Chapter 17

Use of Prebiotic, Probiotic and Synbiotic Growth Promoters in the Modern Poultry Farming: An Updated Review

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ABSTRACT

One of the biggest and rapidly emerging global health challenges is antimicrobial resistance (AMR) which is included among the top ten priorities of the WHO. Several factors, such as the overuse, misuse, or underutilization of antibiotics in clinical settings, are associated with antibiotic resistance. Furthermore, overwhelming use of antibiotics is a major factor in the rise in antibiotic resistance in the environment and in foodborne pathogens. Probiotics, prebiotics, and synbiotics provide the most sustainable substitutes for antibiotics in these restrictive and difficult circumstances. Prebiotics combined with probiotics have a beneficial effect in terms of growth performance, carcass yield and intestinal morphology of the modern poultry farming, thereby avoiding the rising AMR.

KEYWORDS
Broilers, Non-antibiotic, Growth promoters, Antimicrobial resistance

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INTRODUCTION

The widespread use of antibiotic growth promoters in poultry reduces the intestinal pathogens but leads to the antibiotics residue in poultry products (Mathur and Singh, 2005), thereby increasing the incidence of AMR. Currently, researchers are in continuous search for an effective antibiotic substitute such as prebiotics, probiotics, acidifiers, and phenolic compounds (Baurhoo et al., 2009).

The medical use of antibiotics has been constantly increasing and their effectiveness against diseases is decreasing which results in widespread AMR. One of the major factors of AMR is the widespread use of antibiotics in cattle and poultry production. Therefore, to improve poultry performance and prevent and treat infections, it becomes necessary to discover alternatives to the usage of antibiotics such as probiotics, prebiotics, acidifiers, and phenolic compounds for poultry diet as growth promoter (Baurhoo et al., 2009). Use of antibiotics and probiotics resulted in better FCR in birds fed probiotics supplemented diet (Gao et al., 2017). Probiotics have better effect than salinomycin on production performance in broiler and as use of probiotic reduced the *E. Coli* (Ritzi et al., 2014). Probiotics has an impact on growth performance such that birds fed a diet containing protexin, primalac and calciparine had greater weight gain and improved FCR (Shabani et al., 2012). Probiotics had a beneficial effect on digestibility, performance and microflora composition (Mountzouris et al., 2010).

Probiotics are defined as "dietary supplements containing live microorganisms that positively impact the host organism through their advantageous effects linked to the enhancement of the microbial balance within the intestine." The performance of broilers is enhanced when probiotics are added to their diet. The livability of birds fed supply with *Lactobacillus spp*. or *Lactococcus lactis* was enhanced (Brzoska et al., 2012). Prebiotics are indigestible dietary supplements that particularly stimulate the growth or activity of one or more types of bacteria in the gastrointestinal tract and improving the health of the host (Hajati and Rezaei, 2010). Prebiotics are also thought to aid in the growth of chickens. Broilers fed a prebiotic-rich diet consumed more feed and had greater feed conversion rates (FCRs) (Kamran et al., 2013).

Prebiotics supplementation improved the breast and thigh yield (Piray et al., 2007) and reduced the cost of production in broiler diet (Peric et al., 2009).

Two naturally occurring functional polysaccharides with well acknowledged health-improving qualities are abundant in yeast cell walls: Oligosaccharides mannan and β-D-glucan. *Mannan oligosaccharides,* present on the outer layer of autolyzed yeast cell walls, bind harmful bacteria to stop them from colonizing the stomach, preventing infections and the release of toxins (Fowler et al., 2015). Mannan oligosaccharides also enhance gut health by improving the functional structure of the intestines (Ganner and Schatzmayr, 2012). Recent researches had focused on the importance of MOS to improve the microbial profiles, intestinal microarchitecture, production performance and humoral immunity in the broiler (Sohail et al., 2012).

The outermost layer of yeast (*Saccharomyces cerevisiae*) cell walls is the source of commercial mannan oligosaccharides, which are feed additives. Utilizing 0.05% MOS reduced *E. coli* and increased lactobacilli levels in the intestines of birds (Kim et al., 2011). Additionally, enzymatic hydrolysis of agricultural wastes like copra meal produces *mannan oligosaccharides*. (Ariandi and Meryandini, 2015).

