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Review Article

Probiotics supplementation supports gut health, performance, and immune response in poultry coccidiosis

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ABSTRACT: Coccidiosis is an important parasitic disease that consistently jeopardizes optimal productivity and the potential of the poultry industry worldwide. It substantially affects profitability causing losses estimated to be over USD 14 billion annually. To mitigate its impact, various research efforts have explored different control strategies, including the use of probiotics and other dietary supplements. This article provides a comprehensive review of how probiotics influence bird performance, gut health, management practices, and the immune response to this debilitating disease. Evidence suggests that probiotics enhance the efficacy of anticoccidial agents and offer a promising alternative to the use of synthetic compounds as growth promoters in poultry production. Their role has become increasingly important, especially in light of rising resistance to conventional anticoccidial drugs, concerns over drug residues in poultry products, and its implication for public health. As a result, probiotics are rapidly gaining acceptance as growth promoters, thus replacing synthetic drugs in the poultry industry.

Keywords: Anticoccidial agent, dietary supplement, natural growth promoter, poultry health, probiotics.

INTRODUCTION

Generally speaking, poultry refers to domesticated birds raised primarily for commercial purposes, such as ducks, geese, guinea fowl, chicken, etc (Anas *et al.*, 2018). According to Mottet and Tempio (2017), the poultry business is a significant and expanding agricultural subsector in the modern world. Commercial chicken production is growing due to the growing need for animal protein and the growing global population (UN-DESA, 2017; Malik *et al.*, 2016; Adewole, 2012). The chicken is an important poultry bird whose provision of meat and eggs substantially boosts agricultural production (Fatoba and Adeleke, 2018).

Coccidiosis is the most well-known parasitic disease affecting the poultry industry today (Geetha and Palanivel, 2018; Abudabos *et al.,* 2017; Muthamilselvan *et al.*, 2016). It causes significant financial losses (El-Shall *et al.,* 2022; Hayajneh *et al.,* 2018) exceeding 14.4 billion USD annually worldwide (Blake *et al.,* 2020). Due to Eimeria resistance (Arabkhazaeli *et al.,* 2013), traditional disease control methods are becoming less successful (Blake and Tomley, 2014; Kadykalo *et al.,* 2017) as well as expensive (Dalloul and Lillehoj, 2006; Blake *et al.,* 2020). Non-traditional and alternative methods are being pursued (Tsiouris *et al.,* 2021; Adhikari *et al.,* 2020; Awais *et al.*, 2019).

The gut microbiota has been branded a "hidden metabolic organ" (Chen *et al.,* 2020; Nicholson *et al.*, 2012) due to the profound effects it has on immunological function, nutrition, host metabolism, and physiology (Shehata *et al.*, 2022; Aziz *et al.*, 2017). Probiotics are among the many approaches that can alter the gut microbiota and lower the incidence of enteric diseases (Fesseha, 2019; Hassan *et al.*, 2012). Probiotics are increasingly being used in humans and animals as an alternative to antibiotics (Abd El-Ghany, 2021; Getabalew *et al.*, 2020; Reda, 2018), and evidence of their effectiveness is growing (Abd El-Moneim *et al.,* 2020; Erdogmus *et al.,* 2019).

The gastrointestinal microbiota can be preserved normally by probiotics, which are live, nonpathogenic microorganisms (Cai *et al.*, 2022). Probiotics include microbial species of the genus Lactobacillus (Mookiah *et al.,* 2014), Bifidobacterium (Pedroso *et al.,* 2013), Enterococcus and Bacillus (Mountzouris *et al.*, 2010), and non-bacterial (yeast or fungal) species like *Candida pintolopesii*, *Aspergillus oryzae* (Daskiran *et al.,* 2012), Saccharomyces (Aluwong *et al.,* 2013), non-pathogenic *Escherichia coli*, Streptococcus (Ferreira *et al.*, 2011; Markowiak and Slizewska, 2017), etc. which are currently used with variable effects on poultry production. In order to understand the factors influencing probiotic activity and develop guidelines for probiotic applications, it is necessary to regularly examine research findings. Therefore, the purpose of this review is to provide a brief overview of the impact of probiotic supplementation and its effect on gut health, performance, management, and immune response to coccidiosis in poultry from studies around the globe.

Selection and mechanisms of probiotic action

Milk, fermented foods, faeces, and gut microbiota are natural sources from which probiotics can be isolated (Fontana *et al.,* 2013). According to Morelli and Capurso (2012), the two major probiotics found in traditional fermented products are lactic acid bacteria and bifidobacteria; numerous other probiotic sources have been found and are being employed for commercial purposes (Forkus *et al.,* 2017; Sanders *et al.,* 2019). Standard selection criteria for probiotic strains include competitive exclusion of pathogens (Gadde *et al.,* 2017), capacity to adhere to gastrointestinal mucosa, and tolerance to gastrointestinal conditions (Smith, 2014). Probiotics are also chosen according to how well they can withstand the processes involved in production, shipping, storing, and application while maintaining their viability and desired qualities (Doron and Snydman, 2015; Wondwesen and Moges, 2017; Broom and Kogut, 2018).

The mechanisms of action of probiotics are complex and not completely understood (Ajuwon, 2016). The mechanisms suggested from studies (Figure 1) include the following: the secretion of antimicrobial substances (Abd El-Moneim *et al.*, 2020; Vieco-Saiz *et al.*, 2019; Shivaramaiah *et al.,* 2014) such as bacteriocins, oxygen peroxide, antibiotics, free fatty acids, etc.; the modulation of the immune system and intestinal environment like pH (Anas *et al.,* 2018; Taherpour *et al.*, 2012; Dalloul *et al.*, 2003); the improvement of beneficial intestinal microbiota (Zhou *et al.*, 2020); nutrients, and so forth (Lee *et al.,* 2007a; Muhammad *et al.,* 2021).

