and based on milk concentrations, it is 1.9 times better. The relative response in milk Se concentration is much higher than the response in blood because milk protein has about twice as much methionine as do proteins in whole blood; therefore, it is twice as likely that Se-met will be incorporated into milk protein than blood protein. Milk protein is synthesized constantly and removed from the cow two or three times a day. Therefore, Se-met

concentrations in milk reach steady state within a few days after Se-yeast supplementation has begun. Once a red blood cell is made, it does not synthesize protein and red cells live 100 to 130 days. Therefore, it would take 3 or 4 months of supplementation for whole blood concentrations to reach steady-state. Many of the experiments that measured whole blood Se did not last that long, so the measured difference probably was less than maximal differences. Lastly, a substantial portion of the Se in whole blood is in selenoenzymes, which based on GSH-px is less responsive to source of supplemental Se than other proteins. This would dilute the response in whole blood Se concentrations when Se-yeast is fed. Good clinical data are needed to determine the true difference in bioactivity of Se from selenite and Se-yeast. In lieu of those data, the best estimate of relative difference between selenite and Se-yeast available currently is GSH-px activity because it reflects biological activity of Se, not availability of met. Based on those data, Se from Se-yeast, on average, is about 1.2 times more bioactive than Se from selenite.

### **Factors to Consider When Choosing a Se Source**

#### *Antagonists to Se absorption*

Selenite and Se-met are absorbed from the intestine by completely different mechanisms. Factors that antagonize absorption of selenite are not likely to have the same effect on absorption of Se-met. Diets with 0.2% added sulfate-sulfur reduced true absorption of Se from selenate by 20% (Ivancic and Weiss, 1999). When sulfate is present, Se from Se-yeast would be about 50% more available than Se from inorganic sources (compared with 30% when sulfate is not excessive). Sulfate is unlikely to have an effect on Se-met absorption. Although this is not a likely problem, diets that provide high concentrations of digestible met will reduce availability of Se from Se-yeast because of competition for absorption sites in the intestine.

#### *Body retention of Se*

Cows fed Se-yeast have higher concentrations of Se in almost all tissues than do cows fed selenite. Much of this Se is in proteins as Se-met. As proteins in the body are turned over, Se-met is released and if broken down can provide Se for selenoenzyme synthesis. Cows fed selenite have a much lower body reserve of Se than cows fed Se-yeast. This could be beneficial in periods of high Se demand and in unexpected periods of low Se supply. Increased body reserves may be especially beneficial for newborn calves. Calves borne from cows fed Se-yeast have higher concentrations of Se in tissues and often much higher GSH-px activity than when cows are fed inorganic Se. In addition, colostrum from cows fed Se-yeast contains more Se than colostrum from cows fed selenite, thereby increasing the difference in Se status of the calves. Feeding cows some Se-yeast during the last 60 days of gestation may have beneficial effects on calf health by improving the Se status of the calf.

#### *Costs of supplement*

Diets with 0.3 ppm of supplemental Se provided by Se-yeast will cost about 5 cents/day per lactating cow more than will diets with selenite and 2 or 3 cents/day more for dry cows (approximately \$17 annually for each cow, assuming a 305 day lactation). If supplementation rate was reduced 20% to account for higher bioactivity of Se-yeast, the annual cost is about \$14. The cost of an ingredient should not be the primary concern; return on investment is what matters. Unfortunately data are not available to determine whether return on investment (via improved health) differs between inorganic Se and Se-yeast.

### **Recommendations and Conclusions**

The benefits and disadvantages of each type of Se supplement are summarized in Table 2. The

Se-yeast has numerous advantages over selenite, but the question remains, "Is it more profitable to use Se-yeast?" In situations where antagonists are not a concern, inorganic Se is probably the most cost-effective option for lactating cows. If antagonists are present, some or all of the Se should be provided by Se-yeast. To ensure adequate Se status of calves, providing a portion of the supplemental Se as Se-yeast in dry cow diets is a good idea. Current regulations permit using a combination of Se sources as long as the total supplemental Se does not exceed 0.3 ppm in the total diet. Usually using a combination of nutrient sources is better than relying on a single ingredient. Some data with other trace minerals show benefits when a combination of inorganic and organic sources are used compared with either all organic or all inorganic. The same may be true for Se. In my opinion, if antagonists are not present in feed or water, lactating cows should be supplemented with Se that is predominantly from inorganic sources. If antagonists are present, the predominant Se source should be Se-yeast. Because of potential benefits to the newborn calf, a larger proportion of Se (maybe 50%) in dry cows diets should come from Se-yeast, even when antagonists are not present.

