

# Leucine

## Table of Contents

summary

Biological Functions

- Protein Synthesis

- Energy Metabolism

- Muscle Growth and Development

Overview

Therapeutic Applications

- Neurodegeneration

- Parkinson's Disease

Chemical Structure

Leucine in Health and Disease

- Role in Muscle Health

- Metabolic Effects

- Potential Risks

Supplements

- Uses

- Dosage

- Safety and Side Effects

- Storage and Disposal

Dietary Sources

- Animal-Based Sources

- Plant-Based Sources

- Protein Supplements

Research and Developments

- Overview of Research Contributions

- Funding and Support

- Conflict of Interest

- Mechanisms of Action

- Applications in Nutrition and Industry

- Future Research Directions

Check <https://storm.genie.stanford.edu/article/1150295> for more details

Stanford University Open Virtual Assistant Lab

The generated report can make mistakes.

Please consider checking important information.

The generated content does not represent the developer's viewpoint.

## summary

Leucine is an essential branched-chain amino acid (BCAA) that plays a vital role in protein synthesis, muscle growth, and metabolic regulation. As one of the three BCAAs, alongside isoleucine and valine, leucine is primarily found in high-protein foods such as meat, dairy, and legumes. Its unique structure, characterized by an isobutyl side chain, distinguishes it from other amino acids and is integral to its metabolic functions, particularly in muscle tissue where it is predominantly processed[1][2][3].

Notably, leucine is a powerful stimulator of muscle protein synthesis, largely through its activation of the mechanistic target of rapamycin (mTOR) signaling pathway. This pathway is crucial for regulating cell growth and protein synthesis, making leucine particularly significant for athletes and individuals engaging in resistance training. Supplementation with leucine has been linked to improved muscle mass and recovery, especially in older adults, highlighting its importance in combating age-related muscle loss, known as sarcopenia[1][2][4][5].

In addition to its anabolic properties, leucine also influences energy metabolism, promoting glucose uptake and fatty acid oxidation. These metabolic effects are essential for maintaining stable energy levels and may contribute to improved insulin sensitivity and lipid profiles, making leucine a potential candidate for managing metabolic disorders such as diabetes[1][6]. However, excessive intake of leucine can lead to adverse effects, including nutrient imbalances and potential health risks, underscoring the importance of balanced consumption within a varied diet[6].

Leucine's therapeutic potential extends beyond nutrition, as research is ongoing into its applications for neurodegenerative diseases and its role in modulating neuronal health. Studies are exploring the use of leucine-rich compounds as inhibitors for dual leucine zipper kinase, which may offer new avenues for treating conditions like Alzheimer's and Parkinson's disease[1][7]. The multifaceted roles of leucine in health and disease continue to make it a prominent focus in nutritional science and medical research.

## Biological Functions

Leucine plays a critical role in various biological processes, particularly in protein synthesis, energy metabolism, and muscle development. It is one of the branched-chain amino acids (BCAAs) that significantly influences anabolic pathways, including the

mechanistic target of rapamycin (mTOR) signaling pathway, which is essential for regulating cell growth and protein synthesis[1][2].

## Protein Synthesis

Leucine is a potent stimulator of muscle protein synthesis. It activates the mTOR pathway, which enhances the translation of mRNA into proteins, thereby promoting muscle growth and repair[1][2]. Research indicates that supplementation with leucine can improve protein synthesis, especially in older adults, and may be mediated through epigenetic modifications that affect growth hormone regulation[1]. This pathway is crucial for maintaining skeletal muscle mass and function, as protein synthesis is essential for the development and maintenance of muscle tissues[1][2].

## Energy Metabolism

In addition to its role in protein synthesis, leucine also influences energy metabolism. It enhances glucose uptake and utilization in peripheral tissues, which regulates energy balance by promoting energy expenditure and inhibiting energy storage[1]. Furthermore, leucine stimulates fatty acid oxidation by activating AMP-activated protein kinase (AMPK), leading to improved mitochondrial function and energy production[1][2]. This process is significant for maintaining stable energy levels in the body, especially in skeletal muscle, which serves as a major site for the clearance of serum free fatty acids[1][2].

