Selenium is essential

Selenium

• keeps the immune system in balance
• protects against oxidative stress
• is important for the thyroid
Selenium: a brief overview

1. Selenium is an essential trace element

2. Selenium deficiency is common in Germany\(^{[A]}\)

<table>
<thead>
<tr>
<th>Selenium deficiency(^{[B]})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
</tr>
<tr>
<td>&lt;80 µg/l</td>
</tr>
<tr>
<td>Whole blood</td>
</tr>
<tr>
<td>&lt;100 µg/l</td>
</tr>
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</table>

3. Selenium deficiency can have negative effects on our health\(^{[C]}\)

4. Selenium deficiency can make certain viruses more virulent\(^{[D]}\)

5. Selenium administration in cases of selenium deficiency can support the effect of vaccinations\(^{[D, E]}\)

6. Selenium deficiency can be an indication of another disease

7. Examination of selenium status

8. Have your doctor measure your selenium status. If the selenium test reveals a selenium deficiency, the statutory health insurance covers the costs of prescription selenium drugs.

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\(^{[D]}\) Huang Z et al. *Antioxid Redox Signal, 2012 Apr 1; 16(7): 705-43*.

# Summary

**selenase® at a glance**

- **Corrects selenium deficiency**[^A]
- **Is safe:**
  1) No known side effects[^A]
  2) Few interactions with other medicines[^A]
  3) Broad therapeutic range[^A]

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What is selenium?

Selenium is an essential trace element. That means selenium is essential for life. Every single cell needs selenium. At the same time, selenium only occurs in very small amounts in the body (5–15 milligrams). However, selenium content in the body is two-thirds lower in countries with selenium-poor soils than in countries with selenium-rich soils (Table 1).[1]

### Selenium content in the body

<table>
<thead>
<tr>
<th>Country</th>
<th>Total amount of selenium in the body in countries with low-selenium soils</th>
<th>Total amount of selenium in the body in countries with selenium-rich soils</th>
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</thead>
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<tr>
<td>Poland</td>
<td>approx. 5.2 mg</td>
<td>approx. 13.0–20.3 mg</td>
</tr>
<tr>
<td>New Zealand</td>
<td>approx. 3.0–6.1 mg</td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td>approx. 6.6 mg</td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


*Table 1*
Which organ is the most selenium-rich?

Regardless of the total amount of selenium in the body, there are particularly selenium-rich organs in the body.\textsuperscript{[1,3]} The highest selenium concentration is found in the kidney and decreases in the order liver $\rightarrow$ testicles $\rightarrow$ spleen $\rightarrow$ heart $\rightarrow$ prostate $\rightarrow$ lung $\rightarrow$ muscle $\rightarrow$ brain (\textit{Fig. 1}).\textsuperscript{[4,5]}

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{selenium_in_organ.png}
\caption{Selenium in the organs}
\end{figure}

* measured per gram wet weight

Created according to:
What do we know about selenium?

Jens Jakob Berzelius, a Swedish chemist, discovered the metal selenium in 1817. He named the newly discovered element after the Greek moon goddess Selene. Selenium wasn’t really researched until the 20\textsuperscript{th} century. It was not until 1957 that it was discovered that selenium was an essential trace element.\textsuperscript{[6]} In the 1970’s it became clear that selenium deficiency can cause diseases.\textsuperscript{[7]}

Selenium plays a special role among the trace elements. In 1986 it was shown that selenium is incorporated into proteins as part of the amino acid selenocysteine (Fig. 2).\textsuperscript{[8]} Current selenium research involving over 30,000 publications (PubMed, Nov. 2018) shows how important selenium is for our health.

The special role of selenium

* selenium independent

Created according to: Benstoem C et al. Nutrients. 2015 Apr 27; 7(5): 3094-118. Selenium and its supplementation in cardiovascular disease--what do we know?
What makes selenium so special?

Selenium plays a special role among the trace elements. While, for example, iron is bound in the active center after the formation of hemoglobin, the incorporation of selenium takes place via a highly complicated biosynthesis process.

Proteins consist of amino acids, which in turn are encoded in the genetic code by 3 bases, the so-called codons. Start and stop codons are available for reading the mRNA. UGA (Uracil – Guanin – Adenin) stands for a stop codon. At least that’s what they thought for a long time. UGA also stands for the selenium-containing amino acid selenocysteine. To enable the cell to distinguish between UGA selenocysteine and a stop codon, nature has developed a highly complex biosynthesis involving several special proteins (Fig. 3). The more complicated a process is, the more error-prone it becomes. In recent years, several mutations have been found in selenium biosynthesis proteins in humans that can lead to various congenital diseases.

Complex biosynthesis of selenoproteins


Fig. 3
Mutations in selenium biosynthesis

Congenital metabolic disorders are increasingly being recognized as the cause of diseases. The number and range of diseases due to defects in selenium use, transport and metabolism is constantly growing (Fig. 4)\textsuperscript{[11, 12]}.\n
The first congenital metabolic disorder due to a mutation in a selenoprotein was identified in 2001. Mutations of selenoprotein N (SEPN1) cause so-called SEPN1-related myopathies.\textsuperscript{[12]} Patients suffer from early-onset muscle weakness and atrophy, mainly affecting the axial muscles, leading to scoliosis.

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*Fig. 4*
Selenium is incorporated by means of a highly complicated biosynthesis process.
Why do we need selenium?

At a glance

- Selenium plays an important role in the immune system\(^\text{(16)}\)
- Selenium is essential for the thyroid
- Selenium deficiency impairs sperm quality\(^\text{(25)}\)
- Preferential treatment of the brain in selenium deficiency
- Selenium also protects our brain in old age
- Selenium is important for the brain development of the fetus

Selenium is necessary for many metabolic processes in the body (Fig. 5). Selenium’s best known function is as an antioxidant\(^\text{(13)}\). Along with catalase and superoxide dismutase, the selenoprotein glutathione peroxidase is one of the three musketeers of antioxidative defense. However, selenoproteins fulfil many more important functions, some of which have not yet been fully researched. Selenium is essential for the thyroid and the brain\(^\text{(14,15)}\). Immune system functions also suffer from an inadequate selenium supply\(^\text{(16)}\). A massive selenium deficiency can cause cardiomyopathy\(^\text{(8)}\). In men, sperm production suffers, which can lead to infertility\(^\text{(17)}\).
Why do we need selenium?

