# Effects of L-histidine on Growth Performance, Meat Quality, Plasma Antioxidant Capacity, and Muscle Imidazole Dipeptide Content in Broiler Chickens (Postprint)

**Authors:** Hu Meng, Zhang Haijun, Wang Jing, Qi Guanghai, Wu Shugeng

**Date:** 2017-10-10T00:00:00+00:00

## Abstract

This experiment aimed to investigate the effects of dietary L-histidine supplementation on growth performance, meat quality, plasma antioxidant capacity, and muscle imidazole dipeptide content in broiler chickens. Three hundred healthy 1-day-old Arbor Acres (AA) male broiler chicks with similar body weight were randomly divided into 5 groups with 6 replicates per group and 10 chickens per replicate. The control group was fed a basal diet, while the experimental groups were fed experimental diets supplemented with 250, 500, 1,000, and 2,000 mg/kg L-histidine in the basal diet, respectively. The experimental period lasted 42 days. The results showed: 1) L-histidine reduced the feed conversion ratio of broilers during the late growth stage (22-42 days of age), with the 250 and 2,000 mg/kg supplementation groups being significantly lower than the control group ($P<0.05$). 2) L-histidine had no significant effects on eviscerated yield, breast muscle percentage, thigh muscle percentage, abdominal fat percentage, drip loss, shear force, and pH ($P>0.05$). 3) L-histidine linearly increased the plasma total antioxidant capacity and the activities of glutathione peroxidase and total superoxide dismutase at 42 days of age ($P<0.05$). 4) L-histidine increased the contents of carnosine and anserine in muscle at 42 days of age; compared with the control group, the carnosine contents in the 500, 1,000, and 2,000 mg/kg supplementation groups increased by 40.58%, 42.75%, and 33.70% ($P<0.05$), respectively, and the anserine content in the 1,000 mg/kg supplementation group increased by 37.80% ($P<0.05$); quadratic curve fitting of muscle carnosine and anserine contents indicated that the imidazole dipeptide content in muscle was highest when the L-histidine supplementation level was 1,276 mg/kg. In conclusion, dietary L-histidine supplementation can improve feed conversion ratio, enhance plasma antioxidant capacity, and increase muscle imidazole dipeptide content in broiler chickens. Under the conditions of

this experiment, dietary supplementation of 1,000-2,000 mg/kg L-histidine was optimal. Considering the increase in muscle imidazole dipeptide content, the appropriate dietary L-histidine supplementation level was 1,276 mg/kg.

## Full Text

# Effects of L-Histidine on Growth Performance, Meat Quality, Plasma Antioxidant Capacity, and Muscle Imidazole Dipeptide Contents in Broilers

**HU Meng, ZHANG Haijun, *WANG Jing, QI Guanghai, WU Shugeng***

(Key Laboratory of Feed Biotechnology, Ministry of Agriculture; National Engineering Research Center of Biological Feed; Feed Research Institute, Chinese Academy of Agricultural Sciences, Beijing 100081, China)

**Abstract:** This experiment was conducted to investigate the effects of dietary L-histidine supplementation on growth performance, meat quality, plasma antioxidant capacity, and muscle imidazole dipeptide contents in broilers. A total of 300 one-day-old healthy male Arbor Acres (AA) broiler chicks with similar body weight were randomly allocated into 5 groups with 6 replicates per group and 10 birds per replicate. The control group was fed a basal diet, while the experimental groups were fed the basal diet supplemented with 250, 500, 1,000, or 2,000 mg/kg L-histidine. The experiment lasted for 42 days. The results showed: (1) L-histidine decreased the feed-to-gain ratio during the late growth period (22–42 days of age), with the 250 and 2,000 mg/kg groups being significantly lower than the control group ($P<0.05$). (2) L-histidine had no significant effects on dressing percentage, breast muscle rate, leg muscle rate, abdominal fat rate, drip loss, shear force, or pH of muscle ($P>0.05$). (3) L-histidine linearly increased plasma total antioxidant capacity and the activities of glutathione peroxidase and total superoxide dismutase at 42 days of age ($P<0.05$). (4) L-histidine increased muscle carnosine and anserine contents at 42 days of age; compared with the control group, carnosine content increased by 40.58%, 42.75%, and 33.70% in the 500, 1,000, and 2,000 mg/kg groups, respectively ($P<0.05$), while anserine content increased by 37.80% in the 1,000 mg/kg group ($P<0.05$). Quadratic curve fitting of muscle carnosine and anserine contents indicated that the maximum imidazole dipeptide content was achieved at a dietary L-histidine supplementation level of 1,276 mg/kg. In conclusion, dietary L-histidine supplementation can improve feed conversion ratio, enhance plasma antioxidant capacity, and increase muscle imidazole dipeptide contents in broilers. Under the conditions of this experiment, dietary supplementation with 1,000–2,000 mg/kg L-histidine was optimal, and the appropriate supplementation level was 1,276 mg/kg when considering the maximization of muscle imidazole dipeptide content.

