MichaelMooney.net
Research Review
Analysis of Studies from the National Library of Medicine

Number 3, April 2004

WHY I CREATE RESEARCH REVIEWS

I am frequently asked about forms and dosages of nutritional supplement ingredients.

Research Reviews provide information to answer these questions.

Scientific references are cited and text from abstracts is included to provide research details.

I evaluate ingredients by the following criteria:

1) Is it natural and normal to the human body?
2) Has it had a long history of safe use in humans?
3) Is it supported by science or traditional herbal wisdom?
4) Is it nutritionally effective?
5) Is it cost-effective?
6) Is it concentrated enough that optimal doses can be supplied in a reasonable amount of tablets?

The Safety and Effectiveness of Selenium As Selenite, Selenomethionine, and "Food-Grown-Type" Selenium

Fiction: The selenite form of selenium is toxic.

Fact: There are no reports of selenite in supplements causing any toxicity.

Fiction: Selenite is neither absorbable nor effective.

Fact: Selenite is not only very highly absorbable, but it is so effective, it has been proven to stop Keshan Disease (a type of heart failure) in millions of children, with no toxic effects.

Fiction: Selenomethionine and "food-grown-type" selenium are safer and more effective forms of selenium.

Fact: Neither selenomethionine nor "food-grown-type" selenium have been proven as safe or as effective as selenite in long-term human studies.

INSIDE

The Safety And Effectiveness Of Selenium As Selenite, Selenomethionine And "Food-Grown-Type" Selenium

I have been asked why selenite is a preferred form of selenium rather than selenomethionine or "food-grown-type" selenium. (There are several versions of "food-grown-type" nutrients made by different companies, including "bio-cultured-type," "food-state-type," and "whole-food-probiotic-type" nutrients. If you look at the left column on the front cover, you'll see the six standards an ingredient or a form of an ingredient should meet to be considered a best nutrient source. Below I answer some questions about selenite, selenomethionine and "food-grown-type" selenium. Typical questions are:

1. Isn't selenomethionine safer than selenite?
2. Isn't selenomethionine superior to selenite?
3. Aren't selenomethionine and "food-grown-type" selenium more absorbable and bioavailable than selenite?
4. Hasn't "food-grown-type" selenium been proven to be the best in many studies?

No Population Studies On The Safety Of Selenomethionine No Safety Studies Of "Food-Grown-Type" Selenium

Only one study that looked at the safety or toxicity of selenomethionine that was located in a search of the National Public Library of Medicine. It was a study of aquatic organisms, not humans where researchers from the University of California reported that selenomethionine was 30 times more toxic than selenite in one species of aquatic organisms. The also reported that earlier researchers in 1971 and 1976 had found selenomethionine to be approximately 10 times more toxic than selenite.[1] No studies that looked at the safety or toxicity of "food-grown-type" selenium were located.

Selenium As Selenite Proven Safe And Effective With Millions

There are, however, many studies the detail the safety and effectiveness of selenium as selenite with large populations in China where selenite has been used to eradicate a type of lethal heart disease (Keshan Cardiomyopathy) that occurs predominantly in an area of northeast China with 10 million occupants. Although adults do get the disease, the most susceptible populations are children between the ages of 2 and 7 and women of child-bearing age.[2] The fatality rate of Keshan Disease was 50% within 5 years of contracting the disease until selenite therapy was discovered.[3] Below is a summary of a report by the Keshan Disease Research Group of the Chinese Academy of Medical Sciences that details the effectiveness of selenite in eradicating Keshan Disease in a group of children 1 to 9 years of age over a 4-year period of time. [4]

1974 - 83% reduction in Keshan disease with selenite
- 54 cases of Keshan disease in 3985 children who did not receive selenite (13.5%)
- 10 cases of Keshan disease in 4510 children who received selenite (2.2%)

1975 - 89% reduction in Keshan disease with selenite
- 52 cases of Keshan disease in 5445 children who did not receive selenite (9.5%)
- 7 cases of Keshan disease in 4510 children who received selenite (1.0%)

1976 - almost complete elimination of Keshan disease in the children
- Because of the positive effects seen in the previous two years, all the children in the study were given selenite in 1976. This resulted in a reduction to only 4 cases of Keshan's in the 12,579 children who received selenite. (0.32%)

