Effects of Resveratrol on Skeletal Muscle Fiber Type Transformation in Livestock and Poultry and Its Mechanisms: Postprint

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Abstract

Resveratrol is a polyphenolic compound widely present in nature in plants such as grapes and peanuts, exhibiting extensive biological activities including antioxidant, anti-tumor, anti-aging, and cardiovascular protective effects. In recent years, research on the function of resveratrol in skeletal muscle fiber type transformation has garnered increasing attention. Studies have demonstrated that resveratrol can induce the conversion of glycolytic muscle fibers to oxidative muscle fibers, thereby improving the meat quality of livestock and poultry. This review will integrate the latest research findings to summarize the effects of resveratrol on skeletal muscle fiber type transformation and its underlying mechanisms, providing a theoretical foundation for its application in animal husbandry.

Full Text

Influence of Resveratrol on Skeletal Muscle Fiber Type Transition in Livestock and Its Mechanism

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Abstract

Resveratrol is a polyphenolic compound widely distributed in plants such as grapes and peanuts, exhibiting extensive biological activities including antioxidant, anti-tumor, anti-aging, and cardiovascular protective effects. In recent years, research on resveratrol' s role in skeletal muscle fiber type transition has gained increasing attention. Studies have demonstrated that resveratrol can induce the transformation of glycolytic muscle fibers to oxidative muscle fibers, thereby improving meat quality in livestock. This review synthesizes recent research findings to summarize the effects of resveratrol on skeletal muscle fiber type transition and its potential regulatory mechanisms, providing a theoretical foundation for its application in animal production.

Keywords: resveratrol; polyphenolic compound; skeletal muscle fiber type transition; mechanism

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The excessive pursuit of meat yield has led to a significant decline in livestock meat quality, making its improvement an urgent priority. Muscle fibers are the fundamental units of muscle, and their types and composition represent major factors influencing meat quality in livestock and poultry. After birth, muscle fiber number remains constant, but continuous interconversion occurs between fiber types [1]. Numerous factors affect muscle fiber type transition, including environment, age, species, and nutrition. Muscle fibers can adapt to external stimuli through reciprocal transformation among subtypes. Resveratrol is a polyphenolic compound widely found in nature in plants such as grapes and peanuts, produced as a phytoalexin in response to biotic or abiotic stress [2-3]. Research has shown that resveratrol possesses broad biological activities, including antioxidant [4-5], anti-tumor [6], anti-aging, and anti-angiogenic functions [7]. Recent studies have revealed that resveratrol also exerts regulatory effects on skeletal muscle fiber type transition. Dietary resveratrol supplementation not only enhances antioxidant capacity in finishing pigs but also alters the expression of various myosin heavy chain (MyHC) isoform genes, thereby improving meat quality [8]. This suggests that resveratrol could serve as a feed additive in animal production with potential application value. Therefore, this review integrates the latest domestic and international research to summarize the effects of resveratrol on skeletal muscle fiber type transition and its potential regulatory mechanisms, providing a theoretical basis for its application in livestock production.

1. Muscle Fiber Types and Their Relationship with Meat Quality

Muscle fibers constitute the basic units of muscle, and their types and composition determine growth performance and meat quality in livestock and poultry. Based on the proportion of MyHC isoforms, MyHC can be classified into four subtypes: MyHC I, MyHC IIa, MyHC IIx, and MyHC IIb [9-10], all of which are expressed in porcine skeletal muscle. Type I represents slow oxidative fibers, type IIa fast oxidative fibers, type IIx intermediate fibers, and type IIb fast glycolytic fibers. This classification system is currently widely accepted for skeletal muscle fibers.

The composition and distribution of muscle fiber types directly affect meat quality. Serra et al. [11] found that in porcine psoas major and semitendinosus muscles, 24-hour postmortem pH, intramuscular fat content, and meat color were positively correlated with type I fiber proportion. Similarly, Ryu et al. [12] reported that meat tenderness and color were negatively correlated with type IIb fiber proportion but positively correlated with type I and IIa fiber proportions. These findings indicate that higher proportions of type I fibers correlate with better meat quality, whereas higher proportions of type IIb fibers correlate with poorer meat quality.

Additional research has shown that increased type IIb fiber proportion elevates muscle shear force, thereby reducing meat tenderness, while increased type I fiber proportion decreases shear force and improves meat quality [13]. Numerous studies have demonstrated the close relationship between oxidative fiber proportion and meat quality through measurements of meat color, postmortem pH, tenderness, water-holding capacity, drip loss, and cooking loss.