Prevalent use of Antibiotics in Broiler Diet

Antibiotics are compounds with antibacterial properties that are being used in veterinary and human medicine to treat and prevent infections. They also work as growth boosters in animal feed. The physiological and metabolic capabilities of food-producing animals are compromised by antibiotics, which either eradicate or suppress the growth of bacteria and related microbes. Antibiotics come in two varieties: bactericidal and bacteriostatic. Antibiotics are bactericidal act by eradicating the microorganisms they are intended to combat. Antibiotics that are bacteriostatic stop the organism's cells from proliferating rather than killing it, maintaining a steady population level. These authors also mentioned that a lot of antibiotics function by attaching themselves to the enzymes' active sites, which makes the enzymes inactive. Thus, an antibiotic can halt essential cellular functions or prevent the production of new proteins during cell growth by blocking an enzyme (Phillip et al., 2004; Mathur and Singh, 2005).

The supplementation of 20g/ton of virginiamycin had improved weight gain than control diet. Likewise, bird fed with diet having 50 g/ton of narrow spectrum antibiotic BMD had higher weight gain. The supplementation of antibiotics had beneficial effect on growth performance. The addition of antibiotics in broiler diet increased weight gain. Intestinal length and weight were greater in birds fed with virginiamycin than bacitracin methylene disalicylate (Miles et al., 2006; Jian-mei et al., 2010).

Antibiotics have been extensively used in the livestock and poultry sectors during a period of fast management change from low-performance, free-range farming to a more controlled and intensive husbandry sector since their discovery more than 50 years ago. Certain antibiotics have been shown to suppress and restrict the growth of bacteria (*Clostridium perfringens*) that are known to be detrimental to chickens (Ferket et al., 2002).

Alternatives for Antibiotic use in Poultry

Reducing the use of antibiotics in human healthcare has been seriously considered due to the fear that antibiotics used in cattle and poultry production decrease their effectiveness. In nations that have discontinued utilizing antibiotic growth promoters, the prevalence of necrotic enteritis linked to Clostridium perfringens in poultry has increased (Immerseel et al., 2004). *Clostridium perfringens* is a significant food-borne pathogen that is thought to be responsible for 248,000 instances of food-borne disease in the US each year (Mead et al., 1999). Therefore, to improve poultry performance and prevent and treat infections, alternative methods to the usage of antibiotics must be found. Probiotic bacteria and organic acids have the potential to serve as viable substitutes for antibiotics in the growth stimulation and feed conversion efficiency enhancement of agricultural animals (Spring, 2003).

Use of Probiotics in Broiler Diet

Since the public's concern over antibacterial growth-promoting substances has grown and some farmers are choosing to use probiotics instead of antibiotics, the use of probiotics in the chicken business is of great interest (Jian-mei et al., 2010). Probiotics have been shown to improve newborn survival, reduce or prevent diarrhea, accelerate growth, improve feed efficiency, and strengthen the immune system as shown in Table 1 (Tollba et al., 2004).

Probiotics have a variety of advantageous effects, such as immuno-stimulation, the inhibition of enteric pathogens, and the preservation of a balanced gut microbiota (Tannock, 2004). Breeders supplementing their diet with probiotics saw increased egg production, decreased cracked eggs, and improved weight gain and feed conversion in their broiler chickens (Fuller, 1989).

Using a lactobacillus-based probiotic supplement for 42 days significantly improved the broiler's weight gain and food conversion ratio (Jin et al., 1988). When Bacillus subtilis was added, laying hens' eggshell thickness and feed conversion increased, which reduced the number of cracked eggs (Pedroso et al., 1999). It has been discovered that probiotics added to chicken feed increase egg weight, food conversion ratio, and egg output. Layers that were fed a meal containing 153g CP/kg of *Lactobacillus* produced larger eggs than those that were fed a diet that was comparable but did not contain *Lactobacillus* (Nahashon et al., 1996). The improved performance of chickens given probiotic supplements may be linked to changes in the microstructure of the gut, namely in the areas of villus height, goblet cell count, and crypt depth. Probiotics are therefore competitively priced, and their usage of antibiotic growth promoters makes them equally alluring as the growth promoters themselves. Probiotics may be beneficial for health in a number of ways, such as immuno-stimulation, anti-inflammatory responses, pathogen exclusion and death in the digestive system, and decreased bacterial contamination of processed broiler carcasses (Edens, 2003).

