

Isoleucine

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summary

Isoleucine is an essential branched-chain amino acid (BCAA) crucial for human health, with the chemical formula $C_6H_{13}NO_2$ and a molecular weight of approximately 131.17 g/mol. This amino acid is vital for protein synthesis, energy metabolism, and various physiological processes, playing a significant role in muscle growth and recovery, especially in athletic contexts.^{[1][2]} Unlike some amino acids, isoleucine cannot be synthesized by the human body and must be obtained through dietary sources, which include both animal and plant-based foods such as meat, dairy, legumes, and soy products.^{[3][4]}

As one of the building blocks of proteins, isoleucine contributes to the formation of hemoglobin and helps regulate blood sugar levels, making it critical for maintaining energy balance and metabolic health.^{[5][6]} It also influences immune function by serving as a fuel source for immune cells, thereby enhancing the body's response to infections.^{[7][8]} Notably, isoleucine has gained attention for its role in athletic performance, with studies suggesting that supplementation may aid in muscle recovery and reduce exercise-induced muscle soreness.^{[9][10]}

Despite its importance, the efficacy and safety of isoleucine supplementation remain subjects of debate. While it is frequently included in sports nutrition products, research has produced mixed results regarding its benefits in enhancing performance or muscle mass when adequate dietary protein is consumed.^{[3][11]} Additionally, certain metabolic disorders, such as Maple Syrup Urine Disease (MSUD), can impair the metabolism of isoleucine and other BCAAs, leading to serious health concerns.^[3] As interest in amino acid supplementation continues to rise, ongoing research aims to clarify isoleucine's potential therapeutic applications and its long-term effects on health and performance.^{[12][13]}

Chemical Structure

Isoleucine is an essential branched-chain amino acid with the chemical formula $C_6H_{13}NO_2$ and a molecular weight of 131.1729 g/mol^[1]. It is represented by the IUPAC name (2S,3S)-2-amino-3-methylpentanoic acid, and its CAS Registry Number is 73-32-5^{[1][14]}. The chemical structure of isoleucine features a central carbon atom bonded to an amino group ($-NH_2$), a carboxyl group ($-COOH$), a hydrogen atom, and

a branched aliphatic side chain that significantly influences its biochemical behavior and properties[2][3].

Isoleucine exists in two stereoisomeric forms: L-isoleucine and D-isoleucine. L-isoleucine, the naturally occurring form, is often denoted as (2S,3S)-2-amino-3-methylpentanoic acid, while D-isoleucine has the (2R,3R) configuration[1][15]. The presence of a branched side chain, which includes bulky nonpolar R-groups, is characteristic of branched-chain amino acids (BCAAs), which also include leucine and valine[3][16]. This branching plays a crucial role in the amino acid's hydrophobic interactions and its overall function in biological systems[16].

Understanding the chemical structure of isoleucine is essential for studying its role in protein synthesis, muscle metabolism, and nutritional requirements, particularly in relation to growth and recovery processes in both humans and animals[17].

Biological Role

Isoleucine is one of the essential amino acids that play critical roles in various biological processes within the body. As a building block of proteins, isoleucine is vital for protein synthesis, contributing to growth, tissue repair, and energy metabolism[5][18]. It serves not only as a structural component of proteins but also as a signaling molecule, influencing metabolic pathways and cellular functions[19].

Protein Synthesis and Energy Metabolism

Isoleucine is involved in the formation of hemoglobin, the oxygen-carrying component of red blood cells, which is crucial for maintaining oxygen levels in tissues[6]. Additionally, it participates in energy production by helping to break down food and provide energy, especially during physical activity and stress[18][20]. As part of the branched-chain amino acids (BCAAs), which also include leucine and valine, isoleucine is particularly important for muscle growth and recovery, making it a focus for athletes and individuals engaged in intense exercise[20].

Immune Function

Isoleucine has been recognized for its role in enhancing immune function. It is utilized by immune cells, such as lymphocytes and neutrophils, as a fuel source and a precursor for the synthesis of new immune components[7][8]. Studies have demonstrated that supplementation with BCAAs, including isoleucine, can improve the immune response by enhancing the phagocytic function of neutrophils and the activity of natural killer cells, which are essential for fighting infections[7].

Metabolic Regulation

The amino acid also plays a role in regulating blood sugar levels by influencing glucose metabolism. Research indicates that isoleucine can enhance glucose utilization in the intestines and muscles, thus contributing to better blood sugar management[5][7]. Furthermore, isoleucine aids in the detoxification of nitrogenous waste,

particularly ammonia, by providing the carbon skeleton necessary for synthesizing glutamate and glutamine, which are crucial for ammonia detoxification[\[6\]](#).

Dietary Sources

Isoleucine is one of the essential branched-chain amino acids (BCAAs) that plays a crucial role in protein synthesis, immune function, and energy regulation. It is vital for human health, and obtaining sufficient amounts through diet is necessary since the body cannot produce it independently.

Animal-Based Sources

Animal proteins are considered complete sources of isoleucine, as they contain all nine essential amino acids in adequate amounts.