1977 - 100% successful

- All 12,747 children in the study this year were given selenite.
  No new cases of Keshan Heart Disease (Zero %)

The Keshan Research Group authors in a later report,[1] stated that because of the success of selenite therapy, the study group was expanded to other communities. They reported an 87% reduction of Keshan Disease in those communities within 5 years (1976 to 1980):

- 1713 cases in 1,107,568 children who did not receive selenite (2 cases per 1000 children)
- 88 cases in 323,872 children who received selenite (0.27 cases per 1000 children)

The authors, in a follow-up report in 1984, go on to state, "*From 1973 on, similar work has shown the same trends…In all intervention programs, the oral administration of selenite carried out in several provinces on millions of people, using sodium selenite tablets…All results show that selenite has proved to be effective in reducing the incidence, morbidity, and fatality of Keshan disease*." [1]

The authors of the study stated that the following doses were used: [3]

Children 1-5 years old took 500 mcg (micrograms) of selenite per week. (71 mcg/day)
Children 6-10 years old took 1000 mcg of selenite per week. (142 mcg/day)
Children over 11 years old took 2000 mcg per week. (285 mcg/day)
Adults took 4000 mcg per week. (571 mcg/day)

The study authors stated, *"....there were no untoward side-effects. In some individual cases there was nausea after ingestion, but this was overcome by taking (selenite) after meals*."

In addition, in 1984, 1.06 million people in the northeast of China were given table salt with selenite in it. The incidence of Keshan Disease dropped from 25.23 people per 100,000 down to 2.7 people per 100,000 (an 89% decrease).

The authors of the study reported that "…*there were no side-effects observed in the 1.05 million people in 3 years*." [2]

Safe Levels Of Selenite Intake

Various researchers have suggested different upper limit levels before the beginning signs of minor toxicity occur. In 1986, Koller reported that selenite toxicity did not start until dosing reached about 5000 micrograms per day.[6]

In 1995, Yang and Xia from the Chinese Academy of Preventive Medicine, after examining the data from the Keshan Disease Prevention program, estimated the lowest level of beginning signs of toxicity for anyone was about 600 micrograms per day.[5]

The United States National Academy of Sciences' Institute of Medicine reported that the *Lowest Observed Adverse Effect Level* (LOAEL) ever noted for selenium is 910 micrograms per day. (See http://www.supernutritionusa.com/vitamin.safety.doses9-02.pdf *Fact Vs Fiction #5: Vitamin and Mineral Safety and Effectiveness*, page 5.) Dietary supplement doses of selenium are far below this level, generally 50 to 250 mcg per day.

Selenite was used in the U.S.A. at doses of 25 to 100 mcg for about the first ten years of popular use, starting in about 1980. Over the years, as records of selenite's safe use and effectiveness have accumulated, the dosage was gradually increased to the 200 to 250 mcg dosages commonly used today.

Selenite at 200 mcg has already been used by hundreds of thousands of people for many years with no reports of toxicity. The Institute of Medicine states that 800 micrograms of selenite is so safe that there has never been a report of toxicity at this dosage.[7]

Selenomethionine: Claims Of Superiority Dispelled

Marketing campaigns have claimed that selenomethionine is superior to selenite, but independent research and lab studies find that there is little, if any, difference in the body's use of either form. Below I look at selenomethionine claims of superior absorbability and bioavailability.

Absorbability Comparisons

Although there are claims that selenomethionine is better absorbed than selenite, a 1986 study found that in chicks, "regardless of the chemical form, selenium is efficiently absorbed." [8]

But there are conflicts in other studies. One 1990 study from the Department of Human Nutrition at the University of Maryland found that selenomethionine was absorbed more than selenite with women.[11]

Then in 1994, a study at the University of Oregon found that selenite was taken up over 8 times more than selenomethionine in the absorbing area of the intestine of rats (the brush border membrane vesicles). [9]

In 1996, a combined study by Oregon State University and the Chinese Academy of Preventive Medicine found that the binding of selenite to the brush border membrane vesicles was higher than selenomethionine. [10]

Bioavailiability Comparisons

Although there are claims that selenomethionine is more bioavailable than selenite, reports vary regarding how long each form of selenium is held in the tissues and retained in the body. Different tissues retain more selenomethionine; others retain more selenite. Selenomethionine is metabolized more rapidly than selenite, but selenite is excreted from the body faster. This is valuable information but it does not ultimately tell about bioavailability, which is the nutrient's availability to the body for use in healthy body chemistry.