## Muscle Growth and Development

Leucine is particularly important for muscle growth and hypertrophy. It is involved in the regulation of various signaling pathways that contribute to muscle cell development and maintenance. For instance, the activation of the mTORC1 complex by leucine not only promotes protein synthesis but also supports mitochondrial biogenesis, thereby enhancing muscle function and growth[1]. Studies have demonstrated that leucine supplementation can lead to increased muscle protein, fat, and lactose production in dairy cows, highlighting its role in promoting growth in different species[1]. Additionally, the cytoskeleton in muscle cells, which is essential for maintaining structural integrity and facilitating growth, is influenced by the actions of leucine on muscle cells[2].

## Overview

Leucine is an essential branched-chain amino acid (BCAA) that plays a crucial role in protein synthesis and metabolic regulation. It is one of the three BCAAs, along with isoleucine and valine, and is primarily found in high-protein foods such as meat, dairy, and legumes[8].

## Therapeutic Applications

# Neurodegeneration

There is ongoing investigation into the development of dual leucine zipper kinase inhibitors as potential treatments for neurodegenerative diseases. These inhibitors may help modulate the effects of leucine in neuronal health and function, presenting new avenues for therapeutic interventions in diseases such as Alzheimer's and Parkinson's.

## Parkinson's Disease

Leucine-rich repeat kinase 2 (LRRK2) has been identified as a significant therapeutic target for Parkinson's disease. Recent updates suggest that modulating leucine metabolism and signaling pathways may play a role in mitigating the progression of this neurodegenerative disorder.

## Chemical Structure

Leucine is classified as a branched-chain amino acid (BCAA) with the chemical formula  $C_6H_{13}NO_2$ , and a molecular weight of 131.17 g/mol. Its structure includes an amino group, a carboxylic acid group, and a distinct isobutyl side chain that differentiates it from other amino acids. The presence of this branched side chain plays a crucial role in the metabolism of leucine, as it is primarily processed in muscle tissue rather than the liver, which significantly influences its role in energy production and muscle protein synthesis[3][9].

In terms of its biochemical properties, leucine is characterized as a non-polar, aliphatic amino acid, reflecting its hydrophobic nature. This hydrophobicity is an important factor in the formation of protein structures, as it influences how proteins fold and interact with one another[1][10]. Furthermore, leucine's unique structure allows it to participate in various metabolic pathways, particularly those related to muscle growth and recovery, making it an essential nutrient for athletes and individuals engaged in resistance training[11].

## Leucine in Health and Disease

Leucine is an essential branched-chain amino acid (BCAA) that plays a significant role in various physiological processes and has been associated with numerous health benefits. As a vital component of protein metabolism, leucine is crucial for promoting muscle protein synthesis, thereby supporting muscle growth, repair, and maintenance[12][3]. It is particularly important for individuals engaged in physical activity, as well as for older adults experiencing age-related muscle loss.

## Role in Muscle Health

Leucine is known to stimulate the mTOR pathway, which is essential for protein synthesis and cell growth[12][11]. Supplementation with leucine has shown promising effects in improving muscle mass and function, especially in older adults who often

exhibit a diminished anabolic response to dietary protein[4]. Research suggests that increasing leucine intake may counteract muscle loss associated with sarcopenia, a condition characterized by the progressive loss of skeletal muscle mass and strength in aging populations[5][4].

Additionally, leucine acts as a potent anticatabolic agent, meaning it can help prevent muscle breakdown during periods of atrophy or intense exercise[13][14]. Studies have demonstrated that intravenous leucine administration can significantly reduce protein degradation in healthy individuals[4]. However, the long-term effects of leucine supplementation on muscle mass remain a subject of ongoing research, as some studies have shown variable results regarding its influence on muscle protein synthesis[15].

## Metabolic Effects

Beyond its role in muscle health, leucine also affects metabolic processes, particularly concerning insulin signaling and glucose metabolism. The co-consumption of leucine with glucose has been shown to enhance insulin secretion and lower blood sugar levels, making it potentially beneficial for individuals managing diabetes[6][1]. However, caution is advised for those with hypoglycemia, as excessive leucine may further lower blood sugar levels when combined with diabetic medications[6].

Leucine's influence on metabolic pathways extends to lipid metabolism as well, where it may improve insulin sensitivity and lipid profiles in individuals[1]. Some evidence suggests that leucine supplementation could enhance fatty acid oxidation and mitochondrial function in muscle and adipose tissue, contributing to improved metabolic health[4].

## Potential Risks

While leucine is associated with several health benefits, excessive intake can lead to adverse effects. High levels of leucine may inhibit the production of certain vitamins and contribute to deficiency diseases if not balanced with other nutrients[6]. Therefore, it is essential to consider leucine intake within the context of a balanced diet.

