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ANTIBIOTICS RESISTANCE IN POULTRY AND ITS SOLUTION

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ABSTRACT

The poultry sector has grown quickly over the past three decades. This has led to increased use of antibiotics as both medicinal and growth-promoting drugs. Concerns about the emergence of antibiotic resistance in bacterial populations, the presence of antibiotic residues in poultry products, and the increasing consumer demand for products free of antibiotic residues have accelerated the search for alternatives that could replace antibiotics without causing a loss in productivity or product quality. These alternatives to antibiotics in chicken include the use of organic acids, probiotic microorganisms, prebiotic substrates that encourage the establishment of beneficial bacterial populations, or symbiotic (combinations of prebiotics and probiotics), which boost production and maintain bird health. Phytobiotics, antimicrobial peptides, herbal medications, vitamins and minerals, and plant extracts are more examples. Probiotic organisms compete with pathogenic organisms for colonization sites in the gastrointestinal tract, redirect fewer nutrients to harmful microorganisms and the toxins they produce, and stimulate the immune system. Prebiotics also present an option since they change the immune system and intestinal microorganisms to prevent pathogens from colonizing the gut and to promote the growth of healthy microflora. However, further research is required to select probiotic, prebiotic, or synbiotics either alone or in combination that can result in the selection of strains capable of functioning well in the gastrointestinal system. Using synbiotics is still a preferable method for improving poultry production. Researchers can utilize the information in this review to further their understanding of antibiotic alternatives for poultry birds without sacrificing the welfare or performance of the birds.

INTRODUCTION

The poultry business has experienced unprecedented expansion over the past three decades and is currently acknowledged as one of the agricultural sector's fastest-growing subsectors. This has occurred as a result of an increase in the consumption of eggs and meat due to their accessibility, affordability, and abundance in necessary nutrients that can make up for dietary deficiencies in important minerals, vitamins, and amino acids (Dhama et al., 2014a). The genetic potential of the birds, the availability of high-quality feed, the provision of ideal environmental conditions, and the prevention of disease outbreaks have all benefited from the utilization of high growth contributing elements. Since this is where most nutrient intake occurs, intensive research has been done recently on poultry bird gut health in an effort to increase output (Rinttila & Apajalahti, 2013). Next to the skin, the gastrointestinal system is the organ most frequently exposed to environmental infections (Yegani & Korver, 2008). Therefore, maintaining good gut health and function is crucial for poultry production to ensure proper health and output. The general health and performance of birds will be hampered due to poor gut function and health, which also affects nutrient digestion and absorption, ultimately affecting the economics of chicken production. Due to their widespread availability and low cost, antibiotics are frequently utilized in the production of chicken around the world. By enhancing gut health and lowering subclinical infections, it has transformed the intensive poultry industry to enhance growth, productivity, and feed conversion efficiency. Inclusion of antibiotics at low concentrations improves gut health by lowering the pathogen load and aids in the prevention of subclinical illness, which is typically ongoing in birds even in well-run poultry facilities. The thickening of the intestine, which increases food absorption, is one of the positive benefits of administering antibiotics. Thus, by lessening host and pathogen rivalry and minimizing microbial adherence and invasion to the gut wall, it can preserve the host's vital nutrients. It also reduces the generation of poisonous amines, which prevents stress in birds. The effect of antibiotics is more obvious in birds kept in unclean conditions and fed a diet that is relatively low in vitamins and/or amino acids, which clearly shows the antibiotics' nutrient-sparing effect. The first antibiotic to be used in veterinary medicine was penicillin G, which was initially made available in 1947 for intramammary infusions. Since then, regulating animal health in agriculture has become impossible without the use of antibiotics. Food animals, especially chickens, are given antibiotics by a variety of ways, including injections, orally in feed, and intravenously in water. Chlortetracycline, furazolidones, fluroroquinolones, oxytetracycline, sulphonamides, gentamicin, and quinolones are frequently used antibiotics for both preventative and therapeutic purposes in poultry (Athar & Ahmad, 1996; Kodimalar et al., 2014; Anderson & Macgowan, 2003; Luangtongkum et al., 2006; Martinez e (Naeem et al., 2006). The use of antibiotics in chicken is being questioned despite their enormously favorable effects due to the rise in antibiotic resistance (Tiwari et al., 2014a). When an antibiotic is administered to a food animal at a dose below what is considered therapeutic, the sensitive population of bacteria is eradicated, leaving only the varieties with peculiar characteristics that are resistant to the effect. Then, as they proliferate and become the dominating bacteria. Through mutation or plasmid-mediated transfer, the resistant population so created passes on the genetically specified resistance to succeeding offspring as well as to other bacterial strains (Catry et al., 2003). Through the consumption and handling of meat contaminated with these infections, humans may come into contact with a population of such resistant bacteria (Van den Bogaard & Stobberingh, 2000). Once acquired, these bacteria can colonize a person's digestive tract and spread the genes that cause antibiotic resistance to other bacteria in a person's endogenous microflora, making it more difficult to treat bacterial infections effectively (Ratcliff, 2000; Stanton, 2013). There has been a major drive to identify alternative treatment options for common chicken diseases because of the drug resistance linked to the use of antibiotics in poultry production. By suppressing infections and enhancing nutritional digestion and absorption, antibiotic alternatives are required to maintain the gut's health and functionality. Utilizing whole grain cereals, live microbial cultures, fermentable sugars, and feed processing/sterilization are a few strategies to reduce the use of antibiotics in chicken. Organic acids, probiotics, prebiotics, synbiotics, herbal medicines, vitamins, minerals, and plant extracts (essential oils), among others, are notable substitutes in the production of poultry (Dhama et al., 2014a). The following are the qualities of alternatives:

1. It should significantly boost performance.
2. It shouldn't be used much as a therapeutic tool in either human or veterinary medicine.
3. It shouldn't harm the healthy gut flora in any negative ways.
4. It shouldn't contribute to the spread of drug resistance.
5. It shouldn't result in cross-resistance to other antibiotics at levels of actual use.
6. It shouldn't be absorbed from the intestines into edible tissue.
7. It shouldn't encourage the shedding of Salmonella.
8. It must not be carcinogenic or mutagenic
9. It should be easily biodegradable
10. It shouldn't cause environmental pollution
11. 11. Neither the birds nor the people who handle it should be poisoned.

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However, more research is required to select probiotic, prebiotic, or synbiotics either alone or in combination that can result in the selection of strain/s capable of performing effectively in the gastrointestinal tract. Even combined supplementation of prebiotics and probiotics, known as synbiotics, is a better strategy for enhancing production. The current research highlights beneficial antibiotic alternatives for chicken production systems, such as organic acids, probiotics, prebiotics, synbiotics, vitamins, and minerals, as well as herbal medicines, plant extracts, phytobiotics, and antimicrobial peptides. Researchers can utilize the review's information to carry out additional study on antibiotic alternatives for poultry birds without sacrificing the animals' welfare or performance.

METHOD RESEARCH

The research method used in this study is a qualitative descriptive method. The type of data used in this study is qualitative data, which is categorized into two types, namely primary data and secondary data. Sources of data obtained through library research techniques (library study) which refers to sources available both online and offline such as: scientific journals, books and news sourced from trusted sources. These sources are collected based on discussion and linked from one information to another. Data collection techniques used in this study were observation, interviews and research. This data is analyzed and then conclusions are drawn.

RESULT AND DISCUSSION

Replacements to antibiotics

Role of Organic acids in replacement of Anitibioics

Due to their antibacterial activity against a variety of pathogenic bacteria, their capacity to generate a pH drop in the gut, and their potential to increase nutrient utilization in chicken diets, organic acids are being evaluated as one of the viable antibiotic alternatives in recent years (Eidelsburger et al., 1992; Boling et al., 2000; Kil et al., 2011). These have either been utilized as a single acid or as a mixture of various acids (Wang et al., 2009). The European Union has approved the use of organic acids and their salts in chicken as being safe (Adil et al., 2010). Basically, fatty acids and carboxylic acids with the chemical formula R-COOH, where R denotes the acids' chain lengths, are included in the category of organic acids. Short chain length organic acids like formic (C1), acetic (C2), propionic (C3), and butyric acid (C4) have been used increasingly frequently in poultry feeding. Citric, lactic, fumaric, malic, and tartaric acids are some more carboxylic acids that are employed (Dibner & Buttin, 2002). Most organic acids with antimicrobial action have a pKa value (defined as the pH at which the acid is half dissociated) in the range of 3 to 5. In general, organic acids are weak acids that are only partially dissociated. Salts of calcium, potassium, or sodium are also readily available for organic acids. Due to their less volatile nature and solid state, salts are favoured since they are odorless and simple to handle during the processing of feed. Additionally, organic acids have a lower potential for corrosion and are more soluble in water (Huyghebaert et al., 2011). These can be utilized in feed and water. The following are the suggested successive mechanisms of action for organic acid's bactericidal effects: The initial acid form of organic acids can pass through the bacterial cell wall. Then, once inside the bacterial cell, the penetrated organic acids dissociate into the conjugated base form (non-protonated form), causing a decrease in intracellular pH. This stressful environment for the bacteria causes cellular dysfunctions, which prevents bacterial growth (ManiLopez et al., 2012). On the other hand, sorbic acid interferes with membrane proteins and makes the bacterial cell more permeable (Abdelrahman, 2016). Organic acids play a role in the production of poultry by reducing the pH of the animal's feed and gastrointestinal tract (GIT), enhancing nutrient retention in the diet, and inhibiting the growth of infections (Afsharmanesh & Pourreza, 2005; Mroz, 2005). The ability of an organic acid to lower pH in feed and the GI tract is probably reliant on the GIT's pH circumstances and the pKa values of the organic acid in question (Kim et al., 2005). The upper portion of the GI tract has a more noticeable pH reduction. In addition to controlling normal gut flora, application in drinking water ensures pathogen reduction and subsequently crop (Açkgöz et al. 2011; Hamed & Hassan 2013). In the closest portion of the gastrointestinal tract, organic acids are easily absorbed. Due to their capacity to make the gut environment more acidic, intestinal protease enzyme activity improves, leading to improved nutrition absorption and utilization. This may be because acidic digestion may be kept in the GI tract for a longer period of time, giving the GIT more time to digest nutrients (Kidder & Manners, 1978; Mayer, 1994). In addition to preventing the buildup of harmful metabolites, inhibiting undesired bacteria makes more nutrients available to the host, increasing feed utilization efficiency. Additionally, gut pH stabilization improves the efficiency of all digesting enzymes. In feed sanitation programs, organic acids are employed as feed additives and preservatives. It prevents feed deterioration and increases the shelf life of perishable food ingredients by suppressing the growth of harmful microorganisms. Short chain fatty acids, volatile fatty acids, and weak carboxylic acids are examples of organic acids that are frequently employed to reduce the pathogenic microbial load, which includes Salmonella and Escherichia coli. Organic acids also lessen pathogen colonization on the gut wall, protecting epithelial cells from harm. Short chain fatty acids, when applied daily, enhance the proliferation of epithelial cells, speed up intestinal healing, improve villous height, and ultimately boost absorption capacity. By breaking through the phospholipid layer of the bacteria, medium chain fatty acids (MCFA) kill it. They also change the cell membrane by creating pores that allow contents to flow out (Hermans & De Laet, 2014). It offers the residing pathogens an early pathogen barrier. Propionic acid totally inhibits feed mycotoxin and is a powerful mold inhibitor (Zha & Cohen, 2014). Salmonella Gallinarum counts in crop and caecal contents were lowered when chicks were fed propionic acid continuously. Salmonella levels in the carcass and feces samples were both decreased by the addition of 0.36% calcium formate.