What do we need selenium for?

- Antioxidant
- DNA repair
- Immune system
- Reproduction
- Heart
- Brain
- Thyroid

Created according to:
Huang Z et al. Antioxid Redox Signal. 2012 Apr 1; 16(7): 705-43. The role of selenium in inflammation and immunity: from molecular mechanisms to therapeutic opportunities.

Fig. 5
Selenium and the immune system

Selenium plays an essential role in the immune system. Two points make this clear:

- Selenium deficiency impairs the function of the immune system.
- Mutations that impair the biosynthesis of selenoproteins can lead to a defect in T cell proliferation.

Selenium deficiency and risk of infection

Selenium is particularly important for the proper functioning of the acquired immune system. Normally, there is a balance between a TH1 and TH2 immune response. If there is a selenium deficiency, the immune system becomes imbalanced, which promotes autoimmune diseases and allergies (Fig. 6). At the same time, the ability of the immune system to defend itself against viruses or tumor cells decreases. Thus selenium deficiency can increase the aggressiveness of viruses, for example. In contrast, a high dose of sodium selenite can enhance the TH1 immune response and thus protect against infections.

Selenium administration at vaccinations

An intact immune response is the basis for a successful vaccination. For example, the effectiveness of influenza vaccination may decrease in older people, possibly due to an age-related decrease in the immune response. Selenium deficiency also reduces the functioning of the immune system. Therefore it was obvious to check the effects of selenium supplementation before vaccination.

Several trials combined selenium supplementation, alone or as part of micronutrient supplementation, with influenza vaccination in elderly people. The result: selenium can improve the immune response in older people. The selenium form and dosage, however, play a role. Too little selenium (50–60 µg per day) showed a lower or no effect. Too much organic selenium (200 µg per day), as shown in a small trial with selenium yeast, was not beneficial either.

Another trial investigated the effect of selenium supplementation at polio vaccinations. In the double-blind trial, 66 adults with a serum selenium concentration of approximately 80 µg/l received a placebo, 50 or 100 µg selenium per day in the form of sodium selenite. Sodium selenite increased the activity of the immune system compared to the placebo group and the poliovirus clearance after vaccination (Fig. 7). Even when the immune system was put to the test with a renewed polio vaccination using live vaccine, the selenium group showed an increased response of the immune cells, especially the TH1 lymphocytes.
High-dose sodium selenite enhances TH1 differentiation


Fig. 6

Sodium selenite improves poliovirus clearance


Fig. 7
Selenium and the thyroid

The thyroid is the organ with the highest selenium content in the body and is therefore particularly sensitive to selenium deficiency.\cite{15} Like iodine, selenium is essential to the thyroid. Selenoproteins are required to form active thyroid hormone (T3) and to degrade the resulting hydrogen peroxide to water.

The hormones produced by the thyroid influence overall physical development. For example, they control energy and bone metabolism, digestive function, cardiovascular functions and the mental state. Therefore, a selenium deficiency has a negative effect on the body due to the insufficient formation of an active thyroid hormone. In addition, an inadequate selenium supply leads to a lack of protective proteins and thus to destruction of thyroid tissue (Fig. 8).
WHY DO WE NEED SELENIUM?

Effects of selenium deficiency on the thyroid

1. Lower selenium status
   - Reduced activity of deiodinase
   - Reduced activity of glutathione peroxidase
   - Impaired conversion of thyroid hormones
   - Increased oxidative stress
   - Thyroid disorders
   - Increased inflammation disposition


Fig. 8
Male infertility

There is a hierarchy in the distribution of selenium in the human body. Where the selenium supply is most important, the body will always try to ensure a sufficient selenium supply. It’s the brain and the testicles.

Without selenium nothing works in sperm production. If there is a selenium deficiency, the sperm quality suffers (Fig. 9). This can lead to infertility.

The additional intake of selenium can correct infertility due to a selenium deficiency.\textsuperscript{[26,27]}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{selenium图表.png}
\caption{Influence of selenium deficiency on sperm quality}
\end{figure}


\textit{Fig. 9}
Selenium and the brain

Our brain is not only preferred to receive sufficient energy. The brain also gets extra attention with the selenium supply.

The brain contains only 2.3% of the total amount of selenium in the body. But if the selenium supply is insufficient, the brain retains selenium at the expense of other organs. Thus, the activity of the selenoprotein glutathione peroxidase, which is one of the most important factors in reducing oxidative stress, decreases by more than 90% in the liver when there is a selenium deficiency. In contrast, activity in the brain decreases by only 10% (Fig. 10). This is very important because brain cells are extremely sensitive to oxidative stress. Without the preferential treatment of the brain, the neuronal damage caused by oxidative stress would be immense.

![Preferential treatment of the brain with selenium deficiency](image)


Fig. 10
Selenium supply in old age

Studies with older people have shown that a low selenium status is associated with a poorer result in cognitive tests.\textsuperscript{[29,30]} Conversely, this means that a long-term adequate intake of selenium is advantageous for maintaining the intellectual abilities of older people.

Selenium status in expectant mothers

But it is not only in old age that selenium protects our brain. Selenium is also important for brain development in the fetus. The fetus needs active thyroid hormone from the mother for proper brain development, as it cannot yet produce the hormone itself (Fig. 11). However, a selenoprotein is required to activate the thyroid hormones.\textsuperscript{[15]} If the pregnant woman consumes too little selenium daily, this can have an effect on the cognitive development of the child, for example.\textsuperscript{[31,32]}
Maternal selenium is important for fetal brain development

1st trimester
- visual attention
- visual processing
- gross motor skills

2nd trimester
- visual-spatial skills
- fine motor skills

3rd trimester
- language, memory
- attention, IQ

Brain development

- Dependence on maternal T4 production
- Fetal neonatal potential

Modified according to: La Gamma EF et al. NeoReviews 2016; 17: e394. Transient Hypothyroxinemia of Prematurity.