The standard test of actual bioavailability is the increase in glutathione peroxidase activity after selenium supplementation. Selenium is an important component of glutathione peroxidase, one of the most important antioxidants in the body. If glutathione peroxidase activity increases after selenium supplementation, this means the selenium is absorbed and utilized by the body, so it is "bioavailable."

To look at true bioavailability, I reviewed the scientific literature in the National Library of Medicine for studies on changes in glutathione peroxidase activity after selenium supplementation. I found 13 studies comparing glutathione peroxidase activity of selenite and selenomethionine, 9 with animals, 3 with humans, and I study that reviewed 9 other human studies.

Animal Studies Comparing Bioavailability

1977 In rats, increases in glutathione peroxidase activity were "*roughly similar*" with both forms of selenium.[12]

1982 In humans, the increase in glutathione peroxidase activity was "*not significantly greater for Semet (selenomethionine)…than for selenite*…".[13]

1987 In rats, the bioavailability of selenomethionine was greater than selenite.[14]

1988 In rats, "*Tissue (glutathione peroxidase) activities were not different between the two*…"[15]

1988 In rats, "…*there were no differences in glutathione peroxidase activity tissues of rats fed SeMet (selenomethionine) and rats fed selenite*."[16]

1990 In monkeys,"…n*o differences in liver or muscle [glutathione peroxidase levels*…"[17]

1991 In rats, "*Rat pups given intraperitoneal selenite….had higher liver and kidney glutathione peroxidase activity than pups given the same amount of selenium as intraperitoneal selenomethionine*."[18]

1996 In pigs, "…*serum [glutathione peroxidase] activity was generally similar….for either source*."[19]

1997 In rats, "*relative activity of liver glutathione peroxidase was….sodium selenite 81%, SeMet (selenomethionine) 80%*…" [20]

Of the 9 studies above, only one showed that selenomethionine supplementation produced more glutathione peroxidase activity. One other showed selenite supplementation produced more glutathione peroxidase activity, and 7 studies showed each produced about the same glutathione peroxidase activity.

Human Studies Comparing Bioavailability

1982 In humans, the increase in glutathione peroxidase activity was *"not significantly greater for Semet (selenomethionine)… than for selenite…"* [13]

1988 In 139 people, selenite and selenomethionine "*gave steady state levels of [glutathione peroxidase] after one month of supplementation.*" [21]

1994 In 57 elderly people, *"The effect of organic (selenomethionine) and inorganic (selenite) selenium on the activity of [glutathione peroxidase] in plasma and erythrocytes showed a nearly identical increase…."*[22]

1995 In a review of nine studies involving 583 people from different countries, it was observed that "*Saturation of platelet [glutathione peroxidase] activity occurred at lower selenium levels when selenite…[was]... used than with the organic forms (selenomethionine and food-Se).*" [23]

In these 4 studies, 3 showed both selenomethionine and selenite caused approximately the same increases in glutathione peroxidase activity, and 1 reviewed 9 studies from around the world that all showed selenite increased glutathione peroxidase activity more than selenomethionine.

Summary Of Bioavailability Studies Dispels Claims Of Selenomethionine Superiority

In the 13 studies above, 1 indicated that selenomethionine gave rise to higher glutathione peroxidase activity than selenite, 2 indicated that selenite gave rise to more glutathione peroxidase activity than selenomethionine, and 10 indicated that both selenomethionine and selenite gave approximately similar rises in glutathione peroxidase activity.

Using glutathione peroxidase activity, the standard test for bioavailability, there seems to be little, if any difference in either form's bioavailability.

Selenite May Offer More Health Benefits

In a 1976 study with chicks, selenite was found to be effective in promoting weight gain and preventing a certain illness in chicks (exudative diathesis). Selenomethionine was less effective.[24]

In the study below, selenite was effective at protecting against the Coxsackie virus in children but selenomethionine did not, even at higher potencies than selenite.

Cermalli C, and associates. Selenite inhibition of Coxsackie virus B5 replication: implications on the etiology of Keshan disease. Journal of Trace Elements and Medical Biology 2002;16(1):41-46. c.cermelli@unimo.it.