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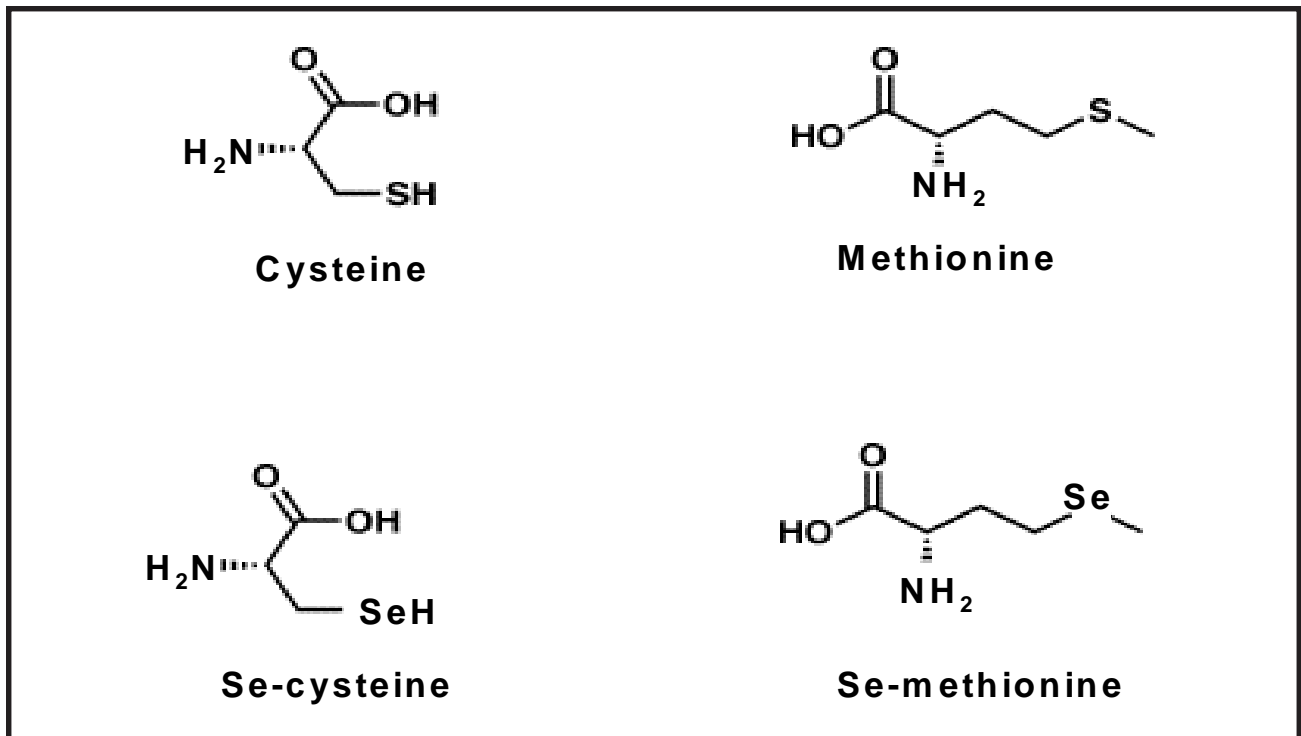
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**Table 1.** Sources of data used in Figures 3, 4, and 5.