Fig. 11
Selenium must be ingested through food.
Do we consume enough selenium?

At a glance

Little selenium in the soil – little selenium in the food

The healthier the diet, the lower the selenium intake

The EFSA (European Food Safety Authority) recommends an intake of 70 μg selenium per day for adults [40]

In Germany we consume too little selenium [41]

Selenium content in German food is too low overall

Brazil nuts – ideal for selenium supply or hidden source of danger?

Selenium cannot be produced by the body itself and must therefore be ingested through food. [35] Insufficient selenium intake affects up to one billion people worldwide. [34]
Little selenium in the soil – little selenium in the food

Germany soils – like most of its neighbors – is poor in selenium.\textsuperscript{[35, 36]} The selenium content of German arable soils is between 0.074 – 0.194 mg/kg (Fig. 12). The optimal selenium content is significantly higher at 0.6 – 4.0 mg/kg.\textsuperscript{[78]} Soils with a selenium content between 0.1 – 0.6 mg/kg are classified as deficient. In the USA, the selenium content of soils is between 0.1 – 5.32 mg/kg.\textsuperscript{[37]} German soils contain little selenium due to geological developments. Since plants can only absorb selenium from the soil, grain in Germany, for example, contains only about one tenth of the amount of selenium found in American grain.\textsuperscript{[79, 82]}

Farm animals are largely fed with indigenous, selenium-poor feed. As a result, farm animals throughout Europe are affected by a greatly increased risk of diseases caused by selenium deficiency.\textsuperscript{[80]} Therefore, EU farm animals are often fed selenium-enriched fodder.\textsuperscript{[80]}

Also, selenium is added everywhere in pet food in order to avoid a selenium deficiency and its negative effects.\textsuperscript{[81]} For humans, on the other hand, it is difficult to sufficiently cover their selenium needs with food.

German soils predominantly contain too little selenium
### Selenium content in German soils

<table>
<thead>
<tr>
<th>Region</th>
<th>Selenium Content (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schleswig-Holstein</td>
<td>0.194</td>
</tr>
<tr>
<td>Mecklenburg-Western Pomerania</td>
<td>0.149</td>
</tr>
<tr>
<td>Lower Saxony</td>
<td>0.155</td>
</tr>
<tr>
<td>Bavaria</td>
<td>0.074</td>
</tr>
<tr>
<td>Baden-Württemberg</td>
<td>0.086</td>
</tr>
<tr>
<td>Hesse</td>
<td>0.142</td>
</tr>
<tr>
<td>Rhineland-Palatine</td>
<td>0.114</td>
</tr>
<tr>
<td>North-Rhine-Westphalia</td>
<td>0.121</td>
</tr>
<tr>
<td>Rhineland-Palatine</td>
<td>0.114</td>
</tr>
<tr>
<td>Lower Saxony</td>
<td>0.155</td>
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<td>Bavaria</td>
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</tr>
<tr>
<td>North-Rhine-Westphalia</td>
<td>0.121</td>
</tr>
<tr>
<td>Bavaria</td>
<td>0.074</td>
</tr>
</tbody>
</table>

**Optimal selenium concentration:** 0.6 – 4 mg/kg

The selenium content was not checked in the remaining states.

Created according to:


*Fig. 12*
A healthy diet versus an adequate supply of selenium?

Those who eat a healthy diet are able to supply the body with all the necessary minerals it needs. That is our fundamental conviction. But it appears that in fact this is not always the case. According to the German Nutrition Society, a healthy diet looks like this (Fig. 13):
75% of selenium uptake is via meat, cereals, dairy products and fish (Fig. 14). The proportion of vegetables and fruit in the selenium intake is just 7%. [39]

The comparison with the DGE requirement for a healthy diet and the distribution of a selenium-rich diet is clearly contradictory. To put it bluntly: “The healthier the diet, the lower the selenium intake”.


Fig. 14
How much selenium does an adult need?

The EFSA (European Food Safety Authority) recommends an intake of 70 micrograms (μg) of selenium per day for adults, and between 55 and 70 μg of selenium per day for adolescents, depending on age and weight.[40]

Recommended daily amount of selenium (RDA)

The daily recommended amount of selenium (RDA of selenium) of the German Society for Nutrition (DGE) is 60 μg per day for adult women and 70 μg per day for adult men.[76] These values are published jointly by the D-A-CH countries (Germany, Austria and Switzerland) and are based on a reference body weight of 70.7 kg for men and 60 kg for women.[77] A daily selenium intake of 1 μg/kg was assumed for healthy individuals.

EFSA, the equivalent of DGE in the EU, has similar values. The background for this assessment is, among other things, a study in which an amount of 50–60 μg selenium per day was not sufficient to achieve an optimal concentration of the selenium transport protein selenoprotein P.[43] EFSA therefore recommends 70 μg selenium per day for adult men and women.[40]

Limitations of the RDA of selenium

Overweight people have a higher risk of selenium deficiency. The background for this is the reference body weight used in the DGE recommendation. The average body weight in Germany in 2013 was 84.3 kg for men and 68.4 kg for women.[44] For a healthy average German, 70 μg or 60 μg of selenium per day are sufficient. With increasing body weight, the daily recommended amount of selenium may no longer be sufficient. In addition, the body can require significantly more selenium in the case of disease. In intensive care medicine, for example, up to 1,000 μg selenium per day are used to correct a selenium deficiency or to achieve a stable selenium status in the reference range.[45]
Do we consume enough selenium in Germany?