Broilers given blends of organic acids as opposed to antibiotic groups showed an increase in Lactobacilli population and a decrease in coliforms and Clostridia, according to Akyurek et al. (2011). Similar to this, chickens fed with acetate, propionate, and butyrate salts had lower levels of Salmonella in their caecum thanks to the production of antimicrobial peptides (Sunkara et al., 2011; Sunkara et al., 2012). When used in combination, organic acids cocktail is said to be more effective at preventing the growth of intestinal pathogens such E. coli and Salmonella than antibiotic growth promoters (Hassan et al., 2010; Hamed & Hassan, 2013). As potential broad-spectrum inhibitors of metallob-lactamases (MbLs), Nheterocyclic dicarboxylic acids and pyridyl-mercapto-thiadiazoles can be utilized in concert with beta lactam antibiotics to combat drug-resistant serotypes (Abdelrahman, 2016).

Oxalic acid, which is found in plant sources, has an impact on the calcium availability, particularly in chickens that lay eggs. This oxalic acid creates calcium oxalate salts that are insoluble (Jadhav et al., 2015). The experiments of Tang et al. (2007) that fed the birds with Lactobacillus strains showed an increase in calcium solubility and availability, which is linked to its capacity to lower the gut pH because of the generation of lactic and acetic acids.Organic acids also lessen the likelihood of re-infection and the pathogen contamination of litter, which lowers the bacterial burden on chicken birds. More research is needed to clarify the mode of action of dietary organic acids and their effects on the growth performance of broiler chickens by different combinations of acids and their concentration in feed or drinking water. Organic acids have the power to reduce pH and have been found to reduce pathogens in the GI tract.

Importance of Probiotics

Probiotics are living microbial cultures that are either isolated or combined to help the host's health (Fuller, 1992). Competition with intestinal receptor sites, formation of particular metabolites (short organic fatty acids, hydrogen peroxide, and other metabolites with antimicrobial activity), and immune stimulating effect are all aspects of probiotic bacteria's mode of action (Madsen et al., 2001; Sherman et al., 2009). Lactobacillus, Streptococcus, Enterococcus, Bacillus, Clostridium, Bifidobacterium species, and E. coli are among the microorganisms used as probiotics. Saccharomyces cerevisiae and Aspergillus oryzae are yeast and fungi used as probiotics (Fuller, 1999). Yeast and bacteria have been added as living creatures or as spores. Saccharomyces cerevisiae and Bacillus spp. (spores) are probiotics categorized as non-colonizing species, whereas Lactobacillus and Enterococcus spp. are colonizing species. Saccharomyces is a source of B complex vitamins and high-quality protein. The non-antibiotic functional product yeast extract is recommended as a potential non-antibiotic substitute for reducing pathogenic microorganisms in turkey production because of its immunomodulatory capabilities (Huff et al., 2010). As zootechnical feed additives, yeast cell derivatives are currently becoming more and more important (Witkiewicz et al., 2014). Similarly, feeding Aspergillus awamori (0.05%) increased meat quality by raising the level of unsaturated fatty acids in broiler chicken breast meat and improved growth performance by releasing growth promoters (Yamamoto et al., 2007).Probiotics are used largely to build healthy intestinal flora with the goal of preventing or lessening the disruptions brought on by enteric pathogens (Dhama et al., 2008). In birds with serious illnesses, probiotics do not take the place of medicines, but they are helpful in reestablishing the normal bacterial population. The physiological condition of the bird, the type and concentration of the probiotic strain, persistence in the intestine, ability to survive during feed processing and gastrointestinal track, and compatibility with the natural microbiota of the intestine are all factors that affect the probiotic's effects. The probiotic strain that is deemed optimum must be resistant to bile salts, acid, and digestive enzymes. It should also have the ability to multiply quickly in order to create the microbial population needed to deliver the desired impact. Additionally, the strain selected shouldn't change the gut microflora's susceptibility to antibiotics (Seema & Johri, 1992; Pal & Chander, 1999; Dhama et al., 2011; Mookiah et al., 2014).