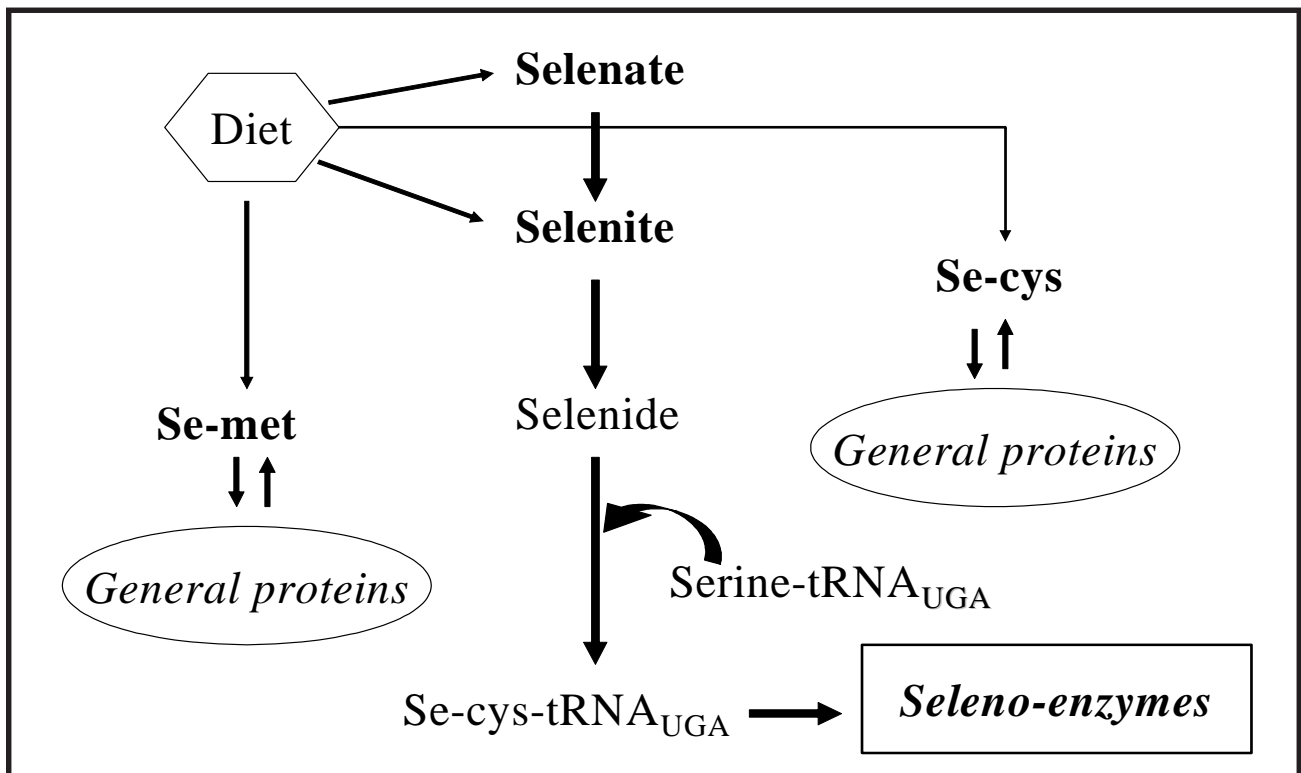
Experiment Code on Figure			Animal Type	Citation
Figure 3	Figure 4	Figure 5		
A	A	A	Beef cows	Awadeh et al. (1998)
B	...	B	Dairy cows	Fisher et al. (1995)
C	C	C	Dairy cows	Knowles et al. (1999) (2 mg)
D	D	D	Dairy cows	Knowles et al. (1999) (4 mg)
E	E	E	Dairy cows	Malbe et al. (1995)
F	...	...	Beef heifers+steers	Nicholson et al. (1991)
G	...	...	Dairy heifers	Nicholson et al. (1991)
...	H	...	Combined	Nicholson et al. (1991)
I	I	...	Growing beef	Nicholson et al. (1993)
J	J	J	Dairy cows	Ortman and Pehrson (1997)
K	K	K	Dairy cows	Ortman and Pehrson (1999)
L	L	...	Dairy heifers	Ortman et al. (1999)
M	M	M	Beef cows	Pehrson et al. (1999)
N	N	N	Beef cows	Gunter et al. (2003)
...	O	...	Dairy heifers	Pehrson et al. (1989)
...	...	P	Dairy cows	Weiss (unpublished)