Probiotics lessen the incidence of enteric infections in chickens and the consequent contamination of poultry products (Patterson and Burkholder 2003). Antibiotics and probiotics increase the cecal microbiomes of broilers that increased Enterobacteriaceae and reduce *Brucellaceae, Erysipelotrichaceae, Coriobacteriaceae* and *Clostridiales* than those fed antibiotic (Neveling et al., 2017). Probiotics result in increased immunity and economic benefits (Gao et al., 2017).

Mode of Action of Probiotics

Being nonpathogenic and having the ability to stimulate the gut microbiota in their host are desirable qualities in a probiotic (Smith, 2014). This is significant because it establishes a symbiotic or commensal interaction. Commensal interactions describe the coexistence of nonpathogenic bacteria and their host, while clear advantages are not always evident. When two distinct species coexist peacefully and at least one of them gains benefits without harming the other, this is known as a symbiotic connection (Hooper and Gordon, 2001). For instance, oral *Lactobacillus plantarum* inoculation resulted in large quantities of immunoglobulin G specific to tetanus toxin fragment C, which triggered immune responses against the 6 produced antigen due to a symbiotic association (Shaw et al., 2000). Conversely, in patients with impaired immune systems, probiotics can occasionally result in infections and GIT disorders.

In the projected 45-day production phase, the GIT is critical to the health and growth of the birds. Gut associate microbial populations are very crucial for properly metabolic physiology of host. For example, probiotics or live Bacillus subtilis strains are being given to chickens to improve GIT physiology including duodenal IgA secretions and feed conversion ratio (FCR) (Sohail et al., 2012; Amerah et al., 2013).

Probiotics are thought to stimulate gut microbiota via a number of mechanisms, such as binding microbial specific receptors within the intestinal mucosa, competing microorganisms for nutrients, and producing antimicrobial agents to suppressing the growth of other microbial population (Hemarajata and Versalovic, 2013; Abd El-Moneim and Sabic, 2019; Abd El-Moneim et al., 2020). There are other possible pathways that probiotics can stimulate against pathogenic microbial populations such as lowering of pH, generation of organic acid and immune regulation of host (Sherman et al., 2009; Abd El-Moneim et al., 2020). They are also believed to be involved in maintaining the integrity of intestinal barrier and immunological tolerance that can negatively affect translocation of pathogenic microbes across intestinal defense (Lee and Bak, 2011). The mechanisms of probiotic action are illustrated in the Fig. 1.