Advantages of probiotics:

1. Enhances gut health by maintaining the desired microbial population equilibrium and lowering diarrheal outbreaks.
2. Slows the spread of infections and lowers mortality
3. Enhances the effectiveness of feed conversations

4. Enhances body weight increase and growth rate
5. Enhances the digestive enzymes, which helps the body absorb nutrients.
6. Controls lipid metabolism to lower circulating cholesterol levels.
7. Boosts the effectiveness of immunizations
8. Contributes to the quick elimination of mycotoxins
9. Lessen the stress related to traveling, vaccination, temperature, and antibiotic administration.
10. Synthetic vitamins of the B complex
11. Produces enteric and litter ammonia, which enhances litter quality
12. Increases intestine short chain fatty acids, which may change the type of bacteria in the gut
13. Has no aftereffects or residues in products
14. Reduces pollution in the environment

Probiotics have a competitive exclusion mechanism of action because they create chemicals that prevent pathogen growth. Additionally, they compete with the pathogens for space in the intestinal epithelium.

Short-chain organic acids (lactic, acetic, and propionic), hydrogen peroxide, and bacteriocins, such as nisin, acidolina, lacocydyna, lacatcyna, reutryna, entrocine, and laktoline, are all products of probiotic bacteria. Probiotic-produced bacteriocins have a strong antibacterial effect against Clostridium perfringens, Salmonella, Campylobacter, and Escherichia coli. According to Mahmood et al. (2014), supplementing feed with probiotics may be a candidate technique for reducing oocysts and necrotic enteritis as well as Eimeria acervulina and E. tenella (Lee et al., 2007). Probiotics also work by stimulating the immune system because of their capacity to adhere to the intestinal mucosa, which enables them to build a natural barrier against disease entrance and therefore improve immunity. Additionally, probiotic immune system stimulation increased the production of immunoglobulins, stimulated the activity of macrophages and lymphocytes, and increased the production of -interferon (Yang & Choct, 2009). The current main reasons for greater usage of probiotics in chicken production are thought to be customer desire for antibiotic-free products, ensuring antibiotic efficacy without therapeutic involvement, and animal welfare promotion (Blanch, 2015). The in ovo injection of probiotic culture is a new method of probiotics feeding, particularly in chicken. The newly hatched chick will have a sterile gastrointestinal tract, therefore it will harbor the microflora when it enters its raising home system and is exposed to diverse environmental bacteria. Although colonization occurs in chicks after hatching (Amit Romach et al., 2004), Pedroso (2009) and Bohorquez reported finding a small number of microorganisms in the prenatal stage of the birds' development (2010). Probiotics are fed to birds, and studies have shown that this reduces the effects of numerous stressors. The newly hatched chicks are similarly subjected to several challenges, including hatching, sexing immunization, dehydration, malnutrition, transit, etc. Numerous in ovo injection experiments have demonstrated that providing necessary amino acids, minerals, carbohydrates, and fatty acids during embryonic development might lessen the effects of stress on broiler growth. Therefore, administering a probiotic culture in an in ovo setting may also aid in helping young children cope with various stresses. In ovo injection of a mixture of probiotic organisms at 17.5 days of incubation dramatically decreased the Salmonella levels in intestines in a broiler experiment (de Oliveira, 2014).

Importance of Prebiotics

Prebiotics are nondigestible feed additives that assist the host by favorably enhancing the growth rate and/or multiplying a small number of beneficial bacteria in the host's colon to improve gut health. These provide food for the beneficial microorganisms in the stomach.