Depending on where they come from, probiotics are categorized as either autochthonous, allochthonous, or fungal (Getabalew *et al.*, 2020; Abdel-Raheem *et al.*, 2012). Autochthonous probiotics, such as Bifidobacterium, *Clostridium butyricum*, Lactobacillus, and *Streptococcus faecalis*, are derived from the gut microbiota and have the ability to efficiently colonize, multiply, and perform specific probiotic benefits in addition to directly replenishing the original bacteria (Mukai *et al.,* 2002). For example, *C. butyricum* efficiently enhanced the number of Lactobacillus and decreased the abundance of *Candidatus arthromitus* and *Brachybacterium sp.,* two pathogenic bacteria (Huang *et al.*, 2019). Autochthonous probiotics share many physiological and metabolic processes with their host. For the benefit of the host, they synthesis nutrients and support regular growth and life activities (Bortoluzzi *et al.*, 2019; Nava and Stappenbeck, 2011). Allochthonous Probiotics, such as *Bacillus subtilis*, *B. licheniformis*, and *B. cereus*, are not closely related to their hosts. Usually, they only temporarily colonize the digestive system (Backhed *et al.*, 2005). The symbiotic relationship between autochthonous and allochthonous microbiota is characterized by the growth and proliferation of autochthonous microbiota by allochthonous microbiota (Whelan *et al.,* 2019). Most Saccharomyces, including *S. cerevisiae* and *S. boulardii,* are the type of fungi that are used as probiotics in poultry (Neut *et al.*, 2017; Terciolo *et al.,* 2019).

Effects of probiotics supplementation on gut health and performance

For poultry and other animals alike, gut health is essential to overall health and well-being (Slifer and Blikslager, 2020). The state of the gastrointestinal system affects how much feed is consumed, how it is digested, and how well nutrients are absorbed (Pan and Yu, 2014; Mace and Marshall, 2013). Thus, the new frontier for disease prevention in various species is managing gut health (Wu *et al.*, 2019; Kuttappan *et al.,* 2015). Growth-related nutrient resource allocation is shifted by Eimeria infections to immune responses, which can cause apparent growth performance variations (Teng *et al.*, 2020; Dalloul and Lillehoj, 2005).

The immune system, particularly the local intestinal immunological status, and the precise site of infection in the intestinal tract play a major role in determining how harmful an Eimeria infection will be (Burrell *et al.*, 2019; Jatau *et al.*, 2016). The intestinal presence of Eimeria parasites causes damage to the lining (Sharma *et al.,* 2015; Abdelrazek *et al.,* 2020), epithelial cell sloughing (Engidaw and Getachew, 2018), and disruption of absorption (Fatoba and Adeleke, 2018). These outcomes lead to diarrhoea, reduced feed intake, diminished weight gain, and overall lower productivity (Geetha and Palanivel, 2018; Lin *et al.,* 2020; Zaheer *et al.*, 2022). Numerous systemic functions are impacted by the disruptions in gut health (Dinan and Cryan, 2017).

Probiotics have demonstrated a great deal of promise for

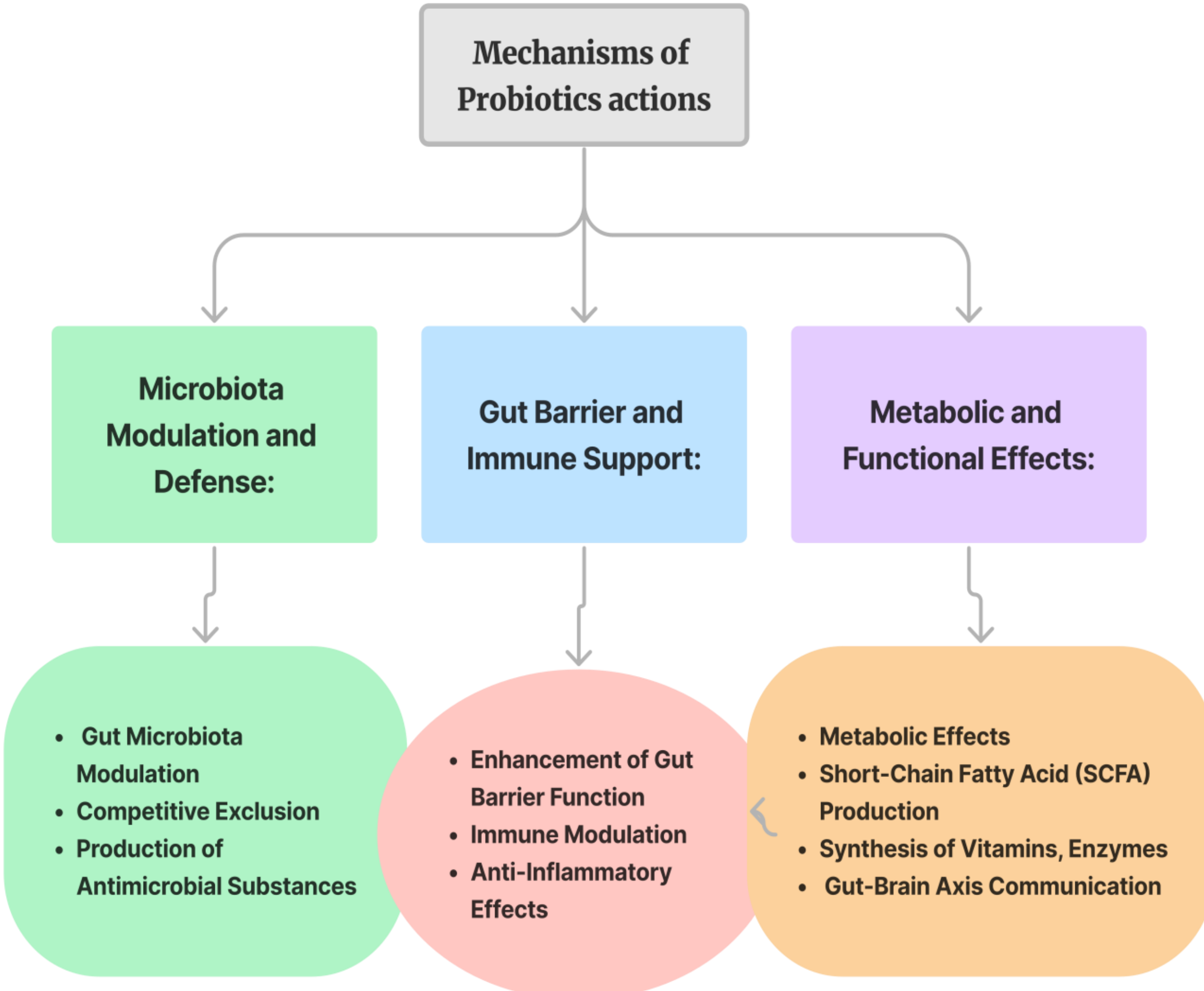

Figure 1. A schematic illustration of the mechanisms of probiotics action.

