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DIETARY BUTYRATE SUPPLEMENTATION ENHANCES PHYSIOLOGICAL RESILIENCE TO HEAT STRESS IN BROILER CHICKENS

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Abstract

Heat stress represents a major physiological challenge in broiler chickens, impairing intestinal integrity, oxidative balance, immune function, and growth performance. This review aimed to evaluate the effectiveness of dietary butyrate supplementation in enhancing physiological resilience of broilers under heat stress conditions. A synthesis of 20 experimental studies published between 2011 and 2025 was conducted, focusing on growth performance, intestinal morphology, antioxidant status, inflammatory responses, and gut microbiota. The results consistently showed that butyrate supplementation improved intestinal villus architecture and strengthened tight junction integrity, leading to better nutrient absorption. In addition, butyrate enhanced antioxidant capacity, likely through activation of the Nrf2–Keap1 pathway, and reduced inflammatory responses via inhibition of histone deacetylase activity and modulation of NF-κB signaling. The most pronounced effects were observed with protected butyrate forms administered at moderate inclusion levels (500–1,000 mg/kg feed), whereas lower doses were less effective and higher doses did not provide additional benefits. The impact on gut microbiota composition was variable, although higher inclusion levels tended to induce broader shifts in cecal microbial populations. In conclusion, butyrate functions as a multifaceted nutritional strategy to improve physiological resilience in heat-stressed broilers; however, further standardized long-term studies are needed to optimize dosage and better understand host–microbiota interactions.

Keywords: butyrate supplementation, heat stress, broiler chickens, intestinal barrier integrity, oxidative stress

Introduction

Heat stress is a major physiological challenge in broiler chickens, as it can compromise intestinal barrier integrity (Nanto-Hara et al., 2020). Elevated ambient temperatures redirect blood flow from the gastrointestinal tract to peripheral tissues, such as the skin and respiratory system, to facilitate heat dissipation (Onagbesan et al., 2023). This splanchnic hypoperfusion induces intestinal hypoxia, which in turn activates oxidative stress and triggers inflammatory signaling within the gut mucosa, thereby disrupting epithelial homeostasis (Onagbesan et al., 2023).

Consequently, structural remodeling occurs in the intestinal epithelium, including villus shortening and crypt deepening, which reduces the absorptive surface area for nutrient uptake (Rostagno, 2020). Heat stress also downregulates the expression and alters the distribution of tight junction proteins, particularly claudins and occludin, compromising mucosal integrity and increasing intestinal permeability. This barrier dysfunction permits luminal antigens and endotoxins to translocate into systemic circulation, leading to "leaky gut" syndrome and endotoxemia (Tabler et al., 2020).

Heat stress further enhances the generation of reactive oxygen species (ROS) beyond the capacity of endogenous antioxidant systems such as superoxide dismutase, catalase, and glutathione peroxidase (Akbarian et al., 2016). This oxidative imbalance induces lipid peroxidation, protein oxidation, and mitochondrial dysfunction, collectively impairing cellular metabolic efficiency and reducing growth performance in broilers (Oke et al., 2024).

These physiological disturbances indicate that heat stress not only compromises productivity but also directly disrupts digestive function and redox homeostasis. Therefore, nutritional strategies that stabilize epithelial integrity, upregulate antioxidant capacity, and modulate immune responses are of critical importance (Liu et al., 2023).

In this context, dietary interventions based on short-chain fatty acids (SCFAs) have emerged as promising alternatives, with butyrate generally regarded as the most effective SCFA in preserving intestinal integrity and attenuating the deleterious effects of heat stress compared to other SCFAs. Butyrate also exerts epigenetic effects via histone deacetylase (HDAC) inhibition, thereby upregulating the expression of antioxidant genes, tight junction proteins, and anti-inflammatory cytokines. This epigenetic mechanism is comparatively strong for butyrate, whereas it is weak or largely absent for other short-chain fatty acids, such as acetate and propionate (Waldecker et al., 2008).