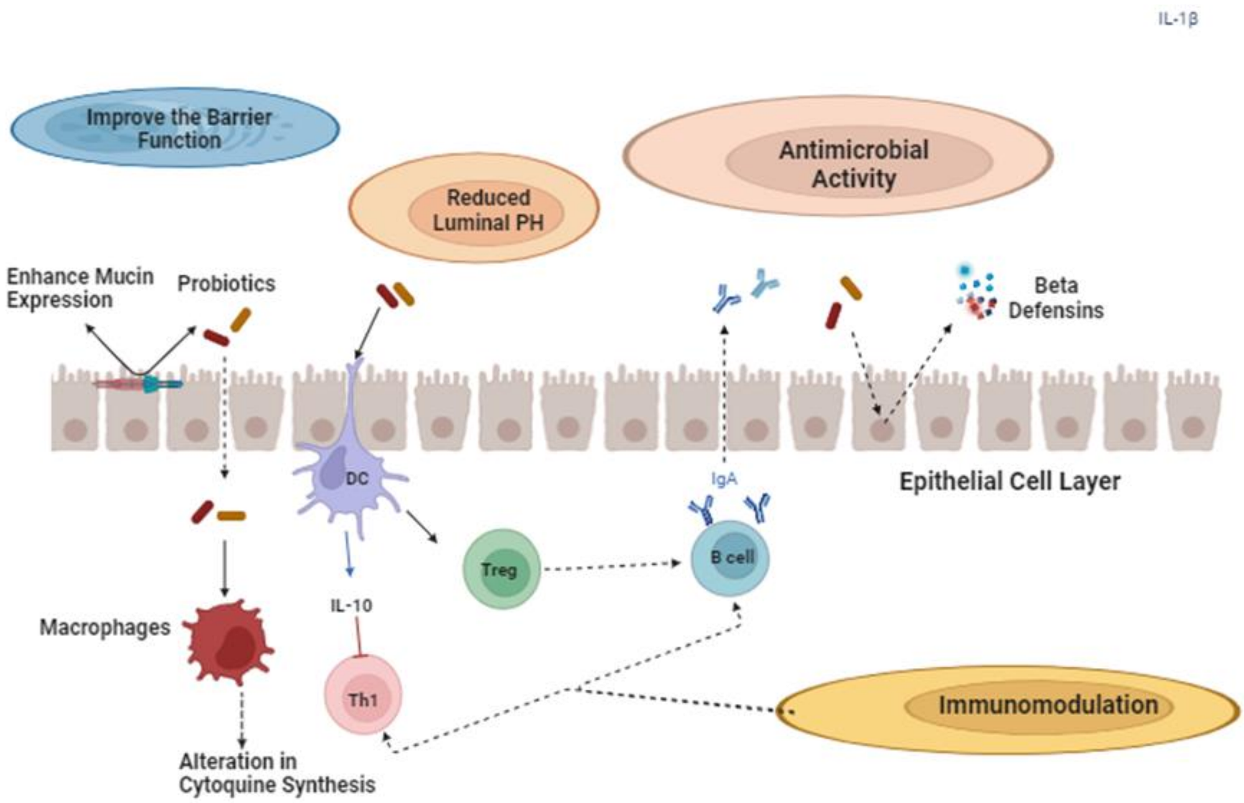

Fig. 1: Mechanism of action of probiotics in broiler diet for better performance and production showing immunomodulation, improved barrier function, antimicrobial activity and reduced luminal pH

Use of Prebiotics in Broiler Diet

Prebiotics are non-digestible food ingredients that specifically act as substrates for microbes (Swanson et al., 2020). The potential to optimize the effects of probiotics in prebiotic formulations is presented by the formation of new molecules upon the combination of prebiotics and probiotics in a single matrix (Cunningham et al., 2021). Lactulose, oligosaccharides (XOS), oligogalactose (GOS), inulin and oligofructose (FOS) are some of the most often occurring prebiotics in diets (Casarotti et al., 2018; Peng et al., 2020). Prebiotics added to meat products improve their nutritional content and affect the way different foods look on the technical side (Pogorzelska-Nowicka et al., 2018).

It has been demonstrated that oligosaccharides reduce the risk of illness, most likely by improving the digestion of some feed components and inhibiting the proliferation of pathogenic species. FOS and MOS are two common oligosaccharides found in animal diets. It has been demonstrated that the majority of prebiotics work to benefit the host by feeding the helpful bacteria while suppressing the pathogenic ones. Prebiotics appear to improve the intestinal bacterial balance in broilers by promoting the growth of nonpathogenic microorganisms and decreasing the colonization of bacteria like *Salmonella* and *E. coli* (Yusrizal and Chen, 2003; Chung and Day, 2004).

Prebiotic had similar effect in replacement to antibiotics in broiler in term of feed consumption and body weight gain (Alonge et al., 2017). Yeast cell wall had greater weight gain and better FCR (Fowler et al., 2015).

Antibiotics can be replaced with MOS without having an adverse effect on the growth performance of broilers (Kamran et al., 2013). Under a *Clostridium perfringens* challenge, dietary mannan oligosaccharide (MOS) at 0.05% can be added to broiler diets to protect them from antimicrobial growth boosters without compromising the broiler's ability to grow (Abudabos and Yehia 2013). Mannan oligosaccharide had similar effect on weight gain and FCR to antibiotics group (Eseceli et al., 2010).

Mannan oligosaccharide had no influence on carcass yield (Leblebicier and Aydoğan 2018). Prebiotic had improved the population of cecal microbiota, enhanced lactic acid producing bacteria and decreased *E. Coli* bacteria (Tayeri et al., 2018). *Bifidobacteria* concentrations are higher in birds fed with *mannan oligosaccharide* (Baurhoo et al., 2009). Further, mannan oligosaccharide improved microbial ecology and morphological development. It does not affect overall performance of birds (Leblebicier and Aydoğan 2018) which shows no influence on feeding behavior, weight gain, and FCR (Yalçinkaya et al., 2008).