Meat: Beef, lamb, and pork are particularly rich in isoleucine, providing more than 100% of the daily recommended intake per serving[\[21\]](#).

Poultry: Chicken and turkey also serve as excellent sources of isoleucine, with comparable amounts to red meats[\[8\]](#).

Seafood: Fish and shellfish are not only rich in protein but also contain significant levels of isoleucine[\[22\]](#).

Dairy Products: Cheese, yogurt, and milk contribute to isoleucine intake, especially for those who consume these regularly[\[8\]](#).

Plant-Based Sources

While many plant-based foods are lower in isoleucine compared to animal sources, several options can provide sufficient amounts, particularly when combined correctly.

Soy Products: Foods like tofu, tempeh, and edamame are complete protein sources, containing adequate isoleucine and all other essential amino acids[\[4\]](#).

Quinoa: This pseudocereal is unique among grains as it provides a complete protein profile, including isoleucine[\[4\]](#).

Legumes: Beans, lentils, and chickpeas can be combined with grains to form complete proteins, offering a good source of isoleucine when eaten in conjunction with methionine-rich foods like rice[\[4\]](#).

Nuts and Seeds: While generally lower in isoleucine than animal products, certain nuts and seeds can contribute to overall protein intake, especially when consumed as part of a varied diet[\[23\]\[4\]](#).

Combining Foods for Adequate Intake

To meet isoleucine needs on a vegetarian or vegan diet, it's important to consume a variety of plant proteins. Combining complementary proteins, such as rice with beans or whole grain bread with peanut butter, can enhance the amino acid profile and ensure adequate intake of isoleucine and other essential amino acids[\[8\]\[4\]](#).

Metabolism

Biosynthesis

Isoleucine is a branched-chain amino acid (BCAA) that is synthesized in plants and microorganisms from pyruvate and alpha-ketobutyrate. This biosynthetic pathway, however, is absent in humans, who must obtain isoleucine through their diet[\[24\]\[25\]](#). The enzymes involved in the biosynthesis of isoleucine include acetolactate synthase, acetohydroxy acid isomeroreductase, dihydroxyacid dehydratase, and valine aminotransferase[\[25\]](#).

Catabolism

Isoleucine is classified as both a glucogenic and ketogenic amino acid. During catabolism, isoleucine undergoes transamination with alpha-ketoglutarate, resulting in a carbon skeleton that is oxidized and split into propionyl-CoA and acetyl-CoA. Propionyl-CoA is subsequently converted into succinyl-CoA, which serves as an intermediate in the tricarboxylic acid (TCA) cycle, contributing to gluconeogenesis. Conversely, acetyl-CoA can enter the TCA cycle or be utilized in the synthesis of ketone bodies and fatty acids[\[26\]](#). This dual metabolic fate of isoleucine underscores its importance in energy metabolism and glucose homeostasis.

Role in Metabolic Health

Isoleucine has been identified as a key regulator of metabolic health, particularly in the context of blood glucose regulation. Studies have shown that increased intake of isoleucine can enhance muscle glucose uptake and oxidation, while simultaneously reducing hepatic gluconeogenesis. This suggests that isoleucine plays a significant role in maintaining blood sugar levels[\[27\]\[28\]\[6\]](#). Additionally, dietary patterns low in isoleucine have been associated with improved metabolic outcomes, such as reduced body weight and enhanced glucose tolerance[\[29\]](#).

Emerging research highlights the intricate relationship between isoleucine and other BCAAs in modulating energy expenditure and metabolic responses. Specifically, lower intake of isoleucine has been linked to strain- and sex-dependent effects on the FGF21-UCP1 axis, indicating a complex regulatory network involving isoleucine and other metabolic pathways[\[30\]\[7\]](#).

Health Implications

Isoleucine, one of the essential branched-chain amino acids (BCAAs), plays a critical role in various physiological processes, particularly in muscle metabolism and energy production. Adequate intake of isoleucine is essential for optimal health and athletic performance.

Nutritional Requirements

For individuals engaging in physical activities, sufficient intake of isoleucine, along with other BCAAs, is vital to maintain energy levels and enhance recovery post-exercise. It is recommended that athletes consume adequate daily amounts of protein, which should include essential amino acids like isoleucine, to support muscle repair and growth[31][32]. The typical dietary sources of isoleucine include meat, dairy, eggs, and certain plant-based foods.

Safety and Dosage

Studies indicate that up to 20 g/day of BCAA supplements, including isoleucine, in divided doses, appear to be safe for healthy individuals[3]. However, specific conditions, such as Maple Syrup Urine Disease (MSUD), can impair the metabolism of BCAAs, including isoleucine, and may lead to serious health complications if left untreated[3]. Additionally, the safety of isoleucine supplementation during pregnancy and breastfeeding has not been extensively studied, so it is advised that women avoid supplementation during these periods unless recommended by a healthcare professional[3].

Potential Benefits

While BCAA supplementation, including isoleucine, has been touted for its ability to enhance athletic performance and promote muscle recovery, research has yielded mixed results regarding its efficacy in this area. Studies have not consistently shown significant improvements in exercise performance or muscle mass with BCAA supplementation when adequate dietary protein is consumed[3][11].