**Keywords:** L-histidine; meat quality; antioxidant capacity; imidazole dipeptide

## Introduction

With rapid social development and improving living standards, consumer demands for meat products have extended beyond nutritional value to include health-promoting properties such as antioxidant capacity, anti-aging effects, and overall health maintenance. Consequently, the development of functional meat products has attracted widespread attention. Imidazole dipeptides, primarily carnosine and anserine, are endogenous bioactive substances in animals that play important roles in antioxidant activity, anti-aging, enhancing muscle buffering capacity, maintaining pH stability, and combating fatigue [1-3]. Recent research has also demonstrated that carnosine possesses pharmacological potential in preventing and treating neurological diseases such as Alzheimer' s and Parkinson' s syndrome [4]. As a functional dipeptide that can accumulate in muscle tissue, carnosine offers broad application prospects for producing enriched meat products.

L-histidine is a semi-essential amino acid in animals but an essential amino acid in poultry production. It participates in tissue formation and serves as the primary precursor for muscle-derived bioactive peptides, exerting its effects mainly through carnosine in vivo. The NRC (1994) recommends L-histidine requirements of 0.35% for broilers aged 1–21 days and 0.32% for those aged 22–42 days. Due to its relatively high content in common feed ingredients (0.23% in corn and 1.1% in soybean meal), L-histidine is generally not deficient in conventional corn-soybean meal diets. However, additional supplementation is required to enhance functional dipeptide accumulation in muscle. Studies have shown that appropriate L-histidine supplementation can improve growth performance in fish [5-6], increase muscle carnosine content [7-8], and enhance antioxidant capacity [9], though research in broiler production remains limited. Therefore, this experiment aimed to investigate the effects of different dietary L-histidine levels on broiler growth performance, meat quality, plasma antioxidant capacity, and muscle imidazole dipeptide contents to provide a reference for its practical application.

## Materials and Methods

### 1.1 Experimental Materials

Arbor Acres (AA) broiler chicks were purchased from Beijing Huadu Broiler Company. L-histidine (purity 99%) was obtained from Hebei Hemei Amino Acid Co., Ltd.

### 1.2 Experimental Design and Diets

A single-factor experimental design was employed. Three hundred one-day-old AA male broiler chicks with similar body weight were randomly divided into

5 groups with 6 replicates per group and 10 birds per replicate. The groups were fed diets supplemented with 0, 250, 500, 1,000, or 2,000 mg/kg L-histidine, respectively. The measured histidine contents in the diets were 0.49%, 0.52%, 0.58%, 0.62%, and 0.70% for days 1–21, and 0.46%, 0.50%, 0.52%, 0.56%, and 0.70% for days 22–42, respectively. The basal diets were formulated according to NRC (1994), *Feeding Standard of Chickens* (NY/T 33-2004), and the *AA Broiler Feeding Manual*. Diet composition and nutrient levels are presented in Table 1 . The experimental period lasted 42 days.

### 1.3 Management Practices

During the experiment, birds had free access to feed and water under 24-hour lighting. The room temperature was maintained at 33°C for the first 3 days, then reduced by 2°C weekly until reaching 24°C, which was maintained thereafter. Management followed the *AA Broiler Management Guide* with routine vaccination and disinfection. The chicken house was well-ventilated, and temperature and humidity were recorded daily at 08:30 and 14:30. Sanitation was performed regularly.