**Table 2.** Benefits and disadvantages of inorganic and Se-yeast.

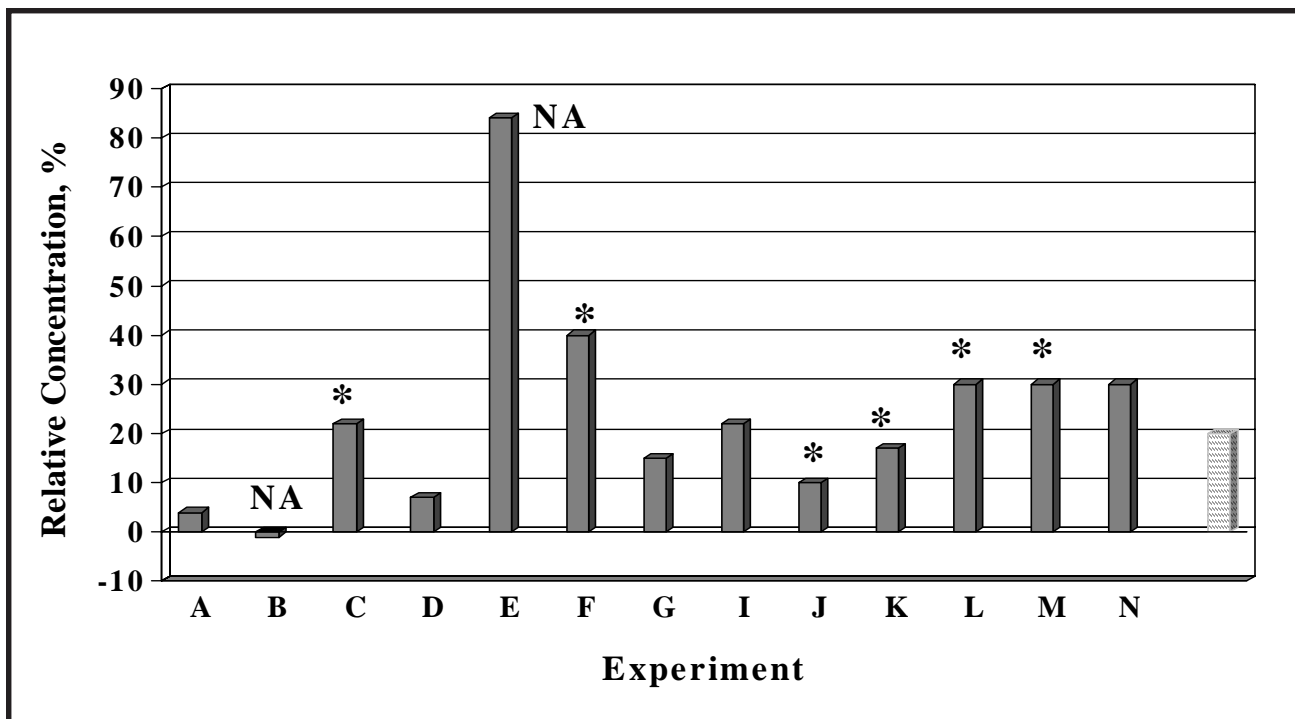
Benefits	Disadvantages
<b>Inorganic selenium</b>	
Cheap	Absorption can be affected by antagonists
Provides adequate Se in many situations	Provides limited body reserves of Se
<b>Se-yeast</b>	
Probably 20 to 30% more available	More expensive
Builds up body reserves of Se	
Increases milk Se (human health benefit)	
Increases colostrum Se (calf health benefit)	
Increased transfer of Se to fetus	
Not affected greatly by absorption antagonists	



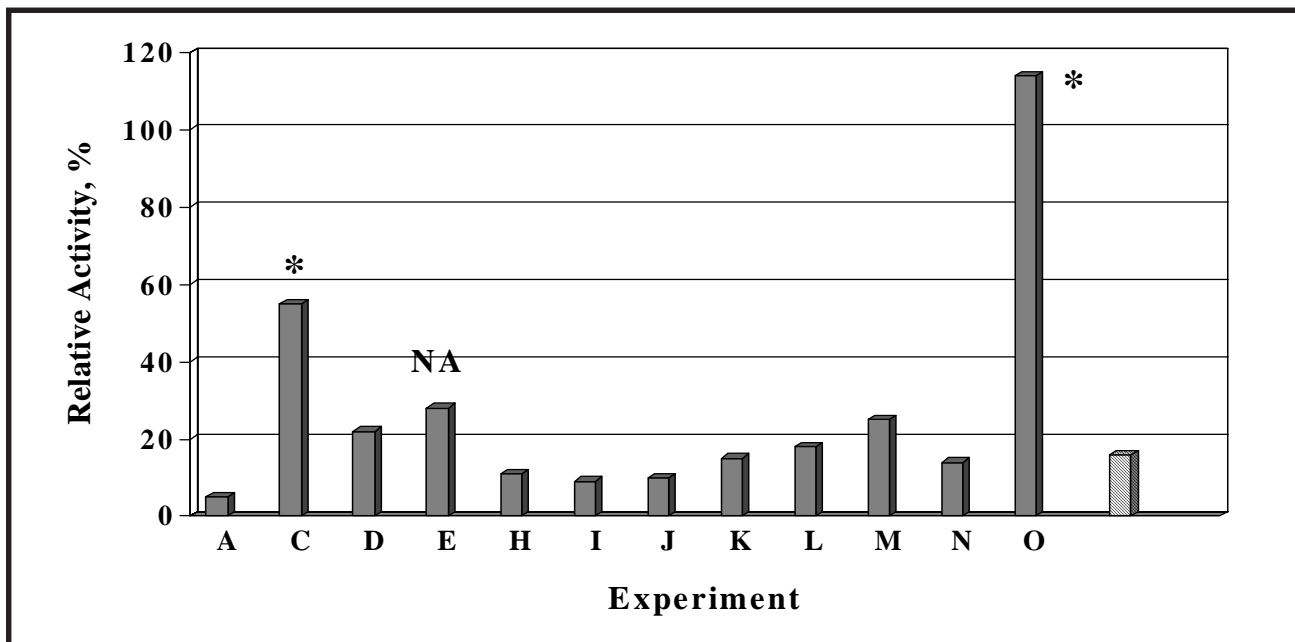
**Figure 1.** Chemical structures of the amino acids, methionine and cysteine, and the comparable seleno-amino acids.