Comment: Keshan disease is a heart disease of unknown cause that was originally reported in children in some areas of China. It is thought to be caused by the Coxsackie virus, but it has also been thought to depend on selenium deficiency, mainly because selenite has been proven to be an effective therapy. This study looked at different forms of selenium, including selenite and selenomethionine and their effect on the replication of the Coxsackie virus. Selenite reduced viral replication, while selenomethionine had no effect even when it was used at a concentration twice as high.

The available scientific evidence does not indicate that selenomethionine is superior to selenite in absorption, bioavailability, safety or effectiveness.

In addition to selenomethionine offering no biochemical advantage over selenite, it costs the consumer about five times more than selenite. I find no nutritional or other reason to use selenomethionine rather than selenite.

"Food-Grown-Type" Selenium Not Studied By Independent Researchers

I have also been asked about claims have been made that "food-grown-type" selenium is proven to be the best form in many studies. This is not true. There is only one known study of "food-grown-type" selenium. It is a test-tube study that was conducted by the single researcher who was paid by the "food-grown-type" raw-materials manufacturer to perform studies. It is not a study of humans or animals and it has never been published in a medical journal.

In the review of published studies in the National Library of Medicine, which examined different forms of selenium for absorption, bioavailability, safety or effectiveness, none were located that examined "food-grown-type" selenium.

In addition to there being no independent scientifically-noted advantage biochemically, "food-grown-type" selenium is about five times more expensive to the consumer than selenite.

While none of the above independent studies looked at "food-grown-type" selenium, the one commercially-sponsored unpublished test-tube study of "food-grown-type" selenium that has been mentioned in promotional materials (Vinson, 1981) stated that "food-grown-type" selenium absorbed only 22% better than selenite.

If this were verified to be true by independent studies, a 22% greater increase in absorption compared to selenite would cost the consumer 500% more than the cost of the same amount of selenite.

"Food-Grown-Type" Selenium May Aggravate Yeast Allergies

It is best to avoid the use of nutrients that may cause allergies. Yeast is allergenic, with as many as 40% of the U.S. population having an acute or sub-clinical allergic reaction to yeast. "Food-grown-type" selenium is supplied in a "base" of yeast. Marketing claims for the yeast in "food-grown-type" nutrients state that the form of yeast that is used will not cause allergic reactions. I find no scientific confirmation to support this claim. I suggest that it is wisest to avoid the use of

nutrients that might cause allergic reactions. Selenite is hypoallergenic, and is known to be safe for use by people who are allergic to yeast.

COMPARISON TABLE

	Criteria	Selenite	Selenomethionine	"Food-Grown-Type" Selenium
1.	Is it natural and normal to the human body?	Yes	Yes	Yes
2.	Has it had a long history of safe use in humans?	Safe with millions	Safe, but no population studies	Safe, but no population studies
3.	Is it supported by science?	Well-supported	Yes	Partly-supported but less than Selenite
4.	Is it nutritionally effective?	Yes	Yes	Partly-supported but less than Selenite
5.	Is it cost-effective?	Yes	No	No
6.	Is it in concentrated enough form that optimal levels can be provided in a reasonable amount of tablets or tablet space?	Yes	Yes	No

Based on the review of the studies above (including selenite's safe and effective use with millions of people), the higher costs of selenomethionine and "food-grown-type" selenium, and the greater concentration of selenite so that it requires less tablets than "food-grown-type" selenium, selenite is the preferred form of these three types of selenium.

The statements in this report have not been evaluated by the Food and Drug Administration. They are not intended to diagnose, cure or prevent any disease.

