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-Invited Review-

Sodium Butyrate Supplementation for Improving Poultry and Rabbit Performance

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ABSTRACT

Sodium butyrate (SB) is a compound that belongs to the class of short-chain fatty acids (SCFA). It is derived from the breakdown of dietary fiber in the colon by gut bacteria. Supplementation of SB in poultry and rabbit diets is of great importance due to its numerous benefits to animal health and performance. Previous studies have shown that sodium butyrate can improve nutrient digestibility, enhance gut health, strengthen the immune system, and reduce the incidence of intestinal diseases in poultry. These favorable benefits eventually contribute to the increased of growth, feed efficiency, and profitability in the poultry and rabbit industries. By improving nutrient digestibility, enhancing gut health, and strengthening the immune system, SB supplementation helps to reduce the incidence of intestinal diseases in poultry and rabbits. This ultimately leads to improved growth, feed efficiency, and overall profitability in the poultry industry. Additionally, SB supplementation can help reduce the need for antibiotics in poultry farming, promoting a more sustainable and environmentally friendly approach to raising poultry. It has efficacy against acid-intolerant species, including *Salmonella sp.*, *Clostridium perfringens*, and *Escherichia coli*. Furthermore, the pH of the gastrointestinal system was successfully decreased by administering SB. These properties make SB a promising alternative for maintaining gastrointestinal health and improving poultry and rabbit performance. Therefore, this review provides insight into the continuous development of novel SB supplements and highlights their potential contribution to poultry and rabbit farms.

Keywords: growth; immunity; intestinal integrity; reproductive performance; sodium butyrate

INTRODUCTION

Poultry and rabbit production, as crucial and fast-developing agricultural subsectors, are necessary to the global animal protein supply (Abd El-Aziz *et al*., 2023). When evaluating nutritional supplementation for monogastric animals such as poultry and rabbits, key parameters such as production and reproductive performance, carcass and meat quality, hematological and biochemical indicators, immune and antioxidant-related factors, and intestinal microbiota and intestinal health, need to be considered. In recent years, the complex interactions between intestinal bacteria, epithelial barriers, and immune cells in the gastrointestinal system have attracted great interest (Liu *et al*., 2019). Various antigens in food and bacteria constantly enter the intestines of animals, impairing their health (Cabezón & Bentez-Ribas, 2013; Wu *et al*., 2018). Gut health has a significant impact on overall poultry and rabbit performance. Several practical strategies, particularly on nutritional supplements, especially organic acids such as sodium butyrate (SB), have been performed to improve gut health. The short chain fatty acid (SCFA) butyrate is mainly produced in the gut of monogastric animals from the cecal microbial fermentation of structural polysaccharides derived from dietary fibers (Melaku *et al*., 2021). Sodium butyrate is easily transformed into butyric acid in the intestine, where it enhances intestinal health through various mechanisms such as decreasing intestinal susceptibility to pathogenic bacteria colonization and increasing the growth performance of birds under stress (Wu *et al*., 2018; Zou *et al*., 2019; Zhao *et al*., 2022). The purpose of sodium butyrate supplementation in poultry and rabbit farming is to optimize health and performance. During carbohydrate and protein digestion, butyrate is produced by beneficial intestinal bacteria and plays a significant role in regulating cell growth and specialization (Hamer *et al*., 2008; Henagan *et al*., 2015). Several studies showed that sodium butyrate not only enhances the intestinal defense system but also reduces oxidative stress, exhibits immunomodulatory and anti-inflammatory effects, and contributes to intestinal integrity and microbial balance (Sauer *et al*., 2007; Chang *et al*., 2014). Furthermore, Yang *et al*. (2018) demonstrated that broiler chicks' intestinal microbiota is positively changed by butyrin, hence improving chicken health.

Feed additives have received much research attention, particularly in the last ten years, for their role in maintaining intestinal health, especially given the EU restrictions on the use of antibiotics in animal agriculture (Hoste *et al*., 2015; Khalifah *et al*., 2023; El-Sabrout *et al*., 2023). Sodium butyrate is a short-chain fatty acid (also called volatile fatty acids (VFAs) that has gained attention for its significant impact on intestinal health, especially in the setting of antibiotic limitations (Elnesr *et al*., 2020). The compound has a molecular weight of 88.12 g/mol, a density of 0.958 g/ml, and a pKa value of 4.82. Due to its corrosive and volatile properties, the sodium salt of butyric acid is employed as an alternative. This choice enables easier manipulation, enhanced stability, and reduced odor (Ahsan *et al*., 2016). Furthermore, SB undergoes rapid conversion into butyric acid in the small-livestock digestive system, hence enhancing intestinal health through several processes (Jiang *et al*., 2015). The addition of SB in livestock diets has been associated with the development of gut wall tissues, boosting symbiotic intestinal microflora growth (Ahsan *et al*., 2016; Wafaa *et al*., 2016), reducing harmful bacteria colonization in the digestive tract, maintaining optimal gut health, improving growth performance, feed conversion ratio, and beneficial bacterial populations (Wu *et al*., 2018; Raza *et al*., 2019), resulting in an increase in marketing body weight. In addition, SB is an energy source with bacteriostatic and immune enhancement properties (Raza *et al*., 2019; Xiao *et al*., 2023). Ahsan *et al*. (2016) and Liu *et al*. (2022) noticed that the presence of butyrate in the digesta of gastrointestinal tract segments of broiler chickens has beneficial effects on the digestive process, gut morphology, and proteolytic enzymatic activities. Short- and medium-chain fatty acids (such as butyric, lauric, and caprylic) have antibacterial effects against some bacterial strains in poultry and rabbits, indicating possible benefits in disease resistance (Marounek *et al*., 2002; Yang *et al*., 2022). The cecum, as a prime location for chicken and rabbit intestinal bacteria, is vital to animal productivity because short-chain fatty acids contribute to internal stability and microbial balance (Angelakis, 2017; Wang *et al*., 2020).

