INE | INSTITUTE OF NUTRITIONAL ENDOCRINOLOGY

Micronutrients: Selenium

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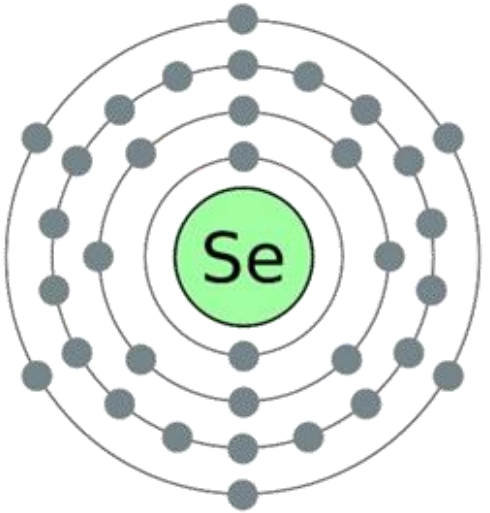
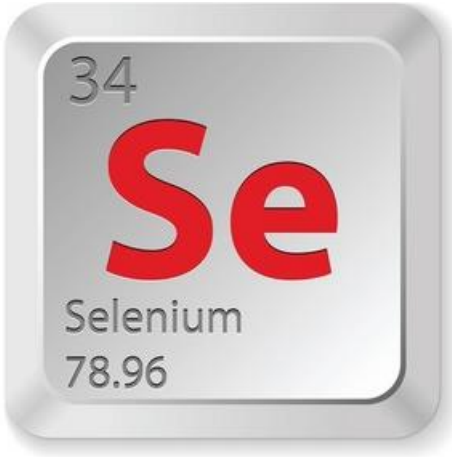
Medical Disclaimer: The information in this presentation is not intended to replace a one-on-one relationship with a qualified health care professional and is not intended as medical advice. It is intended as a sharing of knowledge and information from the research and experience of Dr. Ritamarie Loscalzo, drritamarie.com, and the experts who have contributed. We encourage you to make your own health care decisions based upon your research and in partnership with a qualified health care professional.

Selenium General Info

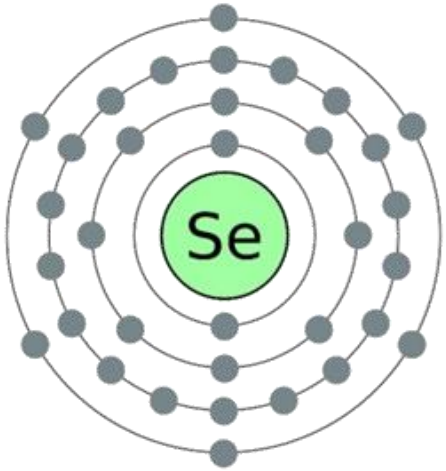
- ✓ Essential micromineral; essential in small amounts, toxic at high levels
- ✓ Very frequently deficient in modern diet
- ✓ Vital for over a number of key enzymes in human body
  - ➢ Selenoproteins
  - ➢ 5-prime deiodinase





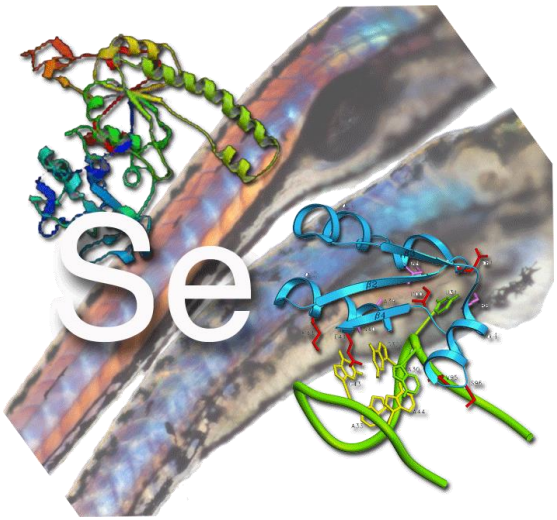
What We Will Cover

- ✓ Why selenium is so important
- ✓ Signs and symptoms of deficiency
- ✓ What happens when excess is consumed
- ✓ Where to find selenium in food supply
- ✓ When to supplement and best types
- ✓ Factors that help or hinder absorption
- ✓ When to use lab testing



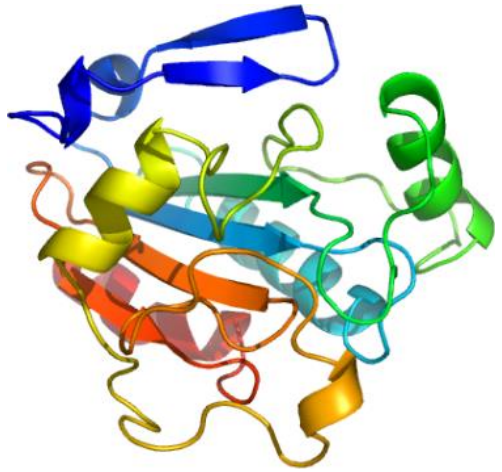
Selenoproteins

- ✓ **25 Selenoproteins identified**
- ✓ **Selenoprotein synthesis**
  - ➢ Selenocysteine is incorporated into amino acid sequence
  - ➢ Forms a functional protein
- ✓ **Only half of the 25 have the metabolic function identified**
  - ➢ Glutathione peroxidases
  - ➢ Thioredoxin reductase
  - ➢ Iodothyronine deiodinases (thyroid hormone deiodinases)
  - ➢ Selenoprotein P
  - ➢ Selenoprotein W
  - ➢ Selenophosphate synthetase
  - ➢ Methionine-R-sulfoxide reductase
  - ➢ 15 kDA selenoprotein (Sep15)
  - ➢ Selenoprotein V
  - ➢ Selenoprotein S