According to Cummings and Macfarlane (2002), the primary functions of prebiotics are altering the GI microflora, stimulating the immune system, preventing colon cancer and reducing pathogen invasion, reducing cholesterol and odor compounds, enhancing gut health by promoting enzyme reactions, reducing ammonia and phenol products, and ultimately reducing production costs (Ghiyasiet al., 2007; Khksar et al., 2008; Peric et al., 2009). The primary prebiotics evaluated in chickens include gluco-oligosaccharides (GOS), fructo-oligosaccharides (FOS), mannan-oligosaccharides (MOS), stachyose, and oligochitosan (Jiang et al., 2006). It should not be hydrolyzed or absorbed in the upper gastrointestinal tract; it should have systemic effects to promote the host's health; it should be palatable as a feed ingredient; and it should be easy to process on a big scale. Prebiotics can be added to chicken diets to reduce the requirement for antibiotics, hence decreasing bacterial drug resistance over time (Patterson & Burkholder, 2003). Prebiotics can help reduce the colonization of pathogens in chicken diets, such as Escherichia coli, Vibrio cholera, S. Typhimurium, and S. Enteritidis (Bailey et al., 1991). The addition of oligosaccharides lowered the total viable counts in the meat and coccus. In addition, prebiotics promote the growth of Lactobacillus and Bifidobacteria and reduce the incidence of harmful gut infections (Dhama et al., 2007) Therefore, prebiotics can be utilized as an alternative to antibiotics to enhance the health and performance of chickens by altering the population of gut microorganisms and boosting the immune system by lowering infections. Additionally, additional research is required to comprehend the specific function and mechanism of action of a single component or combination of components. The bacteria of the hens' gastrointestinal tract influence both their immunity and growth. Prebiotics are renowned for their capacity to encourage the growth of beneficial bacteria (Gibson, 1999; Van Loo et al., 1999), but they also modify the innate immune response by interacting with receptors, boosting endocytosis, and activating cytokines and chemokines (Di Barolomeo et al., 2013). Humans and animals commonly consume fructose polymer inulin as a prebiotic. Despite being indigestible non the intestines, they serve as a substrate for Bifidobacteria growth (Niness, 1999; Kelly, 2008). Inulin also stimulates the ileum's production of secretory immunoglobulin A (SIgA) and the gut's resistance to invading pathogens (Buddington et al., 2002).

Role of Synbiotics

The probiotic and prebiotic mixture, or synbiotics, gives the living culture and feeds them so they have a higher chance of surviving in the bird's intestinal system (Yang et al., 2009; Gaggia et al., 2010). The most well-known synbiotic pro-prebiotic combos are lactitol and lactobacilli, and fructo-oligosaccharides and bifidobacteria (Yang et al., 2009). Intestinal microflora play a significant role in bird health, and if the equilibrium between beneficial microbes is upset, the bird's health and general performance will suffer. This encourages researchers to investigate the impact of dietary supplements in the form of prebiotics, which can be used to boost the establishment of beneficial bacteria and improve poultry bird production. Synbiotics are prebiotics that are supplemented to ensure the growth of probiotics (Huyghebaert et al., 2011). Given that specialized substrate is available for fermentation, adding both probiotics and prebiotics to food could increase the helpful organisms' survival and persistence in the guts of birds (Yang et al., 2009; Adil & Magray, 2012). Synbiotics were successful in enhancing the growth of broiler in chickens' diets (AbdelRaheem et al., 2012; Mookiah et al., 2014). Feeding broiler chickens synbiotics has been demonstrated to improve intestinal architecture and nutritional absorption, resulting in improved performance (Awad et al., 2008; Hassanpour et al., 2013). The best synbiotic effects for chickens have only been revealed in a small number of research (Li et al., 2008). Finding the ideal probiotic and prebiotic ratio and evaluating how well they work together as potential synbiotics must be given careful consideration in order to maintain good health. According to a study by

Madej et al. (2015) in broilers, the development of numerous immune organs was affected when inulin (a prebiotic) and Lactobacillus bacteria were administered in utero.