## Supplements

Leucine is commonly marketed as a dietary supplement, particularly in the sports and nutrition industry, where it is aimed at enhancing muscle growth, recovery, and exercise performance. It is classified as an essential amino acid, meaning it must be obtained from dietary sources since the body cannot synthesize it.[12][1].

## Uses

Although further research is warranted, leucine supplements are generally utilized to help build muscle mass and improve exercise outcomes. The primary mechanism through which leucine exerts its effects is by activating the mechanistic target of rapamycin (mTOR) signaling pathway, which plays a critical role in promoting

muscle protein synthesis.[\[3\]\[1\]](#) Leucine is often taken in conjunction with other branched-chain amino acids (BCAAs) such as valine and isoleucine, particularly in formulations designed for athletes and bodybuilders seeking to optimize their training results.[\[16\]\[3\]](#).

## Dosage

There are no officially established dosage guidelines for leucine supplements; however, a common dosage is around 5 grams per day.[\[14\]](#) The World Health Organization (WHO) recommends that the average healthy adult consume approximately 39 mg/kg of leucine daily. This translates to about 3.1 grams for a person weighing 176 pounds (80 kg). Notably, older adults may require higher intakes to prevent or recover from muscle loss, with recommendations often suggesting around 3 grams of leucine at each main meal, alongside adequate protein intake.[\[14\]\[1\]](#).

## Safety and Side Effects

Leucine supplements are generally regarded as safe when taken at recommended doses, but high doses may lead to adverse effects. Severe side effects can include confusion, elevated blood ammonia levels, and gastrointestinal issues when combined with high doses of whey protein, such as gas and nausea.[\[14\]\[17\]](#) It is essential for individuals to consult with healthcare providers or registered dietitians before starting leucine supplementation, especially if they experience any severe symptoms or have pre-existing health conditions.[\[14\]\[16\]](#).

## Storage and Disposal

Proper storage of leucine supplements is critical for maintaining their efficacy. They should be kept in a cool, dry place and stored in their original packaging, out of reach of children and pets. Supplements should be discarded after one year or as directed on the product label.[\[14\]](#) Individuals are encouraged to consult healthcare professionals about appropriate disposal methods for any unused supplements.

## Dietary Sources

Leucine is an essential amino acid that plays a critical role in protein synthesis and muscle recovery. Various dietary sources provide differing amounts of leucine and other essential amino acids (EAAs), which are important for athletes and those looking to optimize their protein intake.

### Animal-Based Sources

Animal proteins are generally considered high-quality sources of leucine due to their complete amino acid profiles.

**Meat:** Lean cuts of beef, poultry, and pork are rich in leucine. For example, a standard serving of 113.4 g of lean beef provides approximately 3.5 g of leucine along with



a total of 30 g of amino acids, significantly stimulating muscle protein synthesis (MPS)[\[18\]](#)[\[8\]](#).

**Dairy Products:** Low-fat dairy, such as yogurt and milk, also contribute to leucine intake. Dairy proteins, particularly whey, are known for their rapid digestion and high leucine content, making them effective for post-exercise recovery[\[8\]](#).

**Eggs:** Eggs are another excellent source, providing a balance of essential amino acids along with a high leucine content, which can support muscle repair and growth[\[8\]](#).

## Plant-Based Sources

While plant-based proteins tend to have lower leucine content compared to animal sources, they can still contribute effectively to overall leucine intake, especially when consumed in adequate amounts:

**Soy Products:** Foods like tofu and tempeh are good sources of leucine and provide a complete amino acid profile, making them valuable for those on a plant-based diet[\[18\]](#).

**Legumes:** Lentils, beans, and peas contain moderate amounts of leucine and are also rich in other nutrients, but their overall digestibility is often lower than that of animal proteins[\[11\]](#). It is advisable for individuals relying on these sources to consume larger portions to meet their leucine needs[\[18\]](#).

**Quinoa:** This grain is notable for being a complete protein, containing all nine essential amino acids, including leucine, and is a great addition to a balanced diet[\[18\]](#).

## Protein Supplements

Protein powders, especially those derived from whey or soy, can provide concentrated doses of leucine. These supplements are particularly beneficial for athletes looking to quickly replenish their amino acid levels post-workout. Research suggests that targeting higher doses, especially for plant-based protein powders, can help ensure sufficient leucine intake, potentially exceeding the standard recommendations for optimal muscle recovery[\[11\]](#).