improving gut health and poultry performance (Table 1), supporting a balanced and healthy gut microbiota (Wang *et al.*, 2021; Krysiak *et al.*, 2021), and mitigating the detrimental effects of a number of enteric diseases, such as coccidiosis (El Jeni *et al.*, 2021). In a study on induced Eimeria infection, supplementation with Saltose® probiotic decreased intestinal lesions and enhanced gut health as shown by intestinal histologic results (Belih *et al.*, 2015). Probiotics reportedly strengthen the local immune system and improve the gut health of birds, which reduces intestinal damage during the coccidiosis challenge (Ajanya *et al.,* 2018). Probiotic administration through drinking water improved broiler performance (Timmerman *et al.*, 2006). Likewise, growth performance in chicken was enhanced by adding probiotics, such as Lactobacillus cultures and other bacteria, to broiler diets (Mookiah *et al.,* 2014; Zhang and Kim, 2014). After 42 days, broilers given *Lactobacillus acidophilus* supplementation weighed 10.1% more than birds in the control group (Vantsawa *et al.*, 2017). Qiu *et al.* (2022) observed that broilers fed a combination of several Lactobacillus strains and yeast from 1 to 42 days of age showed improvements in body weight gain (BWG) and feed conversion ratio (FCR). The improved state of intestinal configuration and caecal microbial diversity were responsible for the favourable effects of the compound probiotics on the growth performance and health of broilers. These unique impacts from antibiotics show that adding compound probiotics to broiler diets instead of antibiotics is a viable alternative. Awad *et al.* (2009) observed a continuous improvement in body weight increase in chickens fed a Lactobacillus culture. According to Park *et al.* (2020), adding *Bacillus subtilis* to broiler feeds greatly increases body weight gain. Intestinal immunity, epithelial barrier integrity, and growth performance were all markedly improved by the dietary *B. subtilis* 747. The findings suggested that some *B. subtilis* strains could substitute antibiotic growth promoters and have positive effects on the development of young broiler chicks.

Numerous prior studies (Kabir *et al.*, 2004; Khaksefidi

Table 1. Effects of various probiotic preparations on Eimeria parasites.

S/n.	Trade name	Composition	Effect on coccidiosis	Reference
1	BLES	*Bifidobacterium animalis, Lactobacillus casei, Enterococcus faecalis, Saccharomyces cerevisiae*	The gut microbiota analysis of the experimental groups that received BLES and coccidiosis vaccines at 8 and 15 days of age showed a positive correlation with the Enterococcus genus and Lachnospiraceae NK4A136 group. The combination of BLES and coccidiosis vaccination decreased not only the lesion score and OPG values but also the intestinal epithelial abscission caused by coccidiosis vaccines.	Cai *et al.*, 2023
2	Primalac	*Lactobacillus acidophilus, Lactobacillus casei, Enterococcus faecium and Bifidobacterium bifidium*	In comparison to the non-supplemented birds, the probiotic-supplemented birds showed improved body weight and higher body weight gain from day 9 to day 15. On day 15, the supplemented birds' spleen weight was higher. The supplemented group had a far reduced death rate. Probiotic supplementation decreased the gross lesion severity in every intestinal section that was assessed.	Pender *et al.*, 2016
3	Protexin®	*Enterococcus faecium*	Probiotic-treated chickens showed moderate lesion scores and oocyst numbers. Among the challenged groups, the birds administered probiotics and diclazuril had the highest weight increase, lowest lesion score, lowest oocyst count, and lowest fatality rate.	El-Sawah *et al.*, 2020
4	PoultryStar®	*Bifidobacterium animalis subspecies animalis, Lactobacillus salivarius subspecies salivarius*, and *Enterococcus faecium*	Supplementing with probiotics in place of anticoccidials can improve function and lessen the negative consequences of a mixed Eimeria infection.	Ritzi *et al.*, 2014
5	-	*Bacillus subtilis, Clostridium butyricum* and Lactobacillus	Increased levels of proinflammatory cytokines, tight junction proteins, and antioxidant enzymes in the probiotic supplemented when compared to control positive, untreated, challenged chickens	Memon *et al.*, 2021
6	Gro-2-max®	*Bacillus subtilis, Pediococcus pentosaceus, Pediococcus acidilactici, Lactobacillus acidophilus, Saccharomyces cerevisiae*	Probiotics reduced oocyst shedding and infestation, enhanced levels of antioxidant enzyme, serum cholesterol, triglycerides, HDL, ALT, AST, and ALP activities, as well as cecal production of IFN-γ and IL-2.	Nasr El Deen *et al.,* 2021
7	-	*Bifidobacterium animalis subsp. animalis* #503, *E. faecium* #497, *E. faecium* # 589, *L. reuteri* # 514, *L. salivarius subsp. salivarius* # 505, and *Bacillus subtilis* # 588	It was demonstrated that up to 80% of the parasite invasion into MDBK cells was blocked by viable strains of *Bifidobacterium animalis subsp. animalis* #503, *E. faecium* # 497, *E. faecium* # 589, *L. reuteri* # 514, *L. salivarius subsp. salivarius* #505, and *Bacillus subtilis* # 588.	Hessenberger *et al*., 2016.

and Ghoorchi 2006; Nayebpor *et al.*, 2007; Vieira *et al.,* 2008; Ignatova *et al.*, 2009; Sen *et al.*, 2012) have reported that probiotics improve weight gain, carcass yield, and feed conversion ratio in chickens. Probiotic supplements have been shown to improve the feed conversion ratio (FCR) in Eimeria-challenged birds (Bansal *et al.*, 2011; Cao *et al.*, 2013). Probiotic supplementation enhanced the performance of broilers, as evidenced by an increase in weight gain in birds fed probiotics containing Lactobacillus, Bifidobacterium, and *Clostridium species* (Song *et al*., 2015; Nikpiran *et al.*, 2013). It has been reported that probiotics increase broiler growth rate more effectively than avilamycin (Zhang and Kim, 2014). It remains to be determined, though, if the probiotic treatment can be used in place of avilamycin in general. It was however observed that Japanese quails performed better when supplemented *Saccharomyces cerevisiae* (Zhang and Kim, 2014). The potential of probiotics, ranging from non-spore forming to spore formers and yeast, to increase growth rates in commercial poultry production during the course of a coccidiosis challenge has been evaluated by

Table 1. Contd.