### 1.4 Sample Collection and Measurements

**1.4.1 Growth Performance** At 21 and 42 days of age, birds were fasted and weighed by replicate to determine final body weight and calculate average daily gain (ADG). Feed consumption was recorded by replicate during the experimental period to calculate average daily feed intake (ADFI) and feed-to-gain ratio (F/G) for days 1–21, 22–42, and 1–42.

**1.4.2 Slaughter Performance and Meat Quality** At 21 and 42 days of age, one bird per replicate with body weight close to the replicate average was selected, weighed, slaughtered by jugular venesection, and weighed for eviscerated carcass, breast muscle, leg muscle, and abdominal fat.

At 42 days of age, one bird per replicate with body weight close to the replicate average was slaughtered by jugular venesection. The right breast muscle was completely excised, weighed, and used to determine drip loss, shear force, and pH.

**Drip loss:** Within 45 minutes post-slaughter, approximately 30 g of breast muscle with similar texture and uniform shape was weighed (W1), placed in a ziplock bag inflated with nitrogen to minimize contact with the bag interior, suspended with nylon string in a 4°C refrigerator, and reweighed after 24 hours (W2) after gently blotting surface moisture with filter paper. Drip loss percentage was calculated as: $[(W1-W2)/W1] \times 100$.

**Shear force:** Cooked meat samples were trimmed into two rectangular strips (2 cm × 2 cm × 1 cm) along the muscle fiber direction. During measurement, muscle fiber orientation was perpendicular to the blade. A TMS-Pro tenderness

analyzer (Food Technology Corporation, Virginia, USA) was used with parameters set at maximum load 100 N, crosshead speed 150 mm/min, and gap 6 mm. Each sample was tested three times, and the average of six measurements from two strips was recorded as the final shear force value.

**pH measurement:** pH was measured at 45 minutes (pH45min) and 24 hours (pH24h, stored at 4°C) post-slaughter using a pH meter (CyberScan pH310 waterproof pen-type, EUTECH, Singapore). The probe was inserted approximately 1 cm deep into the breast muscle, with the electrode tip completely embedded. Each sample was measured three times and averaged.

**1.4.3 Plasma Antioxidant Capacity** Plasma total antioxidant capacity (T-AOC), glutathione peroxidase (GSH-Px) activity, total superoxide dismutase (T-SOD) activity, and malondialdehyde (MDA) content were determined using commercial kits (Nanjing Jiancheng Bioengineering Institute) following the manufacturer' s instructions.

**1.4.4 Muscle Carnosine Content Instruments and reagents:** High-performance liquid chromatograph (Agilent LC-15, USA), carnosine standard (98%, Sigma, USA), anserine standard (98%, Sigma, USA), homogenizer (Haimen Qilinbeier; QL-901/QL-861), high-speed refrigerated centrifuge (Hunan Hexi Instrument Equipment Co., Ltd.), and methanol (HPLC grade).

**Standard preparation:** Carnosine standard (10 mg) was dissolved in ultrapure water and diluted to 10 mL in a volumetric flask (1 mg/mL stock solution), then further diluted to prepare working standards of 10, 20, 50, 80, and 100 g/mL. Anserine standard was prepared similarly.

**Sample preparation:** At 42 days of age, one bird per replicate with body weight close to the replicate average was slaughtered, and breast meat was collected and stored at -20°C. A 0.5 g sample was minced, mixed with 4.5 mL distilled water, and centrifuged at 4,000 r/min for 10 minutes. The supernatant was collected, mixed with 3 volumes of methanol, frozen at -20°C for 15 minutes, centrifuged at 11,000 r/min, and the supernatant was diluted 10-fold for analysis.

**HPLC conditions:** Separation was performed on an Agilent NH2 column (250 mm × 4.6 mm, 5 m particle size) using 40 mmol/L potassium hydrogen phosphate (pH=6.3) as the aqueous phase and methanol as the organic phase (34% organic phase) at a flow rate of 0.5 mL/min. Injection volume was 10 L, and detection wavelength was 210 nm. Carnosine eluted at 13.1 minutes and anserine at 14.3 minutes [10].