EFSA recommends an intake of 70 µg selenium per day for adults and between 55 and 70 µg selenium per day for adolescents, depending on age and weight. However, the estimated daily intake is only between 34 and 60 µg (Fig. 15).

Insufficient daily selenium intake in Germany

![Chart showing selenium intake in Germany]

Created according to:

*Fig. 15*
Are there foods particularly rich in selenium?

There are selenium-accumulating plants. These plants can be divided into three groups: sodium selenite accumulators (broccoli and cucumber), selenomethionine accumulators (cereals such as wheat and mushrooms) and methylselenocysteine (garlic and onions). However, these plants can only enrich selenium that is present in the soil. Therefore, the selenium content in German food is too low overall.

Brazil nuts – ideal for selenium supply or hidden source of danger?

The question of natural selenium-rich foods is often asked. The answer is usually Brazil nuts. And it is true that no other plant enriches as much selenium in its fruit as the Brazil nut tree. The recommendation is two Brazil nuts a day to meet an adult’s need for selenium. That sounds simple and unproblematic at first. However, there are two major problems with Brazil nuts (Fig. 16).

Brazil nuts and aflatoxins

Aflatoxins are a naturally occurring fungal toxin found in molds. Aflatoxin is one of the strongest naturally occurring toxins and carcinogenic substances. In addition, aflatoxins are heat-stable. This means that only a small part is destroyed during cooking or baking.

EU import ban on Brazil nuts

Brazil nuts in particular are susceptible to aflatoxins, as the warm and humid climate in South America is conducive to the growth of molds (see Fig. 16). The aflatoxin load of Brazil nuts often exceeds the limits set by the EU, which is why a special implementing regulation has regulated the import of Brazil nuts since 2003. As a result, Brazil nuts were temporarily no longer imported into the EU and trade has declined to this day.
Brazil nuts occupy a special position among foods when it comes to radioactivity. Brazil nuts have a radium content per kilogram that is about 1,000 times higher than all other foods in Germany (see Fig. 16). A daily intake of two Brazil nuts results in a value of 160 microsieverts. With an average diet, radiation exposure from food amounts to 300 microsieverts per year. This means that the consumption of two Brazil nuts per day increases the radioactive load by about half. No negative health consequences are to be expected with these values, but the Federal Office for Radiation Protection nevertheless points out that the selenium status can also be improved by dietary supplements.

Created according to:
Bundesamt für Strahlenschutz (The German Federal Office for Radiation Protection), access April 2018.

Fig. 16
Selenium deficiency

At a glance

- Selenium deficiency is widespread in Germany
- A low selenium status may be associated with a higher mortality rate in the long term
- Numerous risk groups
- Risk factor – overweight
- Selenium deficiency – possible indication of another disease

In Europe, for example, selenium deficiency is widespread.\cite{48} A selenium deficit is associated with a variety of diseases.\cite{39} Selenium deficiency diseases include the Keshan and Kashin Beck diseases, which occur in Asia, especially in certain regions of China.\cite{49,50} Keshan’s disease is a cardiomyopathy. The actually harmless Coxsackie virus becomes virulent in a selenium deficiency and can trigger Keshan disease (Fig. 17).\cite{49} Kashin-Beck disease is a disease of the bones and joints. The preventive administration of selenium protects against both diseases.\cite{49,50}

Selenium deficiency in Germany

Selenium deficiency is also widespread in Germany. Women in the EPIC study had a mean serum selenium concentration of 73.2 µg/l and men had 74.3 µg/l (Fig. 18).\cite{48} A selenium deficiency is present in the serum at values below 80 µg/l.\cite{51}
How a selenium deficiency turns harmless viruses unnoticed into killers

Harmless Coxsackie virus → Selenium deficiency → Virulent Coxsackie virus → Keshan disease (cardio-myopathy)

Fig. 17

Deficit selenium status in Germany

Serum selenium concentration [µg/l]

Reference range

Women | Men


Fig. 18
Selenium deficiency – more than just laboratory cosmetics

The two selenium deficiency diseases Keshan and Kashin-Beck do not occur in Europe. Here, the effects of selenium deficiency are more subtle, but no less negative in the long run. For example, a low selenium status is associated with a higher mortality rate in the long term (Fig. 19).[^39]

![Relationship between selenium status and all-cause mortality](image)

Modified according to: Rayman MP. Lancet. 2012 Mar 31; 379(9822): 1256-68. 
Selenium and human health.

Fig. 19
How can you tell a selenium deficiency?

The symptoms of selenium deficiency are non-specific and also occur in connection with other diseases. These include fatigue, poor performance, hair loss and the whitening of fingernails. In addition, liver dysfunction, arthritis, muscle weakness and infertility may occur. Selenium deficiency can limit the function of the immune system and the thyroid. The risk of cancer or cardiovascular disease is increased (Fig. 20).

Who has an increased risk of selenium deficiency?

The risk of selenium deficiency may increase due to both limited intake and increased demand. The daily intake of selenium is significantly reduced in vegetarians, vegans, alcoholics, celiac patients and dialysis patients (Fig. 21). Even with a strongly one-sided diet or patients with malabsorption, too little selenium is absorbed.

Breastfeeding women, patients with diabetes, kidney damage, bulimia, anorexia, diarrhea, obesity, maldigestion and malabsorption have an increased selenium requirement. In cancer patients or in event of surgery, the body consumes significantly more selenium, resulting in a sharp decline in selenium levels.
Effects of a selenium deficit

- **HAIR**: Hair loss
- **BRAIN**: Fatigue, vitality deficiency
- **THYROID**: Impaired thyroid function, hypothyroidism
- **HEART**: Increased probability of cardiovascular disease
- **ORGANISM**: Impaired function of the immune system, increased probability of cancer
- **LIVER**: Liver dysfunction
- **TESTICLES**: Infertility
- **MUSCLES**: Muscle weakness
- **BONES**: Arthritis
- **NAILS**: White coloring of the nails

Created according to:
Huang Z et al. Antioxid Redox Signal. 2012 Apr 1; 16(7): 705-43. The role of selenium in inflammation and immunity: from molecular mechanisms to therapeutic opportunities.


