NST 160
Theil Selenium Lecture 1
October 27, 2004
Selenium Nutrition and Physiology

Reading
Chapter 34: (Reserve BioSci Library) Stipanuk *Biochemical and Physiological Aspects of Human Nutrition*

NST 160 website:
http://nutrition.berkeley.edu/undergrad_class/nst1-60/
Selenium - Chemistry

Atomic number : 34

Periodic Table: Se (34) - same group as S (16) and O (8).
               Se (34) - same period as Mn(25), Fe(26), Cu(29), Zn(30)

Atomic weight (FW) g/mole: 78.9

Outer electron configuration: 3d = 10 (like Zn); 4s = 2; 4P = 4,
                           Se $^{4+}$ and Se $^{6+}$; semiconductor

Solubility: $\text{Na}_2\text{SeO}_4^{-2}$ - 4.4 M
## Elements of Life - Abundance: Period 1 > 2 > 3 > 4

<table>
<thead>
<tr>
<th>Period</th>
<th>Elements</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. H</td>
<td>Hydrogen is not really a group I element</td>
</tr>
<tr>
<td>2. C,N,O</td>
<td>Group I or alkali metal elements</td>
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<tr>
<td>3. Na, Mg, P, S, Cl</td>
<td>Group II or alkaline earth elements</td>
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<tr>
<td>4. Trace/micro”</td>
<td>Transition elements</td>
</tr>
<tr>
<td>5. Micro</td>
<td>Inert elements or Noble gases</td>
</tr>
<tr>
<td>6. -</td>
<td>Group VII or halogens</td>
</tr>
<tr>
<td>7. -</td>
<td>Trace/micro elements</td>
</tr>
</tbody>
</table>

Elements 113-118 have not been made.
Selenium - Physiology

Plasma concentration: (6-8 µg/L)

Plasma transport: in SelP (selenoprotein) and on serum albumin as selenite and selenide

Content (human body): 13-23 mg / 70 kg

Tissue distribution: 61% + muscle + liver+ kidney + blood); 30% in bone (related to thyroxine activity)

Recognition of biological relevance very recent!
1957 –Animal Se deficiency;  1980’s: Humans - Keshan Disease
Selenium - Nutrition

UL (Safe daily intake upper limit): 400 µg/day
RDA: 55 µg/day

Most American diets are Se sufficient.

Sources:
Organ meats: seafoods, muscle meats

Examples: beef liver, lobster tail, shrimp, tuna steak, pork loin

Plants: Variable with soils

Absorption: Seleno-amino acids are 50-90% absorbed

Enhancers: Vitamins A, C, E

Low soil Se/ high vegetable consumption → Se deficiency
(Example: Keshan province in China)
Se Toxicity: Rare overall except in selected geographic areas

Originally thought to be environmental toxin for livestock (1949 = “Awful poison”)

High Se soil

Natural: North and South Dakota, Colorado
Irrigation- San Joaquin Valley reservoir
High Se plants-absorb soluble Se → Se-methionine, Se cysteine)

Toxic effects: Cattle, sheep “blind staggers” / alkaline (soil) disease; anemia, hair loss, paralysis

Toxicity:
Chronic: > 5 ppm in total diet
Acute: 1-10 mg/Kg
Selenium Distribution in the U.S.

Black=Se def.
Grey=Se adeq
Black dots=toxic veg.
Selenium - Deficiency

Keshan’s Disease- Discovered in the 1980’s
  • Readily treated by Se Supplementation- Na SeO₃
  • Mainly in rural poor –low Se soil, low meat diet
  • Urban population – higher meat intake, little affect
  • Myocardial necrosis (Oxidative damage?).
    (Thyroxine deiodinase, key to active hormone synthesis, is an Se protein)
  *Kashan-Beck: Osteoarthiritis – China; may be Se + I deficiencies

*Other: Goiter – New Zealand; linked to iodine deficiency

*Not fully characterized
Selenium and Cancer

Selenium compounds appear to have “anti-cancer” properties

Mechanism:
- Human metabolism of plant selenomethionine?
- Se-protein catalysts?
- Both?