S/n.	Trade name	Composition	Effect on coccidiosis	Reference
8	LactoFeed	*Lactobacillus acidophilus*, *Lactobacillus casei*, *Bifidobacterium thermophilum*, and *Enterococous faecium*	Enhanced broiler performance by altering the morphology and microbiota of the intestines.	Zarei *et al.,* 2017
9	Primalac®	*Lactobacillus sp*. organisms	Oocyst excretion was significantly reduced, according to the data.	Behnamifar *et al.,* 2019
10	PoultryStar® and Immucox I®	*Enterococcus faecium, Bifidobacterium animalis*, Pediococcus and Lactobacillus species, and coccidiosis vaccine containing *Eimeria acervulina*, *E. maxima*, *E. necatrix*, and *E. tenella* oocysts,	In addition to improving performance, a combination of probiotics and coccidiosis vaccinations may offer extra protection against a mixed Eimeria challenge.	Ritzi *et al.,* 2016
11	Biopellt-s	*Bacillus subtilis*, *Enterococcus Faecium* and Dextrose	Body weight increased significantly, whereas erythrogram and death rate did not alter significantly. The results of the biochemical analysis showed a nonsignificant change in the values of AST but a significant drop in the concentration of glucose and total cholesterol. Additionally, histological findings showed that probiotic feed supplements had a protective effect against intestinal and cecal coccidiosis.	Mokhbatly *et al.*, 2013
12	-	*Bacillus subtilis* strains; 2084, LSSAOl, and 15A-P4	The microbial community of vaccinated broilers fed the B. subtilis diet showed the largest percentage of Bacteroidetes and the lowest percentage of Firmicutes. They also showed the highest percentage of Rikenella microfusus. B. subtilis probiotics added to vaccinated broiler feed may lessen the variety of microorganisms found in the cecum.	Wang *et al.,* 2019
13	-	*Bacillus subtilis* 747	Following an infection with E. maxima, it reduced lesion scores. Growth performance, intestinal immunity, and epithelial barrier integrity were all markedly improved.	Park *et al.,* 2020
14	Primalac	Species of Lactobacillus	Decreased fecal oocyst shedding which is indicative of enhanced resistance. An impact on immunoregulation of the local immune system	Dalloul *et al.,* 2005
15	Saltose®	*bacillus licheniformis, Bacillus subtilis, Bacillus pumilus, Enterococcus faecalis, Enterococcus faecium*	Reduced the pathological modifications brought on by coccidiosis.	Belih *et al.,* 2015
16	-	*Enterococcus faecium, Bifidobacterium animalis, Lactobacillus reuteri, Bacillus subtilis*	The multi-species probiotic blend fed to chickens at both levels resulted in higher overall growth performance ($p<0.05$). The groups fed with Bacillus had greater villous height ($P<0.05$) than the infected controls. The group that received Lactobacillus supplementation exhibited the greatest ($p<0.05$) levels of Bifidobacterium and Lactobacillus in the ileum and caecum.	Giannenas *et al.*, 2012;
17	PoultryStar®	*Enterococcus faecium* #589, *Bifidobacterium animalis* #503 and *Lactobacillus salivarius* #505 at a ratio of 6:3:1.	Enhancement of intestinal health and growth performance. Lesion score values and oocyst quantities were lower in probiotic groups. Probiotic groups displayed the highest values of villous height.	Giannenas *et al.*, 2014

Table 1. Contd.

S/n.	Trade name	Composition	Effect on coccidiosis	Reference
18	Enroflorax®, Antox®	Enroflorax: *Enterococcus faecium, Lactobacillus casei, L. plantarum, Pedicoccus acidilactici.* Antox: *Saccharomyces cerevisiae*	The groups that received supplements had improved feed conversion ratios and they exhibited a significant ($p < 0.05$) decrease in oocyst discharge in their feces. The macroscopic lesions of the supplemented groups were similarly lower than those of the positive control. Histopathological investigation of the ceca revealed the supplemented groups had milder lesions as well.	Ogwiji *et al.,* 2022
19	Primalac	*Lactobacillus acidophilus, Lactobacillus casei, Enterococcus faecium*, and *Bifidobacterium bifidum*	The probiotics decreased the severity of mixed Eimeria spp.-induced coccidiosis lesions ($p < 0.01$). It also reduced growth depression brought on by the coccidial challenge.	Bozkurt *et al.,* 2014
20	Gro-2-Max®	*Pediococcus acidilactici, Pediococcus pentosaceus, Acetobacter aceti* and *Bacillus amyloliquefaciens.*	Enhanced the growth performance metrics (feed consumption, FCR, body weight, and body weight gain)	Elkhouly *et al*., 2016
21	Smart ProLive	*Pediococcus acidilactici* and *Bacillus subtilis*	Improvement of growth performance and intestinal health. Probiotic groups had decreased lesion score values and oocyst numbers. The probiotic groups showed the highest villous height values.	Erdogmus *et al*., 2019
22	MF	*Lactobacillus acidophilus* (LASW*), L. fermentum (*LF33), *L. plantarum* (LPL05) and *Enterococcus faecium* (TM39)	The Eimeria-infected chickens' cecal lesion scores (LS) might be considerably lowered by MF. Compared to the chickens in the infected group, the levels of cecal gene expression of anti-inflammatory cytokine, namely IL-10, were significantly greater. Proinflammatory cytokines, such as interleukin (IL)-1β, IL-6, and interferon (IFN)-γ, were found to be significantly lower.	Chen *et al.,* 2016
23	-	Bacillus-based direct-fed microbials (DFMs; eight single strains designated as Bs2084, LSSAO1, 3AP4, Bs18, 15AP4, 22CP1, Bs27, and Bs278, and one multiple-strain DFM product [AVICORR])	Elevated splenocyte mitogenesis infected broilers produced by concanavalin A. Infected chickens fed Bs27 had higher serum nitric oxide levels than those fed Bs2084, LSSAO1, 3AP4, or 15AP4. In chickens fed Bs27, 15AP4, LSSAO1, 3AP4, or Bs18, spleen cell proliferation was promoted by recombinant coccidial antigen (3-1E).	Lee *et al.,* 2010
24	Yeast Grow ® Bio Bird Grow ®	*S. cerevisiae.* *Lactobacillus salivarius* *L. johonsonii*	A significantly greater lymphoproliferative response ($p < 0.05$), greater geomean titers of antibodies, greatly enhanced FCR ($p < 0.05$) and significantly reduced oocyst numbers ($p < 0.05$). Furthermore, there was gain in daily weight that was significantly higher ($p < 0.05$), and greater protection against intestinal and caecal lesions.	Awais *et al.,* 2019
25	-	*Meyerozyma guilliermondii*	Oocysts significantly reduced	Dantán-Gonzalez *et al*., 2015
26	MitoMax ®	*Pediococcus acidilactici* and *Saccharomyces boulardii*	Strengthened humoral immunity in birds to increase their resistance to coccidiosis. The amount of oocysts shed decreased by 10–38% in chickens administered probiotics.	Lee *et al.,* 2007
27	-	*Lactobacillus acidophilus* (LASW), *L. fermentum* LF33), *L. plantarum* (LPL05) and *Enterococcus faecium* (TM39	They lowered the scores for cecal lesions, and were also helpful in reducing the inflammation and growth rate of broiler chickens affected by an Eimeria tenella infection.	Chih-Yuan *et al.*, 2016

Table 1. Contd.