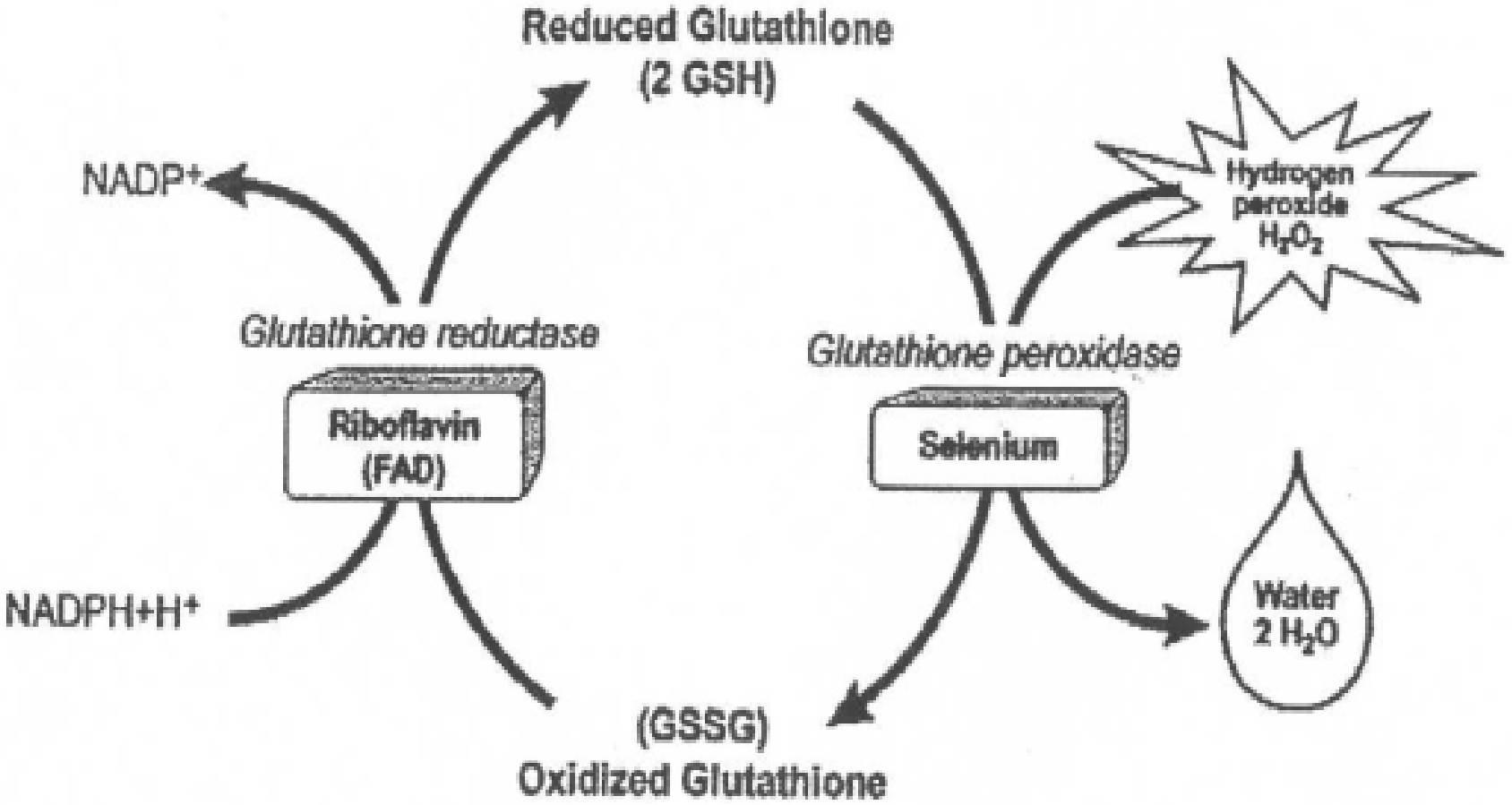
Glutathione Peroxidases

- ✓ Five selenium-containing glutathione peroxidases (GPx) have been identified
  - ➢ Cellular or classical GPx
  - ➢ Plasma or extracellular GPx
  - ➢ Phospholipid hydroperoxide GPx
  - ➢ Gastrointestinal GPx
  - ➢ Olfactory GPx



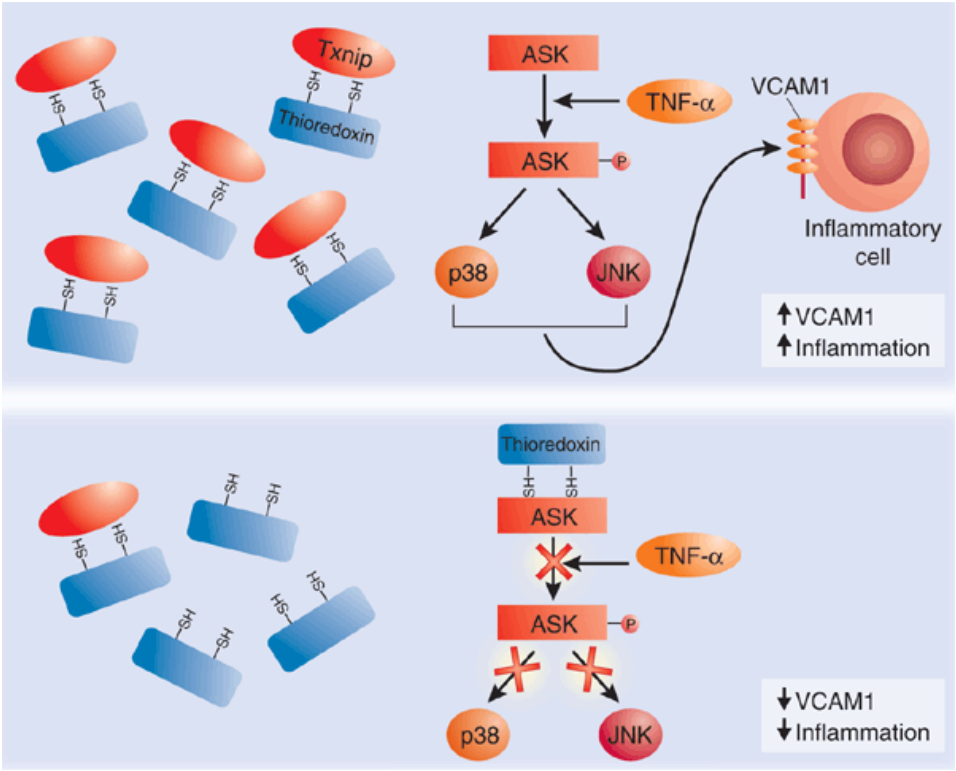
- ✓ Each GPx is a distinct selenoprotein
  - ➢ Reduce potentially damaging reactive oxygen species, such as hydrogen peroxide and lipid hydroperoxides, to water and alcohol by coupling their reduction with the oxidation of glutathione
  - ➢ Sperm mitochondrial capsule selenoprotein protects developing sperm from oxidative damage and later forms a structural protein required by mature sperm

