Department of Animal Science

ANTIBIOTIC ALTERNATIVES IN BROILER PRODUCTION: FEED ADDITIVES

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Poultry production represents one of the largest food industries in the world (Chowdhury and Morey, 2019). Broiler production, in particular, has shown exponential growth in recent decades, possibly because of its comparative advantages in many areas including high quality nutrition, low cost of production, low fat content, appealing taste, short production interval and affordable price. Antibiotics have been used for several decades to enhance broiler production, promote growth performance and protect birds from various pathogens. Despite the importance of antibiotics in livestock farming, improper use has been reported to increase antimicrobial resistance, result in residues in some animal products and cause environmental pollution (Christy et al., 2018; Gonzales et al., 2017). As a result, numerous attempts are being made to replace antibiotics with alternatives such as prebiotics, probiotics, toxin binders, phytogenics, enzymes, oligosaccharides, synbiotics, organic minerals, organic acids and other feed additives (Hashemi and Davoodi, 2011). These alternatives do not lead to deleterious disturbances of the gut flora, are not absorbed from the gut into tissue and do not cause drug resistances (Alghirani et al., 2021a). These feed additives also can enhance performance and have little therapeutic use in veterinary medicine (Alghirani et al., 2021b).

Feed additives

Feed additives are nonnutritive natural products added to the basal diet as minor components of the diet to improve feed quality and food from animal origins and to improve animal performance and health (Ayalew et al., 2022). In addition, they promote ingestion, absorption, nutrient assimilation and growth of animals by affecting physiological processes such as immune function and stress resistance (Jet and Florrencia, 2021). It has been reported that feed additives could be used as antibiotic alternatives in broilers to reduce mortality rates and enhance performance without jeopardizing the environment and consumer health (Medhi et al., 2018). Numerous feed additives have been tested on poultry, particularly the phytogenic feed additive groups, which include essential oils, herbal extracts, organic acids and others such as probiotics, prebiotics and enzymes. Humans have used plant products to naturally treat ailments for centuries (Alghirani et al., 2021b). Plant products were also used in animal feed in early cultures

(Hashemi and Davoodi, 2011). Interest in using phytogenic feed additives has increased in recent years as the poultry industry has shifted to more antibiotic-free and “No Antibiotics Ever” (NAE) production programs. Of 422,000 types of flowering plants, about 50,000 are used for medicinal purposes around the world (El Aziz et al., 2019).

Phytogenics

Phytogenic feed additives (PFAs) are plant-origin extracted compounds that are, according to Madhupriya et al. (2018), natural, less toxic, residue-free feed additives compared with synthetic antibiotics and include a wide range of substances (herbs, spices, essential oils, oleoresins and botanicals). Typical examples of phytogenic feed additives include rosemary derivatives, oregano, thyme, sage, garlic, horseradish, clove, cinnamon, citrus, chili, cayenne, pepper, peppermint and anise (Mountzouris, 2016; Madhupriya et al., 2018). An increasing body of evidence supports that supplementation of phytogenic feed additives in broiler diets improve intestinal functions (Platel and Srinivasan, 2004; Wati et al., 2015), increase nitrogen retention and fiber digestibility, enhance growth performance (Tazi et al., 2014), reduce inflammation (Frankic et al., 2009), and improve antioxidative (Suganya et al., 2016; Cuppett and Hall, 1998) and antimicrobial activities (Jarriyawattanachaikul et al., 2016). Taken together, these results seem to indicate that PFAs have beneficial effects to improve performance and broiler health.