28	-	*Bacillus subtilis*	Following *Eimeria spp*. infection, the intestinal lesion score and OPG were significantly lower in the VBS-CI group (P < 0.05). Furthermore, genera like Romboutsia, Blautia, and Butyricicoccus, as well as microbiota activities like the quorum sensing pathway, may also be strongly linked to these protective properties. These findings suggest that combining the *B. subtilis* and coccidiosis vaccines can enhance efficacy and offer supplementary defense against infection by *Eimeria spp*.	Cai *et al.,* 2022
29	-	*Lactobacillus plantarum*	Enhanced humoral and cell-mediated immunity. Improved serum chemistry (AST, ALT, and LDH) and the activity of tight junction proteins, peptide transporter 1, and antioxidant enzymes.	Mohsin *et al.,* 2022
30	P8 powder	*Lactobacillus plantarum* P8	Decreased oocyst shedding and mortality. enhanced gut barrier function and growth performance. Additionally, the damaged intestinal morphology was improved. In broilers infected with Eimeria, oxidative stress and pro-inflammatory responses were decreased. According to metagenomic study, P8 changed the gut microbiota's composition.	Wang *et al.,* 2021
31	Primalac	*Lactobacillus sp*	While lesion scores were lowered by all treatments, the probiotic alone or in conjunction with other feed supplements proved to be more successful in reducing oocyst shedding. It is possible that probiotics work better to improve humoral and cellular immune responses.	Taherpour *et al.*, 2012
32	-	*Lactobacillus species*	All Lactobacillus species isolates tested, significantly inhibited E. tenella invasion. Steric interference did not affect parasite invasion.	Tierney *et al.,* 2004
33	MitoGrow®	*Pediococcus acidilactici*	Every isolate of Lactobacillus species that was tested greatly reduced the invasion of *E. tenella*. Parasite invasion was not impacted by stem cell intervention.	Lee *et al.,* 2007b
34	Primalac	*Lactobacillus sp.*	The chickens fed probiotics exhibited higher intraepithelial lymphocytes expressing the surface markers CD3, CD4, CD8, and alphabetaTCR and produced fewer oocysts.	Dalloul *et al.,* 2003
35	Biomin	*Enterococcus faecium, Pediococcus acidilactici, Bifidobacterium animalis,* and *Lactobacillus reuteri.*	In every probiotic-treated group, there was a significant (P ≤ 0.05) increase in heterophil oxidative burst. The probiotic + vaccination treatment resulted in a larger (P < 0.05) monocyte oxidative burst. Probiotics may help with vaccination and have the ability to alter the immune response.	Stringfellow *et al*., 2011
36	Avicorr ®	*Bacillus subtilis*	Chickens fed the B. subtilis-enriched feed had considerably (p < 0.05) higher serum nitric oxide levels. Antibodies specific to Eimeria were considerably (p < 0.05) reduced in serum levels by B. subtilis.	Lee *et al.,* 2014

numerous studies around the world (Elkhouly *et al.*, 2016; El-Shall *et al*., 2024 Giannenas *et al.*, 2012; Bai *et al.*, 2013; Afsharmanesh and Sadaghi, 2014). A shift in the microbial communities in the gastrointestinal tract (GIT) which leads to an increase in the production of short-chain fatty acids (SCFA) and immunological regulation could be the cause of the performance differences between the supplemented and non-supplemented birds (Ogwiji *et al.*, 2022; Ney *et al.*, 2023). According to reports, probiotics increase the proliferation and size of intestinal cells and enteric villi in broiler chickens fed *Bacillus subtilis*-based probiotics (Samanya and Yamauchi, 2002; Markovic *et al.*, 2009), as well as the growth rates of the birds (Lei *et al.*, 2013; Afsharmanesh and Sadaghi, 2014). The absorptive capacity of birds is enhanced by larger enteric villi, and the crypts which play a role in the production or replacement of intestinal cells in response to inflammation or any enteric infection (Awad *et al.*, 2009). Increased feed intake (FI) and better feed utilization efficiency were also linked to the higher growth rate observed in the probiotic-supplemented birds (El-Shall *et al*., 2024; Zhang and Kim, 2014).

While probiotics are often promoted as beneficial for poultry health and performance, not all studies report significant improvements in performance and health outcomes in birds challenged with coccidiosis. For instance, Huang *et al.* (2019) found

Table 1. Contd.

37	-	*Bacillus subtilis,* *Bacillus licheniformis,* *Bacillus pumilus,* *Bacillus amyloliquefaciens*	At 6 and 10 days after infection, the Bacillus-fed groups had a 95%–100% better relative body weight growth. Lower lesion scores were observed. The Bacillus-fed group's overall oocyst counts were 10–20 times lower than those of the control group. At three days post-infection, the Bacillus-fed groups displayed distinct gene expression in the caecum, jejunum, and duodenum, among other tissues. Chickens given Bacillus exhibited notable pro- and anti-inflammatory reactions, as well as increased expression of TJ proteins and antioxidants in the ceca, duodenum, and jejunum.	Chaudhari *et al.*, 2020
38	-	recombinant *Lactobacillus plantarum* (co-expressing SO7 and DCpep gene)	Live recombinant L. plantarum immunization resulted in higher serum antibody responses and body weight gains in chickens. Based on lesion scores and histopathologic cecum sections, the immunized group showed significantly less pathological damage in the cecum and significantly less fecal oocyst shedding (p<0.01).	Yang *et al.,* 2017
39	-	*Bacillus subtilis*	In the challenged categories, Proteobacteria and Bacteroidota had the greatest reductions. The abundance of several commensal genera, including Clostridium sensu stricto 1, Corynebacterium, Enterococcus, Romboutsia, Subdoligranulum, Bacillus, Turicibacter, and Weissella, which play roles in butyrate production, anti-inflammation, metabolic reactions, and the modulation of protective pathways against pathogens, increased when probiotic supplements were added when Eimeria infection was present.	Memon *et al.,* 2022