The Glutathione Oxidation Reduction (Redox) Cycle



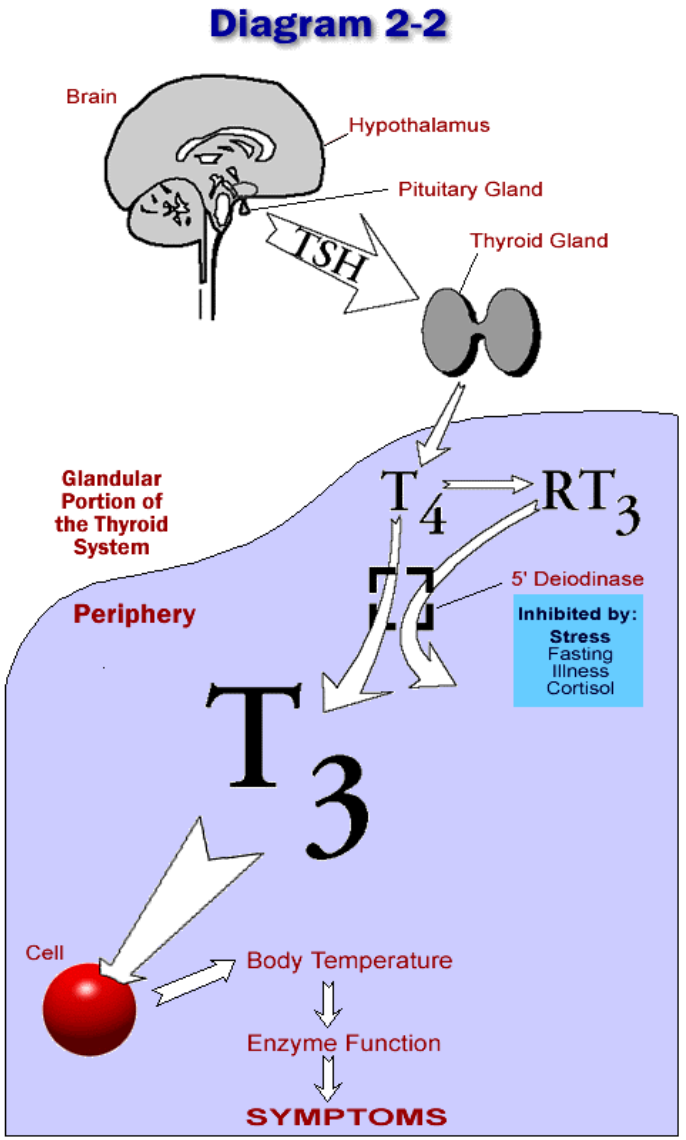
Thioredoxin Reductase

- ✓ Regeneration of thioredoxin and several antioxidants along with Vitamin C
- ✓ Reduced thioredoxin is important for regulating cell growth and viability



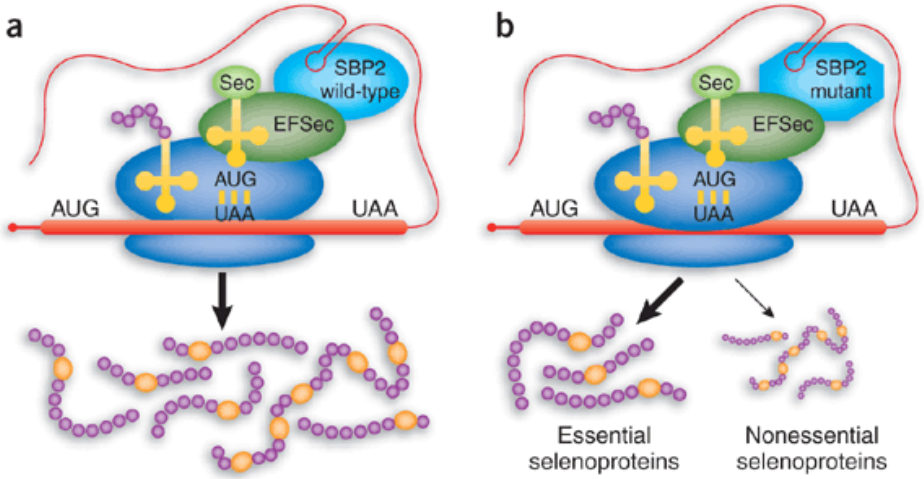
Iodothyronine Deiodinases

- ✓ The thyroid gland
  - ➢ T3 is created by removal of one iodine atom from T4 in a reaction caused by selenium-dependent deiodinase enzymes
- ✓ Three different selenium-dependent iodothyronine deiodinases (types I, II, and III)
  - ➢ Activate and inactivate thyroid hormone by acting on T3, T4, or other thyroid hormone metabolites
- ✓ Selenium is essential for normal development, growth, and metabolism



