



German Journal of Veterinary Research





# Review

# Alternative approaches to antimicrobial use in the turkey industry: Challenges and perspectives

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This article is published in the special issue: Turkey Diseases, Production and Management



Article History: Received: 31-May-2021 Accepted: 04-Jul-2021 \*Corresponding author: Jesse L. Grimes E-mail: jgrimes@ncsu.edu

#### Abstract

Poultry production has experienced a major shift with the prohibition of the use of antimicrobials and antibiotics as growth promoters. The industry in general, and more specifically turkey producers, are facing a changing world in that many consumers have a perception and certain beliefs about food production while the truth maybe something else. Additionally, perception has become a reality when it comes to consumer acceptance, which affects consumer purchasing behavior. In this regard, in many cases and genres, the public perception of antibiotic use in turkey production can be generally negative. The truth that antibiotics and other antimicrobials can be beneficial to both turkeys and consumers is lost. Therefore, turkey producers are accepting the challenge to rear turkey flocks without growth promoting antibiotics or antimicrobials. In some cases and some locales, this has become the law. In other markets, consumer desires and purchasing habits are the driving force for change. Turkey producers are scrutinizing production practices to ascertain and provide the optimal environment for turkey production. In addition, alternatives to antibiotics are being developed, tested, evaluated, and used for turkey production in increasing frequency. These include, but not limited to, probiotics (direct-fed microbials), prebiotics, organic acids, essential oils, spices, and plant and yeast extracts. Researchers are joining forces with turkey producers to develop use plans for these feed additives that, in most cases, are not the same as for antibiotic administration. Turkey producers have become proactive in developing these plans and are preparing to provide exceptional quality products that will meet consumer acceptance. However, more research focusing specifically on turkeys is certainly needed so that these alternative approaches can be optimized to meet the turkey production necessities.

Keywords: Turkey production, Bedding, Litter, Litter management, Litter moisture Citation: Gernat, A. A., Santos, F. B. and Grimes, J. L. 2021. Alternative approaches to antimicrobial use in the turkey industry: Challenges and perspectives. Ger. J. Vet. Res. 1 (3): 37-48. https://doi.org/10.51585/gjvr.2021.3.0018

# Brief discussion of the word "Natural" and "Organic Production"

Agriculture and food animal production have changed and evolved significantly over the last century, and the use of land for food production has increased significantly (Dallimer et al., 2009). Similarly, poultry production has evolved and become considerably more efficient. Considering the turkey industry specifically, the U.S., as the largest turkey producer in the world, produced about 7.5 billion pounds of turkey meat in 2019 (ERS-USDA, 2021; NASS/USDA, 2021). However, there is an increasing concern regarding the "industrial food production system", which will be briefly discussed below, and the turkey producers are significantly affected by these concerns for several reasons. A major reason that turkey production is affected by the changing trends is the prohibition of the use of antimicrobials as growth and health promoters because turkeys are naturally more prone to infections (Tumpey et al., 2004), and the production cycle is longer (Caucci et al., 2019).

The words antimicrobials and antibiotics can cause several reactions and prompt different feelings in consumers when they are spoken or heard. One common reaction is fear; consumers are against the use of antimicrobials in food producing animals, such as turkeys and chickens, because of antimicrobial resistance and other concerns (Marshall and Levy, 2011; Goddard et al., 2017; Cornejo et al., 2018). However, when "natural" alternatives to synthetic drugs are used, the concerns lessen (Gyawali and Ibrahim, 2014). Why are consumers more inclined to the word "natural"? What does it mean to be "natural"? Is there any evidence that "natural" alternatives to antimicrobials are safer than their synthetic counterparts are? Do turkeys need to be raised using antibiotics or antimicrobials as health or growth promoters?.

Changing trends in food consumption can distinctly influence consumer's perspectives on farming, food production and processing, and animal welfare (Goddard et al., 2017). Therefore, the ongoing changes in the market and consumer preferences force the poultry industry to change in order to meet these preferences and "keep up" with consumer demands. However, even if consumers are demanding that turkeys are produced without the use of antimicrobials, animal welfare becomes a challenge when turkeys get sick and require antimicrobial treatment. In consequence, bird management and rearing practices will need to change to adapt to these demands and reduce (hopefully avoid) animal suffering (Goddard et al., 2017).