In the context of oxidative stress, butyrate exhibits superior efficacy compared with other SCFAs by enhancing the activities of key antioxidant enzymes, including glutathione peroxidase (GPx) and superoxide dismutase (SOD), and by maintaining cellular redox balance through stabilization of the reduced glutathione/oxidized glutathione (GSH/GSSG) ratio in heat-stressed broilers (Lan et al., 2020; Sarker et al., 2025). In contrast, acetate and propionate primarily regulate systemic energy metabolism rather than intestinal barrier function. Acetate mainly influences lipid metabolism and energy homeostasis via activation of GPR41 and GPR43, while propionate predominantly modulates hepatic gluconeogenesis and appetite regulation. Although both SCFAs exert modest anti-inflammatory effects and contribute to microbial homeostasis, their capacity to restore epithelial integrity, attenuate oxidative stress, and upregulate tight junction protein expression is generally lower than that observed for butyrate (Tedelind et al., 2007; Yoshida et al., 2019; Cao et al., 2021; Du et al., 2024).

Given these multifaceted actions, butyrate represents a promising nutritional strategy to enhance broiler resilience to heat stress by modulating intestinal morphology, strengthening anti-

oxidant defenses, and regulating immune responses. Therefore, this review aims to critically evaluate recent studies published between 2011 and 2025 on the effects of dietary butyrate supplementation in heat-stressed broilers. It is hypothesized that butyrate supplementation improves physiological resilience and growth performance by enhancing gut integrity, reducing oxidative stress, and attenuating inflammatory responses.

Methodology of the review

A structured literature search was conducted using PubMed, Scopus, and Web of Science to identify relevant studies published between 2011 and 2025. Search terms included "butyrate," "sodium butyrate," "calcium butyrate," "broiler," "poultry," "heat stress," "intestinal morphology," and "antioxidant," combined using Boolean operators (AND/OR). Studies were included if they involved broiler chickens, evaluated dietary supplementation with sodium butyrate or its derivatives (including salt or protected forms serving as butyrate donors), and reported at least one outcome related to growth performance, intestinal morphology, antioxidant responses, immune function, or gut microbiota. Only peer-reviewed experimental trials were considered. As this study is a review based exclusively on previously published data, no ethical approval or animal experimentation clearance was required.

The initial database search yielded a total of 63 records. After removal of duplicates, 54 records remained and were screened based on titles and abstracts. Of these, 20 records were excluded due to irrelevance to the study objectives or failure to meet the inclusion criteria. Subsequently, 34 full-text articles were assessed for eligibility. Following full-text evaluation, 14 articles were excluded because of ineligible interventions or irrelevant outcome measures. Ultimately, 20 studies met all inclusion criteria and were included in the qualitative synthesis, as illustrated in the PRISMA flow diagram (Figure 1).