### 1.5 Statistical Analysis

Data were analyzed using one-way ANOVA in SPSS 16.0 software, followed by F-test and Duncan' s multiple comparison test. Differences were considered significant at $P<0.05$.

## Results

### 2.1 Effects of L-Histidine on Broiler Growth Performance

The effects of dietary L-histidine supplementation on broiler growth performance are presented in Table 2 . During the early growth period (1-21 days), L-histidine had no significant effects on final body weight, ADG, ADFI, or F/G ($P>0.05$). During the late growth period (22-42 days), L-histidine decreased F/G, with the 250 and 2,000 mg/kg groups being significantly lower than the control group ($P<0.05$). Additionally, F/G decreased linearly with increasing L-histidine supplementation ($P<0.05$), while final body weight, ADG, and ADFI were not significantly affected ($P>0.05$). Over the entire growth period (1-42 days), L-histidine had no significant effects on ADG, ADFI, or F/G ($P>0.05$).

### 2.2 Effects of L-Histidine on Broiler Slaughter Performance

Table 3 shows the effects of dietary L-histidine supplementation on broiler slaughter performance. L-histidine had no significant effects on dressing percentage, breast muscle rate, leg muscle rate, or abdominal fat rate at 21 or 42 days of age ($P>0.05$).

### 2.3 Effects of L-Histidine on Broiler Meat Quality

The effects of dietary L-histidine supplementation on broiler meat quality are presented in Table 4 . L-histidine had no significant effects on drip loss, shear force, or pH of breast muscle at 42 days of age ($P>0.05$). However, shear force tended to decrease linearly with increasing L-histidine supplementation ($P=0.061$).

### 2.4 Effects of L-Histidine on Broiler Plasma Antioxidant Capacity

Table 5 presents the effects of dietary L-histidine supplementation on broiler plasma antioxidant capacity. At 21 days of age, L-histidine linearly and quadratically decreased plasma T-AOC ($P<0.05$) but had no significant effects on plasma GSH-Px, T-SOD, or MDA content ($P>0.05$). At 42 days of age, L-histidine linearly increased plasma T-AOC and the activities of GSH-Px and T-SOD ($P<0.05$), while MDA content was not significantly affected ($P>0.05$) but numerically decreased with increasing L-histidine supplementation.

### 2.5 Effects of L-Histidine on Muscle Carnosine and Anserine Contents

Table 6 shows the effects of dietary L-histidine supplementation on muscle carnosine and anserine contents. L-histidine increased muscle carnosine and anserine contents at 42 days of age. Compared with the control group, carnosine content increased by 40.58%, 42.75%, and 33.70% in the 500, 1,000, and 2,000 mg/kg groups, respectively ($P<0.05$), while anserine content increased by 37.80% in the 1,000 mg/kg group ($P<0.05$). Based on the regression relationship between

dietary L-histidine level and muscle dipeptide content, the maximum carnosine content was achieved at 1,284 mg/kg, maximum anserine content at 1,271 mg/kg, and maximum total imidazole dipeptide content at 1,276 mg/kg supplementation.

### 2.6 Feed Cost Analysis

Table 7 presents the effects of L-histidine supplementation on broiler production costs. The cost per kg of weight gain was 4.13, 4.18, 4.34, 4.69, and 5.21 RMB/kg for the control, 250, 500, 1,000, and 2,000 mg/kg groups, respectively, increasing with higher L-histidine supplementation levels.