A significant trend that has become an important type of food production system is organic production or organic farming. Production of organic foods, specifically poultry and eggs, is increasing in North America and very popular in Europe. This is partly due to consumer perceptions that organically produced food is healthier, that poultry and other livestock are raised in a more humane way, and that organic agriculture is sustainable; and as for marketing poultry and eggs, these perceptions are a reality (Scanes and Christensen, 2019). Consumers are pressuring the food industry to produce foods with "natural" ingredients, but the true definition of what "natural" means has not been defined yet (Petty, 2015; FDA, 2018).

Words such as organic and natural are frequently found on food labels, but do consumers really know what they mean? Does the food industry? Food labels can sometimes be misleading to the public, especially to people who are not familiar with or unaware of the complex processes used to produce food. In addition, appropriate wording and statements are not always used, and this affects food markets around the world because it leads to distrust and misinformation (BEUC, 2018; IFIC, 2020). That might result in the rise of unnecessary concerns and unfounded arguments. This situation can be aggravated by the fact that there are different food markets worldwide with their regulations and standards, which producers and the food industry must adhere to if they want to sell their products to these markets.

Educating the public with a wide variety of backgrounds, cultural differences, and customs can be a challenge. As mentioned earlier, it is important to emphasize different requirements and regulations in different countries as to what is considered organic or "natural". In fact, the U.S. Federal Food, Drug, and Cosmetic Act §321 defines food as "(1) articles used for food or drink for man or other animals, (2) chewing gum, and (3) articles used for components of any such article" (21 U.S.C. 321(f)), and clearly does not include the word natural. Therefore, the way food and all the other components involved in producing food are described deserves attention. Ultimately, the goal should be the same, independently of where food is produced. Growers and the food industry should be focused on the production of nutritious and wholesome foods and food products.

In the U.S., the Food and Drug Administration (FDA) is responsible for regulating and supervising food and animal feed production. Interestingly enough, the agency does not define or regulate the use of the word "natural" on the label of foods. However, the FDA published a proposed rule in 2015, in which the agency states that it was "previously considered establishing a definition for the term "natural" when used in food labeling", and in a previously proposed rule, it was "stated that the word "natural" is often used to convey that a food is composed only of substances that are not man-made and is, therefore, somehow more wholesome" (FDA, 2015, 2018). Yet, this policy was not intended to address food production, processing, or manufacturing methods, including thermal technologies such as pasteurization, or irradiation methods, or any other methods such as the use of pesticides. In addition, the FDA did not consider whether the term "natural" should be used to describe any nutritional or health benefit, which leaves no formal definition of what "natural" means when used in food or feed labels, leaving the term natural open for interpretations (Hansen, 2013; FDA, 2018). Unlike the FDA, the United States Department of Agriculture (USDA) regulates the use of natural claims when applied to meat, poultry, and eggs (FSIS/USDA, 2005). According to the USDA, a "natural" food is "a product containing no artificial ingredient or added color and is only minimally processed".

Another potential point of confusion, as mentioned briefly above, is the organic production system, sometimes referred to as organic farming. Most often than not, consumers assume that foods labeled "natural" are organic, hormone-free, and antibiotic-free (Rigby and Cáceres, 2001; Eyinade et al., 2021). However, it should be clear that organic production has its own rules and approved process and should not be considered a synonym of natural. In the U.S., the use of the word "organic" in food labels is regulated by the National Organic Program, which is administered through the USDA (AMS, 2021). In fact, based on the 2017 Census of Agriculture, there were a total of 129 organic turkey farms in the U.S. (NASS/USDA, 2020). The National Organic Program has established several guidelines for organic production systems, which include various requirements for certification. The guidelines related to animal production provide information about practices such as land requirements, livestock feed, healthcare, living conditions, slaughter, marketing, and labeling. It is also important to mention that organic certification is a complex (and costly) process and, because of that, there is a possibility that many small turkey farmers are producing organic turkeys but are not being accounted for because of lack of certification.

In Europe, the Council Regulation (EC) No 1804/1999 contains the basic rules of organic animal agriculture (ECDC/EFSA/EMA, 2017). These rules have similar goals as those of other countries, which include raising healthy animals in addition to producing safe, wholesome foods for humans, and they take into consideration animal welfare, husbandry practices, disease prevention, and veterinary treatments. Organic food production can be very challenging in Europe, and even though it is developing rapidly, the growth rates differ between the western and eastern parts of the continent (Mutlu, 2007). Additionally, it is important to highlight that there are different markets in Europe based on poultry product consumption. For example, Austria (mainly eggs) and France (mainly chicken meat) have the highest market share in the European countries for poultry, and for that reason, these countries potentially have stricter regulations for poultry products (von Borell and S'orensen, 2004).