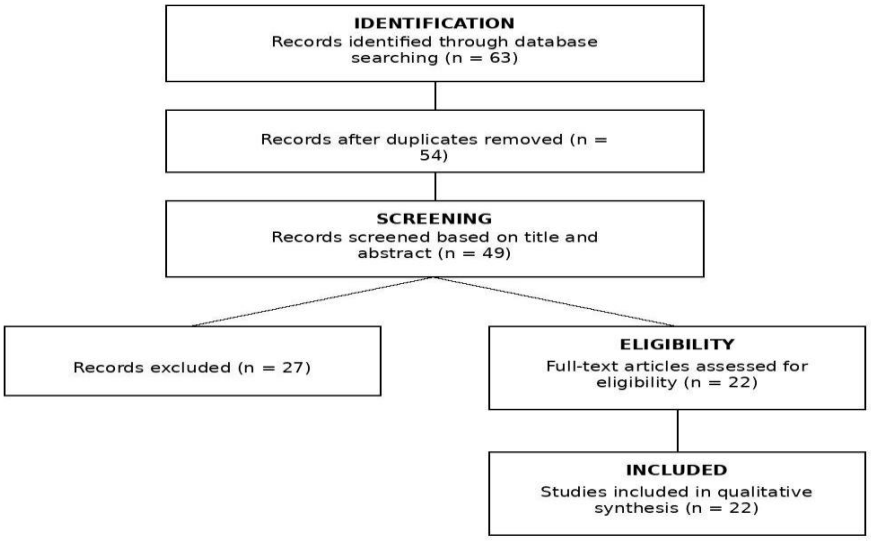

Figure 1. PRISMA flow diagram of the study selection process

The included trials evaluated different butyrate formulations, including unprotected sodium butyrate, protected sodium butyrate, and protected calcium butyrate. Dietary inclusion levels were categorized as low (≤500 mg/kg feed), medium (>500–1,000 mg/kg feed), or high (>1,000 mg/kg feed), under experimental conditions ranging from thermoneutral environments to simu-

lated heat stress. Data were extracted on butyrate type, inclusion level, diet formulation, and measured outcomes, including body weight gain, feed conversion ratio, intestinal morphometric indices (villus height and crypt depth), antioxidant enzyme activities, cytokine expression, and gut microbiota composition. Extracted data were subsequently organized into thematic categories encompassing intestinal morphology, nutrient utilization, antioxidant defense, inflammatory modulation, and microbial responses.

Physiological responses of broilers to dietary butyrate under heat stress

Dietary supplementation with butyrate exerts multifaceted physiological effects in broiler chickens, particularly under conditions of heat stress. A synthesis of 20 experimental studies indicates consistent improvements in intestinal morphology, antioxidant capacity, and inflammatory regulation, accompanied by more variable effects on gut microbiota composition. An overview of these performance- and gut-related responses across different experimental conditions is summarized in Table 1, which collectively highlights the broad spectrum of physiological outcomes associated with dietary butyrate supplementation. Importantly, these responses are not uniform but are strongly influenced by the chemical form of butyrate, dietary inclusion level, and the intensity of thermal challenge imposed on the birds (Ruixia et al., 2024; Zhao et al., 2022).

Table 1. Effects of dietary butyrate supplementation on growth performance and intestinal parameters in broilers

Study	Butyrate form and dose	Conditions	Performance outcomes
Niu et al., 2025	Sodium butyrate, 800 mg/kg feed	Heat stress (32 ± 2°C)	↑ Protection against lung injury, adaptation to heat stress, and body homeostasis
Ismael et al., 2025	Coated sodium butyrate, 300–500 mg/kg feed	Commercial diet	↑ Average daily gain (ADG), feed conversion ratio (FCR), villus height and villus-to-crypt ratio, digestive enzymes (lipase, protease), serum protein, urea, and serum aspartate aminotransferase
Zhao et al., 2022	Chemically protected sodium butyrate, 1,000 mg/kg feed	Normal rearing conditions	↑ Body weight gain, FCR, VH:CD in the small intestine, concentrations of total SCFAs, and digestive enzyme activities (α-amylase, lipase, and trypsin)
Akram et al., 2024	Sodium butyrate, 0.1%–0.5% feed	Broilers injected intraperitoneally with *Escherichia coli* lipopolysaccharide at 16, 18, and 20 days of age (0.5 g/kg body weight) to induce systemic inflammatory stress	↑ ADG, FCR, expression of CLDN1, TJP1, MUC6, and IL-10 genes, and relative intestinal length
Lan et al., 2020	Sodium butyrate, 300–1,200 mg/kg feed	Normal rearing conditions (starter phase 33 ± 1°C gradually reduced to 24°C) with Newcastle disease and infectious bronchitis vaccination	↑ ADG, relative weight and length of the small intestine (duodenum, jejunum, ileum), pancreas and thymus weight, antibody titer against Newcastle disease vaccine
Tang et al., 2021	β-Hydroxy-β-methylbutyrate, 0.05–0.15% feed	Commercial diet under normal rearing conditions	↑ ADG, breast yield, a*, lipid metabolite alterations ↓ FCR, abdominal fat, drip loss, L*
Sadurní et al., 2022	Protected sodium butyrate, 500–2,000 mg/kg feed	Oral inoculation with *Eimeria* spp. (575 *E. acervulina*, 345 *E. maxima*, 1150 *E. mitis*, 575 *E. tenella*)	↑ Goblet cell count, lauric and myristic acid levels in abdominal fat ↓ Intraepithelial lymphocyte count
Mátis et al., 2022	Protected butyrate, 0–1,000 mg/kg feed	Commercial diet under normal rearing conditions	↑ Growth performance, intestinal barrier integrity (claudin and MCT1 protein expression), SCFA concentration and composition, and cecal microbiota balance

