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GUT DYSBIOSIS: CAUSES AND PREVENTION STRATEGIES – A REVIEW

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Abstract

Gut dysbiosis in poultry presents a major challenge, requiring a comprehensive approach to sustain optimal gut health and ensure animal welfare. This review emphasizes the importance of integrated management practices and explores alternatives to antibiotics, including probiotics, prebiotics, synbiotics, postbiotics, phytogenic compounds, medicinal plants, and organic acids. Additionally, it advocates tailored nutritional strategies specific to broiler strains and highlights the potential of advanced biotechnologies for poultry nutrition and health management. Maintaining effective gut health is essential not only for animal welfare but also for the economic sustainability of poultry farming. Given the implications of antibiotic use in poultry for human health, the "One Health" approach is critical for recognizing the interconnection between animal, human, and environmental health. Research should prioritize understanding host-microbiome interactions, developing innovative therapies, and enhancing diagnostic tools for early detection and intervention in gut dysbiosis. Addressing this complex issue requires collaboration among researchers, veterinarians, feed manufacturers, and poultry producers to create sustainable solutions that improve animal health and production efficiency, while reducing reliance on antibiotics and implementing a holistic strategy that encompasses various aspects of poultry management. The industry can mitigate the adverse effects of gut dysbiosis and promote the overall health and welfare of broiler chickens.

Key words: gut malfunction, poultry health, sustainability, poultry farming, dysbiosis treatment strategies

Gut health has become an increasingly crucial indicator of animal performance and overall health, particularly following the discontinuation of antibiotic growth promoters (AGPs) in animal feeds. The ban on AGPs has led to more frequent occurrences of gut health issues, commonly referred to as dysbacteriosis or dysbiosis, particularly in broiler chicken farms (Ducatelle et al., 2023; Shaufi et al., 2023). For many years, it has been widely acknowledged that AGPs mask the underlying gut health problems by inhibiting bile salt deconjugation and reducing intestinal inflammation (Lin, 2014; Smith, 2019).

Similar to other animals, chickens harbor a complex gut microbiota that plays a critical role in regulating the gut physiology, nutrient absorption, metabolism, and maturation of the immune system (Shaufi et al,. 2023; Wang et al., 2023). Healthy chickens maintain a well-balanced intestinal microbiota that is essential for optimal gut function and immune competence. However, various stressors, including early life infections, suboptimal nutrition, overcrowding, poor air quality, inadequate bedding, and environmental stressors, can disturb this balance, allowing pathogenic bacteria to proliferate. Research has indicated that the composition and structure of the gut microbiome are significantly influenced by host genetics (Wen et al., 2021). Further studies have demonstrated that gut microbiota influences intestinal barrier integrity, immune system development, and nutrient metabolism (Akinyemi et al., 2020; Li et al., 2021).

Since the ban on AGP, numerous strategies have been adopted to maintain the sustainability and productivity of poultry farming. These strategies include the use of exogenous enzymes, probiotics, prebiotic fortification, and bacteriophage application (Gadde et al., 2017). The selection of appropriate feed additives or a combination

of them in broiler chickens depends on a thorough understanding of the role that each additive plays in shaping the gut microbiota composition and its functional outcomes, as well as the interactions between the microbiota and the host (Shehata et al., 2022).

Data for this narrative review were gathered from peer-reviewed articles, industry reports, government publications, and databases, including PubMed, Scopus, Google Scholar, and Web of Science. This review provides updated information on gut dysbiosis and management techniques to improve poultry health, reduce losses, and increase farming profits. The included studies were published up to 2024, focusing on the impact of gut dysbiosis and malfunction on poultry health and production, and addressing areas such as causes and treatment strategies for sustainable poultry farming practices. Initial screening was conducted based on titles and abstracts to identify relevant studies. The full-text articles were further reviewed to ensure their relevance to the research questions posed in this study.

Key data related to the effects of gut dysbiosis on poultry production, mitigation strategies, and sustainability were extracted, categorized, and documented in a structured format. The number of selected articles, opinion articles, research notes, reviews, and book chapters related to review subjects was 103 (58 articles, 43 review articles, 1 research note, and 1 book chapter), covering the period from 1993 to 2024.

The objective of this review was to describe the causes and preventative measures for gut dysbiosis in commercially raised broiler chickens and to provide insights into the composition and role of the gut microbiota. By identifying the key factors that influence gut health and exploring alternative approaches to antibiotics, this review aims to offer sustainable solutions to optimize broiler chicken performance and welfare.

Definition and overview

The complex microbial system, known as gut microbiota, exerts significant effects on host health (Chen et al., 2019, 2023). Gut microbiota consists of a diverse group of microorganisms that colonize the gut of living hosts. Diverse groups of microorganisms include bacteria, viruses, protozoa and other functional microorganisms. Many studies on gut microbiota have shown that they can produce health-promoting metabolites, such as vitamins, digestive enzymes, and antimicrobial peptides, which help improve the intestinal environment and prevent the invasion of pathogenic bacteria (Li et al., 2023; Wickramasuriya et al., 2023). Therefore, the gut microbiota is recognized as a new ecosystem essential for host health. Gut microbiota is a reservoir of bacterial communities composed of a diverse range of bacteria from several genera and species arranged in a dense and abundant population; however, they mainly belong to four different phyla: *Firmicutes, Bacteroidetes, Proteobacteria,* and *Actinobacteria* (Stanley et al., 2016). It is believed that the ratio of the microbiota, especially *Bacteroidetes*, maintains a stable microbial structure. The gut microbiome is thought to be significantly influenced by several factors including disease, sex, diet, and environmental factors (Huang et al., 2018; Taylor-Bowden et al., 2024). The increasing complexity of modern broiler production environments that negatively affect gut function, specifically the gut microbiota, is highly relevant in the context of gut health. Gut dysbiosis is a valuable term to describe the imbalance between symbionts and dysbiotic hosts (Ducatelle et al., 2023). Thus, gut dysbiosis is largely related to the composition and abundance of the gut microbiota. Maintaining a balanced microbiota might be beneficial for enhancing poultry productivity and health by positively modifying the microbiota and subsequently supporting gene expression, both during colonization and in relation to other bacteria, as well as during nutrient absorption and immune function (Attia et al., 2018).

Causes of gut dysbiosis

The small intestine possesses a highly developed natural immune system, designed to protect against harmful bacteria that come into close contact with the epithelial cells or the underlying lamina propria (Veldhuizen et al., 2013; Yacoub et al., 2015), contributing to maintain a balanced relationship among beneficial gut microbiota.