2. Effects of Resveratrol on Muscle Fiber Type Transition

Although muscle fiber number does not change after birth in livestock and poultry, fiber types can transition under the influence of various factors such as environment, age, and nutrition to adapt to external demands. Muscle fiber transition can occur from slow to fast fibers or from fast to slow fibers, following the pattern: I IIa IIx IIb [14]. Resveratrol is a polyphenolic compound widely present in nature in plants such as grapes and peanuts [2]. Many researchers have investigated its biological activities, including antioxidant [4-5], anti-aging [7], and energy metabolism regulation [15-16]. Recent studies have revealed that resveratrol also influences skeletal muscle fiber types.

Lagouge et al. [16] supplemented a high-fat diet with 400 mg/kg resveratrol and found that it significantly increased mitochondrial size, maximal oxygen consumption, and citrate synthase activity in mouse gastrocnemius muscle, while also improving endurance. This suggested that resveratrol might affect oxidative fiber expression. Subsequent analysis revealed that resveratrol significantly elevated the expression of myoglobin and troponin 1 (Tn1) genes in mouse gastrocnemius muscle, further confirming its promotion of oxidative fiber expression. By increasing mitochondrial size and enzyme activity, resveratrol enhanced maximal oxygen consumption and elevated oxidative fiber proportion in muscle. Changes in energy metabolism substrates and products in muscle likely represent part of the mechanism through which dietary resveratrol alters fiber type expression.

Price et al. [17] subsequently demonstrated that resveratrol supplementation in a high-fat diet significantly increased MyHC IIa and MyHC IIx mRNA expression while decreasing MyHC IIb mRNA expression in mouse gastrocnemius muscle. In soleus muscle (SOL), resveratrol significantly increased MyHC I, MyHC IIa, and MyHC IIx mRNA expression while decreasing MyHC IIb mRNA expression. These results indicate that resveratrol promotes oxidative fiber expression and suppresses glycolytic fiber expression in both glycolytic and oxidative muscles.

In myoblasts, overexpression of forkhead transcription factor (FoxO1) induces fiber transition from oxidative to glycolytic types. As a natural inhibitor of FoxO1, resveratrol alone did not significantly affect the expression of various fiber subtypes, but when added after FoxO1 overexpression, it antagonized the FoxO1-induced transition from slow to fast fibers and significantly increased myoglobin and Tn1 expression [18].

Additionally, feeding Duchenne muscular dystrophy (MDX) mice 100 mg/kg resveratrol daily for 6 weeks increased type I and IIa fiber proportions in both SOL and extensor digitorum longus (EDL) muscles. However, increasing the dosage and extending the treatment period (500 mg/kg · d for 12 weeks) did not affect the expression of fiber subtypes [19].

Long-term feeding of a high-fat/high-sugar diet to primates reduced MyHC I expression while increasing MyHC IIa and MyHC IIx expression in SOL, and resveratrol supplementation reversed this transition. Resveratrol also promoted the conversion of fast to slow fibers in primate plantaris muscle [20].

In poultry and swine studies, dietary resveratrol delayed pH decline in broiler breast and thigh muscles, reduced drip loss and shear force, and improved meat color [21]. However, supplementation with 50 mg/kg resveratrol had no significant effect on meat quality in normal or PRRSV-vaccinated finishing pigs [22]. In contrast, other research showed that adding 300 or 600 mg/kg resveratrol to finishing pig diets increased 24-hour postmortem pH and myoglobin content in longissimus dorsi muscle while reducing shear force and drip loss [8]. This study also found that resveratrol increased MyHC IIa mRNA expression and decreased MyHC IIb mRNA expression in longissimus dorsi muscle, with no significant differences between the 300 and 600 mg/kg groups.

These findings collectively demonstrate that appropriate resveratrol dosage is crucial for optimal efficacy. In summary, resveratrol can induce the transition of glycolytic fibers to oxidative fibers, though factors such as supplementation level influence its effects on fiber types.

3.1. Through Signaling Pathways

Muscle constitutes the primary component of livestock carcasses, serves as a major metabolic organ, and represents one of the main products of animal production. Since muscle is composed of muscle fibers and fiber type is closely related to meat quality, understanding the patterns of fiber type composition changes, the main factors influencing fiber types, and their regulatory mechanisms is essential. Muscle fiber formation is regulated not only by myogenesis-related genes such as myogenin [23] and myocyte enhancer factor (MEF2) [24] but also by various signaling pathways.