Mode of Action of Prebiotics

Prebiotics can affect poultry directly by affecting host systems like immunological responses, or indirectly by changing the gut microbiota's fermentation patterns and composition. When prebiotics are fermented by gastrointestinal bacteria, short chain fatty acids are thought to be the main inhibitory mechanism against pathogens; however, other processes, such as interference with adhesion, may also take place. Prebiotics are linked to a wide range of processes and roles in the avian GIT microbiota, such as immune system interaction, GIT morphological modification, and competitive exclusion of pathogens (Ricke, 2018).

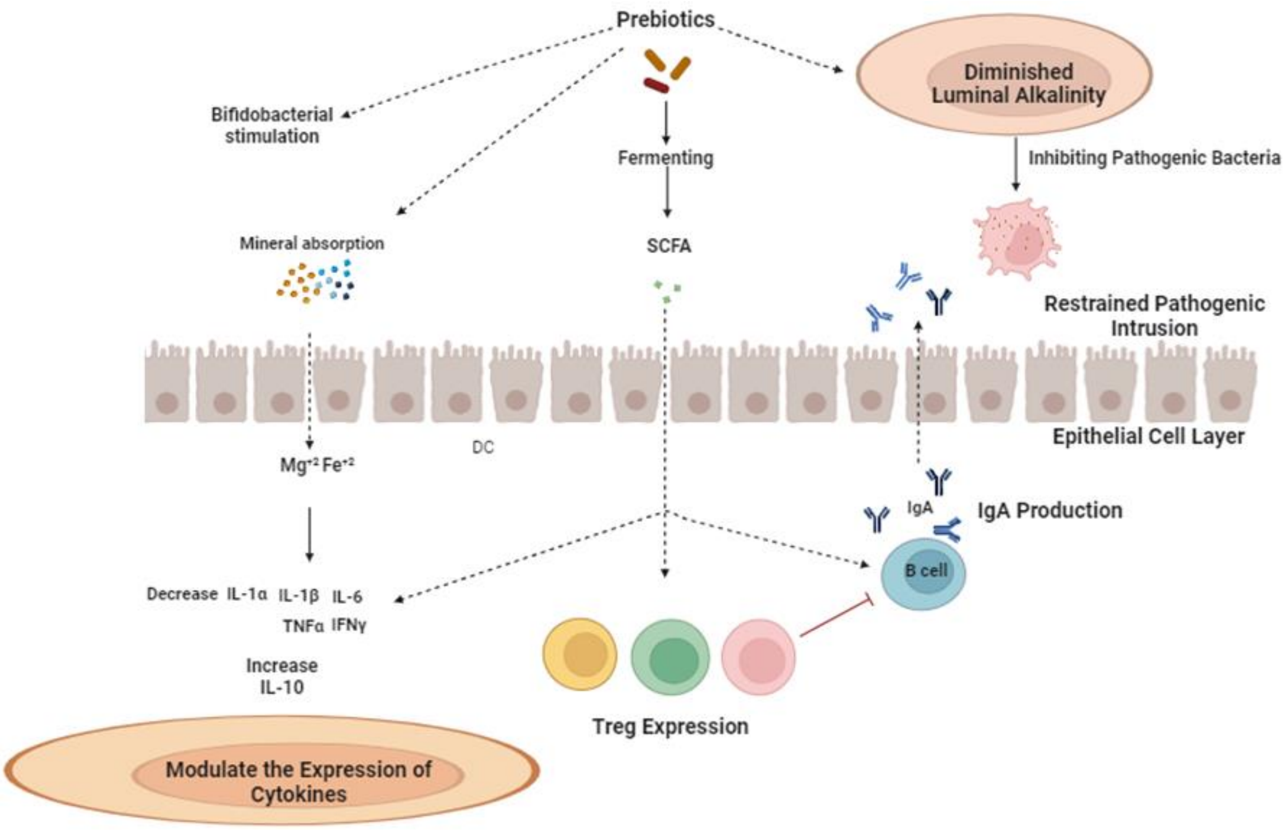

Fig. 2: Mode of action of prebiotics in improved poultry production by diminishing luminal alkalinity, IgA production, elevated mineral absorption, bifidobacterial stimulation and modulating the expression of cytokines.