Anti-oxidant Se proteins
- Glutathione peroxidase, thioredoxin reductase,
- Met sulfoxide reductase

Methylselenol (CH$_3$SeH) has anticancer activity:
- Se Met (Dietary Plants) $\rightarrow$ CH$_3$SeH $\rightarrow$ apoptosis of malignant cells
Selenium Biochemistry

1973: glutathione peroxidase recognized as Se-protein

Se in two amino acids:

Selenocysteine (Sec)
  Synthesized in plants, animals and bacteria

Selenomethionine Se-Met:
  Synthesized in plants.
  Found in human diets - cereals, vegetables.
  Converted to Sec

pka: selenocysteine - 5.3
pKa: cysteine - 8.3

Sec is negatively charged at pH 7 like aspartate and glutamate.


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Selenium- Selenoproteins

1. Oxidative metabolism rates: Tissue T4 deiodinases - convert T4 to T3

Thyroxine (T4) made in thyroid, circulates in blood; cells convert T4 to T3, which binds thyroid hormone receptor; Multiple forms, many cell types

2. Cellular redox control: Thioredoxin* (Trx) Reductase (TrRX)

Trx-S₂ + NADPH + H+ → Trx-(SH)₂ + NADP⁺

All cell types, multiples forms

Expression changes in differentiation and cancer

*Thioredoxins: a group of small (~ 12 kDa) redox proteins, present in all cells converts glutathione ox, a hexa-peptide (GS-SG) to 2 glutathione (GSH), a tripeptide
Selenium- Selenoproteins (cont.)

3. Resistance to oxidative damage - Glutathione Peroxidase (GPX)
   Reverse membrane (lipid) oxidation; destroy \( \text{H}_2\text{O}_2 \).
   \[ 2 \text{GSH} + \text{ROOH} \rightarrow \text{ROH} + \text{H}_2\text{O} + \text{GSSG}; \ R= \text{fatty acid} \]

Multiple GPX forms

   RBC GPx, first Se-protein identified; all cells-GPX1
   Plasma- GPX 3
   Enterocyte GPX-2*
   Liver GPX -1,3,4

Se dietary deficiency response is hierarchal
   \( \text{GPX4} < \text{GPx3} < \text{GPX 1} \)

*Predict GPx 3 sensitivity [Se]- High? Low?
Selenium- Selenoproteins (cont.)

4- Plasma Se transport, antioxidative activity - Sel P

5. Methionine sulfoxide reductase- Sel R

6- “Orphan” Se proteins: ~ 10-30
   Detected with surveys of DNA sequences for SECIS (Sec Insertion Sequence) elements
Selenocysteine – Structure, DNA Code

Cysteine

Seleno - Cysteine

Cysteine

Cysteine

Selenocysteine

Stop

UGU

UGC

UGA

UGA

One codon – two uses

AUG Methionine

AUG Start

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Summary

Selenium Nutrition and Physiology

a) Toxicity: known before physiological requirement
b) Sufficiency: range narrow
c) Deficiency: cardiomyopathy; Goiter (+ I- def.); osteoarthritis
d) Cancer: Se derivatives have anti-tumor activity
e) Distribution:
   All cells
   Hi-Blood, Liver, muscle, bone
   Cell-specific isoforms
f) Source: Cereals, vegetables

Selenium Biochemistry

a) Two amino acids:
   Selenocysteine – synthesis: humans, animals, plants, bacteria
   Selenomethionine- synthesis: plants, converted to Sec in animals and humans
b) Se catalysts: antioxidant peroxidases, reductases (GPx, TrRX, SelR) and T4 deiodinases
c) Se regulation: protein-specific and hierarchal
d) Sec DNA code: 21st codon; second use UGA termination codon