Independently of the production system, poultry production is an important industry in the U.S. and many other countries in the world. U.S. turkey producers raised 228.5 million turkeys in 2019, while 903.2 thousand of them were organically produced (NASS; NASS/USDA, 2020). These are significant numbers expected to grow as predicted by the U.S. Poultry and Egg Association (2021). Likewise, in Europe, organic farming has grown 70% over the last ten years, placing the European Union as the second largest consumer of organic food in the world (European Commission, 2019).

Clearly, organic production is well accepted in Europe, and organically produced food is generally sought for by the general population (Rigby and Cáceres, 2001; Bostan et al., 2019; Evinade et al., 2021). Germany has the largest market for organic foods in the EU (Janssen and Hamm, 2012). After the German reunification in 1990, land used for organic production increased rapidly (Mutlu, 2007). By the 2000s, only about ten years later, organic agriculture spread to all the regions of Germany with the support of the Federal Organic Farming Scheme (BOEL) and the National Organic seal establishment (Haccius and Lünzer, 2000). Eastern Germany currently has the highest distribution of organically managed land compared to all agricultural areas. Whereas southern Germany, especially Baden-Württemberg and the Bavaria States, have vital importance for organic farming due to the larger number of organic farms (Mutlu, 2007).

In terms of poultry meat consumption, including conventional and organic production, China ranks first, followed by the U.S. and the European Union (FAO, 2010). Chicken meat dominates in terms of poultry meat consumption worldwide, while the average consumption of turkey meat and products is estimated to be close to 5 kg/capita/year compared to 15.5 kg/ capita/year for chicken in Europe (Magdelaine et al., 2008). These numbers are very significant, and the Food and Agriculture Organization of the United Nations (FAO) estimated that almost 95 million tons of poultry meat was produced in 2008, and global poultry meat consumption has been increasing steadily (FAO, 2010).

Although there are many factors that can affect consumption rates worldwide, consumers' trust and confidence is a critical factor that should be considered. Consumers, especially the younger generations, are requiring more information about the food they are eating, including their origin and how they were produced (Desbouys et al., 2019). As mentioned earlier, one of these requirements is the production of food animals, such as turkeys and chickens, without the use of antimicrobials or "antibiotic-free" (Foster Farms, 2015; Kirchhelle, 2018). Because of that, researchers and the food industry are searching for solutions and alternatives to meet these preferences and demands. However, once management practices changes are adopted, new challenges arise, such as the emergence or reemergence of certain diseases and problems in performance.

# The challenges of antibiotic-free production

With the ban of the use of antibiotics and antimicrobials as growth promoters, problems that had been controlled for many years reappeared. In addition to infections, multidrug resistance and safety issues are significant challenges currently faced by the poultry industry (Table 1). Even though antibiotics and other antimicrobials can be safely used and should be used to treat infections (therapeutically), once birds are given any type of antimicrobials, they become automatically ineligible to be sold as organic or labeled as organically produced, which is a challenge to some producers. Currently, there is no optimum solution to this issue, which involves, among other factors, animal welfare, and food safety.

Antimicrobial agents have been used extensively in poultry production and were usually administered in the feed or drinking water (Gyles, 2008). The most common reasons these compounds were used include growth promotion, disease prophylaxis, metaphylaxis, and therapy. Usage and regimen vary among countries and regions; for example, antibiotics for growth promotion were banned in the European Union in the late 1990s but were permitted in the U.S., Canada, and in most of the other poultry producing countries (Gyles, 2008). In 2017, the FDA made the use of medically important antibiotics for growth promotion prohibited in the U.S. (FDA, 2021). Therefore, with the ban, specific antimicrobials, which could prevent the growth and spread of pathogens, such as bacteria and fungi, were only allowed therapeutically not as a prophylactic method and required a prescription from a veterinarian

Without the use of prophylactic antimicrobials, certain microorganisms, especially opportunistic bacteria, can colonize birds and spread throughout the poultry farm (Casewell et al., 2003). The most common bacteria of food safety concern found in poultry are *Salmonella* spp., *Campylobacter jejuni* and *C. coli*, and *Escherichia coli* (Gyles, 2008). Consumer Reports reported that, in one survey, most ground turkey food

Table 1: Positive aspects of antimicrobial use and challenges of antibiotic-free poultry production.