## Research and Developments

### Overview of Research Contributions

Research on leucine has significantly advanced our understanding of its role as a branched-chain amino acid (BCAA) essential for protein synthesis and metabolic regulation. The conceptualization and composition of key studies have been spearheaded by various authors, including SR and RA, while HZ has contributed to analysis and MZ has provided proofreading support. Collectively, all authors have approved the submitted versions of their work, reflecting a collaborative approach to the investigation of leucine's biological functions[\[1\]](#).

## Funding and Support

The research into leucine has been bolstered by substantial financial backing from several national programs, including the 14th and 13th Five-Year Plan Key Research and Development Programs (2021YFD1600702, 2017YFD0800200), as well as the key program of the State Key Laboratory of Sheep Genetic Improvement and Healthy Production (2021ZD07; NCG202232). Additionally, support has been provided through the Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD), P.R. China[\[1\]\[7\]](#).

## Conflict of Interest

Researchers in the field have consistently declared that studies on leucine were conducted without any commercial or financial relationships that could pose a potential conflict of interest. This transparency underscores the integrity of the research findings in the scientific community[\[7\]](#).

## Mechanisms of Action

Leucine is recognized for its pivotal role in stimulating muscle protein synthesis through activation of the mTOR signaling pathway[\[12\]](#). This amino acid not only supports muscle growth and repair but also regulates blood sugar levels and promotes the development of muscle and bone tissues[\[19\]](#). Studies have demonstrated that leucine supplementation can enhance various physiological parameters, including lipid and glucose metabolism, exercise tolerance, and even counteracting certain skeletal muscle dysfunctions associated with diseases[\[12\]\[19\]](#).

## Applications in Nutrition and Industry

Beyond its nutritional applications, leucine is being explored in the pharmaceutical and biotechnological sectors. Its biochemical properties facilitate its use in drug formulation, particularly in creating chiral pharmaceuticals that enhance therapeutic efficacy while minimizing side effects. Non-natural leucine derivatives have emerged as valuable tools in drug development and enzyme inhibition studies, leading to a greater understanding of leucine's role in cellular functions and its potential therapeutic applications[\[3\]](#).

## Future Research Directions

Ongoing research is imperative to fill existing gaps in the literature regarding leucine supplementation and its effects on health, particularly in aging populations and those engaging in regular physical activity. This includes examining optimal dosages and understanding potential side effects[\[20\]](#). Such inquiries will inform dietary recommendations and further validate leucine's importance in nutrition and metabolic health.

## References



- [1]: [Research progress in the role and mechanism of Leucine ... - Frontiers](#)
- [2]: [Unraveling the transcriptomic effects of leucine supplementation on ...](#)
- [3]: [International Society of Sports Nutrition Position Stand: protein and ...](#)
- [4]: [Leucine: Definition, Structure, Benefits, Sources and Uses](#)
- [5]: [Branched-Chain Amino Acid Metabolism Disorders - Merck Manuals](#)
- [6]: [Leucine Supplementation: A Novel Strategy for Modulating Lipid ...](#)
- [7]: [Optimal Protein Intake Guide & Calculator - Examine.com](#)
- [8]: [Leucine - Memorial Sloan Kettering Cancer Center](#)
- [9]: [The effectiveness of leucine on muscle protein synthesis, lean body ...](#)
- [10]: [Where to Find Leucine in Food and How to Feed Elderly ... - Frontiers](#)
- [11]: [Leucine - an overview | ScienceDirect Topics](#)
- [12]: [How Leucine Supports Muscle Health and Other Benefits](#)
- [13]: [Leucine Supplement: Potential Benefits and Considerations](#)
- [14]: [Leucine | Dosage, Benefits & Side Effects - Myprotein US](#)
- [15]: [Research progress in the role and mechanism of Leucine in ...](#)
- [16]: [Branch-Chain Amino Acids: Uses and Risks - WebMD](#)
- [17]: [Protein Recommendations for Athletes - My Sports Dietitian](#)
- [18]: [The Effect of Leucine Supplementation on Sarcopenia-Related ...](#)
- [19]: [Leucine - Metabolite of the month - biocrates life sciences ag](#)
- [20]: [Amino acids regulating skeletal muscle metabolism: mechanisms of ...](#)
- [undefined]: [Skeletal muscle protein metabolism in the elderly: Interventions to ...](#)