*Fig. 20*
Risk groups for selenium deficiency

<table>
<thead>
<tr>
<th>one-sided nutrition</th>
<th>obesity</th>
<th>alcoholics</th>
</tr>
</thead>
<tbody>
<tr>
<td>vegans</td>
<td>celiac patients</td>
<td>vegetarians</td>
</tr>
<tr>
<td>cancer patients</td>
<td>dialysis patients</td>
<td>diabetes</td>
</tr>
<tr>
<td>breastfeeding mothers</td>
<td>surgery</td>
<td>maldigestion</td>
</tr>
<tr>
<td>vegans</td>
<td>diabetics</td>
<td>malabsorption</td>
</tr>
</tbody>
</table>

Created according to:


Fig. 21
Risk group vegetarians and vegans

More and more people are changing their diet and becoming vegans or vegetarians in the belief that they are doing something good for their health. The finding of a North American trial supports this theory. As a result, the risk of colorectal cancer among vegetarians in the USA is 22% lower.

Does this also apply to Europeans?

The evaluation of European trials comes to a different conclusion. European vegetarians suffer from intestinal cancer just as frequently as “omnivores”. Only vegetarians who also eat fish have a reduced risk of colon cancer.

What’s the difference?

The eating habits of Americans and Europeans are comparable. A noticeable difference can be seen in the selenium status. US vegetarians have significantly higher selenium levels than European vegetarians.

Risk factor vegetarian diet

Why is a vegetarian diet a risk factor for selenium deficiency? In the western industrial nations, 75% of selenium intake results from consuming meat, cereal and dairy products as well as fish.

Vegetarians do not use meat and fish as selenium sources, which reduces the daily selenium intake by about 30%. With vegans the picture looks even darker. Their daily selenium intake is reduced by about 75%.

Considering the fact that European “omnivores” also consume too little selenium every day in most cases, selenium intake can reach dangerously low levels.
Overweight as a risk factor

Since the daily selenium requirement is designed for people of normal weight, a higher selenium requirement is associated with increased body weight. In addition, overweight often leads to an increase in oxidative stress (Fig. 22).\textsuperscript{[59,60]} One of the main tasks of selenoproteins is the reduction of oxidative stress. Conversely, increased oxidative stress increases the daily selenium requirement.

Increased selenium requirements in obese people

Modified according to: Manna P, Jain SK. Metab Syndr Relat Disord. 2015 Dec; 13(10): 423-44. \textit{Obesity, Oxidative Stress, Adipose Tissue Dysfunction, and the Associated Health Risks: Causes and Therapeutic Strategies}.
Selenium intake for overweight and obese people

A larger-scale clinical trial conducted in Newfoundland with over 3,000 participants was able to prove the increased need for selenium in overweight and obese people with indisputable figures.\textsuperscript{[52]} In North America, the selenium supply is usually sufficient to meet daily needs.\textsuperscript{[1]} Nevertheless, daily selenium intake based on body weight was 15\% lower for overweight people (BMI 25 – 29.9) and about 30\% lower for BMI over 30 (obesity) compared to people of normal weight (Fig. 23).\textsuperscript{[52]}

Selenium and body fat

Body weight is composed of different elements: besides the bones and muscles, it also includes body fat. During the investigations in Newfoundland, the daily selenium intake was additionally determined in relation to the proportion of body fat.\textsuperscript{[52]} As with body weight, the daily selenium intake per kilogram decreased as the proportion of body fat increased (Fig. 24). So the decisive factor is the body fat percentage, not the muscle mass. Expressed in numbers, each microgram of selenium more per kilogram consumed per day correlated with a 3–6\% decrease in body fat.\textsuperscript{[52]}

Each additional microgram of selenium per kilogram correlates with a lower body fat percentage
Reduced selenium intake in overweight patients

![Graph showing daily selenium intake per kilogram of body weight for normal weight (BMI 18.5–24.9), overweight (BMI 25–29.9), and obesity (BMI ≥ 30) patients.]

Classification according to BMI

- Normal weight (BMI 18.5–24.9)
- Overweight (BMI 25–29.9)
- Obesity (BMI ≥ 30)


Fig. 23

Low selenium intake with higher body fat content

![Bar chart showing percentage of body fat in weight for low, mean value, and high daily selenium intake in men and women.]


Fig. 24
Selenium deficiency – possible indication of severe disease

Regardless of the disease, the selenium status decreases with the severity of the disease. This effect occurs in patients in intensive care as well as in cancer patients. The serum selenium concentration is therefore an independent marker for mortality in the intensive care unit or the survival probability of breast cancer patients (Fig. 25).

A selenium deficiency is not only a sign of an inadequate selenium supply, but can also be an indication of a serious illness in which selenium consumption has increased sharply.

2.5-fold increase in 5-year all-cause mortality in selenium deficiency

![Graph showing 2.5-fold increase in 5-year all-cause mortality in selenium deficiency](image)


*Fig. 25*
What is the selenium status?

At a glance

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimum selenium status in serum</td>
<td>approx. 130 µg/l</td>
</tr>
<tr>
<td>Average selenium status of Germans</td>
<td>75 µg/l</td>
</tr>
</tbody>
</table>

The selenium status is determined in the blood and expressed in micrograms per liter. An optimal selenium supply achieves the maximum activity of the selenoproteins. However, the maximum activity of the different selenoproteins lies at different selenium concentrations in the blood. For the glutathione peroxidase the value is 95 µg/l, for the selenium transport protein selenoprotein P 124 µg/l selenium in serum (Fig. 26).[62,63] If one looks at the German average with this value in mind, Germany must be regarded as an area with a pronounced selenium deficiency. The average selenium value of Germans is 75 micrograms per liter in serum.[48]
WHAT IS THE SELENIUM STATUS?