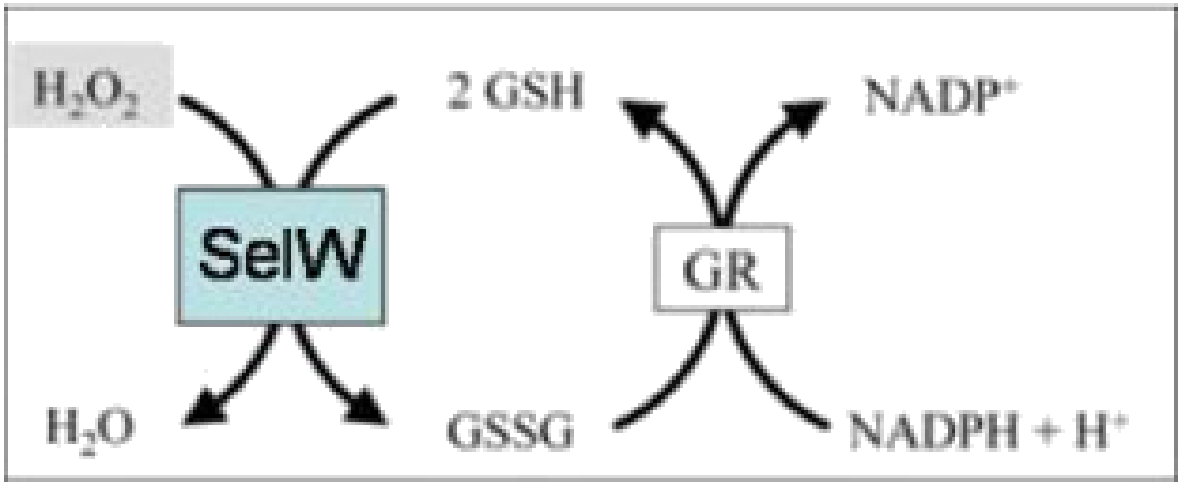
Selenoprotein P

- ✓ Found in plasma
- ✓ Associated with vascular endothelial cells (cells that line the inner walls of blood vessels)
- ✓ Primary function is transport for selenium
- ✓ Also an antioxidant that protects endothelial cells from damage induced by such compounds as peroxynitrite, a reactive nitrogen species (RNS)



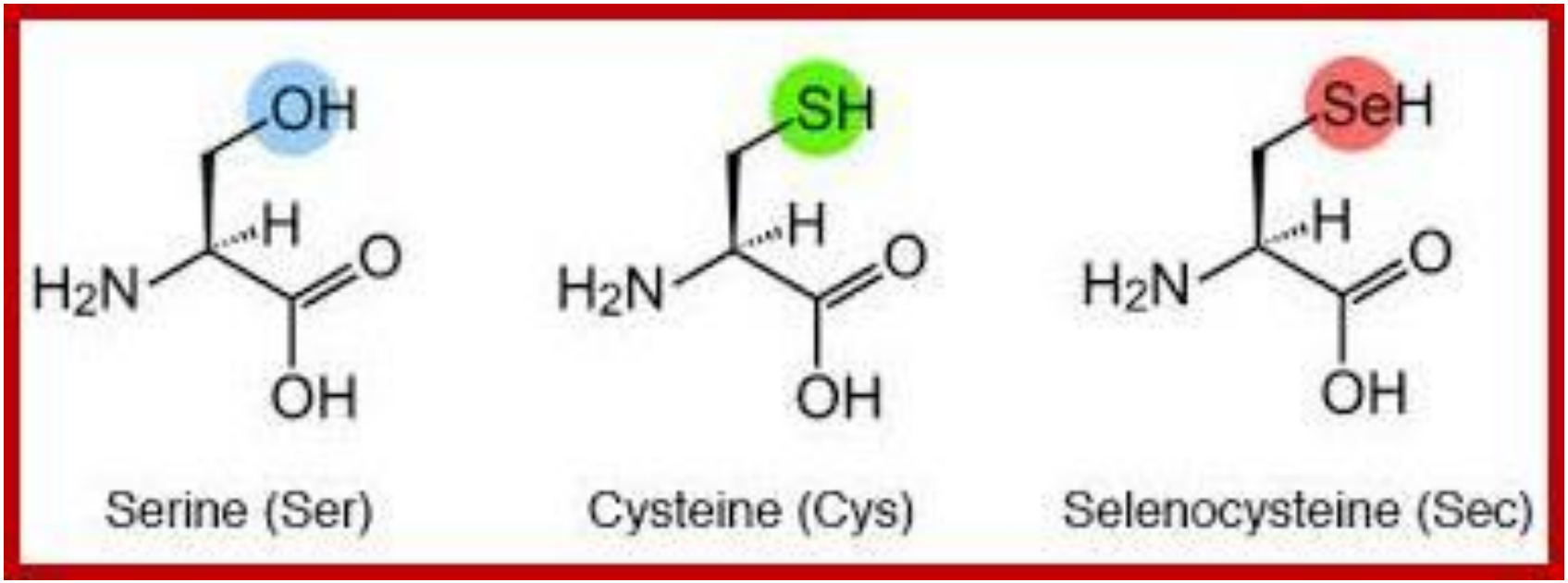
Selenoprotein W

- ✓ Found in muscle
- ✓ Plays a role in muscle metabolism
- ✓ There is about 80% commonality of this selenoprotein with six different species of animals



