

Methionine

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summary

Methionine is a sulfur-containing essential amino acid with the chemical formula $C_5H_{11}NO_2S$, integral to various biological functions in humans and other organisms. Classified as one of the building blocks of proteins, methionine plays a critical role in initiating protein synthesis and acts as a precursor for vital metabolites, including S-adenosylmethionine (SAM), a key methyl donor involved in numerous biochemical processes, such as DNA methylation and detoxification pathways.[\[1\]\[2\]\[3\]](#) Its unique structure allows methionine to participate in redox reactions and metal coordination, further highlighting its importance in cellular physiology.[\[4\]\[5\]](#)

As an essential amino acid, methionine cannot be synthesized de novo in humans and must be acquired through dietary sources, predominantly found in animal products like meat, fish, and dairy, as well as some plant sources such as legumes and nuts.[\[6\]\[7\]\[8\]](#) The amino acid's role extends beyond mere nutrition; it has significant implications for immune function, metabolic processes, and antioxidant defense, positioning methionine as a crucial element in maintaining overall health and well-being.[\[5\]\[9\]](#) Furthermore, research has suggested potential therapeutic applications of methionine modulation in conditions such as cardiovascular diseases and cancer, thus emphasizing its relevance in clinical settings.[\[8\]\[10\]](#)

Controversially, while methionine is essential for health, excessive intake, particularly in supplemental forms, may lead to adverse effects, including increased levels of homocysteine, which is linked to cardiovascular risks.[\[11\]\[12\]](#) Additionally, methionine deficiency can result in growth issues and metabolic dysfunction, especially in vulnerable populations. This duality underscores the necessity for balanced dietary intake to optimize the health benefits of this essential amino acid while mitigating potential risks.[\[13\]\[14\]](#)

In summary, methionine is a vital amino acid with multifaceted roles in human health, dietary requirements, and metabolic regulation, marking its significance in both nutritional science and clinical research.[\[15\]\[9\]](#)

Chemical Structure

Methionine is classified as a sulfur-containing essential amino acid, with the chemical formula $C_5H_{11}NO_2S$ [\[1\]\[16\]](#). Its structural representation includes a central carbon atom, known as the α -carbon, which is bonded to an amino group (NH_2), a carboxyl group ($COOH$), and a side chain containing a sulfur atom[\[2\]\[17\]](#). The IUPAC name for methionine is (2S)-2-amino-4-(methylsulfanyl)butanoic acid[\[18\]](#).

The molecular structure of methionine can be described as $CH_3-S-(CH_2)_2-CH(NH_3)$ [\[4\]](#). This unique structure allows methionine to play various roles in biological systems, including metal coordination and redox reactions, as well as contributing to the stabilization of protein structures[\[19\]\[20\]](#). Methionine, along with cysteine, represents the only amino acids that contain sulfur, highlighting its significance in biochemical processes[\[4\]\[5\]](#).

In addition to its role as a building block for proteins, methionine serves as a precursor for several important sulfur-containing molecules that are vital for cellular functions, including tissue protection and DNA modification[\[5\]](#). Its ability to chelate heavy metals further emphasizes its importance in biological systems[\[16\]](#).

Biosynthesis

Methionine biosynthesis occurs primarily in plants and microorganisms, belonging to the aspartate family of amino acids, which also includes threonine and lysine. The process is crucial because methionine is an essential amino acid that cannot be synthesized *de novo* in humans and other animals; they must obtain it through their diet[\[3\]\[21\]](#).

Pathways of Methionine Biosynthesis

The biosynthesis of methionine can be divided into two main domains: sulfur assimilation, which involves the reduction and biosynthesis of cysteine, and the subsequent conversion to methionine through several biochemical pathways[\[22\]](#).

Enzymatic Reactions

Initial Conversion: The process begins with aspartic acid, which is converted to 2 aspartyl semialdehyde through the action of aspartate kinase (AK). This conversion is subject to feedback inhibition by the accumulation of threonine and lysine, thereby regulating methionine synthesis[\[23\]](#).

Formation of Homoserine: 2 aspartyl semialdehyde can either proceed towards lysine synthesis or be transformed into homoserine via two reduction steps[\[3\]](#).

Cysteine and Homocysteine: The next steps in methionine biosynthesis depend on the interaction with cysteine or hydrogen sulfide.

