

# Ornithine

## Table of Contents

summary

Chemical Structure

Biosynthesis

Biological Functions

- Metabolic Pathways

- Role in Muscle Function and Health

- Clinical Significance

Dietary Sources

Health Implications

- Role in Urea Cycle

- Therapeutic Benefits

- Chronic Disease Connections

Clinical Applications

- Hepatic Encephalopathy

- Metabolic Disorders in COVID-19

- Clinical Efficacy and Safety

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## summary

Ornithine is a non-proteinogenic amino acid with the molecular formula  $C_6H_{13}N_2O_2$ , playing a crucial role in various metabolic processes, particularly in the urea cycle, where it is instrumental in detoxifying ammonia and producing urea.<sup>[1][2]</sup> Characterized by its unique structure, which includes a central  $\alpha$ -carbon bonded to two amino groups and a carboxyl group, ornithine is categorized as a dibasic amino acid, highlighting its basic properties in biological systems.<sup>[3][4]</sup> Its significance extends beyond nitrogen metabolism, influencing the biosynthesis of polyamines essential for cellular functions such as cell growth and DNA stabilization.<sup>[1][5]</sup>

Notably, ornithine's metabolic importance has led to its exploration in therapeutic contexts, particularly for conditions like hepatic encephalopathy and muscle function enhancement.[\[6\]\[7\]](#) The compound L-ornithine L-aspartate (LOLA), derived from ornithine, has been studied for its potential benefits in liver function and ammonia detoxification, reflecting ornithine's clinical significance in managing liver diseases and metabolic disorders.[\[7\]\[8\]](#) Additionally, ornithine supplementation has gained attention for its role in improving muscle recovery and reducing fatigue during intense physical activity, making it popular among athletes and those with specific metabolic needs.[\[9\]\[10\]](#)

Controversies surrounding ornithine primarily involve the quality and consistency of clinical studies evaluating its efficacy, particularly in therapeutic applications for hepatic encephalopathy and metabolic health.[\[11\]\[8\]](#) Concerns about biases and the need for larger, more rigorous trials remain, underscoring the importance of further research to validate the benefits of ornithine supplementation and its derivatives.[\[11\]](#) Overall, ornithine's multifaceted roles in metabolism and potential therapeutic applications contribute to its growing recognition in both scientific and clinical communities.

## Chemical Structure

Ornithine is a non-proteinogenic amino acid with the molecular formula  $C_5H_{11}N_2O_3$  and a molecular weight of 132.16 g/mol[\[1\]\[2\]](#). It is characterized by a structure that includes a central  $\alpha$ -carbon atom, which is bonded to a carboxyl group ( $-\text{COOH}$ ), an amino group ( $-\text{NH}_2$ ), a hydrogen atom, and a distinctive four-carbon side chain. This side chain also terminates with an additional amino group ( $-\text{NH}_2$ ), categorizing ornithine as a dibasic amino acid[\[1\]\[2\]\[3\]](#).

The IUPAC name for ornithine is 2,5-diaminopentanoic acid, highlighting its two amino groups[\[4\]](#). Its isoelectric point (pI) is approximately 9.71, which is the pH at which the molecule carries no net electric charge[\[2\]\[12\]](#). The presence of the two amino groups contributes to the basicity of the molecule, influencing its behavior in biological systems and interactions with other biomolecules[\[1\]\[2\]](#).

## Biosynthesis

L-Ornithine is primarily synthesized through the urea cycle, which is a crucial metabolic pathway in animals for the detoxification of ammonia and the production of urea. The cycle involves several enzymatic reactions that convert ammonia into urea, with L-ornithine serving as a key intermediate. The initial step requires the conversion of ammonia into carbamoyl phosphate, which subsequently combines with L-ornithine to form L-citrulline. The pathway continues through a series of reactions, ultimately leading to the formation of urea and regenerating L-ornithine for further cycles of the pathway[\[1\]\[5\]](#).