little effect of probiotic supplementation on broiler growth. Abd El-Moneim *et al.* (2020) also observed that probiotic supplementation had minimal effects on immune response and growth performance in poultry production. Some studies have as well reported that probiotic supplementation does not significantly improve the body weight of birds infected with Eimeria parasites (Rahimi *et al.*, 2011; Wolfenden *et al.*, 2011; Khan *et al.*, 2019). Probiotic and prebiotic formulations have a protective impact, according to Abu-Akkada and Awad (2015), which lessened the harmful effects of coccidiosis but was not linked to a discernible improvement in growth performance. Nava *et al.* (2007) found that while probiotics helped in maintaining gut microbial balance, they did not significantly enhance immune responses or reduce lesion scores in chickens infected with *Eimeria tenella*. Similarly, Bai *et al.* (2013) found that in birds with coccidiosis, the use of probiotics had no significant (p<0.05) effects on weight gain, feed conversion ratio, or survival rates. They made clear that the timing and amount of probiotics taken could have an impact on the results, and that some strains of probiotics may be less effective than others in coccidiosis management.

According to research, there could be a variety of factors influencing how well probiotics work, including variations in the bacterial strains they contain, how they are prepared, and how much of them are taken (Patterson and Burkholder 2003; Mountzouris *et al.*, 2007). The physiological state of the bird, the actual microbiota already present in the gut, the dose and type of strains used for probiotics culture, the mode of administration, and the timing/duration of application in relation to pathogen challenge are additional factors that may contribute to the variability caused by probiotics (Brisbin *et al.*, 2011; Ajuwon, 2016; Huyghebaert *et al.*, 2011). It has been observed that co-supplementing with bacterial and yeast probiotics increases growth and survival rates (Amer and Khan, 2012). Probiotics that are exclusive to a particular species have more health benefits than those obtained from other host species, and multispecies probiotics (MSPB) are more effective than mono-species probiotics (Timmerman *et al.*, 2004; Timmerman *et al.*, 2005).

Application of probiotics in the management of poultry coccidiosis

Probiotics may be able to treat chicken coccidiosis, according to a number of scientific investigations (Ogwiji *et al.*, 2022; Elkhouly *et al.*, 2016). The optimum use for them is as a feed additive substitute for synthetic anticoccidial agents. In chicks infected with mixed Eimeria species, Poultry-Star®, a multi-species probiotic containing Bacillus, Lactobacillus, Enterococcus, and Pedicoccus, decreased lesion scores and oocyst shedding (Ritzi *et al.*, 2014). In broiler chicks that had been infected with *Eimeria tenella*, the anticoccidial impact of the probiotic Smart-ProLive® (containing *Pediococcus acidilactici* and

Bacillus subtilis) was assessed (Erdogmus*et al.*, 2019). The probiotic had a similar effect as using salinomycin in terms of feed conversion ratio and intestinal health.

A crucial factor in determining the extent of coccidiosis infection is lesion scoring (Bould *et al.*, 2009; Adamu *et al.*, 2013; Sharma *et al.*, 2015). In chickens with coccidiosis, the use of probiotic organisms has been shown to significantly reduce microscopic lesions (Ritzi *et al.*, 2014; Chen *et al.*, 2016). According to Ritzi *et al.* (2014), less intestinal lesion scores represent less harm and a higher likelihood of recovery for sick birds. According to Lee *et al.* (2010), after an *Eimeria maxima* challenge, birds that received a Bacillus-based direct-fed microbial supplement had significantly improved health outcomes. Broiler chickens were reported to have acquired immunity against Eimeria infection by adding Saccharomyces-based probiotics to their feed, which also increased geomean titers and prevented the production of intestinal lesions (Awais *et al.*, 2019). By causing damage to the oocysts' resistant structure and restricting their growth, the probiotic *Meyerozyma guilliermondii*, which was isolated from chickens, decreased the viability of *Eimeria tenella* oocysts (Dantan-Gonzalez *et al.*, 2015). When fed to coccidiosis challenged birds, the commercial probiotic Mitomax® (containing *Pediococcus acidilactici* and *Saccharomyces boulardii*) raised the level of antibodies against mixed Eimeria challenge in broiler chicks and reduced the amount of Eimeria oocysts shed in feces (Lee *et al.*, 2007a).

Furthermore, intestinal lesions and ulcers usually induced by *E. tenella* were considerably reduced in another study with a multi-strain probiotic combination containing lactic acid bacteria (*Lactobacillus acidophilus, L. fermentum, L. Planetarium*, and *Enterococcus faecium*) (Chih-Yuan *et al.*, 2016). In broiler chickens, dietary yeast cell walls decreased the amount of infection and oocyst shedding of a combination of *Eimeria acervulina, E. maxima*, and *E. tenella* (Elmusharaf *et al.*, 2007). Less damage to the intestinal epithelium is indicated by less severe lesion scores, which increases the likelihood that infected birds may recover from the disease. The efficacy of probiotics Fermacto®, which contains *Aspergillus orizae*, and Primalac®, which contains Lactobacillus, in preventing coccidiosis in broiler chicks was investigated by Behnamifar *et al.* (2019). The study found that probiotic supplements can improve performance and lessen the harmful consequences of a mixed Eimeria infection in chickens.

In addition, probiotic supplementation decreased the gross lesion severity in every intestinal segment assessed in the *in ovo* administration of PrimaLac®, indicating that this could be used as a technique to mitigate the detrimental consequences of coccidiosis (Cox and Dalloul, 2015). Also, better performance, carcass yield, and meat quality were observed in free-range broiler chickens that were given dietary probiotics, prebiotics, and coccidiosis vaccinations (Takahashi *et al.*, 2005). Probiotic supplementation has been shown in numerous studies to significantly reduce the number of other intestinal pathogens (Higgins *et al.*, 2007; Ghareeb *et al.*, 2012). This could be very advantageous for the bird, since certain microorganisms, like Salmonella and Clostridium, often exacerbate Eimeria infections and vice versa (Macdonald *et al.*, 2017). Studies have shown that probiotics may help prevent a variety of intestinal diseases, such as salmonellosis and necrotic enteritis, which frequently occur as secondary bacterial complications of coccidiosis (Jayaraman *et al.*, 2013; Tellez *et al.*, 2012; Al-Khalaifah, 2018).