When cysteine reacts with homoserine, cystathionine is produced, which is subsequently cleaved by cystathionine- 3 synthase and cystathionine- 2 lyase to yield homocysteine[\[3\]\[24\]](#).

If homocysteine is formed from free hydrogen sulfide, this reaction is facilitated by O-acetylhomoserine aminocarboxypropyltransferase, leading directly to homocysteine, which can then be methylated to produce methionine[3][23].

[3]

[15]

Regulation of Methionine Biosynthesis

The regulation of methionine biosynthesis is complex and involves multiple layers, including transcriptional control. Key transcription factors, such as SREBP-1c and NF- κ B, can modulate the expression of genes encoding enzymes in the methionine metabolic pathway, such as methionine adenosyltransferase (MAT), which catalyzes the formation of S-adenosylmethionine (SAM) from methionine and ATP[15][20].

In plants, particularly maize, the enzymes cystathionine- γ -synthase, aspartate kinase, and serine acetyl transferase play critical roles in regulating sulfur flux towards methionine synthesis. Up-regulation of these enzymes has been linked to enhanced methionine accumulation in seeds[23][24]. Genetic manipulation of these pathways is being explored to increase methionine content in crops, highlighting the potential for bioengineering to improve nutritional quality[21].

Biological Functions

Methionine is a vital amino acid involved in numerous biological processes essential for human survival. It plays a significant role in initiating the immune system, producing important molecules, and participating in metabolic functions within the body[2][5]. The chemical formula of methionine is $C_5H_{11}NO_2S$, and like all amino acids, it possesses a structure consisting of an amino group, a carboxyl group, and a hydrogen atom attached to a carbon atom[2].

Metabolic Functions

Methionine serves as a precursor for several key metabolites. One of its principal functions is the conversion to S-adenosylmethionine (SAM), the primary methyl donor in biological methylation reactions. SAM is crucial for the methylation of DNA, proteins, and lipids, playing a vital role in gene regulation, cell signaling, and energy production through the formation of creatine and phosphatidylcholine[23][25]. Furthermore, methionine is involved in the trans-sulfuration pathway, leading to the production of cysteine, which is subsequently utilized to synthesize glutathione—often referred to as the "master antioxidant" due to its protective role against oxidative stress[5][11].

Protein Synthesis

In the context of protein synthesis, methionine is recognized as the initiating amino acid for translation. The AUG codon of messenger RNA (mRNA) signals the start of protein synthesis, wherein the initiator tRNA binds to the ribosome to commence the translation process[\[26\]\[15\]](#). This property underscores methionine's fundamental importance in cellular function, as it serves not only as a building block for proteins but also as a critical regulator of various metabolic pathways.

Interaction with Other Metabolic Pathways

The methionine cycle is intricately linked with the folate cycle, forming a comprehensive metabolic network known as one-carbon metabolism. In this context, methionine can be synthesized from homocysteine in a reaction dependent on folate, illustrating its connection to broader nutrient metabolism[\[15\]](#). The regulation of methionine metabolism is tightly controlled at multiple levels, including transcriptional, post-transcriptional, and post-translational mechanisms, which ensure that enzyme activity aligns with the cell's energy status and nutritional availability[\[27\]\[11\]](#).

Dietary Sources

Methionine is an essential amino acid that must be obtained through diet, as the human body cannot synthesize it. It is crucial for various physiological functions, including protein synthesis and metabolism. The dietary sources of methionine can be broadly categorized into animal and plant-based foods.

Animal Sources

Animal foods are often considered "complete" sources of protein, containing all nine essential amino acids, including methionine.

Meat: Beef, pork, and lamb are rich in methionine. For instance, muscle meats typically provide significant amounts of this amino acid, supporting muscle growth and repair[\[6\]](#).

Fish: Fish such as salmon, tuna, and cod are also excellent sources of methionine, contributing to overall protein intake and essential amino acid levels[\[7\]](#).

Dairy Products: Milk, cheese, and yogurt are good sources of methionine and contribute to daily protein requirements[\[28\]\[29\]](#).

Plant Sources

While most plant foods are lower in methionine compared to animal sources, some still provide reasonable amounts. It is important for individuals following plant-based diets to combine different food sources to ensure adequate intake.