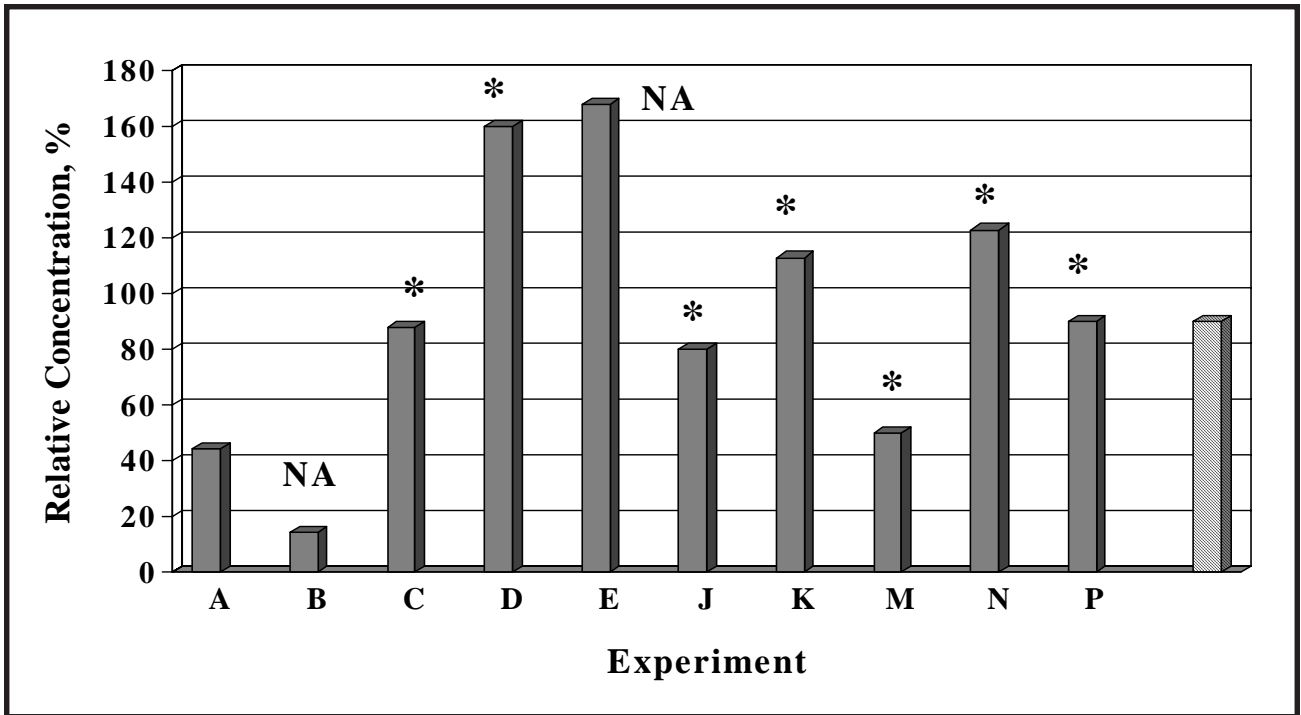
**Figure 2.** Simplified pathways of selenium metabolism.