Figure 1 illustrates the various causes of gut dysbiosis, highlighting factors such as infections, dietary imbalances, environmental stressors, and the overuse of antibiotics, all of which can disrupt the natural balance of the gut microbiota and compromise gut health.

The factors affecting balance and development of the gut microbial ecosystem can be external and internal of the organism. The most common causes of gut dysbiosis include pathogen overgrowth, nutritional imbalances, mycotoxin contamination, antibiotic usage, suboptimal management practices, removal of feed additives, vaccinations, infections, stressors, toxic compounds, and genetic predisposition (Rinninella et al., 2019).

The relevance of the first 15 days of chickens life for gut health development has been extensively discussed (Attia et al., 2013; Lilburn and Loeffler, 2015). Several studies have documented substantial shifts in gut bacterial populations within the first, five to seven days of life, highlighting the susceptibility of young birds to dysbiosis. This vulnerability is often due to mechanical damage from feed transitions, severe coccidiosis, or viral infections, which can alter the gut environment and promote pathogen overgrowth.

Historically, industrial practices to address these issues (e.g. vitamin supplementation and the overuse of antimicrobials) have been prevalent but are increasingly considered unsustainable (Shehata et al., 2022). These interventions disrupt the ecological community of beneficial bacteria, posing significant risks for gut dysbiosis. The negative alterations in the equilibrium and functionality of the gut microbiota are further exacerbated by pathogen transmission through external and internal sources, slowing the maturation of the gut microbiota and metabolite production (Pickard et al., 2017; Wei et al., 2021).

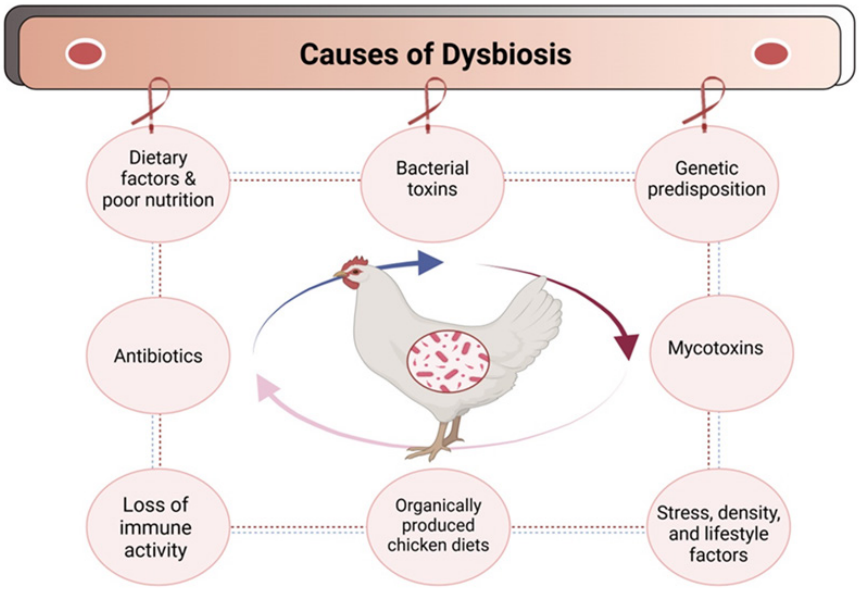


Figure 1. The various causes of gut dysbiosis

Mycotoxin contamination of animal feed is another significant issue that affects gut health (Attia et al., 2016). The inclusion of probiotics, prebiotics, organic acids, essential oils, medicinal plants, their bioactive components, and nanoparticles with strong antimicrobial properties as feed additives has been suggested. These strategies can help to detoxify aflatoxins, improve gut function, and enhance the overall health of animals (Abo El-Maaty et al., 2024).

Dietary factors

Dietary stresses, such as excessive protein intake, can lead to intestinal inflammation and gut microbiota imbalances, or "dysbiosis". When feed protein is inadequately digested and absorbed, it serves as a substrate for the gut microbiota, promoting the proliferation of proinflammatory bacterial populations (Gilbert et al., 2018). Given the increasing consumer demand for organic poultry production, where the use of antibiotics is often discouraged, alternative dietary strategies that enhance growth and health have gained traction and have been successfully applied to commercial meat production (Abo El-Maaty et al., 2024).

A well-formulated diet plays a crucial role in supporting gut health, especially during the early stages of an animal's life, when the gut microbiota is still established. Nutritionists are becoming increasingly aware of the need to carefully consider the impact of dietary changes on gut health to advance poultry nutrition science (Ducatelle et al., 2023). High-performance commercial chicken breeds are characterized by exceptionally high feed intake, which places considerable stress on the gut, particularly on absorptive epithelial cells lining the small intestine. These cells are essential for nutrient absorption and their continuous renewal is vital for maintaining gut integrity.

Epithelial cells undergo rapid turnover to counteract stress and damage and are produced by cell division in the crypts. These cells gradually mature as they migrate up the villi, where they develop receptors and enzymes required for nutrient absorption. However, under stressful conditions, such as dietary imbalances or infections, epithelial cells at the tips of villi undergo apoptosis and are shed into the intestinal lumen (De Grande et al., 2020). This increased cell loss can lead to villus shortening and crypt elongation as the gut attempts to compensate by accelerating cell production in the crypts. Measuring villus-to-crypt ratio is a valuable criterion for assessing intestinal health. For example, studies have shown that replacing inorganic zinc sulfate in broiler diets with a zinc amino acid complex improved villus length and villus-to-crypt ratio, suggesting that inorganic zinc may impose oxidative stress on epithelial cells (De Grande et al., 2020).

In conclusion, the incorporation of health-promoting dietary components has a significant potential for maintaining freshness and controlling broiler health. Combined with active gut-protective dietary components, these strategies are particularly effective in managing dysbiosis, thereby enhancing overall poultry performance and welfare.

Impact of mycotoxins on gut dysbiosis

Mycotoxins produced by fungi are among the most critical anti-nutritional factors present in poultry feeds, posing significant challenges to poultry health and performance. Recent research has highlighted the physiological and immunological effects of both low and high levels of mycotoxin exposure. Tissues with high rates of protein synthesis and turnover, such as those in the gastrointestinal tract (GIT), are particularly susceptible to the detrimental effects of mycotoxins. Many mycotoxins and their metabolites inhibit protein synthesis, which is vital for the maintenance and function of these tissues (Yunus et al., 2011).