Pearce et al., 2025	Unprotected sodium butyrate or protected calcium butyrate, 260 mg/kg feed	Commercial diet under normal rearing conditions	↔ ADG, FCR, average daily feed intake (ADFI), intestinal barrier morphology and function, cecal pH, volatile fatty acids (VFA) concentration ↓ Expression of inflammatory genes, tight junctions in cecum, cecal tonsils, and spleen
Dunisławska et al., 2024	*In ovo* sodium butyrate (0.3% solution, 0.2 mL per egg)	Under normal rearing conditions	↑ FCR, thigh muscle water-holding capacity, breast muscle pH ↔ Body weight, carcass composition, breast muscle pH ↓ Intramuscular fat in breast and thigh muscles
Mallo et al., 2021	Protected sodium butyrate, 1,000 mg/kg feed	Under normal rearing conditions	↑ ADG, FCR, gross energy metabolizability, intestinal VFA profile, beneficial cecal microbiota, intestinal villus height and morphology
Letlole et al., 2021	Coated sodium butyrate, inclusion level not specified (used with or without zinc bacitracin 500 mg/kg feed)	Commercial diet under normal rearing conditions	↑ Intestinal villus height, VH:CD, gut health ↓ FCR
Nazir et al., 2025	Microencapsulated butyric acid, 300 mg/kg feed	Standard commercial rearing conditions	↑ ADG, FCR, carcass traits, villus height, VH:CD, immune organ weights, Newcastle disease titers
Wan et al., 2022	Protected sodium butyrate, 1,000 mg/kg feed	Standard commercial rearing conditions	↑ Weight gain and FCR
de-Cara et al., 2023	Protected sodium butyrate, 2,000 mg/kg feed	Standard commercial rearing conditions	↔ Carcass traits ↓ Meat lipid oxidation, drip losses
Melaku et al., 2024	New-type protected sodium butyrate, 800 mg/kg feed	Standard commercial rearing conditions	↑ ADFI, ADG, VH, VH:CD, ZO-1, claudin-1, occludin, mucin-2, serum IL-10 ↓ FCR, pro-inflammatory TNF-α, MDA
Pascual et al., 2020	Microencapsulated sodium butyrate, 500 mg/kg feed	Standard commercial rearing conditions	↔ ADFI, ADG, FCR, jejunum morphology, slaughter results, meat quality, myopathy occurrence (overall) ↓ Spaghetti meat rate in females
Gu et al., 2025	Coated sodium butyrate, 250, 500, and 1,000 mg/kg feed	Standard commercial rearing conditions	↑ Breast meat shear force, pH_4h, inosinic acid, polyunsaturated fatty acids (C16:1, C18:2, C22:4, C22:6) ↔ Plasma biochemical indices
Sarker et al., 2025	Sodium butyrate, 0, 500, and 1,000 mg/kg feed	Heat stress, 35°C compared to normal conditions of 25°C	↑ Spleen weight, VH and VH:CD ↓ Crypt depth, inflammatory cytokines (NF-κB, TGF-β, IFNγ), downregulated gut barrier gene expression (occludin, ZO-1, claudin-1)
Ruixia et al., 2024	Sodium butyrate, 1,200 mg/kg feed	Heat stress, 34°C during 10.00–18.00 and 24°C at other times	↑ ADG, VH, VH:CD, jejunal tight junction proteins (occludin, claudin-1, ZO-1) ↓ FCR, crypt depth, IL-1β, TNF-α, TLR4 and NF-κB mRNA expression, serum endotoxin, D-lactic acid, diamine oxidase activity