## Discussion

### 3.1 Effects of L-Histidine on Broiler Growth Performance

Histidine is an essential amino acid for broilers, with NRC (1994) recommendations of 0.35% for 1–21 days and 0.32% for 22–42 days. Modern genetic improvement has substantially enhanced broiler growth performance, altering nutrient requirements considerably. Haug et al. [11] reported that 0.3% dietary L-histidine supplementation reduced 28-day body weight by 13.9%, possibly due to histidine excess reducing feed intake and affecting growth. Kopeć et al. [9] found no significant changes in body weight or feed conversion when feeding 0.217% L-histidine for 42 days. Joonghyuck [12] reported that 10% blood meal supplementation (rich in histidine) did not affect growth performance or F/G. Variations in broiler strain, management, and dietary histidine-to-other-amino-acid ratios can all influence histidine requirements. Zhao et al. [13] demonstrated that appropriate L-histidine supplementation improved growth performance and intestinal enzyme activities in juvenile Jian carp. Dietary supplementation with 0.95% L-histidine significantly improved growth performance and feed conversion in stinging catfish [14]. Additionally, long-term consumption of low-histidine diets significantly reduced protein turnover rates in animals [15]. These findings indicate that different histidine levels exert varying effects on animal growth performance, with moderate supplementation potentially improving performance while excessive amounts may be detrimental. The current study showed that L-histidine did not significantly affect 42-day body weight but improved F/G during 22–42 days, with the best effect observed at 2,000 mg/kg supplementation, while having no significant impact during 1–21 days or the overall period. Research has identified toxic effects of excess histidine [3], and studies in mice demonstrated that histidine can reduce feed intake [16]. After consuming high-histidine diets, increased histamine production may occur, and as a neurotransmitter, histamine can reduce feed intake through nervous system regulation. In this experiment, L-histidine did not affect feed intake but improved feed conversion by increasing ADG. The imidazole group of L-histidine can bind metal ions such as copper and zinc, promoting their intestinal absorption and, through various copper- and zinc-dependent enzymes, enhancing animal growth performance. In this study, ADG increased during 22–

42 days in L-histidine-supplemented groups, improving feed conversion. Considering both body weight and feed conversion, 250 mg/kg supplementation was optimal. Son et al. [17] reported that L-histidine inhibited oxidative stress-induced inflammatory responses in human intestinal epithelial cells, improving gut health. Whether the increased ADG in this study was related to improved intestinal function warrants further investigation.

### 3.2 Effects of L-Histidine on Broiler Slaughter Performance

Current literature on L-histidine effects on broiler slaughter performance is limited. Kralik et al. [18] found no significant changes in carcass, breast muscle, or leg muscle weights when supplementing diets with 0.1%, 0.2%, or 0.3% L-histidine. Hu et al. [19] reported that 0.5% carnosine supplementation during 1–21 days significantly increased breast and leg muscle weights. Studies have shown that L-histidine can improve insulin resistance by suppressing pro-inflammatory factor expression [20], and insulin plays a crucial role in regulating protein metabolism in broilers [21]. Therefore, dietary L-histidine may regulate protein synthesis and muscle development by affecting insulin secretion. The current study found no significant effects of L-histidine on slaughter performance, consistent with Kralik et al. [18].

### 3.3 Effects of L-Histidine on Broiler Meat Quality and Plasma Antioxidant Capacity

Meat quality is a critical economic indicator in broiler production. Superior meat quality enhances consumer acceptance and extends product shelf life and storage time. Shear force reflects meat tenderness, with lower values indicating more tender meat. Previous research found that different L-histidine levels had no significant effects on drip loss, cooking loss, shear force, or pH in broiler muscle [16]. Thornton et al. [22] reported that rumen-protected L-histidine supplementation had no significant effect on beef shear force. Calpain and calpastatin are antagonistic enzymes that regulate meat tenderness through protein hydrolysis in muscle. Calpain is a calcium-dependent protease activated by calcium to increase tenderness. Rowe et al. [23] found that oxidative conditions inactivate calpain and activate calpastatin. L-histidine participates in redox reactions and may regulate meat tenderness by modulating calpain activity. Carnosine can regulate cellular calcium channels, and histidine may indirectly affect meat tenderness through carnosine. This study showed that dietary L-histidine supplementation had no significant effect on shear force, though values were numerically lower than the control group, possibly due to modulation of calpain activity.