Table 1. Summary of the causes, methods, and remarkable findings of the gut dysbiosis

Causes of dysbiosis	Method	Findings	Reference
1	2	3	4
Antibiotics	Used a commercial antibiotic (Metaxol®) containing 100 mg sulfamethoxazole and 20 mg trimethoprim/ml in the drinking water, for 3 days at 5 days of age compared to control non-treated chicks.	• Antibiotic significantly affected the microbiota in GIT	(Greene et al., 2023)
	Compared control and chicks exposed to diclazuril, enrofloxacin, and their mixture at 1:1 for 14 days and then not exposed for a withdrawal period of 15 days.	• Oral treatment with antibiotics altered the microbial metabolic profiles and gut microbiota composition in chickens, causing long-lasting changes (during the withdrawal phase) • Prevented the return to the original microbial community and led to the formation of a new one	(Elokil et al., 2020)
	For 14 days Cobb broiler chickens were supplemented with antibiotics (tylosin, bacitracin methylene disalicylate, and virginiamycin) and two ionophores (salinomycin and monensin) and compared to control non-supplemented broiler chicks.	• The growth-promoting effect of AGPs may be due to a combination of factors, including enhanced metabolism and utilization of dietary carbohydrates and lipids as well as improved energy harvest • Antibiotics showed a strong tendency to enrich butyrate- and lactic acid-producing bacteria while reducing bile salt hydrolase-producing bacteria	(Robinson et al., 2019)
	Investigated the impact of zinc bacitracin (55 g/ton), halquinol® (30 g/ton); virginiamycin (16.5 g/ton) enramycin (10 g/ton); and avilamycin (10 g/ton) on the cecal microbiota of broiler chicken, compared to a control group.	• Halquinol was the only drug that did not affect microbial membership compared to the control group • Treatment with antimicrobials did not affect microbial structure in the cecum of any of the studied groups	(Costa et al., 2017)
Mycotoxin	To identify impacts of mycotoxin during the growth period of broiler chickens, a 34-day feeding trial was conducted. Sources of *Fusarium*-contaminated wheat (11.4 mg/kg deoxynivalenol [DON] and clean wheat (<0.5 mg/kg DON) were used. Control and DON diets were provided to broilers according to treatments (control, DON 1 to 14 d, DON 15 to 21 d, DON 22 to 34 d, and DON 1 to 34 d).	• Results indicate that DON-induced growth suppression may be a result of adverse effects on intestinal morphology during later growth phases of broiler	(Wang and Hogan, 2019)
	Broiler chicks received a control diet and the control diet with 4 mg/kg deoxynivalenol (DON) + 3 mg/kg fumonisins (FUM) each with eight replications.	• The birds may be at risk for necrotic enteritis due to dietary DON and FUM contamination, even at subclinical levels, which changed the composition of bacteria in the cecum, dysregulated intestinal processes, and decreased the gut immune response	(Shanmugasundaram et al., 2023)
	Pathological scores of the broiler's small intestines on the 5th, 7th, and 10th day were compared to the control group. 7th day was chosen to analyze the small intestine tight junctions, histomorphology, and cecal biota of the broilers that received diets contaminated with deoxynivalenol (DON).	• The findings demonstrated that the damage to the small intestine grew worse over time, that the broiler chicks' small intestinal villi were broken • The small intestine's tight junctions were disrupted, the cecal biota was out of balance, and the chicks' development performance decreased on the seventh day • They concluded that DON could impair the intestinal tract's structural integrity and functionality, disturb the intestinal biota, and ultimately result in decreased broiler performance	(Wan et al., 2022)
	A review was conducted to comprehensively discuss the role of mycotoxins (zearalenone, trichothecenes, aflatoxins fumonisins, and ochratoxins) toward gut health and gut microbiota.	• It was found that mycotoxins can modify the composition of the gut microbiota; in certain investigations, these changes have been recorded down to the species level. The majority, if not all, of the impacts of mycotoxins showed detrimental effects on intestinal health, with beneficial bacteria being reduced and gut pathogens increasing	(Liew and Mohd-Redzwan, 2018)

Table 1 – contd.

1	2	3	4
Stress factors	Review carried out to explain how heat stress causes a disturbance in the commensal gut microbiota in pigs and broilers.	• Numerous studies have demonstrated that supplying probiotics, synbiotics and prebiotics to broilers can effectively prevent heat stress-induced disruption of the gut barrier by modifying the gut microbiota and supporting all important structural, biochemical, and immunological components of the intestinal barrier • When compared to broilers that were not supplemented and were subjected to heat stress, most studies revealed that broilers fed probiotics, prebiotics, or synbiotics altered the gut microbiota in favor of beneficial ones and improved gut barrier function • These improvements were accompanied by an increase in productivity, health, and/or welfare	(Ringseis et al., 2022)
	14-day-old female broiler chicks were divided into two treatment groups with different housing temperatures for 28 d: a control group (C) at 24 to 26°C and a heat stress (HS) group at 34 to 38°C.	• Through taxon-based and beta diversity analyses, it was determined that heat stress had a significant impact on the makeup of the gut microbiota. Specifically, the phylum-level composition of the heat stress group had a higher concentration of *Firmicutes*, *Tenericutes*, and *Proteobacteria* than the control group, while the HS group had a lower concentration of *Bacteroidetes* and *Cyanobacteria* than the control group • Furthermore, the HS group exhibited a higher composition of *Anaeroplasma* and *Lactobacillus* phyla compared to the control group. Conversely, the HS group displayed a lower composition of *Bacteroides*, *Oscillospira*, *Faecalibacterium*, and *Dorea* genera • Heat stress impaired the feed conversion ratio while considerably lowering average daily growth and average daily feed intake	(Shi et al., 2019)
	A study was run to describe dysbiosis in broilers (Ross 308) during one production round and to identify risk factors. Fifteen farms in Flanders (Belgium) were followed up, with visits at days 10, 17, 20, 24 and 28 of production.	• Following necropsy, gastrointestinal abnormalities and coccidiosis were scored • Lesions of *Eimeria acervulina* were the most common, followed by lesions of *Eimeria maxima* and *Eimeria tenella*. In the period between day 10 and day 20, the average gut appearance score (GAS) increased. The incidence of gastrointestinal anomalies at day 10 may be predictive of scores later, as seen by the high correlations observed between the GAS at days 10, 17, and 20 • In older female birds, when there was a potential *E. tenella* infection, and in farms with better productivity and sanitation, there was a less incidence of intestinal abnormalities and GAS	(Caekebeke et al., 2020)