In microorganisms, particularly in strains such as *Corynebacterium glutamicum*, L-ornithine biosynthesis can also occur through the tricarboxylic acid (TCA) cycle and specific metabolic adjustments. This organism has been genetically modified to

enhance L-ornithine production by manipulating various pathways, demonstrating the ability to increase the yield significantly through gene disruption and overexpression strategies. For instance, the engineered strains have shown improvements in L-ornithine accumulation by altering enzyme expression levels in the metabolic pathway[13][14].

Furthermore, L-ornithine plays a vital role in the biosynthesis of polyamines, such as putrescine, spermidine, and spermine. The enzyme ornithine decarboxylase catalyzes the decarboxylation of L-ornithine, which is the first step in polyamine synthesis. These polyamines are essential for numerous cellular functions, including cell division and the stabilization of DNA, thus highlighting the importance of L-ornithine in both biosynthetic pathways and physiological processes[1][5].

The synthesis of L-ornithine is interconnected with other nitrogen metabolism pathways, particularly the arginine-succinate shunt, which balances the urea cycle with L-arginine synthesis. This interconnection ensures that the necessary intermediates are available for various biosynthetic processes, further emphasizing the metabolic significance of L-ornithine in nitrogen metabolism[1].

## Biological Functions

Ornithine is a non-proteinogenic amino acid that plays a crucial role in various metabolic processes within vertebrates. One of its primary biological functions is as an intermediate in the urea cycle, which is essential for the detoxification of ammonia produced during amino acid metabolism[5][15]. In this cycle, ornithine is converted into citrulline and subsequently to arginine, with the latter being a precursor for the synthesis of nitric oxide, an important signaling molecule in the body[15].

## Metabolic Pathways

Ornithine serves as a metabolic precursor not only for arginine but also for other compounds involved in critical biochemical pathways. For example, ornithine can be synthesized from arginine through a process called hydrolysis, which also produces nitric oxide[15]. This conversion is significant as nitric oxide plays a vital role in vasodilation and neurotransmission, highlighting the importance of ornithine in cardiovascular health and brain function[16].

## Role in Muscle Function and Health

Research indicates that ornithine supplementation may have beneficial effects on muscle function and fatigue. It is sometimes used in dietary supplements to help reduce muscle fatigue, particularly during intense physical activity[15]. Additionally, studies have shown that ornithine can influence muscle metabolism and growth, particularly in conditions of high-fat diet-induced obesity, where it has been associated with improvements in muscle density and strength over time[9].

## Clinical Significance

In clinical contexts, ornithine is also investigated for its potential therapeutic applications, particularly in the management of liver diseases such as non-alcoholic fatty liver disease (NAFLD). L-Ornithine L-Aspartate (LOLA), a compound derived from ornithine, has been explored for its hepatoprotective properties and ability to improve liver function by facilitating ammonia detoxification and reducing oxidative stress in liver tissues[\[6\]\[9\]](#).

## Dietary Sources

Ornithine, a non-essential amino acid, is primarily synthesized in the body from arginine, but it can also be obtained from various dietary sources. Major contributors to ornithine intake include animal-based foods such as meat, fish, dairy products, and eggs[\[17\]\[1\]\[18\]](#). These sources provide not only ornithine but also other essential amino acids crucial for protein synthesis and muscle repair, making them particularly beneficial for individuals engaged in physical activities or muscle recovery[\[1\]](#).

For those following a vegetarian or vegan diet, ornithine can still be sourced from certain plant-based foods. Nuts, particularly coconuts and peanuts, as well as seeds such as sesame and pumpkin seeds, contribute moderate amounts of ornithine[\[17-\]\[18\]](#). Other plant-based sources include grains like oats and wheat germ, legumes, soybeans, and products derived from soy such as tofu and tempeh[\[17\]\[19\]](#). However, the overall availability of ornithine from these sources is typically lower compared to animal products, which may necessitate supplementation for individuals with increased metabolic needs or those involved in intense physical activities[\[1\]\[18\]](#).