Fructooligosaccharides (FOS) Role in Poultry Production

FOS, which are naturally occurring substances derived from a range of plants, have been added to chicken and swine feed as prebiotic additions. Their potential to enhance animal performance and health has been well investigated (Kumar and Pandey, 2020). They could be substituted for antibiotics at subtherapeutic concentrations. Furthermore, the broiler chicks fed diets supplemented with fructo oligosaccharides show a decreased incidence of intestinal colonization with Salmonella enteritidis compared to those on a control diet. It has been reported that female birds if treated with FOS can improve FCR, weight gain including carcass weight, and overall carcass percentage with longer small intestine (Shang et al., 2015; Yusrizal and Chen 2003).

Mannan Oligosaccharides (MOS)

Use of MOS improve body weight, feed conversion ratio and livability in broiler chickens to help to optimize gut health and bird performance as explained in Table 1 (Spring, 2003; Hooge, 2004). It gives enteric pathogens specialized binding sites (D-Mannose), which lessens the likelihood of the pathogens adhering to the intestinal system. According to Waldroup et al. (2003), there is no discernible impact on feed conversion or body weight. MOS was added to the diet eaten for 0-42 days and 42-56 days, respectively, at an 1g/kg and 0.75g/kg concentration. When MOS was added to broiler feeds, there was an improvement in feed conversion and body weight increase (Parks et al*.,* 2001). When compared to birds fed with control diet, the weight gain, feed conversion, and mortality of birds supplemented with MOS were dramatically enhanced (Hooge, 2004). The performance of the birds treated with MOS and those given antibiotic growth boosters was comparable, but the birds fed MOS had a reduced fatality rate. For chicken production to be lucrative and of excellent quality, gut health must be maintained (Parks et al., 2001). MOS has demonstrated potential in immune system modulation and intestinal pathogen suppression (Spring, 2003). When it came to preventing *Salmonella enteritidis* colonization in chicks, chickens fed with MOS or PKM had hen caecal contents (HCC) that were more efficient than hens fed control feed. In challenged three-day-old chicks, MOS decreased the concentration of *S. typhimurium* 29E and *S. dublin* (Fernandez et al*.,* 2002).

The Nutritional Benefits of Probiotics

The major way that prebiotic supplementation affects the host's nutrition is by its fermentation into short-chain fatty acids (SCFAs), primarily lactate and acetic, propionic, and butyric acids, in the hindgut. By passive diffusion, SCFAs are absorbed through the cecal epithelium and provide mature birds with up to 11% of their metabolizable energy. Since SCFAs lower intestinal pH and encourage protein and mineral solubilization, they may also increase the availability of these nutrients (Feng et al., 2005). Microbial prebiotic-mediated alterations affect the production of vitamins and nitrogen compounds, the breakdown of indigestible feed components, and the facilitation of the elimination of undesirable food components. Cecal microbes contain up to 5% of the genes involved in cofactor and vitamin production and 10% involved in protein and amino acid metabolism (Danzeisen et al., 2011). These genes could be used by the microbes themselves or by the host (Pan and Yu, 2014). Additionally, the grill metagenomics analysis revealed the presence of genes encoding lactase, cellulase, hemicellulase, and arabinoxylanse activity, supporting the microbial digestion of these indigestible food components for the generation of SCFAs as well as amylase and protease activity (Sergeant et al., 2014).

Effect of Prebiotic on Breeder, Broiler, and Layer Performance

MOS addition in the basal diet can improve the immune response in both broilers and layers that can also be analyzed by immune organ indexing (Raju and Devegowda, 2002). The ether extract content in breast muscle was lower with the herbs than with AGP, whereas the EE level in leg muscles was unaffected (Pisarski and Szkucik, 2007).

Prebiotics and BMD can be added to diets to boost growth and improve performance of birds, but better performance has been reported in control group if treated with herbes. The treatment group exhibited considerably higher live weight gain, survival rate, dressing percentage, and profitability in comparison to the control group (Shivakumar and Javed 2005). Consequently, the performance of birds leading to profitability can be enhanced by providing additional herbes as growth promoter.