The GIT is frequently exposed to mycotoxins, often at higher concentrations than other organ systems, due to the direct ingestion of contaminated feed. Moderate and occasional doses of mycotoxins have been shown to impair the functionality of the GIT, leading to disruptions in digestion and nutrient absorption (Murugesan et al., 2015 a). Mycotoxins can also influence lipid and nutrient oxidation, alter the structure of the digestive system, and disrupt the gut microbial population, further complicating the health of affected animals. Moreover, mycotoxins can modulate the immune system, thereby weakening an animal's resistance to infectious diseases. Epidemiological studies have demonstrated a strong correlation between aflatoxin (AF) contamination in broiler feed and outbreaks of Newcastle disease, a significant viral infection in poultry (Yunus et al., 2011). These findings highlight the immunosuppressive potential of mycotoxins that can exacerbate disease susceptibility and worsen the overall health of poultry flocks. Preventive measures such as ensuring proper feed hygiene and employing mycotoxin binders have proven effective in controlling and managing mycotoxicosis in poultry. These strategies help to mitigate the harmful effects of mycotoxin contamination, promote animal health, enhance feed safety, and improve overall productivity (Magnoli et al., 2011).

Impact of antibiotics on gut dysbiosis

Antibiotics have historically played a crucial role in animal farming (Zhu et al., 2021), significantly enhancing the growth performance of broiler chickens and helping to mitigate disease outbreaks (Lee et al., 2012; Chattopadhyay, 2014). These antibiotics, which were previously used as growth promoters, are essential for the prevention and promotion of animal growth. However, prolonged antibiotic use in poultry diets results in an imbalance in the natural gut microbiota. This imbalance occurs when beneficial bacteria are eliminated while non-beneficial bacteria proliferate, ultimately leading to dysbiosis (Ronquillo and Hernandez, 2017; Mehdi et al., 2018). The widespread use of broad-spectrum antibiotics in poultry diets for growth promotion and disease management raises concerns regarding the development of antibiotic resistance in human pathogens. As a result, there is a pressing need for research and development of alternative strategies to replace subtherapeutic antibiotic use. Growing interest in the application of the One Health concept for the use of non-antibiotic alternatives aims to restore and maintain gut health in animal production, thereby significantly influencing the health and welfare of broiler chickens (Shehata et al., 2022). These alternative strategies include probiotics, prebiotics, synbiotics, competitive exclusion agents, bacteriophages, *Bacillus* spp., organic acids, essential oils, and plant-derived compounds (Attia et al., 2023). Furthermore, there is a potential for synergistic effects when combining antibiotics with these non-antibiotic strategies; however, data on such combinations are currently limited. Emphasizing these alternative approaches could help mitigate the negative effects of gut dysbiosis and promote better health outcomes in poultry production systems.

Impact of stress and lifestyle factors on gut dysbiosis

Stress can significantly disrupt gut microbiota, leading to a condition known as dysbiosis. The hypothalamic-pituitary-adrenal (HPA) axis is crucial for mediating physiological responses to stress (Shi et al., 2019). However, inflammatory triggers can manifest more subtly. Environmental stressors that compromise the gut barrier integrity can also induce inflammation (Lambert, 2009). Heat stress is particularly relevant in poultry farming because exposure to various stressors, including heat, overcrowding, transportation, catching, restraining, and handling, activates the HPA axis. This activation stimulates the release of corticosterone, which can alter gut microbiota composition. Stress-induced decreases in short-chain fatty acid concentrations within the cecal digesta, stemming from an imbalance between energy nutritional needs and reduced feed intake, may result in diminished populations of beneficial microorganisms. This imbalance subsequently increases the susceptibility of the host to pathogen colonization (Zhu et al., 2019). Moreover, transport and handling stresses have been shown to compromise intestinal barrier function. In summary, strategies aimed at alleviating stress, enhancing the stability of the gut microbiota, preventing feed deprivation on farms, and reducing inflammation are essential for maintaining a healthy gut microbiome in poultry. The implementation of these measures can promote better health outcomes and overall productivity in broiler chickens.

Impact of genetic predisposition on gut dysbiosis

In human medicine, there is a recognized association between atopic conditions and genetically predisposed individuals, which reflects the polymodal nature of disease development. This phenomenon has also been observed in various other conditions including obesity, diabetes, gastrointestinal diseases, autoimmune disorders, and allergies (Blekhman et al., 2015). Similarly, the chicken genotype has been shown to influence gut microbiota composition (Tůmová et al., 2021).

The composition and distribution of microbial ecosystems in humans and animals are believed to be genetically programmed (Blekhman et al., 2015). It is crucial to conceptualize the microbiota as a functional organ that plays a vital role in the health of the host. The genetic and regulatory foundations of host-microbiota interactions may provide insights into the mechanisms underlying animal health, particularly in breeding strategies aimed at producing resilient animals with robust immune systems. Evaluating the polymorphisms of gene receptors related to bacterial functions in the gut can enhance our understanding of these interactions (Wen et al., 2021). There are some disorders and diseases unlike ordinary infections, they were not brought on by specific bacterial species. Instead, they seem to be caused by either misi-

dentification of the normal microbiota in various bodily contexts or a dysbiosis, which is a change in the normal microbiota (Nibali et al., 2014). Either aberrant microbial colonization or misrecognition of normal microbiota that results in these disorders are likely caused by genetic abnormalities in the identification and response mechanisms that the host utilizes to identify microbial pathogens. To describe this mechanism, the term "genetic dysbiosis" may be used, which is the idea of infectogenomics (Kellam and Weiss, 2006), for which two separate paths have been identified (bacterial proliferation and bacterial recognition). However it was demonstrated that the gut microbial community of chickens was largely independent of host genetics, but the microbiota was highly adapted to the environment of a particular gut location (Wen et al., 2019). These inconsistent findings suggest that the relationship between gut dysbiosis and host genetics requires further research.

These findings suggest a recommendation for selecting genetically healthy animals that exhibit favorable host-microbiota interactions. This approach aligns with the practical application of the One Health concept, which emphasizes the interconnectedness of human, animal, and environmental health. By fostering such interactions, we can enhance the health and well-being of both livestock and humans.