Positive aspects	Challenges	
Eliminate most pathogenic bacteria and fungi	Can lead to antibiotic resistance	
Inexpensive	Increased veterinary costs	
Easy to use	Cannot be used in organic production	
Improve bird performance and health	Raise consumer concerns	

products had fecal contamination and had a 90% instance of bacterial contamination, including Enterococcus and Escherichia coli (Perkins, 2013). Also, the report inferred that Salmonella tolerance was too low. The contamination even included the products labeled "organic". Many or most of the bacteria were found to be resistant to antibiotics; although, the bacteria on the products from birds reared without antibiotics were less likely to be antibiotic-resistant. Therefore, there is a great need to address bacteria in turkey food products. This opportunity must be addressed in the production phase as well as during processing. All of the alternatives to antibiotics, as discussed herein, have some potential to reduce intestinal bacteria of food concern during the production phase. There may also be applications during processing.

Although antibiotics should not be used indiscriminately, they undoubtedly reduce the unwanted microbial load present in the bird and must be used when animals get sick with veterinary supervision and in a controlled manner. Certainly, there are concerns associated with the use of antimicrobials, and they should be clearly understood so that alternatives can be created to help growers raise animals that are safe for human consumption. The selection of resistant bacteria is one serious issue that has been associated with antimicrobial usage (WHO, 1983; Tollefson et al., 1997; McEwen and Fedorka-Cray, 2002; Gyles, 2008; Landers et al., 2012; Tang et al., 2017; El-Sayed Ahmed et al., 2020). In Europe, a high prevalence of AMR was found in poultry production when indicator bacteria such as *Escherichia coli* were tested, which may be caused by widespread antimicrobial mass medication since antibiotics cannot be used as growth promoters (EFSA, 2018; Caucci et al., 2019). Antimicrobial resistance may have several unwanted outcomes, such as antimicrobial therapy failure in animals, reduced productivity, and increased veterinary costs (Caucci et al., 2019). Additionally, resistant bacteria can lead to an increased risk of human infections that are difficult to treat, as well as a higher risk of death due to bacterial infections (Casewell et al., 2003).

Some recent review articles discuss the development of antimicrobial resistance (AMR) and its connection with the use of antibiotics in animal production (Tang et al., 2017; El-Sayed Ahmed et al., 2020). Interestingly, contradicting findings regarding the use of antibiotics for growth promotion in food animals, such as poultry (Aarestrup and Wegener, 1999; McEwen and Fedorka-Cray, 2002) and dairy cattle (Oliver et al., 2011) have also been published. Oliver et al. (2011) examined the impact of antibiotic use in dairy cows on the development of AMR and "conclude that antibiotic use in adult dairy cows has not increased antimicrobial resistance of veterinary pathogens to antibiotics used routinely in the dairy industry". The authors also emphasize the importance of using antimicrobials prudently and when necessary. (Aarestrup and Wegener, 1999) concluded that the risk of promoting AMR in Campylobacter spp. and E. coli  $O_{157}$  found in food animals is low and rare. Unfortunately, there are no recent studies that actually measured the risk of AMR development as a consequence of the use of antibiotics in turkey production; most studies were conducted in the 1990s and early 2000s (WHO, 1983; Tollefson et al., 1997; McEwen and Fedorka-Cray, 2002). Nevertheless, according to the European Food Safety Authority, the AMR prevalence is declining (ECDC/EFSA/EMA, 2017).

Several factors affect and can contribute to the emergence of AMR. According to a study performed in Italy, which is one of the main producers of poultry in Europe, producing more than 1 million tons of broiler meat and almost 310,000 tons of turkey meat, factors such as high density, seasonal and geographical variables, and stress play a role in bird health and risk of diseases (Caucci et al., 2019). This situation is aggravated in turkey production because turkeys are naturally more prone to disease than broiler chickens (Tumpey et al., 2004). The turkey production cycle is inherently longer, making antimicrobials use more likely (Caucci et al., 2019).

Even though antimicrobials are more likely to be used in turkey production than in broilers', their use has been significantly decreasing in the turkey industry. In a previous study, researchers sought to determine the on-farm antimicrobial use in turkey production and concluded that antimicrobial use at the hatchery was reduced by 55% from 2013 and 2017 (Singer et al., 2020). In addition, the use of several antimicrobials in the feed has also been reduced significantly, some of them up to 67%. More importantly, the authors recommended that whenever antimicrobials are used, they should be used consciously and based on a well-designed treatment regimen.