Use of Vitamins and minerals as growth promoters

It has been demonstrated via the development of broilers that the use of minerals and various vitamins can improve the health condition of poultry. The bad health status of birds has increased due to mineral and vitamin supplementation, increasing the farm's cost-benefit ratio (Prescott & Baggot, 1993; Peric et al., 2009). There are many positive effects, including an increase in feed conversion ratio, an improvement in the bird's immune system, and changes to the beneficial microorganisms in the gut and intestine. Vitamins like vitamin C play a significant role in reducing stress, especially during the summer, by increasing feed intake and enhancing feed metabolism (Sahin et al., 2003). Vitamin C also prevents birds from losing weight, which is primarily caused by summer stress. Birds naturally produce the antioxidant vitamin C utilizing the gulonolactone oxidase enzyme, which is not present in guinea pigs or humans (Lin et al., 2006; Khan, 2011). Although vitamin C does not have a suggested dose for birds, its antioxidant properties may help to reduce stress. According to a study, broilers fed vitamin C performed well even when exposed to various environmental stresses (McKee & Harrison, 1995). By keeping minerals, particularly iron, in the reduced ferrous state, vitamin C facilitates the absorption of minerals and plays a significant role in the metabolism of amino acids (McDowell, 1989). L-arginine supplementation and vitamin C administration have improved broiler meat quality. The feed conversion ratio and growth performance in chicken were both boosted by a different vitamin, vitamin E. The recommended dose of vitamin E for a bird is 5 to 25 IU/kg of feed, while larger doses have also improved poultry performance (NRC, 1994). Iron plays a growth-promoting and -inhibiting role, while phosphorus contributes to broiler weight gain (Abudabos, 2012). Because ubiquinone is present in many different systems, vitamin Q is most frequently referred to by this name. This is an inherently occurring, lipid-soluble chemical that is vital to the process of converting energy inside cellular mitochondria (Gopi et al., 2015). As the age goes on, though, their synthesis will become insufficient. Similar to humans, birds, especially those of fast-growing kinds, may not have enough endogenous production due to numerous stressors. Broilers fed a high-energy diet showed an increase in feed efficiency, according to Gopi (2013). Additionally, consumption of the chemical strengthens their lipophilic systems' antioxidant defenses. Through increased energy availability, vitamin Q consumption strengthens the host's defense against different microorganisms, including bacteria, viruses, protozoa, and bacteria (Bliznakov, 1978; Hogenauer, 1981). Both Folkers et al. (1982) and Gopi (2013) noted an increase in broiler haemeagglutination titer (HI) against the Newcastle disease virus and immunoglobulin G production.

Antimicrobials of plant origin / phytobiotics

Phytochemicals, also referred to as phytobiotics, are substances originating from plants that have a variety of effects on plants, animals, and people. These substances are the secondary metabolites created by the plant that give it its distinctive flavor and taste, mostly as a form of defense against pest attack and animal grazing. More than 80,000 substances, including phenols, flavonoids, tannins, saponins, essential oils, etc., have been discovered over the years. These substances were initially regarded as waste materials, antinutritional, and unhealthy ones. However, today's approach to them as antioxidants, digestive aids, and health-promoting compounds is evolving globally (Narimani-Rad et al., 2011). Since its anti-microbial activity has been discovered in various types of organisms (Brut, 2004; Murali et al., 2012), (both gram positive and gram negative organisms). They are mostly utilized as an alternative antibiotic growth promoter in monogastric (poultry and pig) animal production

(Khaksar et al., 2012; Karangiya et al., 2016). They have been reported to favorably change the gut microflora by less harmful organisms, while the particular mechanism of action is still unknown (Salim, 2011). The change in membrane permeability to hydrogen ions (H+) is the most likely mechanism of action. It exhibits antibacterial, antiviral, anti-fungal, and anti-protozoan properties in addition to its antibacterial properties. Their anti-fungal properties are becoming more significant as a result of these compounds' use in environmentally friendly and cost-effective fungicide preparations, as well as in fly-repelling products (Afzal et al., 2010). (Mansour et al., 2011).

The ability of tannins (condensed tannins) to inhibit the growth of intestinal parasites in sheep and goats has been extensively explored. Furthermore, they exhibit strong anti-chicken coccidial action. Large animals (cattle, buffaloes) are affected by the methanogenic suppression action of phytochemicals, especially essential oils (reduces the methane enteric methane production). Phytochemicals have antioxidant properties (both hydrophilic and lipophilic activity). These chemicals are utilized during stressful situations, such as heat stress, due to their antioxidant action (Wei & Shibamoto, 2007). Their antioxidant properties may be useful in enhancing the shelf life of processed meats and minimizing the loss of muscle during the thawing of cold-stored goods (Windisch et al., 2008). These chemicals from plants have characteristic flavors that could be used in diets for humans and pigs. These substances draw customers and enhance ingestion. Currently, essential oils are utilized to make ice cream and other things. They still have some controversy about their use as a flavoring component in poultry production. The body's digestive process is accelerated by the dietary addition of active ingredients or the source of such ingredients. They were discovered to enhance the release of digestive enzymes from the pancreas and liver, specifically trypsin, amylase, and bile (Gopi et al., 2014a). This will contribute to increased feed efficiency and total feed digestibility. However, due to their capacity to connect with the digestive enzymes, certain chemicals, particularly polyphenols, which are more frequently incorporated, have a negative impact on the efficiency of digestion. The capacity to absorb nutrients is also increased by these chemicals through an increase in the length and depth of the intestinal villi. Additionally, they change the system's lipid metabolism by decreasing the action of hepatic 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, which lowers the liver's production of cholesterol (Lee et al., 2004). Utilizing this phenomenon might enable the production of meat and eggs with minimal cholesterol levels (Mohamed et al., 2012). Despite the fact that these substances are generally acknowledged as safe (GRAS), their degree of use is still under question because of the unidentified mechanisms behind their range of activity and the potential for bodily implantation.