Studies of broiler chicken growth performance, particularly at high temperatures, showed continued improvements with increasing SB levels, positioning it as a potential antibiotic alternative. The synergistic effect of SB, xylo-oligosaccharides (XOS), *Clostridium butyricum*, vitamin D_3 (VD_3) and enzymes on improving broiler and rabbit performance was studied and their effectiveness as additives was highlighted. The effects of SB on the reproductive performance of female broiler breeders highlight advances in egg production and quality. In terms of intestinal integrity, as measured by parameters such as villus height, SB supplementation resulted in significant increases in villus length and width. Especially on days 21 and 42, villus length increased remarkably, demonstrating the positive effect of SB. Sodium butyrate also plays a crucial role in the development of intestinal epithelium, serving as an energy source for intestinal epithelial cells and improving barrier function. Notably, SB has been shown to be effective in improving the growth performance of broiler chickens in warm climates and positively affecting egg production, quality, and hatchability of broiler breeders (Lan *et al*., 2020; Xiao *et al*., 2023). Furthermore, Li *et al*. (2022) demonstrated the ability of SB to improve rabbit slaughter performance. In addition, Liu *et al*. (2022) observed a synergistic effect between *C. butyricum* and SB in broiler chickens, emphasizing the need to select the right butyrate supplement based on specific goals.

Therefore, the purpose of this comprehensive review is to provide recent insights into the potential benefits of sodium butyrate supplementation in poultry and rabbit nutrition (Figure 1). This study considered the productive performance, carcass characteristics, meat quality, blood biochemical parameters, immunity, antioxidants, intestinal microbiota, and gut health of poultry and rabbits. It also highlighted the continued development of sodium butyrate research and its significant contribution to the poultry and rabbit industries (Table 1).

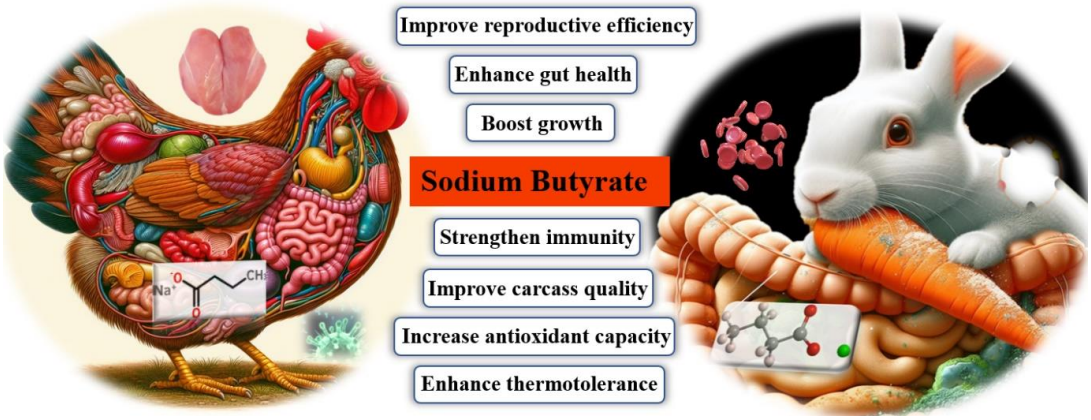

Figure 1. Potential benefits of sodium butyrate supplementation for improving poultry and rabbit performance

Table 1. Summary of the effects of sodium butyrate supplement in chicken and rabbit diets

Productive performance				
Administration	Species	Dose	Effects	References
CSB	Chicken (Broilers)	300-800 mg/kg	Improved egg production, egg quality, and hatchability.	Xiao *et al*. (2023)
SB	Chicken (Broilers)	300 to 1200 mg/kg	Increased body weight, average daily gain, and feed intake.	Lan *et al*. (2020)
CSB	Chicken (Broilers)	1000 mg/kg	Increased weight gain and improved feed conversion.	Wan *et al.* (2022)
SB + *Clostridium butyricum*	Chicken (Broilers)	100 g/t (1.0×10^9 CFU/g) *C. butyricum* spores (CB), 500 g/t sodium butyrate (SB)	Improved growth and intestinal structure.	Liu *et al*. (2022)
CSB + XOS	Chicken (Broilers)	mixture of 1000 mg/kg CSB and 100 mg/kg XOS	Lowered feed conversion rates, increased body weight and average daily gain.	Deng *et al*. (2023)
CSB	Chicken (Broilers)	1000 mg/kg	Improved body weight gain and feed conversion ratio.	Zhao *et al*. (2022)
SB + CF	Chicken (Broilers)	2 mmol/L SB (individually or in combination)	Enhanced feed efficiency and reduced abdominal fat buildup.	Yang *et al.* (2022)
SB	Rabbit	0.5 g/kg to 2.0 g/kg	Marginally increased growth and feed intake.	Carraro *et al*. (2005)
SB	Rabbit	Up to 300 g/ton	Faster weight gain and improved feed conversion.	Abd El-Aziz *et al*. (2012)
Enzyme + SB	Rabbit	500 g/t	Improved production indices.	Abd El-Aziz *et al*. (2020)
Carcass traits				
Administration	Species	Dose	Effects	References
SB	Chicken (Broilers)	300-1200 mg/kg	Increased protein content of breast muscle and decreased drip loss percentage.	Lan *et al*. (2020)
SB + VD_3	Chicken (Broilers)	1 g/kg of the diet SB + 3000-5000 IU/kg of the diet VD_3	Improved meat quality, decreased lightness, cooking and drip loss, increased antioxidant ability, altered fatty acid composition.	Gao *et al*. (2022)
SB + CF	Chicken (Broilers)	2 mmol/L (individually or in combination)	Decreased abdominal fat buildup.	Yang *et al*. (2022)
CSB	Duck	250 g/t	Alleviated egg-laying stress in laying ducks by enhancing immunity and maintaining the intestinal health of the ducks.	Zeng *et al*. (2023)
BAG or CSB	Turkey	3.4 kg BAG/t of feed or 3.3 kg CSB/t of feed	Improved growth performance and protein digestibility and decreased the fecal populations of pathogenic bacteria in turkeys.	Makowski *et al*. (2022)
SB	Rabbit	0.50%	Increased body weights, hind leg weight, and movement.	Li *et al*. (2022)
SB	Rabbit	0 to 2.0 g/kg	Marginally increased growth and feed consumption, no discernible effect on carcass quality	Carraro *et al*. (2005)
SB	Rabbit	500 g/t	Improved carcass attributes such as dressing %, forequarter, hindquarter, and loin	Abd El-Aziz *et al*. (2020)
SB	Rabbit	300 g/t	Improved dressing percentages and increased size of carcass cuts (forequarter, hindquarter, loin)	Abd El-Aziz *et al*. (2012)
Haemato-biochemical parameters				
Supplement	Species	Parameters	Effects	References
SB	Chicken (Broilers)	Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST)	Reduced blood levels of ALT and AST, potentially improving liver function in hot climates	Lan *et al*. (2020)
SB	Chicken (Broiler breeders and progeny)	Immunoglobulin A (IgA), Immunoglobulin G (IgG), Interleukin-1β, Interleukin-4, Total superoxide dismutase, Triglycerides, Total cholesterol, High-density lipoproteins (HDL), Low-density lipoproteins (LDL)	Increased IgA levels in broiler breeders and progeny, increased IgG levels in progeny, reduced interleukin-1β and interleukin-4, increased total superoxide dismutase, altered lipid profiles	Xiao *et al*. (2023)