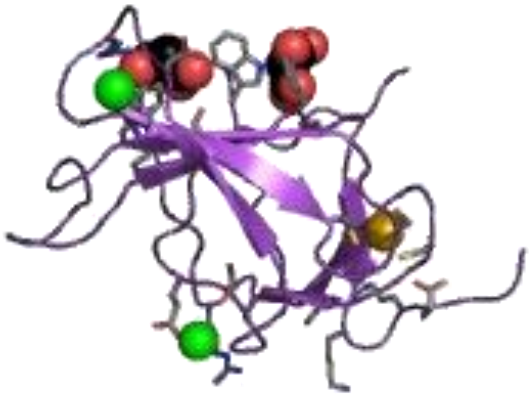
Selenophosphate Synthetase

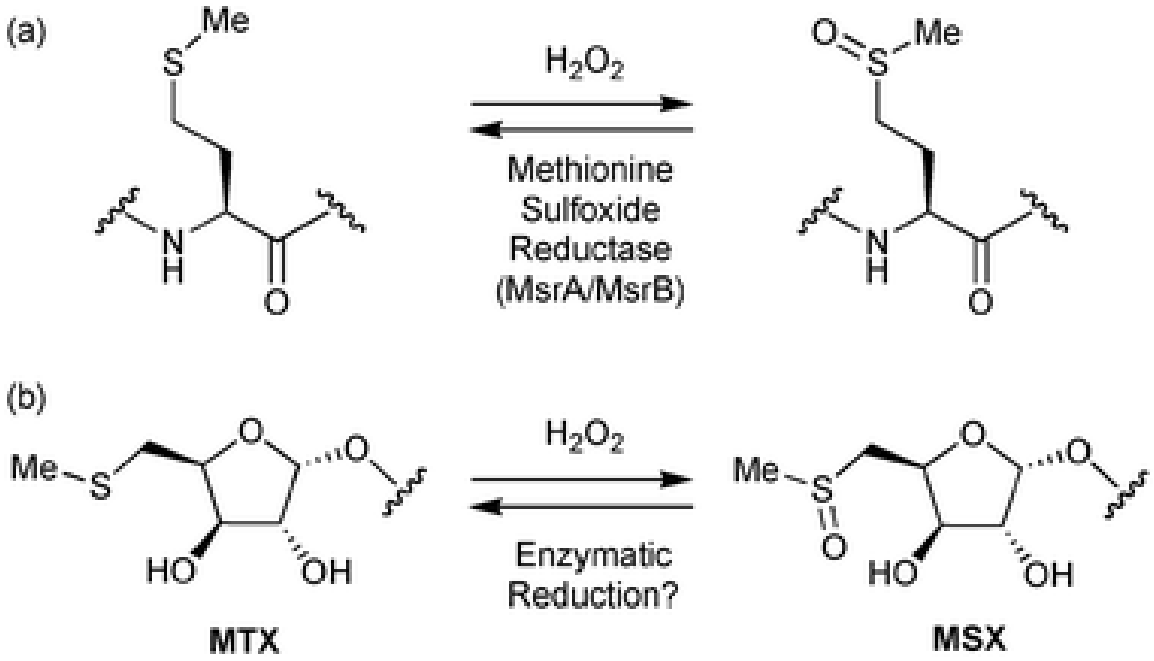
- ✓ Required by the genetic code to incorporate selenocysteine into selenoproteins



Methionine-R-sulfoxide Reductase

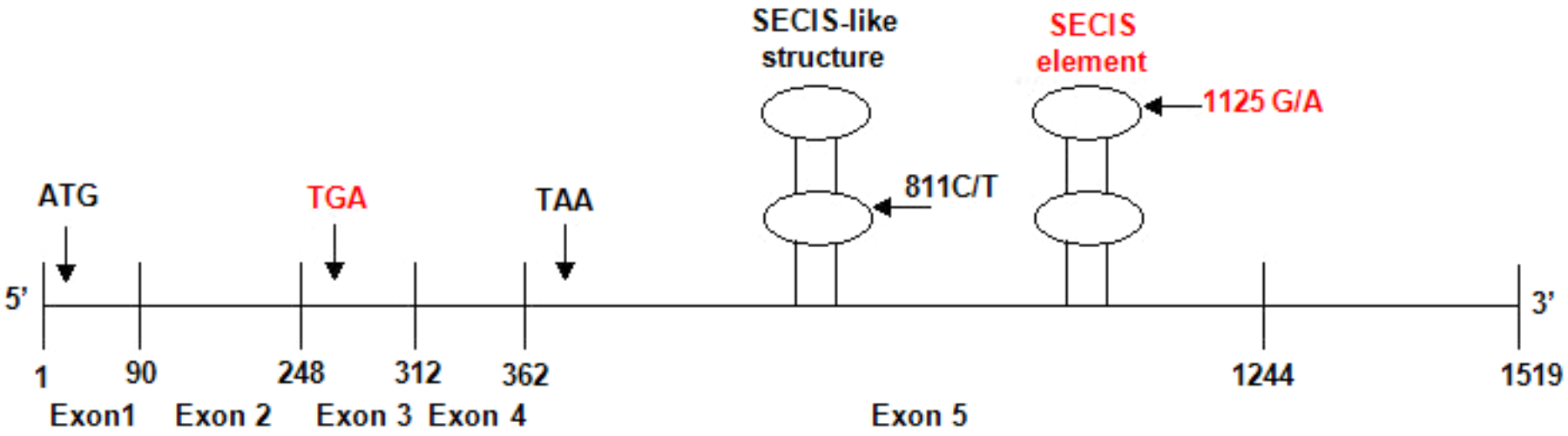
- ✓ Reduction of oxidized methionine residues, using thioredoxin as a reductant
- ✓ Two forms of this selenoprotein





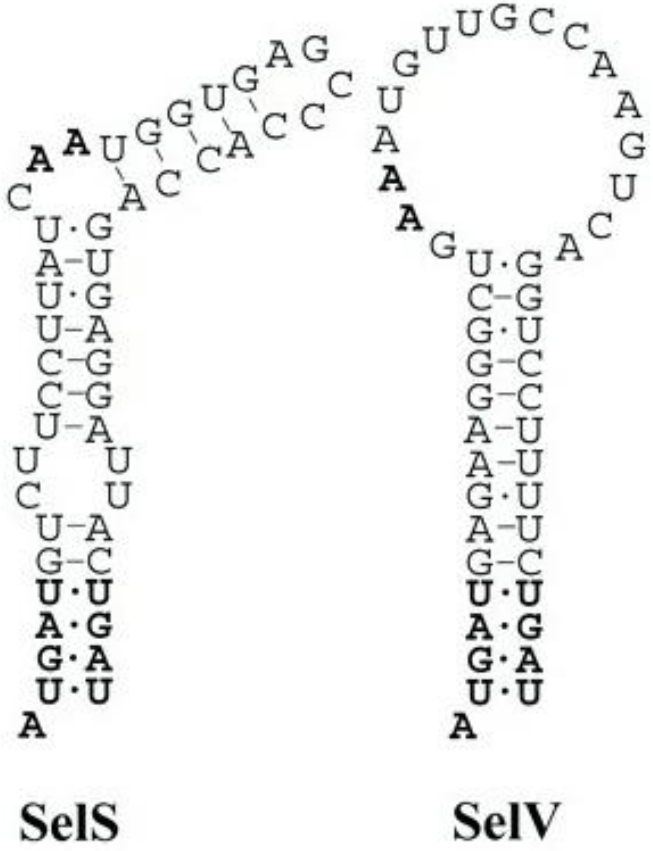
15 kDA Selenoprotein

- ✓ Mammalian protein
- ✓ Located in the endoplasmic reticulum
- ✓ Has a redox function and is also implicated in cancer prevention



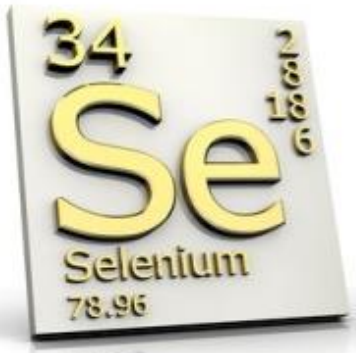
Selenoproteins V and S

- ✓ **Selenoprotein V:** In testes for spermatogenesis
- ✓ **Selenoprotein S:** Also involved in inflammatory and immune responses



