

Selenomethionine

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summary

Selenomethionine (SeMet) is an organoselenium compound classified as a naturally occurring amino acid, with the molecular formula $C_5H_{11}NO_2Se$. Its significance lies in its role as a primary source of selenium in the human diet, predominantly found in high-selenium foods such as Brazil nuts, fish, and certain meats, which vary in selenium content based on geographic soil levels.[\[1\]\[2\]](#) The compound is notable for its incorporation into selenoproteins, crucial for various biological functions including antioxidant defense, immune response, and metabolic health.[\[2\]\[3\]](#)

Research has demonstrated that selenomethionine plays a critical role in synthesizing selenoproteins, which help protect cells from oxidative damage, thereby potentially reducing the risk of chronic diseases such as cancer and cardiovascular disease.[\[4\]\[5\]](#) While supplementation with selenomethionine has been linked to health benefits, including immune function enhancement and thyroid hormone regulation, its efficacy in cancer prevention remains contentious. For example, the Nutritional Prevention of Cancer trial suggested benefits for prostate cancer, while subsequent studies like the SELECT trial found no significant protective effect, highlighting the need for further investigation into selenium's role in cancer prevention.[\[6\]\[7\]](#)

Despite its health benefits, excessive intake of selenomethionine can lead to toxicity, characterized by symptoms such as hair loss, gastrointestinal disturbances, and, in severe cases, selenosis, which poses a public health concern. The recommended upper limit for selenium intake is 400 micrograms per day for adults, underlining the importance of adherence to safe consumption levels to avoid adverse effects.[\[8\]\[9\]](#) As research evolves, the complexities surrounding selenium metabolism, bioavailability, and the implications of supplementation continue to be crucial areas of study, particularly in relation to chronic diseases and overall health outcomes.[\[2\]\[10\]](#)

Chemical Structure

Selenomethionine, with the molecular formula $C_5H_{11}NO_2Se$ and a molecular weight of approximately 196.11 g/mol[\[1\]\[11\]](#), is an organoselenium compound that can be classified as a naturally occurring amino acid. Its IUPAC name is 2-amino-4-(methylselanyl)butanoic acid[\[12\]](#). This compound typically appears as a white crystalline solid[\[1\]\[13\]](#).

Physical Properties

Selenomethionine has a melting point of 267 °C[\[1\]](#), a flash point of 147.8 ± 26.5 °C[\[14\]](#), and demonstrates a polar surface area (PSA) of 63.32 Å²[\[14\]](#). The compound's identity is confirmed through infrared spectroscopy (IR), adhering to the specifications set for its purity, which is ≥ 98% by HPLC analysis[\[3\]\[15\]](#).

Structural Characteristics

The structural characterization of selenomethionine reveals that it possesses a selenium atom substituting the sulfur found in the analogous amino acid, methionine. This alteration contributes to its unique chemical behavior and interaction properties

in biological systems. Molecular docking studies indicate the importance of hydrogen-bond interactions in the binding of selenomethionine with various proteins[16]. The key binding amino acids identified in these interactions include residues surrounding the catalytic and maximum affinity binding sites, which provide insights into its functional roles in enzymatic processes[16].

Sources

Selenomethionine (SeMet) is primarily sourced from various natural foods and supplements. It is commonly found in high-selenium foods such as Brazil nuts, fish, and certain meats, with concentrations often varying by geographical region due to soil selenium levels[16][2]. Research indicates that the average selenium content in plant leaves, such as those from and , can reach as high as 3045 mg Se kg⁻¹, primarily in the forms of methyl-selenocysteine and SeMet[16].

Supplementation studies have also highlighted the effectiveness of selenized yeast, which contains SeMet, in providing selenium for health benefits. For instance, the Nutritional Prevention of Cancer (NPC) trial demonstrated that a daily supplement of 200 µg of selenium, in the form of selenized yeast, was effective in reducing the risk of certain cancers[10]. Moreover, clinical studies have suggested that probiotics enriched with organic selenium might offer an alternative approach to enhancing selenium bioavailability and addressing conditions like inflammatory bowel disease and colon cancer[10][17].

Selenium content in food can be influenced by agricultural practices, with selenium-rich fertilizers being employed to boost levels in crops. This allows for a more consistent dietary intake of selenomethionine through enriched food sources[2][18]. The complexity of selenium metabolism in humans, including its transformation into various bioactive forms, underscores the importance of studying the bioavailability of selenium from different dietary sources to optimize health outcomes[2][10].