Table 1. Continued

SB + EO	Chicken (Broilers)	Blood triglycerides, Total cholesterol, High-density lipoproteins (HDL), Low-density lipoproteins (LDL)	Affected blood lipid profiles, with decreased LDL levels and increased HDL levels, suggesting potential cardiovascular health benefits	El-Katcha *et al.* (2021)
SB	Rabbit	Aspartate aminotransferase (AST)	Elevated AST levels in blood, indicating metabolic and physiological impacts of sodium butyrate on rabbits	Li *et al*. (2022)
SB + muli-enzymes	Rabbit	Total protein, globulin, blood lipids, cholesterol, Albumin-to-Globulin ratio (A/G ratio)	Changes in blood profiles including increased total protein and globulin, altered blood lipids, cholesterol, and A/G ratio	Abd El-Aziz *et al.* (2020)
Immunity and antioxidant related parameters				
Supplement	Species	Parameters	Effects	References
CSB	Chicken (Broilers)	Anti-inflammatory markers (TNF-α, IL-6, IL-10)	CSB significantly reduced TNF-α levels compared to controls and antibiotic-treated groups, with a trend of decreasing IL-6 levels. CSB also increased IL-10 levels.	Wan *et al.* (2022)
SB	Chicken (Broilers)	Antioxidant enzymes (superoxide dismutase, glutathione peroxidase, catalase), Malondialdehyde (MDA)	SB supplementation significantly increased antioxidant enzyme activity and decreased MDA levels, indicating improved antioxidant capacity	Lan *et al*. (2020)
CSB + XOS	Chicken (Broilers)	Total antioxidant capacity, Superoxide dismutase, Interleukin-10, Transforming growth factor-b, Malondialdehyde (MDA), IL-6, Tumor necrosis factor-α (TNF-α)	Increased antioxidant capacity and decreased inflammation markers. The combination showed the most significant effects.	Deng *et al*. (2023)
SB	Chicken (Broiler breeders and progeny)	Immunoglobulin A (IgA), Immunoglobulin G (IgG), Interleukin-1β, Interleukin-4, total superoxide dismutase, triglycerides, total cholesterol, High-density lipoproteins (HDL), Low-density lipoproteins (LDL)	Increased IgA and IgG levels, decreased interleukin levels, increased total superoxide dismutase, and altered lipid profiles.	Xiao *et al*. (2023)
CSB	Chicken (Laying hens)	Malondialdehyde (MDA), Superoxide dismutase (SOD), Total antioxidant capacity (TAC), Diamine oxidase, D-lactic acid	Decreased MDA levels, increased SOD activity, improved TAC, and decreased circulating diamine oxidase and D-lactic acid levels.	Miao *et al*. (2022)
CSB + Antibiotics	Chicken (Broilers)	Superoxide dismutase (SOD), Total antioxidant capacity (TAC), TAC to malondialdehyde (TAC/MDA) ratio	Increased SOD, TAC, and TAC/MDA ratio in the mucosa of the ileum and jejunum.	Zhao *et al*. (2022)
CSB + *Clostridium butyricum*	Chicken (Broilers)	Expression of tight junction proteins, Anti-inflammatory effects	Showed superior efficacy in boosting tight junction protein expression and exerting anti-inflammatory effects compared to CSB.	Liu *et al*. (2022)
SB + Forskolin	Chicken (Broilers)	Necrotic enteritis reduction, Feed efficiency enhancement, carcass composition improvement, expression of host defense, barrier function, and inflammatory response genes	Synergistically improved broiler health by reducing necrotic enteritis, enhancing feed efficiency, improving carcass composition, and modulating gene expression related to host defense and inflammation.	Yang *et al*. (2022)
Gut health				
Supplement	Species	Parameters	Effects	References
SB	Chicken (Broiler breeders and offspring)	Gut microbiota composition, intestinal morphology, Gene expression related to intestinal barrier	Improved intestinal morphology, altered gut microbiota composition, and modulated gene expression related to the intestinal barrier, promoting better immune function and fertility.	Xiao *et al*. (2023)
SB + EO	Chicken (Broilers)	Intestinal villi length, intestinal structure	Improved intestinal villi length and structure, suggesting enhanced digestion and nutrient absorption.	El-Katcha *et al*. (2021)

Table 1. Continued

SB	Chicken (Broilers)	Gut microbiota composition	Altered gut microbiota composition, potentially improving gut health, and reducing the need for antibiotics.	Naghizadeh *et al*. (2022)
CSB	Chicken (Laying hens)	Cecal microbiota composition	Altered cecal microbiota composition, increasing beneficial bacteria and decreasing harmful ones, suggesting a positive effect on gut microbiota balance.	Miao *et al*. (2022)
CSB	Chicken (Broilers)	Intestinal morphology, Gut microbiota composition	Improved small intestinal morphology and altered gut microbiota composition, indicating improved gut health.	Zhao *et al*. (2022)
SB + *Clostridium butyricum*	Chicken (Broilers)	Intestinal integrity, inflammatory cytokine production	Improved intestinal integrity and reduced inflammatory cytokine production, suggesting enhanced gut health and disease resistance.	Liu *et al*. (2022)
SB + Forskolin	Chicken (Broilers)	Intestinal lesions, disease resistance	Reduced intestinal lesions and improved disease resistance against *C. perfringens* infection, potentially through synergistic effects.	Yang *et al*. (2022)
Butyrate	Rabbit	Digestibility of dry matter, growth, feed intake	Improved digestibility, growth, and feed intake, with no substantial impact on intestinal health or meat quality.	Carraro *et al*. (2005)
SB	Rabbit	Tight junction integrity, gut microbiota composition	SB supplementation increased tight junction integrity and altered gut microbiota composition, indicating improved intestinal health.	Li *et al*. (2022)
Gene expression				
Supplement	Species	Parameters	Effects	References
SB + Forskolin	Chicken (Broilers)	Gene expression related to host defense, barrier function, and inflammation	Showed a synergistic effect on gene expression related to host defense, barrier function, and inflammation, potentially enhancing immune function and barrier protection.	Yang *et al*. (2022)
CSB	Chicken (Laying hens)	mRNA expression of TNF-α, IL-6, IL-10	Influenced the mRNA expression of inflammatory cytokines in the jejunum and ileum, suggesting regulation of immune responses.	Miao *et al*. (2022)