Numerous studies have demonstrated excellent outcomes when probiotics and other coccidiosis control techniques are combined in poultry production. In one study, co-administration of the probiotic *Bacillus subtilis* with the coccidiosis vaccination improved the growth performance of broilers. In broilers challenged with *Eimeria sp*., the injection of the *B. subtilis* and coccidiosis vaccine reduced intestinal damage and faecal oocyst discharge (Cai *et al.*, 2022). Lower lesion scores and greater weight gains were the outcomes of the probiotic (Poultry Star®) and coccidiosis vaccine (Immucox I) administration, which improved their protective effect against the *Eimeria acervulina* and *E. maxima* challenge (Ritzi *et al*., 2016). According to Dersjant-Li *et al*. (2016), the intestinal damage and performance loss brought on by the Eimeria challenge were lessened by the combination of exogenous enzymes and probiotics which included *Bacillus species*. Probiotics in combination with anticoccidials, vaccinations, or even plant extracts have been shown to have a more pronounced effect (Chen *et al.*, 2016; Wang *et al.*, 2019). The resistance of the birds was increased and they receive partial protection against coccidiosis when probiotics are taken alone or in conjunction with prebiotics or butyric acid glycerides. Supplementing with probiotics may mitigate the negative effects of coccidiosis to a lesser extent than Salinomycin (Taherpour *et al.*, 2012).

Effect of dietary probiotic supplementation on immune response in poultry coccidiosis

The initial line of defence and source of instant protection against any incoming external challenge is the innate immune system, which is distinguished by its non-specific defence mechanisms (Yu *et al.*, 2021; Birhan, 2019). According to a number of studies (see Table 1), several probiotic strains can activate certain innate immune functions (Bhogoju and Nahashon 2022; Fong *et al.*, 2016; Dalloul *et al.*, 2005). By influencing gut-associated lymphoid tissue (GALT) and promoting the synthesis of immunoglobulins, probiotics improve the immune response. Probiotics have also been shown to raise secretory IgA levels in broiler intestines, which is crucial for mucosal immunity (Kabir *et al.*, 2004). The improvement of local immunity shields the birds against intestinal illnesses, which enhances their general well-being and productivity. Additionally, probiotics affect the immune system of birds as a whole. It has been found that probiotic-fed birds respond better to vaccinations and have higher levels of circulating antibodies (Mountzouris *et al.*, 2007). In light of this increased immune competence, fewer diseases occur, which lowers mortality rates and improves performance.

PrimaLac®, a commercial probiotic, modified gut bacterial populations and mucin production (Smirnov *et al.*, 2005). Additionally, it enhanced the quantity of goblet cells and mucus secreted in the small intestine of the turkey, shielding the intestinal epithelia against infections (Rahimi *et al.*, 2009). Also, probiotics have the power to modify how host cells express antimicrobial peptides. Akbari *et al.* (2008) discovered that probiotic (*Lactobacillus acidophilus*, Bifidum, and *Enterococcus faecalis*) supplementation decreased the expression of antimicrobial peptides in the caecal tonsils, including avian β-defensins (also called gallinacins) and cathelicidins. Coccidia were cultivated (*in vitro*) with the addition of spent culture supernatant (SCS) from both dead and living Lactobacilli. The SCS of the live bacterial group showed the greatest inhibition, suggesting that the lactic acid bacteria released the metabolite which was the anticoccidial component (Tierney *et al.*, 2004). The anti-coccidia action of *Lactobacillus rhamnosus* was demonstrated by the inhibition of oocyst sporulation in *E. acervulina*, *E. tenella*, and *E. maxima* oocysts exposed to its cell-free supernatant (which correlates to SCS) (Biggs and Parsons, 2008). Research has demonstrated that Lactobacillus salivarius generates antibacterial agents that effectively combat Brachyspira hyodysenteriae, Clostridium jejuni, C*. perfringens, Salmonella cholerae suis*, and *Escherichia coli* (Klose *et al.*, 2006).

Probiotic yeasts have been shown to regulate intestinal disorders by the release of antimicrobial peptides, the acidity of the surrounding environment, alteration of immunological and inflammatory responses, and disruption of virulence factors (Hatoum *et al.*, 2012). B-glucans and mannans, two components of yeast cell walls that act as immunomodulators, are linked to immune system modulation by promoting cellular and humoral immunological responses as well as local mucosal IgA production (Gómez-Verduzco *et al.*, 2009). Lee *et al.* (2007a) observed that a *P. acidilactici* based probiotic (MitoGrow®) supplementation increased the resistance of birds and provided partial protection against coccidiosis. There were more parasite-specific antibodies in the bloodstream of the *Eimeria tenella*-infected birds given *P. acidilactici.* According to Dalloul and Lillehoj (2005), broilers infected with *E. acervulina* exhibited enhanced resistance to infection when fed a diet containing Lactobacillus, which indicates it had an immunoregulatory effect on the local immune system.

Probiotic supplementation raises antibody titres against many major pathogens, including infectious bursal disease virus, and New Castle disease virus besides coccidiosis (Apata, 2008; Haghighi *et al.*, 2005; Kabir *et al.*, 2004; Karimi Torshizi *et al.*, 2010; Khaksefidi and Ghoorchi, 2006; Nayebpor *et al.*, 2007). Haghighi *et al.* (2006) found that probiotics (*Lactobacillus acidophilus*, *Bifidobacterium bifidum*, and *Streptococcus faecalis*) given orally to broiler females increased their natural antibody production. Allochthonous probiotics stimulate a robust immunological response in the host, but autochthonous probiotics cause minimal amounts of antibody production (Guo *et al.*, 2021). Numerous studies have demonstrated that chickens given probiotics increased their levels of immunoglobulins, to protect against a range of illnesses (Haghighi *et al.*, 2006; Viertlboeck and Göbel, 2008). Probiotic-treated chickens magnified the numbers of immunoglobulins such as IgG, Ig A, IgM against various disease conditions (Haghighi *et al.*, 2006; Viertlboeck and Göbel, 2008). Supplementing with probiotics has been shown to increase the amount of antibodies produced against *E. acervulina* (Lee *et al.*, 2007a, 2007b). The dynamics of probiotics and immunological responses, as reported by Kabir *et al.* (2004), showed that feeding broilers probiotics containing Lactobacillus increased the generation of antibodies in the birds. Likewise, the addition of MitoGrow® probiotic (*Pediococcus acidilactici*) to broiler chicken feed resulted in an increase in antibodies against Eimeria infection (Lee *et al.*, 2007b).