Biological Role

Selenomethionine (SeMet) plays a crucial role in various biological processes, primarily due to its incorporation into selenoproteins, which are vital for antioxidant defense, immune function, and overall metabolic health. As a naturally occurring amino acid, SeMet is a major source of selenium in the diet, and its bioavailability is critical for maintaining optimal selenium levels in the body[2][3].

Antioxidant Function

One of the primary roles of selenomethionine is its contribution to the synthesis of selenoproteins, such as glutathione peroxidases and thioredoxin reductases, which are essential for protecting cells from oxidative damage[4][5]. These enzymes help neutralize reactive oxygen species (ROS) and reduce oxidative stress, thereby mitigating the risk of chronic diseases, including cardiovascular disease and cancer[19][5]. By participating in redox reactions, SeMet aids in maintaining cellular redox balance, which is critical for cell function and survival[2][4].

Metabolism and Microbiota Interaction

The metabolism of selenomethionine is influenced by the gut microbiota, which can convert SeMet into various metabolites, impacting selenium bioavailability and excretion[2][19]. This metabolic interaction highlights the importance of gut health in selenium utilization and its implications for overall health. Additionally, selenium is known to play a role in cellular and paracellular permeability, affecting the gut barrier function and immune responses[2][20]. Se-deficiency has been associated with compromised gut integrity, leading to disturbances in immune function and increased susceptibility to chronic conditions such as inflammatory bowel disease and diabetes mellitus type 2[2][20].

Hormonal and Signaling Pathways

Selenomethionine also interacts with various hormonal pathways and signaling molecules. The gut microbiota produces signaling molecules that can affect metabolic processes related to the development of cardiovascular risk factors, such as ghrelin, leptin, and glucagon-like peptide 1 (GLP-1)[2][4]. These interactions emphasize the significance of selenium in the regulation of metabolism and appetite, further underlining its biological relevance.

Health Benefits

Selenomethionine, a naturally occurring form of selenium, is associated with several health benefits due to its role as an essential mineral in the human body. Selenium is a crucial component of selenoproteins and enzymes that possess antioxidant properties, which help mitigate oxidative stress by breaking down harmful peroxides that can damage tissues and DNA, potentially leading to inflammation and various health issues[21].

Immune Function

Selenium is known to enhance immune function. Adequate selenium levels are linked to improved immune responses, including chemotactic and phagocyte activities of immune cells, which are essential for combating infections. Selenium also supports the activation and function of T- and B-cells, thus playing a significant role in adaptive immunity[4]. Deficiencies in selenium can result in a weakened immune system, making individuals more susceptible to illnesses[4].

Thyroid Health

Selenium is integral to thyroid function. It is involved in the conversion of the inactive thyroid hormone thyroxine (T4) into its active form, triiodothyronine (T3), through the action of selenium-dependent enzymes called iodothyronine deiodinases[22]. Sufficient selenium intake is crucial for maintaining proper thyroid hormone levels and overall endocrine health.

Cancer Prevention

Research has suggested a potential role for selenomethionine in cancer prevention, particularly prostate cancer. A randomized controlled trial known as the Nutritional Prevention of Cancer Trial indicated that supplementation with 200 micrograms of selenium daily led to a significant reduction in the risk of prostate cancer among men with low baseline levels of selenium[\[6\]\[23\]](#). However, the evidence remains somewhat controversial, and other studies, such as the SELECT trial, have not found a significant protective effect against prostate cancer when combining selenium with vitamin E[\[7\]](#).

Other Health Considerations

Selenium supplementation may also influence various metabolic conditions. Some studies have examined the effects of selenium on glucose homeostasis in individuals with type 2 diabetes, suggesting potential benefits in regulating blood sugar levels[\[8\]](#). However, caution is advised as high doses of selenium can lead to toxicity, resulting in side effects such as fingernail loss, skin rashes, and fatigue[\[8\]](#).

Before considering selenium supplements, it is advisable for individuals to consult healthcare providers, especially if they have conditions such as hypothyroidism or a history of skin cancer, as high selenium intake may exacerbate these issues[\[8\]](#). Additionally, the recommended upper limit for selenium intake is 400 micrograms per day for adults, emphasizing the importance of adhering to recommended dosages to avoid adverse effects[\[21\]\[8\]](#).