Supplementation of ornithine has gained popularity among athletes and those experiencing muscle wasting or liver dysfunction, as it is believed to support biological processes such as muscle recovery and ammonia detoxification[\[1\]\[10\]](#). Ornithine supplements are available in various forms, including capsules and powders, with dosages commonly ranging from 500 mg to 3 grams per day[\[1\]](#).

## Health Implications

### Role in Urea Cycle

L-ornithine is a non-proteinogenic amino acid that plays a vital role in the urea cycle, a crucial metabolic pathway responsible for the detoxification and removal of ammonia and excess nitrogen from the body.[\[17\]](#) Deficiencies in enzymes associated with this cycle can lead to severe health issues, including hyperammonemia, which is a dangerous accumulation of ammonia in the blood.[\[16\]](#) Among urea cycle disorders, ornithine transcarbamylase (OTC) deficiency is the most prevalent, particularly affecting males due to its X-linked inheritance pattern.[\[10\]](#) This genetic disorder can lead to neurological toxicity and requires timely intervention to prevent serious complications such as coma or death.[\[5\]](#)

### Therapeutic Benefits

Recent studies have indicated that L-ornithine supplementation may provide therapeutic benefits for various conditions, including hepatic encephalopathy, which is characterized by the accumulation of toxins in the brain due to liver dysfunction.[\[7\]](#)-[\[11\]](#) Clinical trials have shown that L-ornithine-L-aspartate can significantly improve symptoms associated with hepatic encephalopathy, enhancing health-related quality of life for affected individuals.[\[7\]](#) Additionally, the amino acid has been associated with benefits in muscle growth and recovery, sleep quality, and immune support, making it a valuable component for those engaged in intensive physical training or recovering from injuries.[\[17\]](#)

## Chronic Disease Connections

Emerging research suggests that ornithine may have implications in the management of chronic diseases, such as cancer, Alzheimer's disease, and depression. Its role in nitrogen metabolism and potential immune-boosting properties may contribute to overall health improvement and support in the healing of wounds.[\[17\]](#)[\[10\]](#) Furthermore, the association between elevated ornithine levels and reduced symptoms of chronic illnesses underscores the importance of this amino acid in metabolic and physiological functions.[\[10\]](#)

## Clinical Applications

### Hepatic Encephalopathy

Ornithine, particularly in the form of L-ornithine L-aspartate (LOLA), is utilized in the treatment of hepatic encephalopathy, a severe complication associated with liver disease characterized by neurological disturbances due to elevated blood ammonia levels. LOLA has been shown to play a critical role in ammonia metabolism by promoting the conversion of ammonia to urea in the liver, thus reducing systemic ammonia accumulation[\[8\]](#). The combination of LOLA with lactulose has demonstrated significant improvements in key liver function indicators, enhancing patients' overall prognosis and quality of life[\[8\]](#)[\[11\]](#).

### Metabolic Disorders in COVID-19

Recent studies have indicated that ornithine and its derivatives may be beneficial in managing metabolic disorders associated with COVID-19. Research has highlighted metabolic abnormalities persisting even after hospital discharge in patients who have recovered from COVID-19, suggesting a prolonged recovery trajectory for metabolic balance[\[20\]](#). High-throughput untargeted metabolomic studies are essential for understanding these changes, providing insight into potential interventions involving ornithine supplementation to restore metabolic equilibrium[\[20\]](#).

### Clinical Efficacy and Safety

The safety and efficacy of ornithine as part of combination therapies have been evaluated in several randomized controlled trials. While some studies report significant advantages in using LOLA for treating hepatic encephalopathy compared to traditional treatments, concerns regarding study biases and the quality of included trials remain[8][11]. The lack of blinding in many studies may introduce risks of bias, highlighting the need for larger, multicenter trials to validate these findings and optimize treatment regimens involving ornithine[11].

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