A wide range of plants and their products fall under the PFA category, and, based on their origin, they can be classified as herbs (flowering, non-woody, non-persistent plants from which leaves and flowers are used) or spices (non-leaf parts of plants, including seeds, fruits, bark or roots with an intensive taste or smell) (Windisch et al., 2008; Van Der Klis and Vinyeta-Punti, 2014). They can be used in solid, dried or ground form or as extracts (either crude or concentrated) (Gadde et al., 2017). Essential oils are any class of volatile oils obtained from plants that possess the odor and other characteristic properties of plants and are used chiefly in the manufacture of perfumes, flavors and pharmaceuticals (Suganya et al., 2016). Several plant extracts have proven to have beneficial properties on growth performance, and, through a carryover effect, on improved carcass characteristics and meat quality, along with immune responses in poultry (Alghirani et al., 2021b). The primary bioactive compounds of the PFAs are polyphenols, and their composition and concentration vary according to the plant, parts of the plant used, geographical origin, harvesting season, environmental factors, storage conditions, and processing techniques (Windisch et al., 2008; Applegate et al., 2010).

Numerous plant-based compounds are widely used today as alternatives to antibiotic growth promoters in poultry diets because of their ability against certain bacterial infections (Khaksar et al., 2012; Dhama et al., 2015; Karangiya et al., 2016). For example, cinnamon oil can limit and control the growth and colonization of several bacteria in the intestines by unsealing and disrupting their cell membranes, leading to the disintegration of the cells (Mehdipour and Afsharmanesh, 2018). Cinnamaldehyde from cinnamon oil can be used to balance the microbial population in poultry to enhance their intestinal health because they can selectively inhibit the growth of commensal and pathogenic intestinal bacteria (Reis et al., 2018). A wide variety of herbs and spices (e.g., thyme, oregano, rosemary, marjoram, yarrow, garlic, ginger, green tea, black cumin, coriander and cinnamon) have been used in poultry diets in recent years for their potential application as antibiotic alternatives. In contrast, several other PFAs such as grape pomace, cranberry fruit extract, *Macleaya cordata* extract, garlic powder, grape seed extract and yucca extract tested as growth promoters did not show and effects on performance parameters (Gadde et al., 2017).

Organic acids

Organic acids have been used in animal feeds for several years because of the ban on the use of antibiotics and are considered effective antibiotic alternatives. Organic acids are weak acids that have a carboxylic acid group (R-COOH), nutritional values and antimicrobial effects in animal feed (Peng et al., 2014; French, 2017; Chahardoli et al., 2020). Inclusion of organic acids in broiler diets has been shown to improve protein and carbohydrate digestibility (Adil et al., 2010), fight against pathogenic bacteria, and enhance the feed conversion rate, nutrient utilization and growth rate of broilers (Hassan et al., 2010); Qaisrani et al., 2015). The most commonly used organic acids in broiler diets are acetic, butyric, citric, formic, lactic, malic, propionic and tartaric acids.

Diets that lack high protein quality have more indigestible proteins reaching the gastrointestinal tract (GIT), resulting in high protein fermentation (Diether and Willing, 2019). This causes discomfort to the animal and negatively affects growth rate because of high-volatile fatty acids and production of ammonia and other gases (Bikker et al., 2007). Organic acids help to acidify the GIT environment and improve nutrient utilization (Partanen and Morz, 1999). They suppress pathogenic intestinal bacteria due to their antimicrobial activity, resulting in less bacterial competition for available nutrients, lower levels of harmful bacterial metabolites, improved protein and energy digestibility, and improved avian performance (Baurhoo et al., 2007). Organic acid supplementation affects the histological structure of the GIT, resulting in increased villus length; improving the absorptive ability of the intestinal mucosa, which leads to better nutrient absorption; maximizing nutrient utilization; and improving growth performance (Abd El-Hack et al., 2022). Like other antibiotic alternatives, despite the demonstrated beneficial effects, using organic acids to improve performance lacks consistent results. This can be attributed to various factors including inclusion rates, source of the organic acids and the buffering capacity of other dietary nutrients (Dibner and Buttin, 2002; Kim et al., 2015).