Toxicity and Side Effects

Selenomethionine, a naturally occurring form of selenium, can lead to toxicity and various side effects when consumed in excessive amounts. The estimated maximum safe daily dietary intake of selenium is 400 µg, with functional signs of toxicity expected at intakes of 750-850 µg[\[9\]](#). Chronic exposure to high levels of selenium can result in a condition known as selenosis, which is characterized by a range of symptoms including hair loss, nail deformation and loss, tooth discoloration, gastrointestinal disturbances, and garlic breath[\[8\]\[24\]\[25\]](#).

Symptoms of Toxicity

The symptoms of selenium toxicity can manifest in several ways.

Itchy skin

Diarrhea

Weakening and loss of fingernails and hair

Discolored teeth

Nausea and vomiting

Fatigue

Foul-smelling breath[26][9][24].

In cases of acute selenium toxicity, individuals may experience more severe symptoms such as stomach pain, headache, respiratory issues, changes in blood pressure, and peripheral neuropathy[9][25]. Long-term consumption of high doses of selenium has also been associated with increased risks of various health issues, including diabetes and certain cancers[26][22].

Sources of Toxicity

Toxicity can arise from both dietary intake and the consumption of improperly formulated supplements. Overdoses often occur in randomized clinical trials involving high-dose selenium supplementation, typically exceeding 200 µg/day for extended periods[2][25]. It is important to note that the form of selenium consumed can affect its bioavailability and toxicity levels, complicating the establishment of safe exposure limits[26][9].

Treatment and Management

Management of selenium toxicity primarily involves the discontinuation of the source of excessive intake and supportive care. There is currently no known antidote for selenium toxicity[9][8]. In cases of severe toxicity, particularly from accidental ingestion of large quantities, medical attention should be sought immediately.

Research and Clinical Studies

Cancer Prevention Studies

A comprehensive review conducted in 2018 by Cochrane analyzed ten randomized, placebo-controlled trials involving 27,232 participants, predominantly male (94%) [23]. This review focused on the effects of selenium supplementation, specifically doses ranging from 200 to 500 mcg/day, primarily in the form of selenomethionine, over periods of 2 to 10.3 years. The findings indicated that such supplementation had minimal impact on cancer incidence or mortality rates. The certainty of evidence was rated as high for several cancer types, including prostate, colorectal, lung, and bladder cancers, while it was moderate for breast and nonmelanoma skin cancers. Consequently, the authors concluded that daily supplementation of 200 mcg of selenium does not lower the overall risk of cancer or the incidence of specific cancer types, and highlighted the need for further research to understand potential variations in cancer risk modification based on genetic backgrounds or nutritional status.

Autoimmune Thyroiditis

Selenium's role in autoimmune thyroiditis (AIT), particularly Hashimoto's thyroiditis, has been the subject of various clinical trials. A systematic review and meta-analysis encompassing 16 trials evaluated the effects of selenium supplementation on thyroid

antibodies in individuals diagnosed with AIT. This analysis included 1,494 adults, primarily women, who received selenium doses between 80 to 200 mcg/day (as selenomethionine or sodium selenite) over periods of 3 to 12 months, with most trials being placebo-controlled [23]. The results revealed that selenium supplementation might influence thyroid antibody levels, with additional studies indicating that participants receiving 83 mcg of oral selenomethionine exhibited improved thyroid function compared to placebo counterparts.

Interactions and Toxicity

While selenium supplementation is generally safe, interactions with certain medications can occur. For instance, selenium may heighten the risk of bleeding when taken with anticoagulants such as warfarin or heparin [27]. Additionally, research indicates that cisplatin, a common chemotherapy drug, can deplete selenium levels, though some evidence suggests that selenium may mitigate cisplatin toxicity, warranting further investigation [27]. Long-term studies have shown that high doses of selenium, such as 1600 and 3200 mcg/day, do not present serious toxicity risks, although the effects on immune responses and vaccine efficacy in the context of selenium supplementation remain an area of ongoing research [28].

Future Directions

Emerging research continues to explore selenium's multifaceted roles in health and disease. Recent studies are investigating the potential benefits of selenium supplementation in relation to COVID-19 outcomes, among other conditions, though definitive conclusions are yet to be established [7]. Given selenium's significant presence in the thyroid gland and its implications for thyroid metabolism, ongoing research is crucial to fully understand its therapeutic potential and the varying effects of different selenium compounds [23][27].

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