Selenium status

<table>
<thead>
<tr>
<th>Selenium deficiency</th>
<th>Reference range of selenium in Germany</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean selenium concentration in Germany</td>
<td>Optimal activity of glutathione peroxidase</td>
</tr>
<tr>
<td>Optimal activity of selenoprotein P</td>
<td></td>
</tr>
</tbody>
</table>

Serum selenium concentration [µg/l]

60 70 80 90 100 110 120 130 140

Created according to:


Fig. 26
How is the selenium status determined?

The selenium status is best measured with a blood test at your doctor’s office, preferably in whole blood, as this value indicates the long-term supply (Fig. 27). The serum value only reflects the current supply of selenium. It can happen that the serum value already signals a normal selenium status, while a selenium deficiency can still be detected in whole blood.

* serum contains only 1/3 of the selenium

Fig. 27
Caution – check the actual selenium level

Some laboratories offer selenium measurements. Do not rely on the “selenium deficiency – yes or no” assessment of the laboratory or your doctor, but check your personal selenium level carefully.

Why? Different reference ranges are used in the laboratories, which also almost always show a selenium deficiency only at values below 50–60 µg/l selenium in serum or whole blood. However, a selenium deficiency already begins at values below 80 µg/l selenium in serum or below 100 µg/l selenium in whole blood. These values were determined by the agency for medicinal products and are authoritative (Fig. 28).[51]

### When is there a selenium deficiency?

<table>
<thead>
<tr>
<th>Whole blood</th>
<th>Serum</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 µg/l</td>
<td>80 µg/l</td>
</tr>
<tr>
<td>1.3 µmol/l</td>
<td>1.0 µmol/l</td>
</tr>
<tr>
<td>140 µg/l</td>
<td>120 µg/l</td>
</tr>
<tr>
<td>1.8 µmol/l</td>
<td>1.5 µmol/l</td>
</tr>
</tbody>
</table>

**Selenium deficiency:**
- < 80 µg/l selenium in serum,
- < 100 µg/l selenium in whole blood

Created according to: [Summary of product characteristics selenase® T peroral](#), biosyn Arzneimittel GmbH, November 2017.

*Fig. 28*
biosyn Service Laboratory

The biosyn service laboratory offers you full-service range for the determination of selenium, other trace elements and heavy metals in whole blood, serum, urine or saliva. The significance of selenium determinations for selenium supply is improved by the determination in whole blood.

The analysis is carried out using modern methods such as atomic absorption spectroscopy or photometry. The accuracy of the results is guaranteed by regular participation in official interlaboratory comparisons. Together with the measured values, you receive an evaluation of the results and a comparison with the reference values. Furthermore, therapy recommendations are given for concentrations outside the reference range.

The required material (urine tube or special blood collection system including cannula and protective sleeve, request for analysis and mailing bag) will be sent free of charge on request.

All information is available at http://biosyn.de/service/servicelabor/.

You can print out the complete form via the link “Analysenanforderung” (“Analysis request”).

Otherwise you can order the form as well as the required shipping material by telephone (+49 (0) 711 575 32-00) or by e-mail (information@biosyn.de).

Information is available at:
http://biosyn.de/service/servicelabor/

Trace element and heavy metal measurement at biosyn

Certified laboratory

<table>
<thead>
<tr>
<th>Selenium test</th>
<th>Amtest®*</th>
</tr>
</thead>
<tbody>
<tr>
<td>19.90 €</td>
<td>39.60 €</td>
</tr>
</tbody>
</table>

* Heavy metal mobilization test

biosyn Arzneimittel GmbH · Schorndorfer Straße 32, 70734 Fellbach, Germany
Phone: +49 (0) 711 575 32-00 · www.biosynpharma.com · information@biosyn.de

The information provided must not be understood as a request for a specific treatment or non-treatment or for self-treatment or self-recognition of a possible illness or the like. Information is not a substitute for an examination or treatment by a doctor or a consultation in a pharmacy.
selenase® corrects selenium deficiency

At a glance

<table>
<thead>
<tr>
<th>GMP active ingredient: sodium selenite pentahydrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>selenase®: proven use in numerous RCT studies</td>
</tr>
</tbody>
</table>

The active ingredient in selenase® is sodium selenite pentahydrate. Sodium selenite is an inorganic form of selenium that effectively and safely corrects selenium deficiency.\(^{[51]}\) This has been proven in numerous trials from a wide variety of disciplines (including intensive care, oncology, endocrinology) (Fig. 29).\(^{[45, 64–69]}\)
selenase® effectively corrects selenium deficiency

![Graph showing selenium concentrations before and after selenase® therapy](image)

- Reference range
- Before selenase® therapy
- After selenase® therapy

**Legend:**
- Intensive care
- Oncology
- Endocrinology

* converted from whole blood values

Created according to:
- Bloos F et al. JAMA Intern Med. 2016 Sep 1; 176(9): 1266-76. Effect of Sodium Selenite Administration and Procalcitonin-Guided Therapy on Mortality in Patients With Severe Sepsis or Septic Shock: A Randomized Clinical Trial.

Fig. 29
Is selenium always the same?

At a glance

There are two forms of selenium:
- the inorganic form – main form: sodium selenite
- the organic form – main form: selenomethionine

Sodium selenite: fast and targeted dosage

Selenium is basically available in two forms, inorganic and organic. The most common inorganic form of selenium is sodium selenite. The most common organic form is selenomethionine. When selenium is ingested from food, the predominant form of selenium is selenomethionine.

Why sodium selenite?

The advantage of sodium selenite is that it is absorbed by the body through passive diffusion and quickly converted into selenoproteins. The body also excretes it mainly via the urine, which is why it does not accumulate unnecessarily. The complete path of sodium selenite in the body is precisely regulated by the body.
Why not organic selenium?