Enzymes

Feed enzymes are used to improve feed efficiency, reduce feed cost and create a better environment by reducing the volume of manure produced and phosphorus and nitrogen content excreted (Barletta, 2010). Enzymes are biological catalysts that can speed up chemical reactions. All animals use enzymes to digest feed and supplementing the feed with particular enzymes improves the nutritional value of feed ingredients, increasing digestion efficiency (Llamas-Moya et al., 2019). Enzymes are not new to poultry production and research regarding enzymes in poultry diets has been ongoing since the 1920s (Abd El-Hack et al., 2022). The addition of exogenous enzymes has become the standard to improve digestibility and efficiency of nutrient utilization (Ravindran, 2013) and are essential to the reduction of feed costs. When the price of feed ingredients increases, the use of enzymes in the feed becomes even more economically attractive and provides a more significant return on investment (Barletta, 2010).

Phytase is one of the most important enzymes added to poultry feed. Poultry require dietary phosphorus (P) for maintenance and growth and an adequate amount must be included in the diet. However, a portion of total P in the diet comes from cereal grains and this P is in a form that poultry cannot digest. The majority of P, about 60 percent, is not accessible to nonruminants because it is associated with phytate. Phytate binds to many dietary cations resulting in serious reductions in nutrient availability (Bohn et al., 2008). Phytase is an enzyme that hydrolyzes phytate to inositol and inorganic phosphate (Bilal et al., 2015), making P more available. Hydrolytic enzymes have emerged as feed supplements to improve digestion and absorption of poorly available nutrients, such as dietary phytate (Barletta, 2010).

Synbiotics

Synbiotics are feed additives that combine the use of prebiotics and probiotics for a synergistic effect (Alloui et al., 2013). Few research trials have been conducted to demonstrate the effects of synbiotics on broiler performance, but their use is based on the concept that a mixture of prebiotics and probiotics beneficially affect the host by improving the survival and implantation of probiotic organisms and by selectively promoting the growth or metabolism of beneficial bacteria in the intestinal tract (Gibson and Roberfroid, 1995). Like other antibiotic alternatives, the results when using synbiotics have been somewhat inconsistent. Some trials have shown significant improvement in performance (Awad et al., 2009), while others have shown no difference in performance (Willis et al., 2007). However, synbiotics have been shown to beneficially alter the intestinal microbiota composition and increase villi height and crypt depth in the intestinal mucosa (Jung et al., 2008; Sohail et al., 2012). Therefore, much potential exists for using synbiotics in the future as antibiotic alternatives for improving performance and reducing pathogenic load in the intestines of poultry (Gadde et al., 2017).

Prebiotics

Prebiotics are macromolecules that are either derived from plants or synthesized by microorganisms. A variety of non-starch polysaccharides (NSP) or oligosaccharides have been considered as prebiotics, including mannan oligosaccharide (MOS), fructooligosaccharide (FOS), inulin, oligofructose, galactooligosaccharide, maltooligosaccharide, lactulose, lactitol, glucooligosaccharide, xylooligosaccharide, soya-oligosaccharide, isomaltooligosaccharide (IOS), and pyrodextrins (Patterson and Burkholder, 2003). Mannan oligosaccharide, perhaps the most well-known prebiotic, is derived from the outer cell-wall layer of *Saccharomyces cerevisiae* and has been extensively studied as a prebiotic in poultry diets with favorable results. However, several characteristics should be considered when selecting a prebiotic, including resistance to a gastric acid environment, intestinal/pancreatic enzyme hydrolysis, and absorption across intestinal epithelium (Hume, 2011; Heo et al., 2013; Ricke, 2015). The fermentation of prebiotics by microflora also leads to the production of short-chain fatty acids that act as an energy source for intestinal epithelial cells and thus maintain the integrity of the gut lining (Ferket et al., 2005).