Herbal medicine has gained popularity recently primarily as a result of its advantages over chemical medications, which include reduced or nil toxicity, availability in nature, and appropriate feed additive properties (Khan et al., 2010; Khan et al., 2012a). It is well known that plant components like herbs and spices have antibacterial properties (Nychas & Skandamis, 2003). Essential oils in particular are items made from plant parts that are known to contain active chemicals that have antibacterial properties against bacteria, yeast, and molds. Thymol, eugenol, saponins, flavonoids, carvacrol, terpenes, and their precursors are a few of the main groupings of primary constituents that give essential oils (EOs) their antibacterial properties. Due to the fact that essential oils are volatile chemicals, they have the scent and characteristics of the plants from which they were derived (Oyen & Dung, 1999). The plant parts that can be used to make essential oils include clove buds, onion and garlic bulbs, parsley seeds, fruits, rhizomes, leaves, basil, and tea plants (Nychas & Skandamis, 2003). Examples of substances with strong antibacterial properties are cinnamon barks with high quantities of cinnamamic aldehyde and spices with high levels of eugenol (Davidson & Naidu, 2000). According to reports, essential oils from plants have a broad antibacterial spectrum and are effective against a variety of bacterial and fungal organisms (Tiwari et al, 2009). Numerous biological aspects (plant species, growth environment, and harvest stage), industrial procedures (extraction/distillation), and storage environment all affect the antibacterial property (temperature, light, oxygen level and time). Identification and measurement of the many actions and claims claiming to improve feed efficiency and the health status of poultry birds are still under investigation. The structural conformation of the active components and their concentration both affect the antibacterial capability of essential oils. Currently, attention is growing in herbs that aim to impair bacterial quorum sensing (Goossens, 2016).

Essential oils like thymol and carvacrol have been extensively examined for their antimicrobial properties against a variety of bacteria including L. monocytogenes, S. Typhimurium, and Vibrio parahaemolyticus (Karapinar & Aktug, 1986; Tassou et al, 1995; Dhama et al., 2015a). Cinnamon oil contains cinnamic aldehyde, which has been reported to have antibacterial effects against a variety of bacteria including L. monocytogenes, C. jejuni, and S. enteritidis (Smith-Palmer et al, 1998). Numerous studies on the antibacterial and antifungal properties of eugol, an ingredient in clove essential oil, have been conducted (Deans et al., 1995; Smith-Palmer et al., 1998). It has been discovered that adding EOs to chicken feed improves broiler feed efficiency and body weight (Cross et al., 2002; Bampidis et al., 2005; Cabuk et al., 2006). Similar to this, feeding turmeric powder boosts the immune system by increasing circulatory antioxidant defense (Madpouly et al., 2011). Similar to this, it has been discovered that adding garlic to feed at a level of 3% improves the growth and performance of broiler chicks (Elagib et al., 2013). Blends of several essential oils, such as lemon, basil, oregano, tea, etc., increased body weight gain in broilers and increased egg production with greater feed conversion efficiency in laying quails when added to diets (Khattak et al., 2014). (Cabuk et al., 2014). Recently, it was discovered that broiler bird skin treated with carvacrol, acidified sodium chlorite, or trisodium phosphate effectively inactivated Salmonella Enteritidis and Salmonella Typhimurium (Karuppasamy et al., 2015, Yadav et al., 2016). Numerous plants and their derivatives, including as Aloe vera, Astragalus membranaceus, ginger, garlic, noni, onion, turmeric, and thyme, have been thoroughly studied and employed in the production of poultry (Dhama et al., 2015b). These substances have enhanced broiler growth and elevated layer egg output (Guo et al., 2004; Sunder et al., 2013; Sunder et al., 2014). Resinol, a natural resin acid composition (RAC), has been demonstrated to have antibacterial, antifungal, and antiparasitic activities. When added to feed, it regulated the intestinal microbiota and decreased the percentage of gram-positive population in vitro, in addition to enhancing growth performance (Vuorenmaa, 2015). According to Zhang et al. (2012), broilers fed fermented Ginkgo biloba leaves coupled with Aspergillus niger shown better growth performance. Although the mechanisms of action of many of the plants' active components have been identified, some have been published but not all. According to reports, these herbs' active ingredients enhance the gut's regular microbiota, which increases nutritional metabolism and absorption and promotes greater growth and production (Hashemi & Davoodi, 2011). Trypsin, chymotrypsin, amylase, and lipase activity have all increased as a result of eating turmeric, which is ascribed to its active ingredient curcumin (Khan et al., 2012b). Ginger improves feed digestion and metabolism by increasing the release of digestive enzymes like enterokinases and other essential enzymes (Zhao et al., 2011). Similar to this, adding essential oils to feed boosted the release of digestive enzymes, enhancing feed absorption, and improving broiler activity in general (AlKassie et al., 2011). Free radical production in cells is decreased by the antioxidant qualities of these active principles.