Legumes: Beans and lentils contain methionine, although in smaller quantities compared to animal proteins[\[28\]](#).

Nuts and Seeds: Nuts such as Brazil nuts and seeds like sesame seeds are beneficial sources of methionine and other essential nutrients[\[6\]](#).

Whole Grains: Certain grains, particularly quinoa and oats, can contribute to methionine intake but may need to be combined with other protein sources for a complete amino acid profile[\[7\]](#).

Dietary Recommendations

To meet the dietary requirements for methionine, it is suggested that adults consume a varied diet that includes both animal and plant-based protein sources. This helps to ensure not only adequate methionine intake but also the overall nutritional quality of the diet. The recommended protein intake varies, with adults advised to obtain approximately 10-35% of their total energy from protein sources, which should include adequate levels of essential amino acids like methionine[\[8\]](#)[\[30\]](#)[\[7\]](#).

Health Benefits

Methionine, an essential sulfur-containing amino acid, plays a critical role in numerous physiological functions and health benefits. It is integral to protein synthesis, the metabolism of nutrients, and the production of DNA and various bioactive compounds.[\[9\]](#)[\[31\]](#) Methionine's importance is underscored by its necessity for the synthesis of S-adenosylmethionine (SAM), a key methyl donor involved in numerous biochemical processes.[\[15\]](#)

Antioxidant Properties

Methionine exhibits antioxidant properties, which help protect cells from oxidative stress caused by free radicals. This function is particularly significant as oxidative stress has been implicated in a variety of chronic diseases, including cancer and cardiovascular conditions.[\[9\]](#)[\[32\]](#) Additionally, methionine aids in the detoxification of heavy metals, thus contributing to cellular protection and overall health.[\[9\]](#)

Immune Function

Research indicates that adequate levels of methionine and its derivatives, such as cysteine, are essential for optimal immune function. Deficiencies in these amino acids can impair the immune response and antioxidant capacity, leading to increased susceptibility to diseases.[\[32\]](#)[\[33\]](#) Increasing methionine levels has been shown to improve immune parameters and overall health in various animal studies.[\[32\]](#)

Skin, Hair, and Nail Health

Methionine is thought to nourish the skin, hair, and nails, contributing to their structural integrity and health. The amino acid plays a role in collagen synthesis, a protein crucial for maintaining skin elasticity and strength.[\[9\]](#) While many of these claims require further scientific validation, methionine's involvement in protein synthesis supports its potential benefits in maintaining the health of these tissues.

Potential Risks and Side Effects

Despite its numerous health benefits, excessive intake of methionine may lead to adverse effects. Side effects can include nausea, vomiting, irritability, and drowsiness, particularly when taken in supplement form.[\[12\]](#)[\[11\]](#) Furthermore, high levels of methionine are associated with increased homocysteine production, which is linked to cardiovascular disease risk. Elevated homocysteine levels can harm endothelial function, promote inflammation, and contribute to arterial damage.[\[11\]](#) Therefore, while methionine is vital for health, moderation is essential, especially in supplemental forms.

Deficiency

Methionine deficiency can have significant implications for both health and biological processes. A shortage of this limiting amino acid can constrain animal growth, reduce feed efficiency, and, in extreme cases, lead to nutritional deficiencies.[\[13\]](#) In humans, methionine deficiency is linked to reduced milk protein production, which can further result in excessive nitrogen excretions into the environment.[\[34\]](#)

Effects on Health

Inadequate methionine intake can impact various health aspects. For adults and teenagers, the typical recommended dose of methionine supplementation is 500 mg three to four times a day, with specific considerations for children's dosages depending on age.[\[35\]](#) However, high doses or prolonged use of single amino acids, including methionine, can lead to negative nitrogen balance, adversely affecting metabolism and putting extra strain on the kidneys.[\[14\]](#)

Moreover, in children, prolonged use of single amino acid supplements may result in growth issues.[\[14\]](#) This highlights the necessity of maintaining a balanced diet rich in all essential amino acids to prevent deficiencies and associated health risks.