Dysbiosis can result from any disruption in the microbiota balance, which can be caused by dietary modifications, feed additives, mycotoxins, stress, and other factors. Some of the most significant causes of dysbiosis in poultry are listed in Table 1.

Diagnosis of gut dysbiosis

The diagnosis of gut dysbiosis depends mainly on intestinal histopathological examination and intestinal injury biomarker production, in addition to the use of modern biotechnologies to demonstrate qualitative and quantitative alterations in the microbiota populations.

Symptoms and clinical signs of gut dysbiosis

Several abnormalities have been documented in the gastrointestinal tract of chickens with dysbiosis. Liver atrophy associated with fetal emaciation syndrome is similar to that observed in the livers affected by chronic liver diseases, such as fatty liver disease and inclusion body hepatitis in chickens. Additionally, both liver enlargement and atrophy have been reported to be manifestations of dysbiosis (Xi et al., 2019; De Grande et al., 2020). Hepatic abnormalities are often accompanied by liver necrosis, hepatic lipidosis, and hypertrophy. Generally, in these cases, the liver appears congested, pale, and enlarged; in some instances, it may exhibit an irregular surface.

In broilers, these symptoms typically emerge between 20 and 30 days of age (Wilson et al., 2005). Clinically, key indicators of dysbiosis include paleness, a glistening appearance, orange droppings containing undigested food particles, and wet greasy feces. Additional observations may include foamy cecal droppings, decreased physical activity, increased water intake, reduced feed consumption, impaired growth, and compromised feed conversion efficiency (De Gussem, 2007). These clinical signs underscore the need for effective management strategies to address dysbiosis and its associated complications during poultry production.

Laboratory tests for gut dysbiosis

Laboratory testing targeting specific pathogens is instrumental in developing effective control strategies tailored to the particular pathogens of concern. When considering a partial or complete eradication strategy, it is essential to gather baseline knowledge regarding the current pathogen levels and associated risk factors affecting birds on-site. Thus, adapting rapid laboratory testing tools to evaluate gut integrity and control mycotoxin contamination in poultry farms is vital (Hafez and Attia, 2020). To effectively assess mycotoxin levels in poultry feed, a comprehensive understanding of the occurrence, detection methods, and toxicity associated with each mycotoxin is crucial (Liew and Mohd-Redzwan, 2018; Murugesan et al., 2015 a). However, the poultry industry faces challenges owing to a lack of systematic reviews and conflicting reports regarding the prevalence of additive or interaction effects within the gastrointestinal tract. This inconsistency complicates the provision of clear, evidence-based guidance concerning the interactions between multiple mycotoxins present in the feed.

Over the years, various methods have been employed to study gut microbiota, reflecting significant advancements in the field (Sarangi et al., 2019). Modern techniques, such as predicting the functional profiles of the gut microbiota from 16S rRNA metagenomic data, enable a more comprehensive evaluation of gut dysbiosis (Inoue et al., 2017). Furthermore, investigating the interactions between the gut microbiota and bile acid metabolism could offer insights into both health and disease states, highlighting the complex relationships that exist within the gut ecosystem (Mullish et al., 2018). These approaches not only enhance the understanding of gut health, but also provide a framework for developing targeted interventions that could mitigate the impacts of dysbiosis and mycotoxin contamination, ultimately supporting the overall health and productivity of poultry.

Impact of gut dysbiosis on gut and animal health

Animal health and optimal gut health are inextricably linked in the animal production industry, with gut health being a critical determinant of overall productivity. Research indicates a direct correlation between animal performance and gut health (Kogut, 2019). The gut microbiota serves as a key regulator of the host's well-being, playing a vital role in maintaining cell structure and function, ensuring nutritional balance within the cellular environment, and promoting the immune cell homeostasis necessary for optimal host physiology.

The intestine is equipped with a robust innate immune response designed to protect against pathogenic organisms that come in close contact with epithelial cells or the underlying lamina propria. This defense mechanism includes a combination of digestive enzymes, bile salts, and rapid feed transit, all of which are complemented by a protective mucus layer. Additionally, secretory IgA and host defense peptides such as cathelicidins and β-defensins contribute to this protective environment (Yacoub et al., 2015).

When the gut microbiota is healthy, bird productivity and performance are significantly enhanced (Bindari and Gerber, 2022). Healthy microbiota produce beneficial metabolites, including short-chain fatty acids (SCFAs), indoles, vitamins, and antibacterial compounds, which help increase the absorptive surface of the epithelium. They also support the development of the mucus layer, lamina propria, and the epithelial monolayer (Oakley et al., 2014). In contrast, dysbiosis disrupts the biochemical interactions between the host and microbiome, leading to the proliferation of pathogenic organisms and reducing the effectiveness of commensal bacteria. This imbalance can severely affect the structural and functional organization of the gut microbiota, drastically diminishing microbial diversity and allowing undesired microflora to dominate the intestinal environment.

The consequences of dysbiosis include impaired competitive exclusion of pathogens, reduced synthesis and maintenance of the epithelial barrier through butyrate production, decreased secretion of antibacterial peptides, and diminished immune responses due to the altered secretion of commensal lipopolysaccharides (Pickard et al., 2017; Takiishi et al., 2017; Ma et al., 2022). In particular, the physiological conditions within the intestinal ecosystem are significantly altered, with factors such as microbial population density in the small intestine and the prevalence of gram-negative bacteria on the apical surface of the gut mucosa being critical during both early and late stages of chick production (Pan and Yu, 2014).

To optimize gut health and consequently animal productivity, it is essential to maintain a balanced microbiota, utilize effective management strategies, and incorporate dietary interventions that support microbial diversity and health. This holistic approach is fundamental for enhancing overall animal welfare and performance in poultry production.

Impact of gut dysbiosis on digestive health

The profitability of chicken rearing and overall wellness depend on digestive health. Modification of the intestinal microbiota of poultry has been shown in several studies to improve gut health and prevent harmful infections. In addition to preventing external pathogen colonization, the presence of advantageous native microorganisms in the mucosal layer and related lumen may have several positive effects on host health. Numerous avian diseases, including fatty liver hemorrhagic syndrome, coccidiosis, and pathogenic infections, have been linked to an imbalance in the microbial communities inside members or niches, which is commonly cited as a host health issue (Abd El-Hack et al., 2022). This lowers nutritional consumption and increases the risk of gastrointestinal illnesses in hens. The primary cause of *Enterococcus* expression in young broilers is the underdeveloped intestinal barrier caused by the early age of the birds and their rapid passing rates. According to Attia et al. (2018), heat stress impairs the function of the intestinal barrier and increases the vulnerability of broilers to endotoxemia. The composition of the gut microbiota is crucial for the control of energy balance and nutrient metabolism in chickens. Changes in gene transcription linked to gut barrier integrity and metabolic processes, which are intimately linked to phagocytosis and fatty acid production and secretion, can result from the poor gut health of broilers (Habashy et al., 2017).