References

1. Kiffney P & Knight A. *The toxicity and Bioaccumulation of Selenate, Selenite and Seleno-L-Methionine in the Cyanobacterium Anabaena flos-aquae*. Archives of Environmental Contamination and toxicology 1990;19:488-94.
2. Yang GQ & colleagues. *The role of selenium in Keshan disease*. Advances in Nutritional Research 1984;6:203-31.
3. Yun-Yu C & Ping-Chu Q. *The Effect of Selenium-fortified Table Salt in the Prevention of Keshan Disease on a Population of 1.05 Million*. Biological and Environmental Sciences 1990;3:422-38.
4. Keshan Disease Research Group of the Chinese Academy of Medical Sciences. *Observations on Effect of Sodium Selenite in Prevention of Keshan Disease*. Chinese Medical Journal 1979;92(7)471-6.
5. Yang GQ & Xia YM. *Studies on human dietary requirements and safe ranges of dietary intakes of selenium in China and their application in the prevention of related endemic diseas*es. Biomedical and Environmental Sciences 1995 Sep;8(3):187-201.
6. Koller & colleagues. *The two faces of selenium-deficiency and toxicity are similar in animals and ma*n. Canadian Journal of Veterinary Research 1986 July;50(3):297-305.
7. Institute of Medicine. *Dietary Reference Intakes for vitamin C, Vitamin E, Selenium, and Carotenoids*. National Academies Press, 314-315.
8. Humaloja T & Mykkanen HM. *Intestinal absorption of 75SE-labeled sodium selenite and selenomethionine in chicks: effects of time, segment, selenium concentration and method of measurement*. Journal of Nutrition 1986 Jan;116(1):142-148.
9. Vendeland SC & colleagues. *Uptake of selenite, selenomethionine and selenate by brush border membrane vesicles isolated from rat small intestine*. Biometals 1994 Oct;7(4):305-312.

10. Whanger P & colleagues *Metabolism of Subtoxic Levels of Selenium in animals and Humans*. Annals of Clinical and laboratory Science 1996;26(2):99-113.
11. Mangels AR & colleagues. Selenium utilization during human lactation by use of stable-isotope tracers. American Journal of Clinical Nutrition 1990 Oct;52(4):621-627.
12. Pierce S & Tappel AL. *Effects of selenite and selenomethionine on glutathione peroxidase in the rat*. Journal of Nutrition 1977 Mar;107(3):475-479.
13. Thompson CD & colleagues. *Effect of prolonged supplementation with daily supplements of selenomethionine and sodium selenite on glutathione peroxidase activity in blood of New Zealand Residents*. American Journal of clinical Nutrition 1982 Jul;36(1):24-31.
14. Smith AM & Picciano MG. *Relative bioavailability of seleno-compounds in the lactating rat*. Journal of Nutrition 1987 Apr;117(40:725-731.
15. Beilstein MA & Whanger PD. *Glutathione peroxidase activity and chemical forms of selenium in tissues of rats given selenite or selenomethionine*. Journal of Inorganic Biochemistry 1988 May;33():31-46.
16. Whanger PD & Butler JA. *Effects of various dietary levels of selenium as selenite or selenomethionine on tissue selenium, levels and glutathione peroxidase activity in rats*. Journal of Nutrition Jul;1118(7):846-852.
17. Butler JA & colleagues. *Metabolism of selenite and selenomethionine in the rhesus monkey*. Journal of Nutrition 1990 Jul;120(7):751-759.
18. Lane HW & colleagues. *Effect of chemical form of selenium on tissue glutathione peroxidase activity in developing rats*. Journal of Nutrition 1991 Jan'121(8):80-86.
19. Mahan Dc & Kim YY. *Effect of inorganic or organic selenium at two dietary levels on reproductive performance and tissue selenium concentrations in first –parity gilts and their progeny*. Journal of Animal Science 1996 Nov;74(110:2711-8.
20. Wen HY & colleagues. *Bioavailability of selenium from veal, chicken, beef, pork, lamb, flounder, tune, selenomethionine, and sodium selenite assessed in selenium deficient rats*. Biological Trace Element Research 1997 Jul;58(1-2):43-53.
21. Clausen J & Nielsen SA. *Comparison of whole blood selenium values and erythrocyte glutathione peroxidase activities of normal individuals on supplementation with selenate, selenite, L-selenomethionine, and high selenium yeast.* Scandinavian Journal of Clinical and laboratory investigation 1994 Dec;54(8):585-90.
22. Lassen KO & Horder M. *Selenium status and the effect of organic and inorganic selenium supplementation in a group of elderly people in Denmark*, Scandinavian Journal of Clinical and laboratory Investigation 1994 Dec;54(8):585-90.
23. Neve J. *Human selenium supplementation as assessed by changes in blood selenium concentration and glutathione peroxidase activity*. Journal of Trace Elements in Medicine and Biology 1995 Jul;9(2):65-73.
24. Osman M & Latshaw JD. *Biological potency of selenium from sodium selenite, selenomethionine, and selenocystine in the chick.* Poultry Science 1976 May;55(3):987-994.