Supplementation of probiotics (*Lactobacillus sp*.) in a broiler diet revealed that probiotics could enhance intestinal immunity against coccidiosis by altering the population of intestinal intraepithelial lymphocytes (Abd El-Hack *et al.*, 2020). According to El-Shall *et al*. (2022), adding probiotics (*Lactobacillus sp.)* to broiler diets improved intestinal immunity against coccidiosis by changing the population of intestinal intraepithelial lymphocytes. Another study measured intestine intraepithelial lymphocyte numbers and coccidiosis protection after feeding a Lactobacillus-based probiotic to chicks. The chicks were challenged with *Eimeria acervulina* and given probiotic supplements in their diet. The results of the study showed that probiotics enhanced the local immune response, as evidenced by changes in lymphocyte subpopulations and a decrease in oocyst shedding (Dalloul *et al.*, 2003). Saccharomyces and Lactobacillus based probiotics improved the immunological response and performance metrics in broiler chickens challenged with Eimeria (Awais *et al.*, 2019). Broiler chickens' immunological response and tolerance to the *Eimeria tenella* challenge were greatly boosted by the use of Enroflorax®, which contains *Enterococcus faecium, Lactobacillus casei, L. plantarum*, *Pedicoccus acidilactici*, and Antox®, which contains *Saccharomyces cerevisiae* (Ogwiji *et al.*, 2022).

Probiotics can block pathogen establishment and colonization of the intestinal epithelium by enhancing early creation of a beneficial microbiota, increasing the protective effect and strengthening host tolerance to infection while lowering the requirement for preventative medication use (Patterson & Burkholder, 2003; Ritzi *et al.*, 2014; Rolfe, 2000). Also, by increasing the activity of lymphocytes found in the intestinal epithelial cells, probiotic use contributes significantly to the cellular immune response (Noujaim *et al.*, 2008). Additionally, probiotics have been shown to boost lymphocyte proliferation at the infection site, which boosts the cellular immune response and strengthens immunity against infections such as coccidiosis (Dalloul and Lillehoj, 2006; Viertlboeck and Gobel, 2008). It is believed that the avian heterophil is the mammalian neutrophil's counterpart. Heterophils are the initial line of defence for cells against microbial infections due to their high phagocytic activity and significance as effector cells in innate immunity. Heterophils employ oxidative burst and degranulation as defence mechanisms against phagocytosed pathogens (Harmon, 1998). According to Farnell *et al.* (2006), heterophils isolated from broiler chicks given probiotics containing *B. subtilis, Lactococcus lactis subsp. lactis,* and *L. acidophilus* induced an increase in the oxidative burst and degranulation of the heterophils. According to Stringfellow *et al.* (2011), there was a higher concentration of heterophil oxidative burst in the multispecies probiotic product PoultryStar®. According to research, chicken given probiotic supplements exhibit heterophilic behaviors such degranulation and oxidative burst (Ogwiji *et al.*, 2021).

As pathogen recognition receptors, members of the Toll-like receptor (TLR) family of proteins are highly conserved and recognize molecular patterns associated with microbes that are expressed on infectious agents. They are in charge of starting and controlling the innate response, as well as being essential in pathogen identification. TLR-2 and TLR-4 mRNA expression levels are elevated by probiotic-supplemented diets containing *Lactobacillus fermentum* and *Saccharomyces cerevisiae* (Bai *et al.*, 2013). By adversely influencing the synthesis of inflammatory cytokines and therefore changing the gut microbiota, *Eimeria sp.* suppress host immune responses to facilitate their invasion and colonization in hosts (Lu *et al.*, 2021). In chickens afflicted with the coccidia, *Bacillus subtilis* increased serum nitric oxide (NO) levels (Lee *et al.*, 2014). The activity of different immune cells is modulated by NO. For instance, NO have the ability to enhance macrophage activity, improving their capacity to phagocytize and eliminate Eimeria oocysts (El-Far and Abdou, 2014; Zhao *et al.*, 2021). By enhancing immunological elements that cause sporozoite escape before maturity, *Bacillus species* are able to eradicate Eimeria. Nitric oxide also prevents Eimeria from reproducing by causing sporozoites to escape before they mature (Yan *et al.*, 2021). When compared to fresh sporozoites, nitrate-induced sporozoites have vividly reduced invasive ability and reproductivity in chickens. Gram-positive pathogens like *Campylobacter coli*, *C. jejuni*, *Clostridium difficile*, *C. perfringens, Listeria monocytogenes, Micrococcus luteus, Staphylococcus aureus,* and *Streptococcus pneumoniae* are inhibited from colonizing as well by the antimicrobial factor produced by *Bacillus species* (Khochamit *et al.*, 2015). Feed containing *Bacillus licheniformis* significantly boosted the expression of JAM2 and IL-10 in Eimeria-infected chickens (Chaudhari *et al.*, 2020).

Finally, probiotics added to feed can help offset the negative effects of Eimeria infection on the intestinal health and growth of birds. According to Mohsin *et al.* (2022), probiotics are linked to increased activity of antioxidant enzymes, control of pro-inflammatory cytokines, and tight junctional proteins that protect the body from infections. Additionally, adding probiotics to poultry diets can improve the activity of digestive enzymes, boost the activity of good bacteria in the gastrointestinal system, and control humoral and cellular immunity (Memon *et al.*, 2022).

Conclusions

In conclusion, probiotics have emerged as potent anticoccidial agents, by exploiting the antagonistic relationship between pathogens and the gut microbiota. Given the growing concerns regarding drug residues in chicken products and the increased resistance of *Eimeria* species to conventional treatments, their diverse mechanisms of action make them viable substitutes for existing anticoccidial feed additives. Restoring the gut microbiota's equilibrium is possible using probiotics, and this is essential for preventing Eimeria from colonizing and developing in the intestinal lumen. In addition to improving growth performance and nutrient absorption, probiotics help to preserve gut health by reducing the degree of damage associated with coccidiosis and strengthening the integrity and structure of intestinal epithelia.

Furthermore, it has been demonstrated that probiotics enhance immunological modulation and increase resistance to Eimeria infections by stimulating both specific and nonspecific immune responses. Their role in coccidiosis control is further enhanced by their capacity to regulate the production of metabolites, such as short-chain fatty acids, which makes the environment unfriendly for pathogenic organisms. Thus, probiotics provide a safe and sustainable alternative to curb coccidiosis in poultry, supporting the industry's efforts to use fewer chemicals and antibiotics in animal production.

Therefore, adding probiotics to poultry management plans not only helps with coccidiosis but also promotes general gut health and productivity, opening the door to more sustainable and secure approaches to poultry production.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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