Impact of gut dysbiosis on immune function

It is well known that the gut microbiota plays a role in the host immune system. Commensal microbiota adheres to the intestinal epithelium and is crucial for preserving homeostasis and preventing pathogen colonization (Diaz Carrasco et al., 2019). However, depending on the particular taxonomic makeup and metabolism, they may be advantageous or harmful. Changes in the makeup of gut microbes frequently alter the gene expression profile and immune cell activity, which may modulate immunological responses. In order to help immune cells grow and learn to tolerate commensal microorganisms, recognize and suppress pathogens, and preserve the equilibrium of potentially dangerous commensal microorganisms like *Clostridium perfringens* and *Escherichia coli*, the chicken immune system and microbiota collaborate (Adil and Magray, 2012). Certain bacteria and metabolic products have an indirect effect on immune function by either inducing or suppressing the response, even though certain species may have direct effects.

It is well known that the immunomodulatory properties of *Lactobacilli*, *Bifidobacterium*, and *Akkermansia* boost host immunity by inhibiting the production of proinflammatory cytokines, reducing Th1 and Th17 responses, and boosting the release of anti-inflammatory cytokines while damaging pathogens (Demas et al., 2011). The production of certain probiotic genes involved in various cell wall components is an important method. This makes it possible for probiotic organisms to communicate with the host by releasing certain chemicals and signaling molecules. The metabolic byproducts of beneficial microorganisms also contribute to immunological regulation. A significant portion of tryptophan is broken down into indole, which is then transformed into tryptophan metabolites that may modify immunological pathways and exhibit anti-inflammatory properties (Fernández et al., 2016). Furthermore, SCFAs produced during anaerobic bacterial fermentation have significant anti-inflammatory properties. Butyrate significantly affects the generation of antimicrobial peptides and reg-

ulatory T cells, both of which are critical for intestinal barrier function. Nevertheless, elevated butyrate levels have been shown to reduce the expression of proteins linked to cytotoxic T lymphocytes (Siddiqui and Cresci, 2021). The development and health of broiler chickens are significantly influenced by their gut flora. Reduced nutrition absorption, inflammation, altered gut shape, and increased vulnerability to gut infections and illnesses are all consequences of dysbiotic alterations in the gut microbiota (Hafez and Attia, 2020). The overall development of intestinal adaptive immunity, which is typified by tolerance towards feed and luminal microbial antigens and a protective reaction against pathogenic microorganisms, is significantly influenced by the rich and complex microbiota that live in the lumen of the gut layer (Kogut et al., 2020).

Preventive strategies for gut dysbiosis

Organic acids, plant-derived phytochemicals, probiotics, prebiotics, postbiotics, and phytogenic compounds can all be used to manage enteric dysbiosis. These agents can confer health benefits to the host when administered in adequate amounts at the right time (Attia and Hassan, 2017). Figure 2 shows different preventive strategies for gut dysbiosis.

Dietary modifications and phytogenic additives

Dietary modifications represent a fundamental strategy for mitigating intestinal dysbiosis in broiler chickens. Numerous studies have demonstrated that targeted dietary interventions can significantly influence the composition of gut microbial communities, thereby enhancing poultry productivity (Brown et al., 2012; Blachier et al., 2019). Various dietary approaches have been employed to modify chicken microbiota, regulate the intestinal environment, and increase the population of beneficial bacteria. These approaches involve the use of prebiotics, probiotics, synbiotics, and phytogenic feed additives.

Prebiotics are non-digestible substances that resist hydrolysis by the host's digestive enzymes but serve as substrates for specific beneficial bacteria within the gut. Common examples of prebiotics include inulin, fructooligosaccharides, mannooligosaccharides, xylooligosaccharides, galactooligosaccharides, isomaltooligosaccharides, soybean oligosaccharides and lactulose. Probiotics such as *Lactobacillus* and *Bifidobacterium* species are viable microorganisms that confer health benefits to the host when administered in sufficient quantities (Skvortsova et al., 2018).

Additional studies have highlighted the potential of synbiotics, which are defined as a combination of probiotics and prebiotics that enhance the survival and colonization of live microbial dietary supplements in the gut. Phytogenic feed additives, including essential oils and plant-derived compounds such as carvacrol, cinnamaldehyde, eugenol, thymol, flavonoids, and polyphenols, have also been employed to modify the gut microbiota composition in broilers, as demonstrated in various animal studies (Abd El-Hack et al., 2022).