Silent information regulator 1 (SIRT1) is a member of the nicotinamide adenine dinucleotide (NAD+)-dependent protein deacetylase family and plays an important regulatory role in muscle fiber type. Studies have shown that mice with skeletal muscle-specific SIRT1 overexpression exhibit fiber type transition from glycolytic to oxidative fibers, accompanied by significantly increased expression of peroxisome proliferator-activated receptor γ coactivator-1α (PGC-1α) [25], a key marker gene associated with oxidative metabolism and mitochondrial biogenesis. PGC-1α is closely related to mitochondrial function and oxidative fiber formation; PGC-1α knockout mice show fiber type transition from types I and IIa to types IIx and IIb [26].

Both in vivo and in vitro studies have demonstrated that resveratrol regulates muscle fiber type transition. Ljubicic et al. [19] found that dietary resveratrol supplementation in MDX mice significantly increased type I and IIa fiber proportions in SOL and EDL muscles, while also elevating SIRT1 protein levels and enzyme activity in muscle. Enhanced SIRT1 activity can lead to deacetylation and activation of its downstream target PGC-1α [27]. PGC-1α is known to be highly expressed in type I fibers [28]. Lin et al. [29] showed through transgenic approaches that PGC-1α overexpression in mice enhanced mitochondrial oxidative capacity and increased expression of type I fiber-specific proteins, indicating that PGC-1α promotes slow fiber formation. Research has demonstrated that resveratrol significantly reduces PGC-1α acetylation levels, but in the absence of SIRT1, resveratrol has no effect on PGC-1α acetylation or mRNA expression, suggesting that resveratrol may indirectly regulate PGC-1α expression through SIRT1 [17].

AMP-activated protein kinase (AMPK) regulates mitochondrial biogenesis, type I fiber formation, and endurance capacity during long-term training in mice [30-31]. Price et al. [17] found that resveratrol increased AMPK phosphorylation levels, but in SIRT1-deficient conditions, resveratrol had no significant effect on AMPK expression, suggesting that resveratrol may indirectly regulate AMPK expression through SIRT1. However, other research indicates that resveratrol can act directly by activating AMPK. Um et al. [31] observed that AMPK knockout mice fed resveratrol showed no enhancement in metabolic rate, insulin sensitivity, or mitochondrial function, and expression of genes related to mitochondrial function remained unchanged. This demonstrates that resveratrol cannot exert its metabolic effects in the absence of AMPK, implying that AMPK may be a target of resveratrol action. Additionally, the authors found that resveratrol increased the NAD+/reduced nicotinamide adenine dinucleotide (NADH) ratio, indicating it can indirectly enhance SIRT1 activity.

In summary, resveratrol may promote slow fiber expression by increasing SIRT1 expression, which subsequently activates AMPK and PGC-1α through phosphorylation and deacetylation. Alternatively, resveratrol may directly activate AMPK, thereby increasing the mitochondrial NAD+/NADH ratio to regulate

SIRT1 expression, forming a feedback regulatory loop.

3.2. Through FoxO1

Research has shown that resveratrol regulates FoxO1 gene expression. FoxO1 plays an important regulatory role in myogenesis, inhibiting myoblast proliferation and differentiation [32-34] while also regulating muscle fiber type. Kamei et al. [35] found that FoxO1 transgenic mice exhibited significantly reduced body weight, and microarray and histological analyses revealed that overexpression of FoxO1 decreased the expression of many genes associated with type I fibers, indicating a negative correlation between FoxO1 and type I fiber proportion.

Yuan et al. [18] demonstrated that while resveratrol increased Tn1 and myoglobin expression, this was insufficient to alter the fast/slow fiber composition ratio. However, resveratrol antagonized the FoxO1 overexpression-induced decrease in Tn1 and myoglobin expression and blocked the FoxO1-mediated transition from slow to fast fibers. This suggests that resveratrol' s promotion of oxidative fiber-specific gene expression may be achieved through FoxO1 inhibition.

Conclusion

Resveratrol is a naturally occurring polyphenolic compound with extensive biological functions that has attracted considerable attention. Muscle fibers are the basic units of muscle, and their types and composition are closely related to livestock meat quality. Research has shown that resveratrol can induce oxidative fiber expression and improve meat quality, with the SIRT1/AMPK/PGC-1α pathway and FoxO1 playing crucial regulatory roles in this process. However, research on resveratrol' s effects on muscle fiber type transition in livestock remains limited, with most studies conducted in pathological models, and its specific regulatory mechanisms remain controversial. Therefore, extensive in vivo and in vitro studies are needed to further explore the effects of resveratrol on muscle fiber types in livestock and their underlying mechanisms. This research is essential for improving livestock meat quality and provides a theoretical foundation for animal production.

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