Finding alternatives to replace the prophylactic use of antibiotics and reduce the necessity to use them therapeutically is, therefore, crucial. The high loads of pathogenic microorganisms in the bird, especially in the intestinal tract, is a serious concern to the poultry industry because of productivity losses, increased mortality, and the associated contamination of poultry products for human consumption with these diseasecausing organisms (Hajati and Rezaei, 2010).

Over the years, scientists have tested and evaluated a variety of alternatives to the use of antibiotics to control certain health issues related to animal production (Mehdi et al., 2018; Aziz Mousavi et al., 2018; Gadde et al., 2017; Teillant and Laxminarayan, 2015). Researchers are tirelessly looking for natural, or perhaps less synthetic, alternatives for antibiotics, and some of them are showing promising results (Mikulski et al., 2008; Gyawali and Ibrahim, 2014; Hafeez et al., 2016; Zhai et al., 2018). These alternatives have different mechanisms of action and approaches to reduce the number of unwanted microorganisms. Some examples include probiotics, prebiotics, plant extracts, essential oils, organic acids, and yeast extracts, which will be discussed in more detail below and summarized in Table 2. These alternatives can have a very similar mode of action as regular antimicrobials such as disruption of bacterial cells, or more indirect action such as alteration of the environment to inhibit pathogen growth while promoting the growth of "good" bacteria in the bird intestinal tract (Hafeez et al., 2016).

# **Probiotics and prebiotics**

To prevent and reduce the amount of antibiotics given to animals used for human consumption has been a struggle for farmers. Currently, antibiotics are used when needed therapeutically and in the appropriate dose to keep animals healthy and the animal's welfare protected (FDA, 2021). Having natural alternatives to antibiotics might increase consumers' confidence when purchasing and consuming poultry meat. One safe method of promoting the intestinal health of poultry is by the use of probiotics and prebiotics. Promoting intestinal health can result in lower colonization of the intestinal tract by pathogens (Gadde et al., 2017; Pineda-Quiroga et al., 2019; Zbikowski et al., 2020).

FAO and the World Health Organization (WHO) define probiotics as "live microorganisms which when administered in adequate amounts confer a health benefit on the host" (FAO, 2001; Bajagai et al., 2016), and the health benefits are a result of promotion of a healthy intestinal microbiome that competitively excludes pathogenic bacteria (Hill et al., 2014). With probiotics being considerably sought in the poultry industry, the opportunity to investigate alternatives due to their benefits is receiving significant attention. Some of these benefits include enhanced growth rate, better laying performance and immunity, improved gut histomorphology, and the increase of beneficial intestinal microbiota (Jha et al., 2020).

Probiotic bacteria are known for producing antimicrobial substances that can be just as effective as antibiotics (Alloui et al., 2013). Some of these substances include lactic acid, ammonia, organic acids, alcohols, hydrogen peroxide, lipoteichoic acid, carbon dioxide, and others (Helander et al., 1997). Turkeys have a longer rearing cycle than chickens; therefore, early dosing of probiotics can result in better performance and gut health (Grimes et al., 2008; Russell and Grimes, 2009; Mohammadigheisar et al., 2019). These probiotics can be directly administered in the feed, also known as direct fed microbials (DFMs) or water. However, independently of the administration method, the supplementation of probiotics has been demonstrated to benefit intestinal cytokine production, which can positively affect the intestinal mucosal lining against pathogens (Abd El-Hack et al., 2020b). Other benefits of the use of probiotics in turkey production include improved bird performance, such as improved body weight, weight gain, and reduced cost of production (Torres-Rodriguez et al., 2007; Grimes et al., 2008; Russell and Grimes, 2009; Ezema, 2013). Although different types of probiotics can be effective against various diseases, the main issues found in poultry processing plants are Salmonella and Campylobacter (Gyles, 2008). Charalampopoulos and Rastall (2009) showed that probiotics could efficiently reduce the intestinal colonization of poultry by the pathogens mentioned above.

Unlike probiotics, prebiotics are not microorganisms (Alloui et al., 2013). According to FAO and WHO (2002), "a prebiotic is a selectively nondigestible ingredient that allows specific changes, in both the composition and activity in the gastrointestinal microbiota and benefits the host". In poultry, prebiotics can have various functions and effects; one of those is the selection and stimulation of the growth of specific beneficial gastrointestinal microbiota, which serves as a barrier for pathogen colonization (Ricke, 2018). Supplementation with prebiotics has been shown to affect weight gain significantly, feed intake, feed conversion rate, blood constitutes, and immunoglobulins in turkeys (Aziz Mousavi et al., 2018). Therefore, prebiotics can cause both indirect and direct effects on the bird; indirectly by shifting the composition and fermentation patterns of the gastrointestinal microbiota, or directly by stimulating and/or regulating the hosts' immune system (Ricke, 2018).