Among the different formulations, the release kinetics of butyrate appear to be a key determinant of efficacy. Unprotected butyrate is rapidly absorbed in the proximal gastrointestinal tract, which limits its availability in the distal intestine and constrains its capacity to sustain epithelial integrity and redox balance, particularly under moderate to severe heat stress (Mátis et al., 2019). In contrast, protected butyrate formulations enable gradual release along the distal small intestine and cecum, thereby extending local bioavailability and more effectively preserving intestinal morphology, limiting lipid peroxidation, and supporting antioxidant defenses during thermal challenge (Wan et al., 2022). As illustrated in Table 1, studies employing protected or

coated butyrate consistently report more pronounced improvements in feed efficiency and intestinal morphometric indices than those using unprotected forms.

Beyond formulation, the biological response to butyrate is markedly dose dependent. Low inclusion levels (≤500 mg/kg feed) generally elicit minimal or inconsistent effects on growth performance and intestinal morphology under thermoneutral conditions (Pascual et al., 2020; Sadurní et al., 2022). Nevertheless, under heat stress, certain butyrate derivatives administered at comparable doses have been reported to improve body weight gain, feed conversion efficiency, and litter hygiene, including reductions in *Clostridia* and aerobic bacterial loads in the cecum and litter (Ismael et al., 2025). These findings suggest that thermal stress may increase intestinal responsiveness to butyrate, even at relatively low inclusion levels.

As dietary inclusion increases to moderate levels (approximately 1,000 mg/kg feed), the beneficial effects of butyrate become more consistent and pronounced. Across multiple studies, supplementation at this range enhances villus height, increases the villus-to-crypt ratio, improves antioxidant status, and strengthens intestinal barrier integrity, particularly when broilers are exposed to physiological stressors such as infection or elevated ambient temperature (Sadurní et al., 2022; Zhao et al., 2022). In contrast, further increases in dietary inclusion (≥2,000 mg/kg feed) do not appear to confer proportional benefits and may, in certain contexts, reduce feed palatability or compromise performance efficiency (Bawish et al., 2023), indicating the presence of an optimal inclusion window rather than a linear dose–response relationship.

The magnitude of these dose-dependent effects is further modulated by the severity of heat stress. Under mild thermal challenge, butyrate supplementation often yields limited physiological responses. However, as heat stress intensifies, the protective effects, particularly those associated with protected formulations, become more evident, although supplementation does not invariably restore physiological parameters to thermoneutral baselines (Lan et al., 2020). Collectively, these observations support the interpretation that butyrate functions primarily as a modulator of physiological resilience, mitigating but not fully eliminating the adverse consequences of thermal stress.

The improvements in growth performance observed under these conditions are closely linked to structural and functional adaptations within the intestine. Multiple studies have demonstrated that protected butyrate supplementation promotes epithelial cell proliferation and differentiation, resulting in increased villus height, improved villus-to-crypt ratios, and greater mucosal thickness, even when birds are fed energy- or amino acid-restricted diets (Letlole et al., 2021; Mallo et al., 2021). These morphological adaptations expand the absorptive surface area and enhance nutrient utilization, thereby providing a mechanistic basis for the observed improvements in feed efficiency and weight gain under heat stress.