Note: SB= Sodium butyrate; CSB= coated sodium butyrate; XOS= xylo-oligosaccharides; CF= Coleus forskohlii; VD_3= Vitamin D_3; EO= essential oils

POTENTIAL IMPACTS OF INCORPORATING SODIUM BUTYRATE IN POULTRY AND RABBIT DIETS

Performance Indices (Production and Reproduction)

According to Mátis *et al*. (2022), adding protected butyrate to broiler diets increased growth performance and intestinal integrity by modulating the cecal microbiota and increasing endogenous production of SCFA in the caecum. These findings contribute to a better knowledge of the complicated effects of butyrate, the biologically most active SCFA, on the chicken's overall health and metabolism. Recently, Xiao *et al*. (2023) studied the impact of SB supplementation in chicken diets within the context of intensive rearing conditions. Specifically, the focus was on assessing how this feed additive influences the reproductive performance of broiler parents. The results of the study revealed a significant improvement in egg production performance, as well as enhanced broiler breeder hens' egg quality and hatchability, due to the addition of SB. Furthermore, Gong *et al*. (2020) stated that laying breeder hens' dietary supplementation of SB with some substances, such as beta-carotene and curcumin, can boost their offspring's jejunal immunity through the interaction between host innate immunity selected microbial colonization and microbiota-educated adaptive immunity.

Working on broiler chickens, Lan *et al*. (2020) reported that body weight increased consistently on day 35, as did average daily feed intake (ADFI) from day 22 to day 35. These findings imply that utilizing SB as a supplement in broiler diets could significantly improve growth performance in hot-climate regions.

Wan *et al*. (2022) conducted an in-depth study on the benefits on the growth performance of chemically preserved coated sodium butyrate (CSB) used as an additional feed supplement (1000 mg/kg) in chickens. Based on this assumption, this study investigated the effects of long-term antibiotic treatment or CSB supplementation on the growth of broilers. Results showed that CSB treatment significantly increased weight gain and improved feed conversion ratio (FCR) compared to the control group. This study sheds light on the growth-promoting effects of CSB and highlights its potential as a viable alternative to antibiotics on poultry farms. Furthermore, Liu *et al*. (2022) revealed

that both *C. butyricum* and SB exhibited beneficial probiotic effects in chicks, beating the growth and expression of inflammation-related genes induced by the antibiotic oxytetracycline. They also mentioned that SB can improve the growth and intestinal structure of chicks.

Additionally, Deng *et al*. (2023) evaluated the combination of SB (1000 mg/kg) and XOS (1000 mg/kg) on broiler growth performance. This combination exhibited lower feed conversion rates compared to the control. It significantly increased body weight by 7.93% and average daily gain by 8.67% during days 1-21. Such effects highly demonstrated the growth performance of SB and XOS individually and in combination, highlighting the tremendous growth potential. Likely, El-Katcha *et al*. (2021) conducted a comprehensive study to investigate the effects of essential oils (EO) supplementation in broiler diets with SB on various aspects of broiler performance. The study showed a decrease in the concentration of EO in urine was associated with a decrease in feed intake. Interestingly, the opposite tendency occurred when EO was supplemented with SB in the diet, suggesting minor interactions between these additives and the growth rates of broiler chickens. Of note is the significant improvement in vital parameters such as crude protein, extracted ether, inorganic substances, calcium (Ca), and phosphorus (P), by exposure to EO, the effect of coupling, particularly at low concentrations and for inorganic matter, when EO was paired with SB. These findings highlight the potential of EO, combined with SB, to enhance nutrient utilization and absorption in broiler chickens.

Importantly, concerns about commensal gut microbiota and dysbacteriosis are major obstacles to chicken health. To develop efficient preventative strategies, Naghizadeh *et al*. (2022) aimed to explore how nutritional intervention impacts the microbial ecology of broiler chickens. One group was given standard food without any supplements (control), another group received the same diet supplemented with 500 mg/kg of encapsulated butyrate, and the third group got 68 mg/kg of salinomycin (an ionophore coccidiostat with antibiotic effect). Butyrate showed modest benefits for the broiler gut at the concentrations tested, therefore, further research is needed to find the optimal diet levels of butyrate, especially to replace ionophore coccidiostats in broiler chicken production. Furthermore, Zhao *et al*. (2022) analyzed the impact of CSB addition (1000 mg/kg) on broiler growth performance. The study showed that broiler development performance improved when antibiotics and CSB were included in the diet. This was demonstrated at several points in the trial by raising body weight gain (BWG) and improving FCR.

Regarding broiler rabbits, Abd El-Aziz *et al*. (2012) found that New Zealand white rabbits receiving SB gained weight faster compared to the control group, especially at 8 weeks. Furthermore, a remarkable improvement in feed conversion was observed in rabbits receiving SB throughout the experiment. These results confirm the positive effect of SB up to 300 g/t on rabbit growth. However, the effects of feeding butyrate to young rabbits were investigated in depth by Carraro *et al*. (2005). Sodium butyrate was administered to 220 weaned rabbits at different doses (0, 0.5, 1.0, and 2.0 g/kg) from 28 days of age until they were slaughtered at 70 days of age in an experiment to determine its effects. As a result, feed intake and growth were marginally increased when butyrate was added, but there were no noticeable changes in cecal fermentative activity, intestinal mucosal characteristics at 42 days of age, or slaughter quality of carcasses or meat. There was also no significant effect on overall mortality and morbidity throughout the experiment. Although butyrate supplementation delayed the start of severe colibacillosis, it did not eliminate the requirement for antibiotic intervention. Production efficiency, digestive function, general health, and meat quality were all unaffected by the addition of butyrate. Furthermore, Abd El-Aziz *et al*. (2020) studied the effects of an enzyme and SB-mixed dietary supplement on weaning rabbits' growth performance. They concluded there were no significant differences in the traits studied that were related to growth performance during the experiment. However, the mixture supplement substantially improved most of the production indices, such as growth rate and BWG.