Synbiotics

Nutritional supplements that combine probiotics and prebiotics in a synergistic manner are referred as synbiotics. The idea that a probiotic cannot thrive in the digestive system without its prebiotic substrate is the main justification for utilizing a synbiotic. The probiotic will be more sensitive to low pH, oxygen, and temperature if it does not receive the essential nutrition supply. Prebiotics maintain the colonies of these "good" bacteria by providing better circumstances for probiotics to grow. By taking both probiotics and prebiotics, one can see improvements in one's health state and an increase in the good bacteria in the digestive system. Synbiotics have these beneficial effects in two ways: (1) by enhancing probiotic viability and (2) by optimizing specific health benefits (Sekhon and Jairath, 2010). In commercial broilers, the combination of prebiotics and probiotics improved growth performance and carcass yield with simultaneous growth in intestinal morphology, as compared with antibiotic growth promoters (Ali et al., 2023).

Mechanism of Action

Prebiotics and probiotics combined (known as synbiotics) have a synergistic effect that enhances poultry health. They have the following benefits when added to broiler chicken feed; thicken the intestinal wall, boost resistance, boost the absorption of glucose, increase the levels of short chain fatty acids and lactic acid, reduce the concentration of branched chain fatty acids, encourage the growth of lymphoid tissue associated with the gut and enhance colonization of GALT by T and B cells (Jiang et al., 2022; Nguyen et al., 2022). Combination of prebiotic (MOS) and probiotic (*Bacillus subtilis*) fed to commercial broilers increased the dressing percentage, breast yield percentage and decreased FCR, thereby increasing the surface area for nutrient absorption by increasing villus height and villus area (Ali et al., 2023).

There are two varieties of synbiotics: synergistic and complementary synbiotics. Probiotics and prebiotics, of which more than one can be utilized, form complementary synbiotics. These microorganisms function separately to provide various health advantages. The live bacteria and a selectively fertilized substrate are the two parts of a synergistic synbiotic (Zubair, 2022)**.**

Table 1: Summarized effects of probiotics, prebiotics and synbiotics on birds

	Commonly used	Growth performance	Immune system	Gastrointestinal system	References
Probiotics	*Lactobacillus bulgaricus, Enterococcus faecium, Lactobacillus spp. Bacillus spp. Rhodopseudomonas palustris, Aspergillus oryzae, Candida pinpolopesi.*	Increased growth performance, improved FCR, Plasma cholesterol and triglyceride concentrations reduced Better meat composition, increased feed intake and better weight gain	Elevated Serum KLH-specific IgA, antibody response to ND virus, increased spleen and bursa relative weights.	Digestibility of fat and nitrogen, elevated ceaca microbiota, increased ileal and duodenal villus heights, Improved intestinal microbiota and gizzard weights, Decreased ammonia emission.	(Ricke et al., 2020, Rehman et al.,2020; Sheheta et al., 2022; Rashid et al., 2023)
Prebiotics	*Bacillus licheniformis and Bacillus subtilis,* Fructooligosaccharide and *Bacillus subtilis, Enterococcus faecium, Lactococcus lactis*	Increased growth performance, improved FCR, better weight gain	Improved immunity against salmonella, Development of central and peripheral lymphatic organs, improved gene expression regulation in spleen and ceacal tonsils	Increased ammonia concentration, Enhanced Caeca microbiota, Phenol and cresol decreased in caeca, Elevated acetic acid and butyric acid in caeca	(Ajuwon, K.M., 2016; krysiak et al., 2021; Wu et al., 2022)
Synbiotics	Oligosaccharides, Galactooligosaccharides, Insulin, Sucrose thermal oligosaccharides	Increased weight gain, FCR, feed intake, dressing percentage, carcass, wing, breast, back, thigh, and drumstick percentages, Improved heart, liver and gizzard weights	Development of peripheral and central lymphatic organs, Improvement in gene expression regulation in spleen, GALT development	Increased villus length to crypt depth ratio in the jejunal mucosa, improved villus heights	(Jha et al., 2020; Yaqoob et al., 2021; Khomayezi and Adewole, 2022; Rashid et al., 2023)

Conclusion

From the above discussion, it is concluded that the addition of prebiotics, probiotics, synbiotics or their combination (replacing antibiotics) reduces the risk of AMR. Furthermore, it has a beneficial effect on the poultry in terms of growth performance, carcass yield and intestinal morphology, leading to higher profitability. However, much research is still needed to fully understand the mechanisms involved to maximize the health benefits of probiotics, prebiotics and synbiotics on poultry health and production.

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