Probiotics

Probiotics, also known as direct-fed microbials (DFMs), like many other antibiotic alternatives, have gained greater acceptance as more integrators have adopted antibiotic-free production programs. Probiotics may contain one or more strains of microorganisms and may be given either alone or in combination with other additives in the feed or water (Thomke and Elwinger, 1998). Numerous bacteria (*Bacillus, Bifidobacterium, Enterococcus, Lactobacillus, Lactococcus* spp. and *Streptococcus*) and yeast (*Saccharomyces* spp.) have been investigated as probiotics in poultry with, for the most part, promising results. The majority of the research tested the effects of probiotics in reducing the numbers of pathogenic microorganisms in the GIT, although considerable research examined the effects of probiotics on improving growth and performance in poultry without disease (Gadde et al., 2017). While numerous reports indicate performance improvements in poultry (broilers, layers and turkeys), some reports show limited or no growth-promoting effects. Possible explanations for this inconsistency could be related to differences in the type and dose of the strain used, processing variations, administration time and period, diet and the environment.

Not every probiotic strain is an ideal probiotic organism that can withstand processing and storage, survive in the gastric acid environment of the intestinal tract, adhere to epithelium or mucus in the intestines, produce antimicrobial compounds and modulate immune responses (Edens, 2003; Patterson and Burkholder, 2003; Cheng et al., 2014). Therefore, careful consideration is necessary when selecting individual strains or combinations that will produce maximum beneficial effect *in vivo*.

Heavy metals

Heavy metals such as iron, manganese, copper, zinc and selenium play a vital role in growth and metabolism and are critical for many digestive, physiological and biosynthetic processes (Richards et al., 2010; Attia et al., 2012). In the past, heavy metals have been supplemented in animal diets in the form of organic salts such as carbonates, chlorides, oxides and sulfates (Pierce et al., 2009; Attia et al., 2012), although chelated or organic forms have also been used recently. The movement away from antibiotics and the increase in antibiotic alternative programs have seen the use of trace minerals to increase animal productivity and performance gain importance in recent years, and they are being substituted at levels beyond the recommended nutritional requirements (Gadde et al., 2017). However, the use of metals in excess amounts raises environmental concerns in terms of their accumulation in soil and surface water (Burrell et al., 2004). In addition, excess use of metals has been shown to develop metal resistance concomitant cross-resistance to antibiotics among enteric bacteria in farm animals (Yazdankhah et al., 2014).

Additional antibiotic alternatives such as hyperimmune egg yolk antibodies, bacteriophages, antimicrobial peptides and clay minerals are also receiving attention and are being researched. A variety of alternative products coupled with good flock husbandry practices may eventually be able to replace a substantial portion of antibiotic use for disease prevention and growth promotion purposes, but this will require a comprehensive approach that considers antibiotic alternatives and best management practices as critical parts of a broader, overall flock health management program.

Summary

There is an increasing need for the development of antibiotic alternatives that can help improve performance and maintain optimal health of food-producing animals. This is related to the rise in consumer demand for livestock products from antibiotic-free or NAE production systems. The recent ban on certain antibiotics in the feed has promoted increased use of phytogenics, organic acids, enzymes, synbiotics, prebiotics, probiotics, heavy metals and other alternatives in broiler production. The primary effects provided by these alternative feed additives include enhanced digestion, improved nutrient availability, increased absorbability of nutrients, antioxidant activity, enhancement of gut integrity, improved intestinal health and modulating the host gut microflora. These differing modes of action indicate the possibility of symbiotic, antagonistic, synergistic or even combative effects between alternatives or other feed ingredients. In addition, even though the beneficial effects of many of the alternatives tested have been well documented, there is a general consensus that these products lack consistency, as results often vary greatly from farm to farm, complex to complex and company to company. Care should be taken in the selection of alternatives or their combinations, such that they match the needs of individual production programs. Matching the correct alternative (or perhaps combination of alternatives) to the need, along with sound management practices, will be necessary to maximize performance, maintain productivity and reduce antibiotic use in the poultry industry.

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