Although the bioavailability of selenomethionine is higher than that of sodium selenite, absorption is much more complicated. Selenomethionine is not recognized by the body as a form of selenium, but is confused with the sulfurous amino acid methionine. As a result, selenomethionine is incorporated unspecifically and unregulated into proteins containing sulfur. Some of the sulfur-containing proteins in which selenomethionine is non-specifically incorporated can be regenerated by the body and the selenium contained can be used for the synthesis of selenoproteins. This process does not take place as required, but as a function of methionine conversion. The other part of selenomethionine is unspecifically incorporated into non-regenerable proteins found, for example, in hair and red blood cells. This selenium can no longer be supplied to the selenium cycle, but accumulates in the body. The higher the amount of selenomethionine absorbed, the greater the proportion of selenomethionine that is incorporated into non-regenerable proteins and can thus lead to the accumulation of selenium in the body (Fig. 30).

Therefore, only sodium selenite is authorized as a medicinal product. Selenomethionine or selenium yeast (main selenium form: selenomethionine) may also be used in dietary supplements. It is also safer to take sodium selenite in food supplements or in combination products.
Two forms of selenium: selenomethionine and sodium selenite

- Selenomethionine
- Sodium selenite

- Non-specific incorporation in proteins (instead of methionine)
- Reduction into selenium-hydrogen (H₂Se)
- Synthesis of selenoproteins
- Degradation of excess selenium and excretion mostly via kidney

- Non-regenerable proteins
- Regenerable proteins

- Accumulation in the body (e.g. hair, red blood cells)

Created according to:

Fig. 30
Effect of organic selenium on selenium status

Organic selenium increases the concentration of selenium in the blood faster than inorganic selenium. However, this is largely due to the unspecific binding of selenomethionine. The activity of selenoproteins, on the other hand, does not increase above the level of inorganic selenium using organic selenium. Instead, higher doses showed the opposite: the activity of selenoproteins decreased significantly.

The effect of organic selenium massively increasing the selenium concentration in the blood is problematic due to the so-called U-curve, which shows the effect of the serum selenium concentration on e.g. total mortality. Both low and high selenium levels have a negative effect on health.

Even 200 µg selenium in the form of selenium yeast per day increases the plasma selenium concentration to an unfavorable level of over 200 µg/l (Fig. 31). In a new trial, long-term intake of 300 µg selenium (selenium yeast) per day led to an increase in all-cause mortality. The trial authors noted that this negative effect would probably not have occurred at the same selenium dose in the form of sodium selenite, since sodium selenite is either directly used for selenoproteins or excreted (Fig. 32).

Selenium yeast increases selenium levels in the blood to an unhealthy level

![Selenium yeast increases selenium levels in the blood to an unhealthy level](image)

Selenium is not always the same

Long-term 300 µg selenium

Selenium yeast
Selenomethionine

Sodium selenite

Serum selenium concentration > 250 µg/l*

Total mortality 2.5-fold

Serum selenium concentration ~ 160 µg/l**

Total mortality***

* after 6 months of supplementation
** after 24 weeks of supplementation
*** results of observational studies

Created according to:

Fig. 32
Does selenium also have side effects?

**At a glance**

**High therapeutic index**

300 µg selenium daily for life is a safe dose[^2]

**Side effects of an overdose of selenium:**

- garlic-like breath
- diarrhea
- nausea
- abdominal pain
- fatigue
- hair loss[^2,75]

Selenium poisoning is also known as selenium intoxication or selenosis. What applies to all substances also applies to selenium: it is the quantity that determines the benefit or harm of a substance. This becomes particularly clear when comparing selenium and common salt (Fig. 33).

For example, one takes in 6 grams of table salt per day, which is considered sufficient. 210 grams of common salt, on the other hand, can also lead to death in an adult. That’s just 35 times the amount. However, no one describes table salt as toxic.

In contrast, the lethal dose of sodium selenite is 490,000 µg, almost 3,200 times the daily recommended selenium requirement.

[^2]: Reference for selenium safety dose
[^75]: Reference for side effects of selenium overdose
Therapeutic index for sodium selenite and sodium chloride

Sodium selenite

Recommended amount per day \(^{[A]}\)
70 µg selenium corresponding to 153.3 µg sodium selenite

Amount per day for short-term high-dose therapy \(^{[B]}\)
e.g. 2,000 µg selenium/day corresponding to 4,380 µg sodium selenite

Table salt (sodium chloride)

Orientation value per day (DGE)
6 g table salt (sodium chloride)

Lethal dose \(^{[C]}\)
490,000 µg sodium selenite

Lethal dose \(^{[D]}\)
210 g table salt (sodium chloride)

---


\(^{[B]}\) Summary of product characteristics selenase\(^{®}\) T peroral, biosyn Arzneimittel GmbH, November 2017.


\(^{[D]}\) GESTIS Substance Database. Sodium chloride.
Toxicity of selenium

Selenium poisoning is possible, but only occurs when used incorrectly and uncontrollably. The lethal toxicity of oral sodium selenite intake is 7,000 μg/kg.\(^7\) 4,000–5,000 μg/kg selenium are required to acutely poison oneself with selenium.\(^3\) Chronic poisoning with selenium is also possible. For this purpose, more than 1,000 μg selenium would have to be absorbed per day over a very long period of time, several months to years. With a lifelong daily intake of 850 μg selenium per day, there are no side effects (=NOAEL) (Fig. 34). The EU classifies the lifelong intake of 300 μg selenium as absolutely harmless.\(^2\)

---

**Fig. 34**

Lethal selenium intoxication

---


Signs of acute selenium poisoning

An overdose of selenium may cause side effects. First signs are garlic-like breath, diarrhea, nausea, abdominal pain, fatigue and hair loss.\textsuperscript{[2,75]} In the event of prolonged overdose, nail and hair growth may change and disturbances of the nervous system may occur.

A toxic dose cannot be achieved with products from the pharmacy. The highest dose of dietary supplements available is 200 micrograms of selenium per tablet. One would have to take a very large number of tablets to get into a critical range (Table 2).