Specific Populations at Risk

Certain populations may be particularly vulnerable to the effects of methionine deficiency. For instance, individuals with genetic disorders affecting methionine metabolism, such as homocystinuria, should avoid methionine supplementation, as it can exacerbate their condition.[\[12\]](#) Additionally, individuals with severe liver diseases may experience worsened symptoms with methionine use due to the potential build-up of toxins in the bloodstream.[\[9\]](#)

Supplementation

Methionine is an essential amino acid that must be obtained through diet, as the human body cannot synthesize it. It plays a crucial role in various physiological processes, including protein synthesis, metabolism, and the production of other vital

compounds[14][9]. As a sulfur-containing amino acid, methionine is categorized as a lipotropic, which aids the liver in processing fats[14].

Benefits of Methionine Supplementation

Supplementation of methionine has been shown to enhance the performance of animals, particularly in the context of livestock and dairy production. For instance, studies have demonstrated that dietary methionine can improve feed conversion rates and optimize growth in various animal species[36][37]. In ruminants, methionine supplementation must be carefully managed to prevent degradation by microbes; thus, it is often coated to ensure its release in the small intestine[38].

Increasing methionine levels, such as through products like Mepron®, has been linked to improved reproductive success in dairy cows. This effect is attributed to methionine's role during critical metabolic periods, such as the transition to peak lactation[38][32]. Moreover, it is essential for nutritional strategies to consider phase feeding to meet the differing requirements based on production levels and lactation stages[38].

Practical Applications

In practical nutrition, methionine supplementation can help achieve optimal levels of methionine and cysteine, translating into better animal health and productivity. DL-methionine, being 100% bioavailable, offers excellent handling properties, allowing precise formulation in feed[32]. This supplementation strategy has shown positive impacts on nitrogen utilization and overall farm profitability when evaluating income over feed cost (IOFC)[38].

Considerations and Recommendations

While methionine supplementation can confer significant benefits, it is crucial to balance its intake with other amino acids to avoid excess, which may lead to adverse effects. For example, high levels of cysteine can lower methionine requirements[39]. Additionally, individuals considering methionine supplementation for health purposes should consult healthcare professionals, as appropriate dosages can vary based on specific health needs and conditions[9]. In general, the recommended intake of sulfur amino acids, including methionine, is approximately 15 milligrams per kilogram of body weight per day for healthy adults[9].

Research and Clinical Studies

Overview of Methionine in Health

Methionine, an essential amino acid, has been the focus of various research studies that explore its role in human health and disease. Its metabolism is crucial for numerous biological processes, including methylation reactions, which are vital for DNA synthesis and repair. Clinical studies have investigated the implications of

methionine levels in various health conditions, including cardiovascular diseases and cancer.

Clinical Implications

Hyperhomocysteinemia and Cardiovascular Health

Elevated levels of homocysteine, an amino acid that is derived from methionine, have been linked to impaired endothelial function and an increased risk of cardiovascular diseases. A study indicated that hyperhomocysteinemia after an oral methionine load acutely impairs endothelial function in healthy adults, suggesting that methionine's metabolic pathway plays a significant role in cardiovascular health[\[8\]\[10\]](#).

Methionine and Cancer

Research has also explored the relationship between methionine and cancer. One study found that methionine restriction induced apoptosis in prostate cancer cells through the c-Jun N-terminal kinase-mediated signaling pathway, highlighting the potential of methionine modulation in cancer therapies[\[8\]](#). Another prospective study investigated the relationship between methionine and vitamin B6 intake with the risk of pancreatic cancer, suggesting a complex interplay between these nutrients in cancer development[\[8\]\[10\]](#).

Safety and Side Effects

While methionine supplementation can have beneficial effects, it may also lead to side effects. Commonly reported side effects include drowsiness, nausea, and vomiting, although these often do not require medical attention and may subside as the body adjusts to the treatment[\[35\]](#). It is essential for individuals to consult healthcare professionals before starting or altering methionine supplementation, especially in the presence of other medical conditions such as liver disease or metabolic acidosis, which may be exacerbated by methionine use[\[35\]](#).

Dietary Considerations

Methionine is often provided as a nutrient feed additive in the animal feed industry due to its critical role in protein utilization, metabolism, and overall animal health. The supplementation of methionine in animal diets has been shown to enhance growth performance, reduce nitrogen excretion, and support health during stress conditions[\[37\]](#). The increasing awareness of the benefits of a healthy animal diet is driving the demand for methionine products, which contribute to sustainable practices within the agricultural sector[\[37\]\[40\]](#).

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