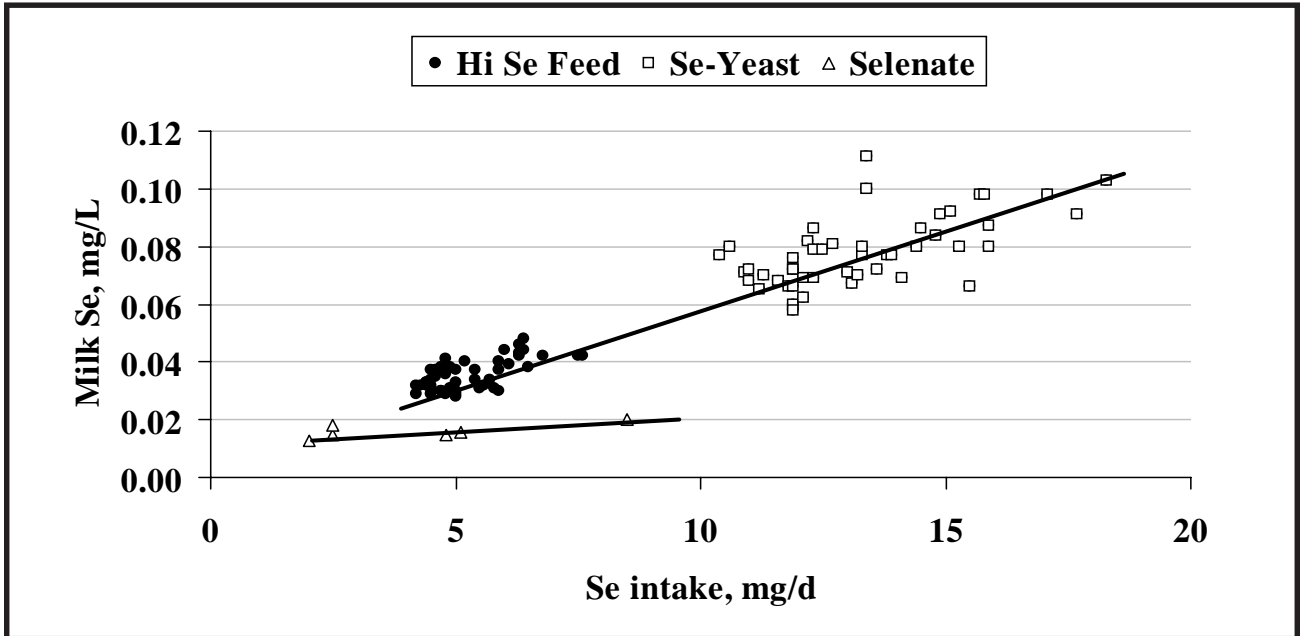
**Figure 3.** Relative increase in concentration of Se in whole blood when cattle were fed Se-yeast compared with selenite. Relative increase calculated as  $(\text{Se-yeast} - \text{selenite}) / \text{selenite} \times 100$ . A value of 0 means that concentrations were equal when Se-yeast or selenite was fed. The hashed bar is the median response. NA = data not statistically compared; \* =  $P < 0.05$ .



**Figure 4.** Relative increase in activity of glutathione peroxidase activity in whole blood when cattle were Se-yeast compared with selenite. Relative increase calculated as  $(\text{Se-yeast} - \text{selenite}) / \text{selenite} \times 100$ . A value of 0 means that activities were equal when Se-yeast or selenite was fed. The hashed bar is the median response. NA = data not statistically compared; \* =  $P < 0.05$ .



**Figure 5.** Relative increase in concentration of Se in milk when cattle were fed Se-yeast compared with selenite. Relative increase calculated as (Se-yeast minus selenite)/selenite x100. A value of 0 means that concentrations were equal when Se-yeast or selenite was fed. The hashed bar is the median response. NA = data not statistically compared; \* = P < 0.05.



**Figure 6.** Concentration of Se in milk when fed: A) a basal ingredients with low concentrations of Se plus supplemental selenite ( $\hat{I}$ ), B) a diet with basal ingredients that contained high concentrations of Se and no supplemental Se (Q, or C) a diet with basal ingredients that contained high concentrations of Se plus supplemental Se from Se-yeast ( $\square$ ). Treatments B and C fit the same line with a slope of 0.0052. Treatment A had a slope of 0.0007.