In parallel with its effects on intestinal architecture, butyrate plays a critical role in maintaining barrier integrity. Supplementation has been shown to upregulate the expression of key tight junction proteins, including occludin, claudins, and tight junction protein-1, as well as mucins such as MUC2, thereby reducing paracellular permeability and limiting endotoxin translocation (Mátis et al., 2022; Yang et al., 2022). These barrier-stabilizing effects are attributed, at least in part, to the dual function of butyrate as a primary energy substrate for enterocytes and as a HDAC inhibitor, which facilitates transcriptional activation of genes involved in epithelial maintenance and repair (Chang et al., 2014).

Stabilization of the intestinal barrier is closely intertwined with modulation of immune responses. Consistent with this relationship, butyrate supplementation exerts dose-dependent anti-inflammatory effects, characterized by suppression of nuclear factor κB (NF-κB) signaling and reductions in proinflammatory cytokines such as interferon-γ, interleukin-6, and tumor necrosis

factor-α under heat stress conditions (Sarker et al., 2025; Zhang et al., 2011). These responses are mediated through HDAC inhibition and activation of G protein-coupled receptors (GPR41, GPR43, and GPR109A), which collectively attenuate inflammatory signaling while promoting regulatory T cell differentiation and interleukin-10 production, thereby contributing to immune homeostasis within the intestinal mucosa (Giuffrida et al., 2019; Pedersen et al., 2022).

Heat stress-induced disruption of intestinal function is frequently accompanied by alterations in gut microbial ecology. Elevated ambient temperatures reduce populations of beneficial taxa such as *Lactobacillus* and *Bifidobacterium* while favoring opportunistic pathogens, including *Escherichia coli* and *Clostridium perfringens* (Kikusato and Toyomizu, 2023). Although protected butyrate supplementation does not consistently modify dominant microbial populations across all experimental conditions, moderate reductions in pathogenic taxa have been reported in some studies (Mallo et al., 2021). More comprehensive sequencing-based analyses further indicate that higher inclusion levels of fat-protected butyrate (approximately 3,000 mg/kg feed) can induce broader shifts in cecal microbial structure, underscoring the context- and dose-dependent nature of butyrate–microbiota interactions (Onrust et al., 2020). The reported effects of butyrate supplementation on intestinal microbiota composition are summarized in Table 2.

Table 2. Microbiota shifts associated with butyrate supplementation

Study	Microbiota outcomes	Key findings
Mallo et al., 2021	↑ *Lactobacillus* ↓ *Clostridium*	↑ Shift in VFA profile, cecal butyrate
Letlole et al., 2021	↑ Stabilized microbiota under antibiotic growth promoter-free diets	↑ Villus morphology ↓ Pathogen pressure
Niu et al., 2025	↑ *Clostridia*, *Firmicutes* ↓ *Staphylococcus*, *Bacteroidetes*	↑ Balance of intestinal and pulmonary microbiota, presence of beneficial microbes
Ismael et al., 2025	↓ *Clostridia*	↓ Aerobic bacteria in the cecum
Zhao et al., 2022	↑ *Candidatus Arthromitus*, *Romboutsia*, *Akkermansia* ↓ *Lactobacillus*	↑ Diversity of ileal microbiota
Akram et al., 2024	↑ *Bacteroidetes*, *Epsilonbacteraeota*, *Cyanobacteria*, *Lentisphaerae*, *Tenericutes*, *Verrucomicrobia* ↓ *Firmicutes*	↑ Diversity and proportion of beneficial bacteria, metabolic functions of the microbiota
Onrust et al., 2020	↓ *Clostridia*	↑ Cecal butyrate concentration, balance of cecal microbiota
Sadurní et al., 2022	↑ *Escherichia coli* ↔ *Clostridium perfringens*	↑ Modulation of intestinal microbiota
Yang et al., 2022	↓ *Clostridium perfringens*	↑ Host defense genes (AvBD9, AvBD10), barrier function genes (MUC2) ↓ Inflammatory gene (IL-1β), intestinal lesions
Wan et al., 2022	↓ Pathogenic bacteria (*Romboutsia*, *Shuttleworthia*)	↓ Number of beneficial bacteria
Melaku et al., 2024	↑ SCFA-producing bacteria (*Peptostreptococcaceae*, *Colidextribacter*, *Firmicutes*, *Oscillospira*, *Erysipelatoclostridiaceae*) ↔ Gut microbiota alpha and beta diversity	↑ SCFA-producing bacteria