Herbal preparations also have antibacterial, antiparasitic, and immunomodulating qualities in addition to their antioxidant and digestive benefits. Although there are immunostimulants available, they have side effects that call for a replacement; as a result, herbal medications can be a superior immunostimulant option. The potential of flavonoids, lectins, polysaccharides, peptides, and tannins as immunomodulators has been well documented. Plants with immunomodulatory qualities include neem, ashwagandha, guduchi, noni, etc., and the effects of these substances are well known (AbdElslam et al., 2013; Bhatt et al., 2013; Latheef et al., 2013a; Latheef et al., 2013b; Tiwari et al., 2014a; Tiwari et al., 2014b). Black pepper, nishyinda, and cinnamon have been reported to have promising growth-promoting effects in broilers without causing any negative side effects (Chowdhury et al., 2009; Mode et al., 2009; Molla et al., 2012; Saminathan et al., 2013). When fed to poultry, a number of herbal extracts have an antibacterial effect, avoiding infectious diseases and promoting the growth of the poultry (Dhama et al., 2014b; Dhama et al., 2015b). Thymol and carvacrol, the active components of thyme, have antibacterial properties, particularly against gram-negative bacterial infections. They penetrate bacterial cell walls and harm cells by attaching to amine and hydroxylamine groups (Juven et al., 1994; Helander et al., 1998; Abd El-Hack et al., 2016). When it comes to Eimeria spp., which causes coccidiosis in chicken, curcumin has a better effect (Khalafallah et al., 2011).

The production of interferon, interleukin, and tumor necrosis factor are all increased by garlic (Hanieh et al., 2010). Garlic's bioactive ingredient, allicin, is thought to have the potential to penetrate pathogen cellular membranes and then bind to important enzymes to disrupt cellular processes. With sufficient ventilation, the eucalyptus oil compounds cineol and eucalyptol have a calming effect on bird respiratory illnesses (Nakielski, 2015). For the advancements in herbal medicine that are focused on finding solutions, comprehensive understanding about each active ingredient and their potential positive or negative effects is necessary (Heinzl & Borchardt, 2015).

The following list of advantages of phytobiotics is based on research from the past (Lee et al., 2004; Windisch et al., 2008; Salim, 2011; Gopi et al., 2014b; Dhama et al., 2014b; Karangiya et al., 2016):

Following are some of the key advantages of phytobiotics:

Reduces the incidence of harmful bacteria, viruses, and parasites in the gut, hence reducing the requirement for antibiotic medication.

1. Favorably changes the microbial community for sustaining gut health.
2. Increases feed efficiency and body weight growth
3. Boosts antioxidant protection against oxidative stress
4. Lowers cholesterol levels by preventing hepatic enzyme activity.
5. Encourages the release of digestive enzymes and nutrition absorption
6. Improve the consequences of heat stress
7. Ecologically sound insecticides and pesticides

Role of Antimicrobial peptides

Host defense peptides, also known as antimicrobial peptides, have an amino acid length of roughly 30 to 60 numbers and are found in all living things. These peptides have immunomodulatory and antibacterial properties that can harm fungi, viruses, and bacteria by concentrating on their cell membranes (Li et al., 2012; Parachin et al., 2012). The favorable effects of several of these antimicrobial peptides, such as their ability to stimulate growth in chicken, have been investigated. Antimicrobial peptides, particularly cecropin A (1-11)-D (12-37)-Asn (CADN), have been examined as growth promoters in chicken, indicating that they may be an alternative to antibiotics in this capacity (Liu-Fa & Jian-Guo, 2012). Studies conducted in vitro revealed that Candida albicans, E. coli, and L. monocytogenes were all significantly suppressed by peptides extracted from chicken leukocytes (Harwig et al., 1994). Campylobacter colonization in chicken is reported to be significantly reduced by bacteriocins, the non-toxic ribosomal antimicrobial peptides released by bacteria on their cell surface (Svetoch & Stern, 2010). These are antimicrobials of a new generation that might be able to get rid of bacteria that are resistant to medication. Nisin is a bacteriocin that has been widely explored for usage in food and for medicinal purposes in chicken (Joerger, 2003). It has been proposed to extract antimicrobial peptides from transgenic plants for use in chicken feed (van t' Hof et al., 2001).

CONCLUSION

Since many years ago, antibiotics have dominated the chicken market as a growth enhancer. However, due to their excessive use, bacteria have acquired a resistance to them, endangering the community of humans by giving rise to infections that are exceedingly drug resistant. Therefore, it is essential to stop using antibiotics to encourage growth and look for alternatives that can help with positive actions. In recent years, a lot of study has been focused on finding alternatives to antibiotics, which has led to increased usage of probiotics, prebiotics, herbal medicines, etc. It is possible that using probiotics, prebiotics, synbiotics, plant extracts, and organic acids will improve digestion and nutrient absorption, alter the metabolism of birds, modulate the immune system, and improve the function and health of the gut by excluding and inhibiting pathogens in the intestinal tract as well as the safety of poultry products for human consumption. However, further research is still required to explore different pairings of these options with a focus on improving productivity. Additionally, efforts are required to investigate additional possibilities where alternatives to antibiotics in poultry production and poultry products with desirable attributes without affecting the welfare of the poultry birds, can be used. This is done in light of the consumers' demand for functional foods.

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