Antioxidant Nutrient Interaction with Selenium

- ✓ **Copper and zinc:** Superoxide dismutase
- ✓ **Iron:** Catalase
- ✓ **Vitamin C:** Thioredoxin reductase maintains the antioxidant function of vitamin C by catalyzing its regeneration from its oxidized form, dehydroascorbic acid
- ✓ **Vitamin E (α-tocopherol):** Limits the oxidation of lipids, preventing damage from vitamin E deficiency in oxidative stress



Seelnium and Iodine Interactions

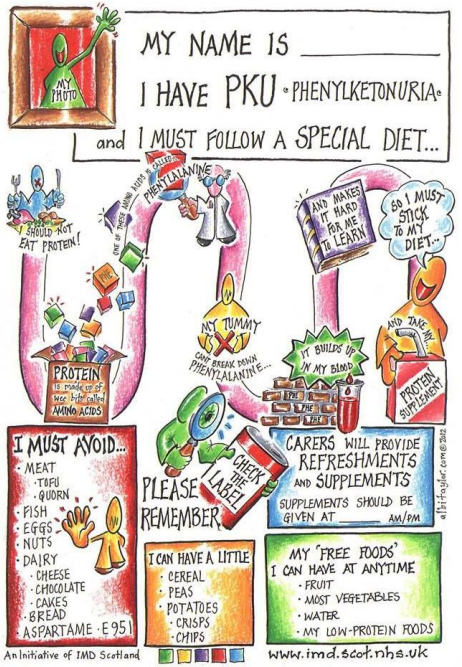
- ✓ Selenium deficiency may exacerbate the effects of iodine deficiency
- ✓ Iodine is essential for the synthesis of thyroid hormone
  - ➢ Selenium supplementation decreases plasma T4
  - ➢ Increased deiodinase activity
  - ➢ Increased conversion of T4 to T3

Selenium Deficiency

- ✓ Results in decreased activity of the glutathione peroxidases and other thioredoxin reductase and thyroid deiodinases
- ✓ Isolated selenium deficiency does not usually result in obvious clinical illness
- ✓ Selenium-deficient individuals appear to be more susceptible to additional physiological stresses

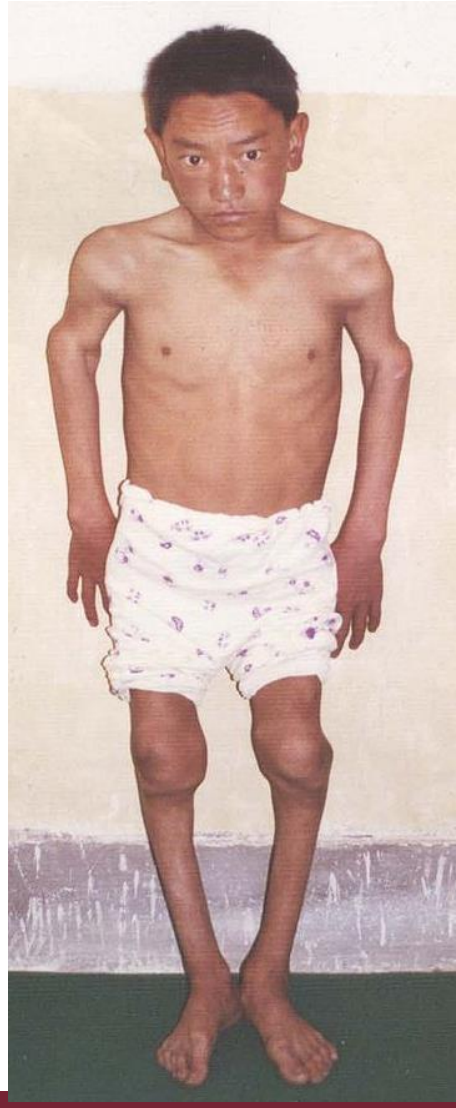
Risks of Selenium Deficiency

- ✓ Chronically ill people who receive total parenteral nutrition without added selenium for prolonged periods of time
- ✓ People who have had a large portion of the small intestine surgically removed
- ✓ Those with severe gastrointestinal problems, such as Crohn's disease ➔
  Impaired absorption
- ✓ Specialized medical diets used to treat metabolic disorders, such as phenylketonuria (PKU), are often low in selenium



Selenium Deficiency and Kashin-Beck Disease

- ✓ Characterized by the degeneration of articular cartilage between joints (osteoarthritis)
- ✓ Associated with selenium-deficient status
- ✓ Affects children between the ages 5 and 13 years
- ✓ Severe forms of the disease may result in joint deformities and dwarfism



Selenium Deficiency and Immune Function

- ✓ Selenium supplementation
  - ➢ Stimulates the immune response
  - ➢ 200 mcg/day of selenium as sodium selenite enhanced immune cell response to foreign antigens
- ✓ Plays a role in regulating the expression of cell-signaling molecules called cytokines, which orchestrate the immune response
- ✓ IV sodium selenite used in alternative cancer centers

Selenium Deficiency and Viral Infection

- ✓ Enhanced progression of some viral infections
- ✓ Oxidative stress induces changes in the expression of some viral genes
- ✓ Cellular glutathione peroxidase protects against myocarditis resulting from mutations in the genome of a previously benign virus
- ✓ Decreased activity of glutathione peroxidase
  - ➢ Increases oxidative damage and the likelihood of mutations in the viral genome

Selenium and Cancer

- ✓ Selenium supplementation
  - ➢ At high levels reduces the incidence of cancer
  - ➢ Significantly reduces tumor incidence
  - ➢ Methylated forms of selenium are the active species against tumors
- ✓ Low plasma selenium concentrations
  - ➢ Even greater risk of liver cancer
  - ➢ Associated with an increased risk of lung cancer