Reducing necrotic enteritis, boosting feed efficiency, and enriching the composition of broiler carcasses were the goals of a separate research by Yang *et al*. (2022) that examined the synergistic effects of sodium butyrate and forskolin, a natural labdane diterpene. In an effort to find antibiotic-free chicken farming options, this study analyzed how butyrate and forskolin worked together to affect growth performance and carcass quality. The broilers were given a supplement consisting of butyrate and *Coleus forskohlii* (CF) extract containing forskolin for 42 days as part of the controlled trial. The results showed that the combined therapy had no significant effect on weight increase, although it decreased feed consumption considerably. In addition, feed efficiency was greatly enhanced, and day-42 broilers that were given a combination of butyrate and forskolin had a marked decrease in belly fat buildup. Nevertheless, no significant effects were seen on pH, drip loss, breast meat color, or carcass yield. It appears that butyrate and forskolin may work together to improve growth performance and carcass characteristics in broilers. Working on layer chickens, Zhang *et al*. (2022) reported that dietary supplementation of CSB (300-800 mg/kg of diet) improved egg production, yolk color, intestinal morphology, and butyrate content, as well as microbial diversity in laying hens.

Carcass Characteristics and Meat Quality

Regarding the work of Lan *et al*. (2020), they aimed to investigate how supplementing the diet with SB (600-1200 mg/kg) affects the meat quality of broilers raised in hot climates. As the levels of SB rose, the findings showed that the protein content of the breast muscle grew significantly linearly, and the drip loss

percentage decreased on days 1 and 3. These results demonstrate that SB is a powerful feed additive for improving the meat qualities of broiler chickens kept in hot weather. In addition, Gao *et al*. (2022) performed a study to clarify the impacts of supplementing broiler chickens with a diet enriched with SB and vitamin D_3 (VD_3) on their meat quality, oxidative stability, and nutritional value. The findings demonstrated that the inclusion of SB in the diet resulted in a decrease in lightness, cooking and drip loss, free fatty acids (FFA), C14:0, C16:0, saturated fatty acids (SFA), C20:4n6, and the n-6: n-3 polyunsaturated fatty acids (PUFA). Simultaneously, there was a rise in DPPH and ABTS levels in the chicken flesh, suggesting an enhancement in antioxidant ability. Significantly, the concurrent presence of elevated VD_3 levels and SB led to an increase in the concentration of polyunsaturated fatty acids (PUFAs) in the chicken flesh. Thus, incorporating SB into the diet greatly improved the quality of chicken meat. This improvement may be mainly attributable to the increased antioxidant capacity and good alterations in physical properties (Gao *et al*., 2022). In addition, the inclusion of SB with increased VD_3 levels showed positive benefits via improving the fatty acid composition. However, it was shown that elevated levels of VD_3 were linked to a reduction in the amino acid content of chicken meat. The results highlight the significant influence of dietary supplements on many elements of broiler chicken meat and stress the need for a comprehensive strategy to enhance both the quality and nutritional characteristics of poultry production.

The goals of a separate trial by Yang *et al*. (2022) were to improve feed efficiency, reduce necrotic enteritis, and improve the carcass composition of broilers. Researchers found that the natural labdane diterpene forskolin and SB worked together synergistically. As a possible antibiotic substitute, this study examined the effects of butyrate and forskolin on chicken development and carcass quality. The 42-day trial involved supplementing the diets of broilers with a mixture of butyrate and *Coleus forskohlii* (CF) extract, which contains forskolin. According to the data, the combined intervention had no significant effect on weight increase, although it significantly reduced feed consumption. Furthermore, a tendency towards increased feed efficiency was statistically significant. Without influencing carcass production, breast meat color, drip loss, or pH, the combination of butyrate and forskolin significantly decreased abdominal fat buildup in day-42 broilers. These results point to the possibility of a synergistic effect between butyrate and forskolin in improving broiler growth performance and carcass characteristics.

Previous research by Abd El-Aziz *et al*. (2012) found that rabbits' carcass quality significantly improved when SB was added to their diets. Dressing percentages were greater in the SB group (300 g/ton) than in the control group. In addition, the group that received SB showed a considerable increase in the size of the carcass cuts, especially in the forequarter, hindquarter, and loin. These results demonstrate that adding SB to rabbit feed improves their growth performance as well as their carcass quality and production. However, an extensive study on the effect of SB on rabbit slaughter performance was conducted by Li *et al*. (2022). The results reveal that adding SB to the rabbit diet causes a considerable increase in carcass weights. This demonstrates the potential of SB as a supplement for rabbits, as their performance improved during execution. On the other hand, the effects of supplementing growing rabbit diets with SB (0 to 2.0 g/kg) until 70 days of age (marketing age) were investigated by Carraro *et al*. (2005). This supplementation tended to increase growth (3.2%). Nevertheless, it did not impact the quality of the carcasses and meat when slaughtered, intestinal mucosal characteristics, or cecal fermentative activity. However, there was no discernible effect on total mortality or morbidity during the research period, and although butyrate supplementation did postpone the start of severe colibacillosis, it did not eradicate the necessity for antibiotic treatment. The study concluded that butyrate's addition had no discernible effect on health, digestive physiology, meat quality, or productive performance. Moreover, Abd El-Aziz *et al*. (2020) examined how different breeds and dietary supplements affected different aspects of the carcass. Although growth performance was unaffected by the breed effect, there were noticeable differences in the majority of carcass attributes. Dressing %, forequarter, hindquarter, and loin were some of the specific carcass attributes that improved noticeably due to the treatment's influence on the breed.

Haemato-Biochemical Parameters

Following the initial findings of Lan *et al*. (2020), this study examined the effects of SB supplementation on liver function in broilers kept in hot climates. Supplementing with SB consistently reduced blood levels of alanine aminotransferase and aspartate aminotransferase, which may positively impact liver function in hot temperatures. Beyond improving their developmental performance, SB has several other positive effects on broilers' health.

Further elaborating on the research conducted by Xiao *et al*. in 2023, this investigation aimed to assess the serum biochemical constituents, antioxidant capacity, and immunological function of female broiler breeders and their progeny. There was a considerable increase in the concentrations of immunoglobulin A in the blood of both broiler breeders and their offspring when maternal supplementation with SB occurred. Furthermore, it resulted in a significant elevation in the levels of immunoglobulin G in the progeny. Interleukin-1β and interleukin-4 were significantly reduced in the progeny, whereas total superoxide dismutase increased in both the offspring and ova. Serum concentrations of triglycerides, total cholesterol, and high-density and low-density lipoproteins were all altered by SB. The findings of this study underscore the capacity of SB to improve the immune system and antioxidant capacity of broiler breeders and their progeny. Additionally, El-Katcha *et al*. (2021) revealed that EO supplements

in water alongside SB significantly affected blood serum parameters, such as protein level, while having no noticeable impact on blood triglyceride or total cholesterol concentrations. In addition, EO used with SB showed a decrease in LDL levels and an increase in HDL levels, suggesting that there may be advantages to cardiovascular health. These results provide more evidence that EO with SB can affect broiler hens' cardiovascular health and lipid metabolism.