Side Effects and Precautions

Excessive intake of isoleucine or other BCAAs may lead to gastrointestinal disturbances, including nausea and abdominal discomfort[11]. Therefore, individuals are encouraged to consult healthcare providers before starting any new supplement regimen, especially those with existing medical conditions or those taking medications regularly[31][32].

Applications

Role in Athletic Performance

Isoleucine, one of the essential branched-chain amino acids (BCAAs), plays a significant role in enhancing athletic performance and post-exercise recovery. Its supplementation has been widely studied, with findings suggesting that it may aid in muscle repair and recovery after intensive workouts, thereby reducing recovery time and enabling athletes to return to training more quickly with less discomfort[9][33]. Athletes commonly use isoleucine to bolster endurance and support muscle integrity during physical exertion, making it a staple among sports nutrition products aimed at providing a competitive edge[34].

Nutritional Supplementation

Isoleucine is often included in dietary supplements designed to enhance exercise and athletic performance. These supplements may come in various forms such as powders, capsules, and bars, and they frequently contain a combination of amino acids, protein, and other ergogenic ingredients[31]. The retail market for sports nutrition supplements, which includes products with isoleucine and other BCAAs, has shown significant growth, indicating a high demand among athletes and fitness enthusiasts[31].

Recovery and Muscle Soreness

The use of isoleucine in post-exercise recovery strategies has garnered attention in recent research. Studies have shown that BCAA supplementation, including isoleucine, can significantly impact muscle recovery, with some evidence indicating improvements in muscle soreness and overall recovery following exercise-induced muscle damage (EIMD)[10][9]. This effect is particularly notable at different time points post-exercise, suggesting a complex interplay between timing and effectiveness of supplementation[10].

Efficacy and Safety Considerations

Despite the benefits associated with isoleucine supplementation, the efficacy can vary depending on numerous factors such as the type of exercise, the level of training, and individual metabolic responses[35]. Furthermore, while dietary supplements can enhance performance, athletes are advised to consult healthcare providers to ensure the safe use of these products, especially considering potential interactions with medications and other supplements[31][33].

Historical Context

Isoleucine, classified as one of the three branched-chain amino acids (BCAAs), alongside leucine and valine, has a significant historical background in biochemistry and nutrition. It was first isolated from hemoglobin by the chemist Frederick G. K. Schenk in 1903, marking its entry into the scientific literature as a distinct amino acid[36].

As an essential amino acid, isoleucine plays a crucial role in human nutrition, necessitating regular dietary intake. It is predominantly found in protein-rich foods such as meat, fish, soy, and dairy products[36][37]. Over the decades, research into isoleucine has expanded significantly, revealing its functions beyond merely serving as a building block for proteins. Studies have indicated that isoleucine is involved in metabolic regulation and signaling processes, contributing to protein, glucose, and lipid metabolism, as well as immune function[36][12].

The understanding of isoleucine has evolved, particularly in the context of athletic performance and recovery. Research has shown that isoleucine, along with other

BCAAs, can enhance muscle protein synthesis and improve recovery after exercise[31]. This led to increased interest in isoleucine supplementation among athletes and bodybuilders, culminating in its inclusion in various dietary supplements aimed at improving performance and recovery outcomes[31].

Furthermore, advancements in biochemical techniques have allowed for the exploration of non-natural derivatives of isoleucine, which possess specialized properties for use in drug development and biotechnology[5]. These derivatives have been shown to enhance the stability and bioavailability of pharmaceutical formulations, thereby widening the applications of isoleucine in therapeutic contexts[5][36].

Related Resources

Data Availability

The datasets related to Isoleucine research can be accessed through various online repositories. Specific names of these repositories and their corresponding accession numbers are available in the relevant literature and supplementary materials provided by the authors[13].

Author Contributions

Research on Isoleucine has seen contributions from multiple authors who have significantly influenced the scope of the studies conducted. Each author has played a critical role in the analysis, preparation, and approval of the manuscripts discussing the effects and benefits of Isoleucine, ensuring a comprehensive understanding of the topic[13][7].

Literature Review

A comprehensive literature review has been conducted, encompassing a wide range of studies related to Isoleucine. The review cites multiple sources, including research articles, abstracts, and book chapters, which provide insight into the amino acid's role in metabolism and supplementation effects on exercise performance and training adaptations[12][7].

Ethical Considerations

Research involving Isoleucine supplementation and its effects has adhered to ethical guidelines. Procedures involving animal subjects are conducted in accordance with the China Agricultural University Animal Care and Use Committee guidelines, ensuring the integrity and ethical treatment of research subjects[7].

Further Research

Despite the progress made in understanding Isoleucine, significant gaps remain in knowledge regarding its long-term effects and safety profiles. Future research should

focus on exploring the amino acid's potential therapeutic applications and its role in various health conditions, thereby contributing to the broader understanding of amino acids in human health[12][7].

Competing Interests

Researchers involved in Isoleucine studies have disclosed that they possess no competing interests, which strengthens the credibility and impartiality of their findings[7].

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