L-histidine possesses strong antioxidant properties, primarily through two mechanisms: direct interaction with free radicals and carbonylated proteins, and indirect antioxidant effects by chelating metal ions that promote oxidative enzyme activity [24]. L-histidine can also affect antioxidant function by altering antioxidant enzyme activities. Kopeć et al. [9,25] found that 0.18% L-histidine

significantly increased plasma GSH-Px activity in turkeys, and 4% histidine-rich blood meal significantly increased plasma GSH-Px and SOD activities. The current results showed that L-histidine supplementation significantly decreased plasma T-AOC at 1–21 days but significantly increased plasma T-AOC, GSH-Px, and T-SOD activities at 22–42 days. Research indicates that excess L-histidine exhibits pro-oxidant effects under in vitro conditions [26]. The decreased plasma T-AOC during 1–21 days may be due to excess L-histidine for broilers at this age, promoting oxidation. During 22–42 days, the antioxidant effect of L-histidine strengthened with bird growth, increasing plasma T-AOC, GSH-Px, and T-SOD activities. L-histidine supplementation increased muscle carnosine content, which scavenges free radicals and carbonyl proteins, so the enhanced plasma antioxidant enzyme activity may also result from reduced oxidative substances and decreased consumption of antioxidants. The imidazole group of L-histidine can chelate metal ions, increasing their intestinal absorption [27], and these metal ions participate in various enzyme systems, so increased plasma antioxidant enzyme activity may also be related to enhanced antioxidant enzyme synthesis due to increased metal ion availability.

### 3.4 Effects of L-Histidine on Muscle Carnosine and Anserine Contents in Broilers

Carnosine is an endogenous functional dipeptide (anserine is a methylated derivative of carnosine) synthesized from -alanine and L-histidine, primarily present in skeletal muscle and brain, and secondarily in heart, kidney, and liver [28]. It possesses antioxidant, anti-aging, anti-fatigue, and pH-stabilizing properties, and shows potential in treating cataracts, autism, and Parkinson' s disease [29]. As a precursor for carnosine synthesis, appropriate dietary L-histidine supplementation can increase muscle carnosine and anserine contents. Kai et al. [30] reported that dietary L-histidine at twice the NRC (1994) recommendation increased muscle carnosine and anserine contents by 72% and 13%, respectively. Haug et al. [11] found that 0.1% L-histidine supplementation increased muscle carnosine and anserine contents by 64% and 10%, respectively. Kopeć et al. [9] reported that 0.18% L-histidine increased muscle carnosine and anserine by 35.24% and 23.33%, respectively. Different L-histidine levels produced varying muscle carnosine contents, indicating that supplementation can regulate muscle carnosine content to enrich meat with this functional dipeptide, providing consumers with higher-quality functional meat. However, Ogata [31] found that combined supplementation of 0.1% -alanine and 0.25% L-histidine in fish diets did not increase muscle dipeptide content, possibly due to species differences in sensitivity to dipeptide precursors, with fish potentially requiring higher precursor levels. The current study demonstrated that L-histidine significantly increased muscle carnosine content and markedly increased anserine content, consistent with anserine being a methylated derivative of carnosine.

Based on the regression relationship between dietary L-histidine level and mus-

cle histidine dipeptide content, appropriate L-histidine supplementation is necessary to increase muscle dipeptide content. At low supplementation levels, dipeptide content increased with supplementation level, but excessive supplementation did not produce satisfactory effects and may inhibit feed intake and reduce growth performance. Amend et al. [32] reported that histidine deficiency reduced muscle carnosine content in rooster breast and leg meat without affecting anserine content, indicating similar synthesis but different degradation patterns for carnosine and anserine in broilers, with carnosine degradation being more sensitive to histidine availability. Therefore, additional dietary L-histidine is necessary to produce meat with high carnosine content. Drozak et al. [33] found that genes such as carnosine synthase and carnosine N-methyltransferase affect carnosine synthesis and content in broilers. L-histidine may increase muscle carnosine content by upregulating carnosine synthase gene expression, though the exact molecular mechanism requires further investigation.

## Conclusions

1. Dietary L-histidine supplementation can improve feed conversion ratio, enhance plasma antioxidant capacity, and increase muscle imidazole dipeptide contents in broilers.
2. Under the conditions of this experiment, dietary supplementation with 1,000–2,000 mg/kg L-histidine was optimal.
3. Considering maximization of muscle imidazole dipeptide content, the appropriate dietary L-histidine supplementation level is 1,276 mg/kg.

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*Note: Figure translations are in progress. See original paper for figures.*