However, SB may have various impacts on different serum indices in different animals; nevertheless, Li *et al*. (2022) investigated this effect in rabbits. According to the study, aspartate aminotransferase (AST) levels in the blood were found to be elevated in rabbits fed a diet consisting of sodium butyrate. These results shed light on the metabolic and physiological impacts of SB on rabbits systemically. In addition, Abd El-Aziz *et al*. (2020) conducted a study to examine the effect of SB on rabbit biochemistry, including blood profiles. According to the findings, several blood profile measurements were changed noticeably when the enzyme and SB combination was added to the diet. In addition to a rise in total protein and globulin, important changes were noted in blood lipids, cholesterol, and the albumin-to-globulin ratio (A/G ratio).

Immunity and Antioxidant Related Parameters

Using broiler chickens as a model, Wan *et al*. (2022) evaluated the effects of CSB (1000 mg/kg) on growth performance and its antioxidant characteristics. The broilers were randomly allocated to these three groups. Comparing the ANT group to the CSB group, the results demonstrated a substantial improvement in the anti-inflammatory and antioxidative properties of the broilers. The levels of inflammatory markers, such as TNF-α, IL-6, and IL-10, were examined in detail in the serum. The results showed that the CSB group had significantly lower TNF-α levels than the other groups. At the same time, compared to the antibiotic group, the CSB group showed a tendency of decreasing IL-6 levels. There was a significant rise in IL-10 levels in the CSB group. Therefore, the results of this study confirm that CSB is an important dietary supplement for broilers since it sheds light on how it might improve their antioxidant defenses.

Furthermore, the study by Lan *et al*. (2020) investigated how broiler hens' resistance to heat-related oxidative stress is affected by three dietary levels of SB (300, 600, and 1200 mg/kg). The levels of superoxide dismutase, glutathione peroxidase, and catalase activity were shown to significantly increase when SB was given to the breast muscle, although malondialdehyde levels exhibited a trend toward decline. These results show that SB might be a potential dietary supplement for broilers in hot regions since it increases their antioxidant capacity, which is optimal for chicken health, in general. Furthermore, Deng *et al*. (2023) have studied how adding XOS and CSB to the feed of broiler chickens affected their antioxidant and anti-inflammatory capabilities. According to the results, total antioxidant capacity, superoxide dismutase, interleukin-10, and transforming growth factor-β levels were all raised when CSB and XOS were added, either alone or in combination. On the other hand, levels of malondialdehyde, IL-6, and tumor necrosis factor-A decreased. Furthermore, out of the five groups, the MIX group showed the most significant effect on antioxidant and anti-inflammatory capacity. This highlights the possibility of CSB and XOS acting as natural alternatives to antibiotics, with improved anti-inflammatory and antioxidant capabilities.

Another study aimed to assess the antioxidant capacity, immunological function, and serum biochemical components in female broiler breeders and their progeny (Xiao *et al*., 2023). The blood levels of immunoglobulin A were considerably elevated in both the broiler breeders and their offspring when SB supplements were given to their female breeders. Furthermore, it resulted in a rise in immunoglobulin G levels in the progeny. The levels of interleukin-1β and interleukin-4 decreased in the offspring and the eggs, respectively, but total superoxide dismutase increased in both groups. Statistically, SB altered the blood levels of triglycerides, total cholesterol, and high- and low-density lipoproteins. Collectively, the findings showed that SB can boost antioxidant levels and immune function in broiler breeders and their progeny. Following, the purpose of the study by Miao *et al*. (2022) was to assess how laying hens' intestinal antioxidant profile was affected by feeding CSB (0, 250, 500, 750, and 1000 mg/kg). A significant decrease in malondialdehyde levels and an improvement in superoxide dismutase activity were seen in the jejunum, whereas an improvement in total antioxidant capacity was observed in the ileum. The levels of diamine oxidase and D-lactic acid in the circulation were consistently decreased when CSB was added to the meal. Results show how effective CSB is in increasing laying hens' intestinal antioxidant capacity and provide important information for bettering the health of these birds in general. There was a marked improvement in antioxidant measurements when antibiotics and CSB were added to the diet.

Moreover, Zhao *et al*. (2022) found that the CSB and antibiotic diets resulted in higher levels of superoxide dismutase (SOD), total antioxidant capacity (TAC), and TAC to malondialdehyde (TAC/MDA) ratio in the mucosa of the ileum and jejunum compared to the control diet. Moreover, an essential aspect of the previous research done by Liu *et al*. (2022) was evaluating the anti-inflammatory response elicited by the dietary supplements. While both *C. butyricum* and SB showed improvements in anti-inflammatory responses, *C. butyricum* had superior efficacy compared to sodium butyrate in boosting the expression of tight junction proteins and exerting anti-inflammatory effects. This comprehensive examination elucidates the specific impacts of several supplements on the anti-inflammatory mechanisms in broiler chickens.

Yang *et al*. (2022) conducted an additional investigation that offers significant knowledge regarding the synergistic impacts of SB and forskolin on diverse facets of broiler well-being. The noted impacts on necrotic enteritis reduction, feed efficiency enhancement, and

carcass composition improvement indicate that these natural substances may have potential as substitutes for antibiotics in the poultry industry. The study's molecular pathways provide insight into the potential mechanisms by which sodium butyrate and forskolin achieve their synergistic effects. The presence of bacterial lipopolysaccharides (LPS) influenced the expression of genes associated with host defense (AvBD9 and AvBD10), barrier function (MUC2, CLDN1, and TJP1), and the suppression of inflammation (IL-1β) in chicken HD11 macrophages. The observed collaborative effect in the expression of these genes implies that the concurrent administration of sodium butyrate and forskolin could potentially bolster the body's innate defense mechanisms, fortify the intestinal barrier against inflammation, and mitigate inflammatory responses. This study adds to the expanding literature concerning the prospective advantages of natural supplements utilized in poultry husbandry, including SB and forskolin. This underscores the significance of comprehending the molecular mechanisms that underlie these effects to advance the industry's pursuit of sustainable and efficacious alternatives to conventional antibiotic utilization.