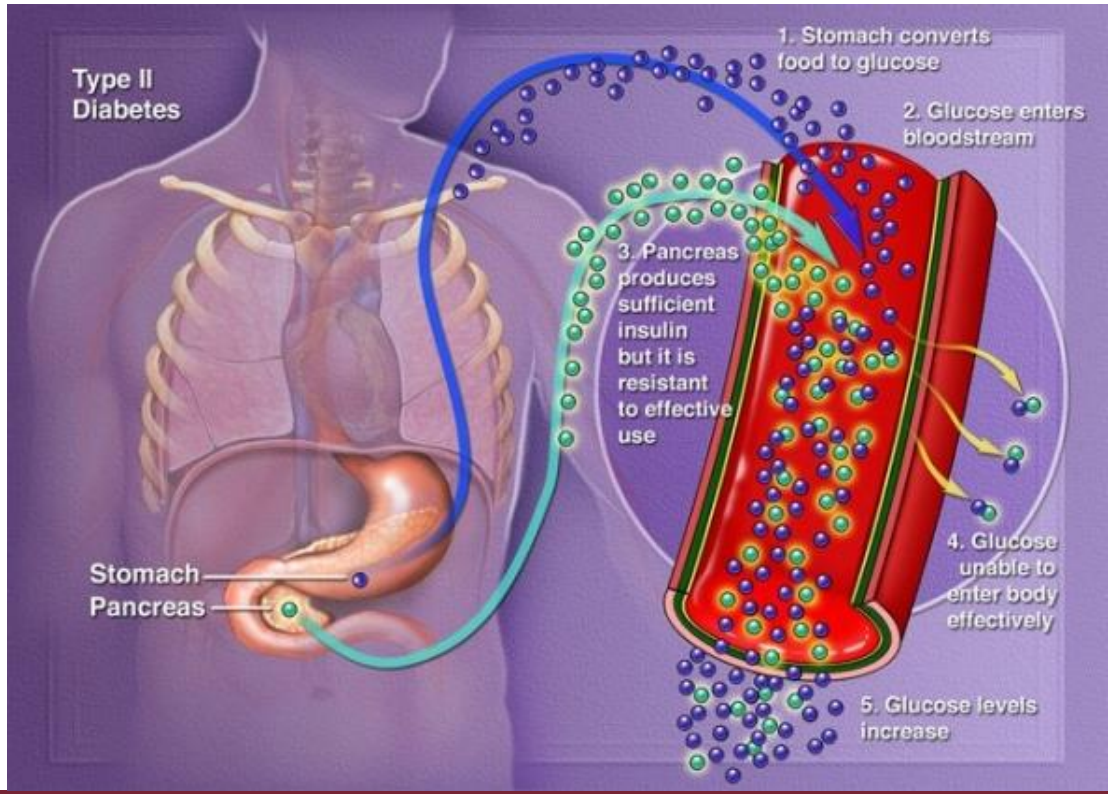
- ✓ Low dietary selenium intake
  - ➢ Associated with increased risk of prostate cancer
  - ➢ IV sodium selenite used as part of alternative cancer treatment

Selenium Deficiency and Cardiovascular Disease

- ✓ Optimizing selenoenzyme activity
  - ➢ Decreases the risk of cardiovascular disease
    - Decreases lipid peroxidation
    - Influences the metabolism of cell-signaling molecules known as prostaglandins
- ✓ Low levels of selenium increases the risk of cardiovascular disease

Selenium Deficiency and Type 2 Diabetes Mellitus

- ✓ Insufficient dietary: can interfere with the body's ability to effectively use insulin
- ✓ Selenium can promote diabetes
- ✓ Supplementary selenium decreases risk

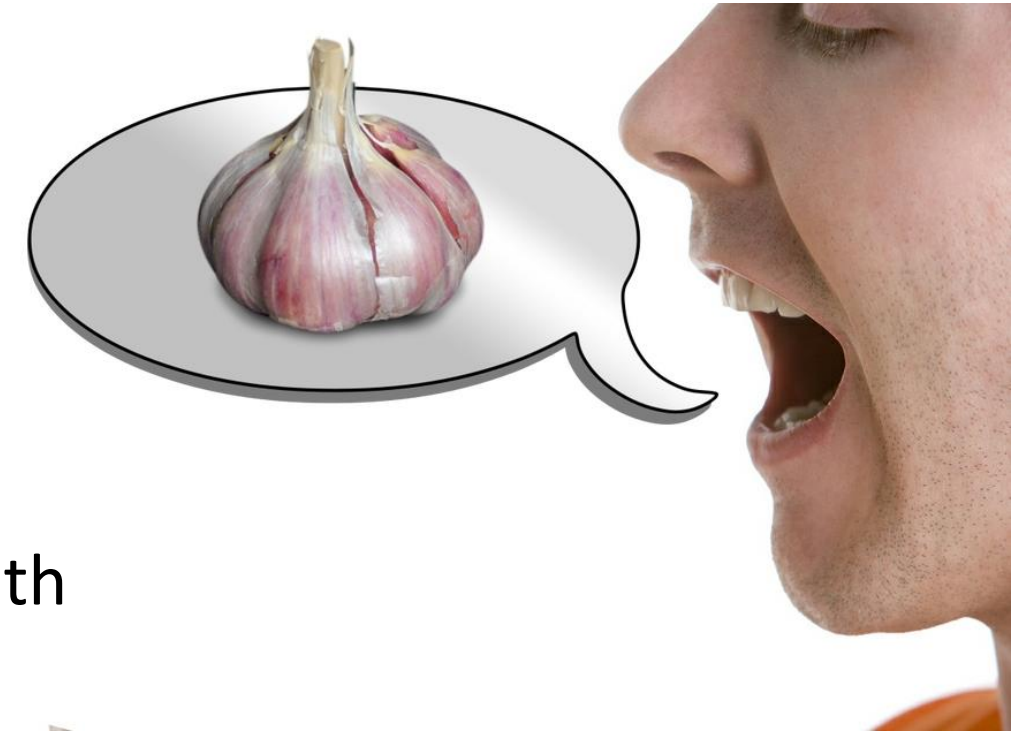


Selenium Deficiency and HIV/AIDS

- ✓ Interaction between selenium and the HIV that causes AIDS
- ✓ Declining selenium levels in HIV-infected individuals
  - ➢ Sensitive markers of disease progression and severity
  - ➢ Even before malnutrition becomes a factor
  - ➢ Associated with a significantly increased risk of death from HIV
- ✓ Adequate selenium nutritional status
  - ➢ May increase resistance to HIV infection
    - Enhances the function of T cells
    - Modifies T cell production of cytokines
- ✓ In HIV infection, increased oxidative stress appears to favor viral replication
  - ➢ Activates specific transcription pathways
  - ➢ Selenium plays an important role in decreasing oxidative stress in HIV-infected cells
  - ➢ Suppresses the rate of HIV replication
- ✓ HIV may be capable of incorporating host selenium into viral selenoproteins that have glutathione-peroxidase activity
- ✓ The immune system and the activity of the virus are affected by selenium nutritional status