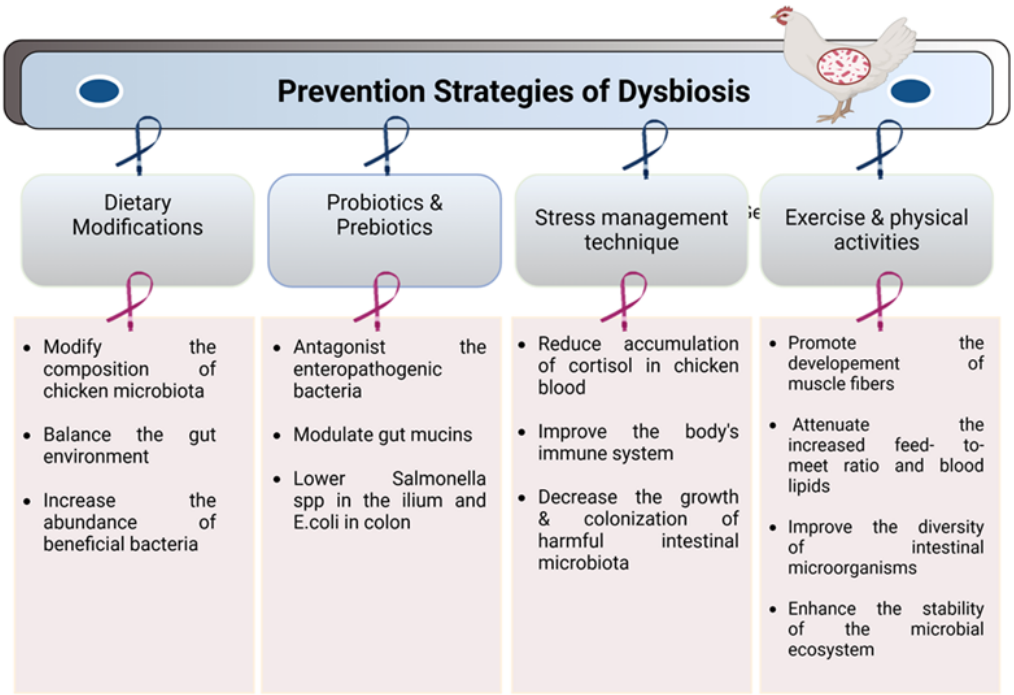


Figure 2. The various preventive strategies for gut dysbiosis

Furthermore, it is important to acknowledge that gut microbiota composition may vary among different broiler breeds. Therefore, selection of appropriate dietary sources is crucial for optimizing the proliferation of beneficial bacteria (Murugesan et al., 2015 b). However, it is essential to recognize that certain bioactive phytochemicals present in phytogenic feed additives may exhibit toxicity to the host in some instances, and may not enhance the growth efficiency of broilers. Consequently, careful consideration of the dosages, combinations, and mechanisms of action of phytogenic feed additives is necessary for diverse subtypes of bioactive compounds.

Impact of probiotics and prebiotics on gut dysbiosis

By reducing harmful bacteria within the intestinal microbiota of poultry, probiotics and prebiotics can enhance immune function, decrease reliance on antibiotics, and improve the overall host welfare. Probiotics, in particular, have demonstrated efficacy in combating enteropathogenic bacteria owing to their antagonistic properties (Al-Khalaifa et al., 2019). The most extensively studied probiotic sources belong to the *Lactobacillus* and *Bifidobacterium* genera. Supplementation with *Lactobacillus salivarius* or *Bacillus subtilis*, when combined with prebiotics, mitigates the adverse effects of coccidiosis (Kailasapathy et al., 2000).

Coccidiosis caused by *Eimeria* species in broilers can be effectively managed through the administration of live *Lactobacillus* and *Bifidobacterium* species. Specifically, *Lactobacillus acidophilus* has been investigated as a probiotic feed additive for newly hatched broilers in conjunction with thymol and yucca extracts. The combination of *L. acidophilus* and yucca extracts has been shown to ameliorate intestinal lesions and enhance production performance (de Freitas et al., 2023; Ahmad et al., 2024).

Moreover, dietary supplementation with *Bifidobacterium longum* subsp. *infantis* in combination with prebiotics has been effective in mitigating the negative effects of lipopolysaccharides on gut health (Abdelrahman et al., 2014). Previous *in vitro* studies have indicated that *Corynebacterium* and *Lactobacillus* species can inhibit *Salmonella enteritidis* (Zihler et al., 2010). Consequently, the inclusion of these probiotics in broiler diets may reduce cecal colonization by *Salmonella* spp. Furthermore, the incorporation of probiotics into feed has been associated with lower concentrations of *Salmonella* spp. in the ileum and reduced levels of *Escherichia coli* in the colon (Attia et al., 2012).

The mode of action of probiotics involves several antimicrobial mechanisms, including high population densities, competition for binding sites and nutrients, production of inhibitory substances, such as bacteriocins, induction of host defense peptides, and synthesis of short-chain fatty acids (SCFAs). Probiotics have been shown to suppress the expression of intestinal tumor necrosis factor-alpha (TNFα) through the promotion of anti-inflammatory cytokines, notably interleukin-10 (IL-10), as well as by enhancing secretory immunoglobulin A (IgA) responses and the upregulation of immunoglobulin G (IgG) in the gut. Furthermore, probiotics can modulate the expression of immune-related genes including MyD88, TLR7, TLR4, IL-10, and CD25. *Lactobacillus* and *Bifidobacterium* species are the most commonly used probiotics, either as single strains or in combination (Taheri et al., 2009; Nallala et al., 2017; Hossain et al., 2021).

An effective candidate for commercial probiotic use should possess several key characteristics: 1) regulatory approval for health claims, 2) proven safety through appropriate assays, 3) demonstrated antimicrobial activity, 4) the ability to adhere to and colonize the gastrointestinal tract (GIT), 5) resilience to GIT environmental conditions and digestive fluids, 6) long-term viability, 7) health-enhancing properties, 8) direct utilization of essential compounds while supplementing limited dietary molecules, 9) safety across sex, 10) genetic stability for prolonged use, and 11) support for immune function, as evidenced by increased IgA in the gut lumen and IgG in the plasma.

The therapeutic efficacy of *Lactobacillus acidophilus* and *Bifidobacterium animalis* against *Enterococcus faecalis* allows them to outcompete indigenous microbiota in poultry by effectively downregulating host defense genes in the gut. One of the most well-studied prebiotics is mannan oligosaccharides, which are derived from the outer cell wall of yeasts, such as components from the *Saccharomyces* yeast cell wall, cellulose, and β-1,3–1,6–glucan. Prebiotics are known to enhance the crude protein content of mammalian diets and promote greater absorption of amino acids, ions, and minerals including manganese (Mn), zinc (Zn), copper (Cu), calcium (Ca), and phosphorus (P). Yeast cell wall components typically contain 25–40% crude protein, high mannose concentrations that contribute to improved gut health, and 20–40% crude fiber (Attia and Abd-El-Rahman, 2001).

Plant-derived compounds such as methyl methionine, sulfonium, and fumaric acid have demonstrated benefits for the gut microbiota in poultry. However, it is important to note that these compounds can exert an inhibitory effect on the gut flora at elevated concentrations. Other organic acids commonly used to mitigate the gastrointestinal burden of pathogens include lactic, formic, benzoic, propionic, butyric, citric, and caprylic acids (Taheri et al., 2009). Medicinal plants, such as ajowan essential oil and oregano, are also used to manage enteric diseases in commercial poultry. However, the incorporation of medicated feeds into therapeutic management does not effectively eliminate pathogenic bacteria and may contribute to the development of antibiotic resistance (Hafez and Attia, 2020).

Alternative strategies include the use of resistant starch-rich sources that promote a favorable microbiota balance in commercial birds. Additionally, fortification with functional nutritional compounds such as nucleotides and antioxidant phytochemicals could prove beneficial in mitigating the clinical manifestations of enteric

diseases in commercial broilers during periods of stress or challenge (Desbruslais and Wealleans, 2022).