Intestinal Microbiota and Gut Health

The recent investigations of (Wan *et al*., 2022; Deng *et al*., 2023) offered substantial contributions to our understanding of how CSB affects the structure and composition of the intestinal microbiota in broiler chickens. The effects of CSB on gut microbiota were compared to those of long-term antibiotic treatment in a study by Wan *et al*. (2022). The gut microbiota was devastated by the long-term use of antibiotics, which increased the population of harmful bacteria (*Romboutsia* and *Shuttleworthia*) and decreased the population of beneficial bacteria (*Alistipes*, *Akkermansia*, and *Bacteroides*). In contrast, CSB continuously lowered deleterious bacteria while increasing helpful microbes, including *Bacteroides*. Propionic acid and total SCFA were both raised after CSB treatment, which raises the possibility that it might regulate intestinal health and serve as an eco-friendly potential natural antibiotic replacer in broiler production. Additionally, improved intestinal health was indicated by higher ileal villus height and a lower villus height to crypt depth ratio (VCR), which was investigated by Deng *et al*. (2023) in broiler chickens fed a combination of CSB and XOS. These findings shed light on CSB as a natural supplement that can regulate the gut microbiota and enhance the health of broiler chickens' intestines. This could be a viable alternative to the traditional use of antibiotics in poultry farming.

The effects of SB supplementation on the composition of the gut microbiota and the function of the intestinal barrier were studied by Xiao *et al*. (2023) in female broiler breeders. By reducing crypt depth in the jejunum and increasing villus height in the offspring, SB supplementation enhanced intestinal morphology, suggesting a favorable impact on the intestinal barrier. Moreover, SB substantially impacted the expression of genes related to the intestinal barrier in the female's jejunum and ileum. It was highlighted that SB may affect the composition of the gut microbiota via changes in microbial diversity in cecal contents, with an increase in the predominance of certain bacterial families as *Ruminococcaceae* and *Lachnospiraceae*. When considered as a whole, these effects help broiler breeders, and their offspring have better immune systems as well as more fertile offspring. Furthermore, El-Katcha *et al*. (2021) explored how broilers' intestinal structures changed when they were given EO supplements with or without SB. Intestinal villi lengthened in the presence or absence of SB, suggesting that EO may improve digestion and nutritional absorption. These results demonstrate that EO can improve the structural features of the broiler's intestines.

On a different note, Carraro *et al*. (2005) investigated the impact of including butyrate in the diet of juvenile rabbits. The findings revealed a combination of outcomes, with a little enhancement in both growth and feed intake. Nevertheless, there were no discernible effects on the fermentative activity in the cecum, the characteristics of the intestinal mucosa, or the quality of carcasses and meat throughout the slaughter process. While butyrate supplementation could not completely remove the necessity for antibiotic treatment, it indicated a possible beneficial impact on health, as seen by the delay in the onset of severe colibacillosis. In general, the addition of butyrate did not substantially impact production performance, digestive physiology, health status, or meat quality. These investigations significantly enhance our comprehension of the diverse impacts of dietary supplements, such as SB and EO mixes, on the shape of chicken intestines, the operation of their barriers, and the composition of their microbiota.

The coexistence of commensal gut microbes and dysplasia presents a significant challenge to the overall welfare of poultry. Thus, Naghizadeh *et al*. (2022) explored how dietary interventions could impact the microbial environment in broiler chickens, which is crucial for developing effective preventive strategies. They were divided into three groups: one group received a standard (control) diet, another group received a basic diet plus an additional 500 mg/kg butyrate supplement, and a third group received salinomycin 68 mg/kg. Remarkably, an increase in possibly beneficial *Ruminococci* and a decrease in potentially harmful *Enterobacteriaceae* reduced the presence of *Lactobacillus salivarius* and *C. perfringens* by the addition of salinomycin. On the other hand, the effect of coated butyrate on these parameters was minimal.

The association between the makeup of the cecal microbiota and the inclusion of CSB in laying hens' diet was also investigated in thorough research by Miao *et al*. (2022). A basic meal supplemented with CSB at 0, 250, 500, 750, and 1000 mg/kg altered cecal microbiota over the course of eight weeks, with an increase in helpful bacteria and a decrease in harmful ones, suggesting a positive effect on gut microbiota balance. These results demonstrate that CSB can change the makeup of the cecal microbiota, which sheds information on how to improve the intestinal health of laying hens.

Sadurní *et al*. (2022) have investigated dietary approaches to improve gut health as a means to find antibiotic alternatives in chicken farming. Sodium butyrate, protected by sodium salts of medium-chain fatty acids, was the main supplement that the researchers employed in their studies on broiler chicken diets. Under ideal conditions, preliminary studies tested 0.5, 1, and 2 kg/t dosages. In young chickens, supplementation at rates of 0.5 and 1 kilogram per ton preserved the amount of mucin-secreting cells in the intestinal barrier, whereas in mature broilers, a rate of 1 kg per ton enhanced the immune system. Sodium butyrate, when protected by sodium salts of medium-chain fatty acids, had protective effects on mucin-secreting cells, which affected the shape of the intestinal mucosa and the makeup of the microbiota, according to a following experiment that focused on broilers challenged with coccidiosis. The results indicated that this feed addition may be effective in improving the digestive system health of young chicks, which might help the poultry industry cut back on antibiotic use. On day 21, the small intestinal architecture, especially the duodenum, jejunum, and ileum, was positively affected by the addition of CSB to the diet. A higher villus height to crypt depth (VH/CD) ratio, indicative of improved intestinal morphology, was observed in comparison to the control and antibiotic diets (Zhao *et al*., 2022).