In addition to its structural, immunological, and microbial effects, butyrate plays a central role in maintaining cellular redox homeostasis under thermal stress. Low-dose supplementation (300 mg/kg feed) is generally associated with modest improvements in antioxidant status, whereas moderate inclusion levels (1,000–1,200 mg/kg feed) consistently reduce malondialdehyde concentrations and enhance antioxidant enzyme activities, including superoxide dismutase and

glutathione peroxidase (Lan et al., 2020). At higher inclusion levels, these responses tend to plateau, suggesting a threshold beyond which additional supplementation does not proportionally enhance antioxidant defenses. These antioxidant effects are attributed to activation of the Nrf2–Keap1 signaling pathway, HDAC-mediated epigenetic regulation of antioxidant gene expression, and improved mitochondrial oxidative efficiency that limits reactive oxygen species generation (de-Cara et al., 2023; Rose et al., 2018). Together, these mechanisms provide a biological basis for the dose-dependent antioxidant improvements summarized in Table 3.

Table 3. Antioxidant responses in butyrate-supplemented broilers

Study	Butyrate form and dose	Biomarkers	Key findings
Lan et al., 2020	Sodium butyrate, 300–1,200 mg/kg feed	SOD, CAT, GSH-Px, MDA	↑ SOD, CAT, GSH-Px ↓ MDA; improved meat quality
Pearce et al., 2025	Na- and Ca-butyrate, 500 mg/kg feed	Cytokines, tight junction proteins	↓ TNF-α, IL-6; ↑ occludin, claudin
Zhao et al., 2022	Chemically protected sodium butyrate, 1,000 mg/kg feed	SOD, total antioxidant capacity (TAC), TAC/MDA	↑ SOD, TAC, TAC/MDA
de-Cara et al., 2023	Protected sodium butyrate, 2,000 mg/kg feed	SOD, CAT, GPx, ferric reducing antioxidant power	↑ Plasma SOD, meat oxidative stability
Melaku et al., 2024	New-type protected sodium butyrate, 800 mg/kg feed	SOD, T-AOC (total antioxidant capacity), MDA	↑ SOD and T-AOC/MDA ratio
Sarker et al., 2025	Sodium butyrate, 0, 500, and 1,000 mg/kg feed	MDA, CAT, GSH-Px	↑ Antioxidant enzyme activities (CAT, GSH-Px), IL-10 expression ↓ Serum MDA
Ruixia et al., 2024	Sodium butyrate, 1,200 mg/kg feed	GSH-Px, SOD, CAT, ROS	↑ GSH-Px, SOD activity ↓ ROS

Conclusions

The evidence reviewed indicates that dietary butyrate supplementation enhances physiological resilience to heat stress by improving intestinal morphology, reinforcing tight junction integrity, strengthening antioxidant defenses, and attenuating inflammatory responses. The most consistent benefits are observed with protected butyrate administered at inclusion levels of 500–1,000 mg/kg feed, particularly under moderate to severe heat stress, whereas lower doses appear insufficient and higher doses provide no additional advantages and may impair feed palatability. Despite these promising outcomes, limited long-term data on intestinal microbiota stability and tissue-specific oxidative stress thresholds underscore the need for further investigations using standardized heat stress models to refine dosage recommendations and to clarify host physiological and microbial adaptive responses.

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