<table>
<thead>
<tr>
<th>Required quantities of tablets containing sodium selenite</th>
</tr>
</thead>
<tbody>
<tr>
<td>For acute toxicity</td>
</tr>
<tr>
<td>approx. 640 tablets 200μg at 70 kg body weight</td>
</tr>
</tbody>
</table>

Based on:
Summary of product characteristics selenase\textsuperscript{®} T peroral, biosyn Arzneimittel GmbH, November 2017.

Table 2

Only the dose makes the poison

(Paracelsus)
Bibliography


38. DGE Nutrition Circle.


45. Bloos F et al. JAMA Intern Med. 2016 Sep 1; 176(9): 1266-76. Effect of Sodium Selenite Administration and Procalcitonin-Guided Therapy on Mortality in Patients With Severe Sepsis or Septic Shock: A Randomized Clinical Trial.


47. Bundesamt für Strahlenschutz, access April 2018.


<table>
<thead>
<tr>
<th><strong>selenase®: application and dosage</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Application</strong></td>
</tr>
<tr>
<td>Proven selenium deficiency that cannot be remedied with food</td>
</tr>
<tr>
<td><strong>Dosage</strong></td>
</tr>
<tr>
<td>50μg selenium daily</td>
</tr>
<tr>
<td>A regular check of the selenium status at appropriate intervals is recommended</td>
</tr>
</tbody>
</table>


biosyn Arzneimittel GmbH

**World market leader for high-dose selenium injections**

biosyn Arzneimittel GmbH is a pharmaceutical and biotech company based in Fellbach, Germany. It specializes in trace elements, is a world market leader for high-dose selenium injections, developer and operator of two unique GMP manufacturing operations for producing active ingredients, and in the biotech sector, is actively involved in the production of glycoprotein isolated from the Megathura crenulata, a sea snail found in California. 70 percent of our sales turnover is realized outside of Germany – in 26 countries all around the world.

With products geared to the areas of intensive care, oncology and endocrinology, biosyn is a partner to hospitals and physicians in private practice, as well as to naturopathic physicians and holistic health practitioners. We pursue research and development and evaluate the current medical-scientific literature as well as engage in modern online marketing. Our mid-sized family enterprise places great value on an open, engaged and customer-oriented corporate culture.
selenase® pharmaceuticals: pharmacy only

**selenase® 50 AP**

Tablets
50 µg selenium per tablet

**selenase® 50 peroral**

Oral solution
at difficulty with swallowing
100 µg selenium per drinking ampoule

**selenase® 50 Mikrogramm Injektionslösung**

Injection solution
50 µg selenium per injection ampoule

Active ingredient: sodium selenite pentahydrate. Subject to sale in pharmacies

---

**Active substances**
Sodium selenite pentahydrate. **selenase® 50 Mikrogramm Injektionslösung, selenase® 50 peroral, 50 µg selenium per ml. selenase® 50 AP, 50 µg selenium per tablet.**

**Indications**
- selenase® 50 Mikrogramm Injektionslösung: Confirmed selenium deficiency that cannot be corrected by diet. Selenium deficiency can occur in conditions of malnutrition or malabsorption, as well as in malnutrition (e.g., total parenteral nutrition).
- selenase® 50 peroral, selenase® 50 AP: Proven selenium deficiency that cannot be offset from food sources. Selenium deficiencies may occur as a result of states of malnutrition and malabsorption, as well as in malnutrition.

**Composition**
- selenase® 50 Mikrogramm Injektionslösung: 1 ampoule of 1 ml solution for injection contains as active substance 0.167 mg sodium selenite pentahydrate corresponding to 50 µg selenium in an 0.9% NaCl-solution. Excipients: Sodium chloride, hydrochloric acid, water for injections. selenase® 50 peroral: 1 drinking ampoule of 1 ml oral solution contains: 50 µg sodium selenite pentahydrate in 0.9% NaCl-solution. Excipients: Sodium chloride, hydrochloric acid, water for injections. selenase® 50 AP: 1 tablet contains 0.167 mg sodium selenite pentahydrate (corresponding to 50 µg selenium). Excipients: gelatin, magnesium stearate (Ph. Eur.), maize starch, sucrose, talcum. Contra-indications: Hypersensitivity to sodium selenite pentahydrate or to any of the excipients. Selenosis. **Side effects:** None known to date if the medicinal product is administered according to prescription. **Form of administration, size of packages:** selenase® 50 Mikrogramm Injektionslösung: 10 and 50 ampoules respectively of 1 ml solution for injection. selenase® 50 peroral: 50 drinking ampoules of 1 ml oral solution. selenase® 50 AP: 20 tablets, 50 tablets, 100 tablets. Subject to sale in pharmacies.
selenase® during pregnancy and lactation

Helps protect cells from oxidative stress

We would be glad to send you our detailed brochure: information@biosyn.de (keyword: selenase® 100 XL / Selenium is essential)

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The tablets are divisible. A varied and balanced diet as well as a healthy lifestyle are of great importance.
Information on biosyn Arzneimittel GmbH

Brochures

We are happy to offer you comprehensive information on the topics of selenium, oncology and thyroid. You can order folders for yourself and your patients free of charge. Please choose from the brochures shown. Order by e-mail: information@biosyn.de (please specify desired materials).

Literature for medical experts

Selenium and oncology
Folder for medical experts
Format: A4, 172 pages

Integrative Oncology
Folder for medical experts
Format: A4, 88 pages

Selenium and the thyroid gland
Folder for medical experts
Format: A4, 132 pages

Information brochures for patients

The immune system guards your health
Patient brochure
Format: DIN long
18 pages
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(keyword “biosynNews international”)

Further information

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You can also find us on coliquio, the free medical network, with our Infocenter Selenium: www.coliquio.de

More information about us is available on our Facebook page and our YouTube channel
Selenium is essential

biosyn Arzneimittel GmbH
Schorndorfer Straße 32
70734 Fellbach
Germany

information@biosyn.de
www.biosynpharma.com
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