When comparing the ileum microbiota to that resulting from the control and antibiotic diets, the study by Zhao *et al*. (2022), utilizing 16S rRNA gene sequencing, showed that CSB supplements greatly boosted microbial diversity. The phylum most commonly identified was *Firmicutes*, whereas the species most commonly found was *Lactobacillus*. CSB changed the ratio of certain genera, which increased the growth of *Akkermansia* and decreased the prevalence of *Kitasatospora*, which was originally in the antibiotic diet. Supporting the idea that CSB might be an appropriate replacement for in-feed antibiotics in the broiler business, researchers demonstrated that incorporating 1000 mg/kg CSB in the diet improved broiler development, small intestine histology, antioxidant status, enzyme activity, and microbiota composition. Additionally, the impacts of nutritional supplements on gut health were also investigated by Liu *et al*. (2022). While the antibiotic oxytetracycline was shown to have negative effects on intestinal structural integrity and inflammatory cytokine production, *C. butyricum* and SB had the opposite effect. Butyrate may be an excellent dietary supplement for improving intestinal health, as it was found to be more effective than other supplements in intestinal enhancement. In addition, after treatment with *C. perfringens*, a compound derived from CF extract that included butyrate and forskolin, significantly reduced intestinal lesions, suggesting an improvement in disease resistance. Yang *et al*. (2022) found that when the drugs were given separately, there was no impact. This highlights the possibility of a synergy between butyrate and forskolin in improving resistance to *C. perfringens* infection.

According to Li *et al*. (2020), sodium butyrate, as an eco-friendly feed additive, can be added to growing broiler rabbit diets instead of antibiotics, as it improves the rabbit intestine's physical, immunological, and microbiological barriers. Furthermore, Li *et al*. (2022) reported that SB positively affected rabbit intestinal health by increasing the integrity of tight junctions in the gut and being beneficial across the microbiota. These data contribute to an overall understanding of the benefits associated with sodium butyrate supplementation in rabbits. The demonstrated improvements in slaughter and serum markers highlight the potential use of sodium butyrate as a feed supplement in rabbit breeding, particularly due to its additional beneficial effects on intestinal health. Promoting intestinal health and maintaining strong barrier function is important for overall animal welfare. Therefore, sodium butyrate has shown the ability to positively influence these traits, indicating the potential for improving the health and performance of the rabbit industry.

Gene Expression

The investigation of how adding CSB to laying hens' diets affected their immunological function was the main goal of a recent study by Miao *et al*. (2022). Over the course of eight weeks, seven hundred and twenty-two 52-week-old Huafeng laying hens were given a standard meal supplemented with different concentrations of CSB (0, 250, 500, 750, and 1000 mg/kg). The results showed that CSB influenced the mRNA expression of inflammatory cytokines (TNF-α, IL-6, and IL-10) in the jejunum and ileum, indicating that it may regulate immune responses. Understanding of CSB's involvement in strengthening the immune function of laying hens is enhanced by this work on its immunomodulatory effects.

A natural labdane diterpene called forskolin and SB were shown to work together in a recent study by Yang *et al*. (2022) to improve feed efficiency, decrease necrotic enteritis, and improve the carcass composition of broilers. These all-natural options might one day replace antibiotics used in chicken raising. The study investigated the molecular mechanisms that caused the impacts. While bacterial lipopolysaccharides (LPS) were present, butyrate and forskolin showed a synergistic effect on the expressions of genes related to host defense (AvBD9 and AvBD10), barrier function (MUC2, CLDN1, and TJP1), and the suppression of inflammation (IL-1β) in chicken HD11 macrophages. This points to a possible synergy between butyrate and forskolin that strengthens barrier protection, reduces inflammatory reactions, and enhances the body's inherent defense systems.

Economic Efficiency

Few studies have looked at the cost-effectiveness of adding SB to the diets of rabbits and poultry. Abd El-Aziz *et al*. (2020) examined the cost-effectiveness of adding SB and a multi-enzyme to two rabbit breeds' diets. Total and net returns were higher in the supplementation groups compared to the control groups across all breeds, even though feed and total expenses were higher in the treatment groups. None of the groups' profitability metrics were as superior as

those for the untreated Rex rabbit breed. Conclusively, the study emphasizes the economic advantages of providing rabbits with a multi-enzyme enriched with sodium butyrate.

FUTURE PERSPECTIVES

Sodium butyrate is identified as a multipurpose additive in the feed that exhibits distinct effects on poultry and rabbits. The remarkable biological impacts expressed by this research include augmented growth rates in rabbits and broilers as well as reproduction efficiency of breeder hens and rabbit females, advantageous influences over the quality of carcass and meat, antioxidant characteristics along with anti-inflammatory abilities, promotion of immune responses, and benefiting control over intestinal microbiota, thus indirectly improving gut health overall. This beneficial substance demonstrates potential as an effective replacement for antibiotics, most notably due to its persistent impact on broiler development even under high-temperature conditions.

Most nutritional investigations focus on enhancing animal intestinal health. Impressively, the synergistic effects observed with a mixture of SB in coated form, XOS, *C. butyricum*, VD_3, and forskolin-containing *Coleus forskohlii* were successful in reducing intestinal lesions and implying an improvement in disease resistance as well as birds' productivity. Furthermore, adding SB to rabbit diets acts effectively when combined with different enzymes, positively affecting their productivity and immunological performance. It also demonstrated beneficial effects on female breeder broilers' reproductive performance as well as intestinal health enhancement, as evidenced by increases in villi length and width, highlighting its diverse characteristics. Moreover, SB effectively regulates gastrointestinal pH, highlighting its potential as a suitable alternative for gastrointestinal health in poultry and rabbits. However, the delivery of more comprehensive domains of studies emerge as critical to determining the comprehensive amounts and frequencies required for effectively administering SB while observing feasible prospects of simultaneously boosting other supplement compositions, fortifying levels of consistency, and applying advanced strategies within rabbit or poultry backgrounds.

Future research revolving around poultry and rabbit farming should prioritize recognizing appropriate quantities maintained by appropriately spaced duration needed while supplementing sodium butyrate, taking into consideration their individuals' relatively unique dietary necessities amongst each one. Exploring the advantages of blending diverse additives holds promise for enhancing poultry and rabbit farming results. Studying the long-term effects of SB on chickens and rabbits, concerning health, productivity, and welfare provides crucial understanding for practical applications. Repeated efforts to progressively tweak nutritional strategies boost the formulation of more competent and ecological practices within poultry-oriented enterprises. Persistence in investigating possible benefits related to health from supplementing feed with sodium butyrate for poultry and rabbits remains at the core of innovative research focusing on this adaptable additive.

CONCLUSION

Sodium butyrate inclusion in poultry (300-500 g/t) and rabbit (300 g/t) diets can enhance immune response, antioxidant capacity, gut wall tissue development, and symbiotic intestinal microflora growth, as well as decrease the colonization of harmful bacteria in broiler digestive tracts, resulting in improved feed conversion ratio, body weight, and product quality, particularly when it is added in the protected forms (such as coated sodium butyrate or butyric acid glycerides) or added in combination with *C. butyricum* or muli-enzymes.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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