Selenium Excess

- ✓ Garlic breath
- ✓ Nausea
- ✓ Diarrhea
- ✓ Skin rashes
- ✓ Irritability
- ✓ Metallic taste in the mouth
- ✓ Brittle hair or nails
- ✓ Loss of hair or nails
- ✓ Discolored teeth
- ✓ Nervous system problems



Recommended Dietary Allowance

Based on the amount of dietary selenium required to maximize the activity of the antioxidant enzyme glutathione peroxidase in plasma

Table 1: Recommended Dietary Allowances (RDAs) for Selenium [6]

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	15 mcg*	15 mcg*		
7–12 months	20 mcg*	20 mcg*		
1–3 years	20 mcg	20 mcg		
4–8 years	30 mcg	30 mcg		
9–13 years	40 mcg	40 mcg		
14–18 years	55 mcg	55 mcg	60 mcg	70 mcg
19–50 years	55 mcg	55 mcg	60 mcg	70 mcg
51+ years	55 mcg	55 mcg		

*Adequate Intake (AI)

Food Sources

Animal Based

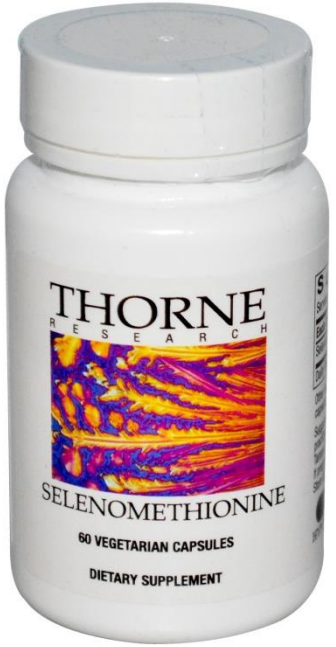
- Tuna
- Halibut
- Sardines
- Ham
- Shrimp

Plant Based

- Brazil nuts 100 mcg each nut
- Wild mushrooms
  - Pine mushrooms
  - Porcini mushrooms
- Reishi/chaga powders
- Chia seeds
- Mustard seeds

Supplements

- ✓ Sodium selenite and sodium selenate
  - ➢ Inorganic forms
  - ➢ Selenate is almost completely absorbed
    - Significant amount is excreted in the urine before it can be incorporated into proteins
  - ➢ Selenite is only about 50% absorbed but is better retained than selenite
- ✓ Selenomethionine
  - ➢ Organic form of selenium that occurs naturally in foods
  - ➢ About 90% absorbed
- ✓ Selenium-enriched yeast
  - ➢ Mainly supplies selenomethionine
  - ➢ The consumer should be aware that some forms of selenium yeast on the market contain yeast plus mainly inorganic forms of selenium
- ✓ Both inorganic and organic forms of selenium can be metabolized to selenocysteine by the body and incorporated into selenoenzymes

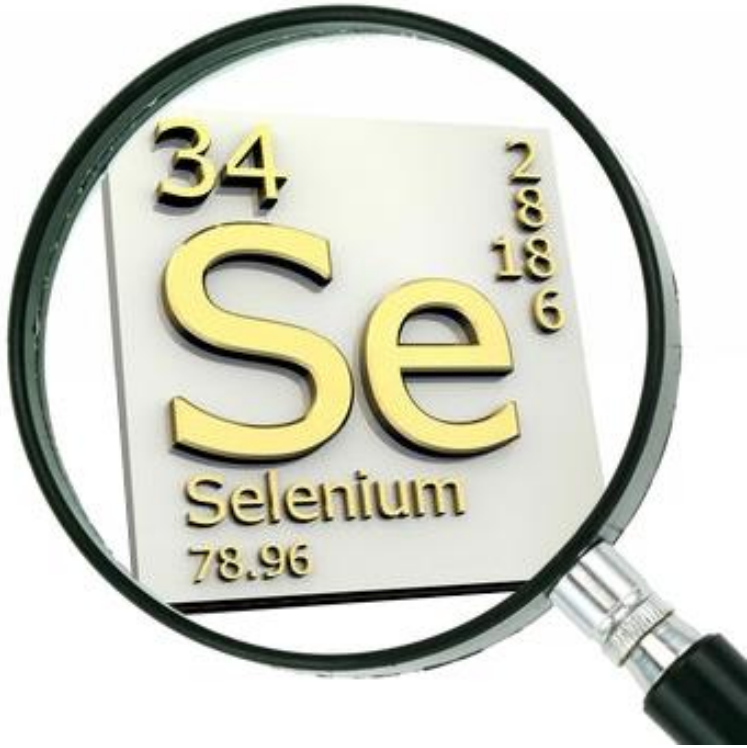


Drug Interactions

- ✓ The anticonvulsant medication valproic acid has been found to decrease plasma selenium levels
- ✓ Supplemental sodium selenite decreases the toxicities of the antibiotic nitrofurantoin and the herbicide paraquat

Selenium Assessment

- ✓Signs and symptoms
- ✓Family history and health history
- ✓Taste test
- ✓Organic acids test
- ✓Toxic and essential elements



References

- ✓ *Advanced Nutrition and Human Metabolism* – Gropper, Smith, and Groff
- ✓ *Modern Nutrition in Health and Disease*. 10th ed. - Shils, Shike, Ross, Caballero, Cousins, eds.
- ✓ *Trace Elements in Human and Animal Nutrition*. 5th ed. - Mertz
- ✓ *PDR for Nutritional Supplements*. 2nd ed. - Hendler, Rorvik
- ✓ Assessment Study: http://www.drritamarie.com/go/AmJCNSeleniumAssessment
- ✓ Linus Pauling Institute: http://www.drritamarie.com/go/LPISelenium