Finally, in the context of antibiotic-treated broilers with intestinal disorders, controlled feeding models suggest that feed restriction may serve as an effective alternative to other dietary modifications. Fasting has been proposed as a strategy to modulate the cecal microbiota, thereby reducing populations of pathogens such as *Clostridium perfringens* in antibiotic-free poultry (Attia et al., 2023). Despite the promising responses observed with dietary inclusion of bioactive compounds, further research is needed to identify specific alternative treatments that can confer similar clinical benefits.

Stress management techniques

Stress can occur at any stage of chicken development and production and is typically categorized into three types: physical, psychological, and social stress. Preslaughter-related stress is of particular concern and often arises from factors such as prolonged fasting, live transport, overcrowding, exposure to elevated environmental temperatures, mixing with other flocks, and queuing (Webster et al., 1993). Additionally, environmental stressors, including high temperature, humidity, mechanical noise, and harsh lighting, can significantly impact chicken welfare.

A critical consequence of these stressors is the accumulation of cortisol in the bloodstream, which can weaken the immune system; diminish the immune response, especially in the gut; and facilitate the growth, colonization, and persistence of harmful intestinal bacteria (Webster et al., 1993; Yang et al., 2011).

One effective strategy for improving animal health and performance under stressful conditions is the application of nutritional strategies to enhance gut conditions (Azad et al., 2010). *Bifidobacteria* and *Lactobacilli*, which produce the protective metabolite acetate, are particularly noteworthy because of their ability to metabolize specific oligosaccharide substrates. Dietary supplementation with probiotics may enhance thermotolerance and mitigate the adverse effects of heat stress on broiler performance and health of broilers under heat stress conditions (Attia et al., 2017).

Vitamin E is a potent antioxidant, playing a vital role in supporting the immune system, and reproductive function of poultry. In particular, vitamin E has been effective in sustaining the population of keystone fibrolytic bacteria in turkeys ceca (Panda and Cherian, 2014).

Impact of exercise and physical activity on gut dysbiosis

Compared to humans and other mammals, only a limited portion of the poultry gut is involved in energy production and exchange, with energy reserves constrained by the muscle structure of broilers. Consequently, increased activity during the early developmental stages can promote muscle fiber development, augment muscle weight, and enhance flesh accumulation. This activity may also mitigate the elevated feed-to-meat ratio and blood lipid levels associated with high-fat diets, thereby improving hyperlipidemia and overall resistance in animals (Maharjan et al., 2021).

Engagement in physical activity has been shown to positively influence the diversity of intestinal microorganisms and to enhance the stability of microbial ecosystems. Conversely, a high population density in cage housing, coupled with a lack of proper activity, can stimulate the hypothalamic-pituitary-adrenal (HPA) axis, resulting in increased glucocorticoid secretion. This hormonal response can further enhance the glucose and fatty acid metabolism. Glucocorticoids are known to inhibit the growth of the gut flora, facilitate intestinal glucose transport, and increase glucose utilization. The stress experienced by animals may lead to increased motility in the small intestine as well as decreased residence times in the stomach, small intestine, and large intestine (Aya et al., 2021).

Chronic stress increases susceptibility to harmful gram-negative bacteria, increases cecal organic matter digestibility, enhances nitroreductase and beta-glucuronidase activities, and increases the likelihood of bacterial translocation into the portal vein. Gut microorganisms play a crucial role in promoting health, stimulating host energy demands, and modulating the degradation rate of dietary polysaccharides to maintain host homeostasis. Beneficial interactions between exercise and the gut microbiota have been demonstrated through significant increases in microbial diversity and abundance among high-performance athletes (Marttinen et al., 2020). Furthermore, improving housing systems could improve animal welfare and contribute to the One Health concept through altering gut microbiota composition towards beneficial bacteria. Recent evidences demonstrated marked differences in cecal microbiota profiles between chickens raised in cage versus cage-free environments (Pires et al., 2024).

Impact of pharmacological interventions on gut dysbiosis

Historically, the prevention of bacterial infections and the enhancement of chicken growth have relied heavily on the use of antibiotics. Consequently, there has been growing emphasis on recommending alternatives to antibiotic growth promoters (AGPs) in animal production, as these alternatives can achieve beneficial effects by promoting growth while enjoying high consumer acceptance in the absence of antibiotic therapies (Shehata et al., 2022). In practice, antibiotics are commonly administered via feeders and drinking water (Sanganyado and Gwenzi, 2019). This administration method is particularly relevant for influencing the intestinal microbiota as it can enhance the proliferation of beneficial bacteria while suppressing pathogenic species. In certain situations, more potent antibiotics are prescribed for broilers, either as medical prophylaxis for disease prevention, or as therapeutic agents for treating endemic or sporadic ill-

nesses. A significant concern regarding the use of antibiotics in animal feed, especially at subtherapeutic dosages, is their contribution to environmental contamination. The emergence of antibiotic-resistant bacteria from livestock poses considerable risks to human health as these resistant strains may be transferred to the human gut following the consumption of contaminated animal food products. Therefore, it is imperative to restrict the use of AGPs as growth promoters in animal husbandry (Hafez and Attia, 2020). Given the challenges associated with antibiotics and public concerns regarding food safety, there is growing interest in utilizing natural microbial solutions to maintain animal health and optimize performance (Zhu et al., 2021).

Conclusion and remarks

Gut dysbiosis in broiler chickens is a complex issue that significantly affects their immune system, digestive health, and overall productivity. The etiology of this condition is multifactorial, encompassing dietary influences, antibiotic usage, environmental stressors, and genetic predispositions. Effective prevention and treatment strategies require a holistic approach that integrates dietary modifications, use of probiotics and prebiotics, synbiotics, organic acids, phytogenic additives, stress management techniques, and judicious application of pharmacological interventions when necessary. As research in this area continues to advance, emerging therapies and technologies present promising opportunities to maintain optimal gut health throughout broiler production. A comprehensive understanding of the intricate interactions among host genetics, environmental variables, and the gut microbiome is essential for developing targeted and sustainable solutions to prevent and manage gut dysbiosis in commercial poultry operations. Addressing this challenge can lead to enhanced animal welfare, improved production efficiency, and the ability to meet the increasing demand for safe and high-quality poultry products.

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Conflict of interest

There is no conflict of interest.

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