Clearly, probiotics and prebiotics are beneficial, and when combined, they can offer a better strategy. The simultaneous use of probiotics and prebiotics is known as synbiotics. It has been shown that the use of prebiotics and probiotics is better than one of them alone since prebiotics supply energy and nutrients for the probiotic bacteria (Markowiak and Śliżewska, 2018; Villagrán-de la Mora et al., 2019). There are specific combinations that work better together or are a better "recipe" for each situation, which also depends on the specific differences in each livestock. Some of the most used combinations are *Bifidobacterium* or *Lactobacillus* with fructooligosaccharides (FOS) and *Lactobacillus* with lactitol (Collins and Gibson, 1999).

Over the years, a surge for finding other alternatives besides prebiotics, probiotics, and synbiotics has emerged for several reasons. For instance, probiotics and prebiotics do not directly kill pathogenic bacteria; therefore, results vary significantly from one flock to another and from one type of production to another (Yirga, 2015; Gadde et al., 2017). Additionally, relying solely on probiotics and prebiotics may not be sufficient to eradicate the presence of certain pathogens because their efficacy will depend on several characteristics such as survival rate of the strain used, dose and frequency used, etc. (Yirga, 2015). Herbs and plant extracts of various forms, including their essential oils, might be such an alternative, as they have been used for over millennia for different purposes (Gyawali and Ibrahim, 2014; Khattak et al., 2014; Gadde et al., 2017). These plant-derived products have gained significant attention in recent years, not only in human medicine but also in the feed additive niche and the poultry science industry in general (Khattak et al., 2014; Hafeez et al., 2016; Zhai et al., 2018).

#### Plant extracts, essential oils, and organic acids

The use of additives, such as essential plant oil or plant extracts, is favorably increasing. When extracted correctly, they are considered natural, non-toxic, and free from residues (Zhai et al., 2018). With successful results, plant extracts have been used for their antimicrobial abilities (Hammer et al., 1999; Akyildiz and Denli, 2016). In the same manner, organic acids have been used widely in the poultry industry to replace synthetic antimicrobials (Wang et al., 2009). There are several plant extracts and organic acids that have been used in the poultry industry with variable results and efficiency (Wang et al., 2009; Adil et al., 2010; Khattak et al., 2014; Hafeez et al., 2016). Thymol (thyme), eugenol (cloves), turmeric, black pepper, carvacrol (oregano), ginger, and curcumin are of most interest to scientists (Suhaj, 2006). These extracts have different types of aldehydes, phenolics, terpenes and other active compounds as part of their composition.

These compounds might have inhibitory effects against a diverse range of pathogens (Swamy et al., 2016). Most of the compounds mentioned above are potent antioxidants, and some of them can have antimicrobial activities (Yanishlieva et al., 2006). Cinnamon (Cinnamomum zeylanicum), known globally as one of the oldest medicinal plants, along with garlic (Allium sativum), can be used in poultry feed as an essential oil or powder (Abd El-Hack et al., 2020a). Cinnamon and its components, mainly cinnamaldehyde and eugenol, when added to poultry diets, have beneficial effects on birds such as antioxidant activity, improved performance, hypocholesterolemic potential, improved microbiological aspects, and improved carcass traits (Abd El-Hack et al., 2020a). Garlic has beneficial effects on the prevention of different diseases or health conditions, not just in humans but also in animals (Khan et al., 2012).

With the poultry industry looking for high levels of efficiency and efficient feed conversions, the turkey industry has managed to stay current when it comes to finding solutions and alternatives for a successful production chain from farm to fork. A study was conducted with unsexed turkeys to investigate the effect of the addition of garlic, ginger, and cinnamon powder on their performance and a few blood factors (Al-Shuwaili et al., 2015). In this study, a 5% inclusion of each ingredient was added to the diets, and some promising results were found. An effect in live body weight, feed intake, feed conversion ratio (FCR), and organ weights (gizzard and liver) were observed, as well as a decreased alanine aminotransferase and aspartate aminotransferase in glucose levels.

A similar study was conducted, where male turkeys were fed diets with added organic acids or plant extracts (Mikulski et al., 2008). In this study, different blends of organic acids (citric, fumaric, orthophosphoric, and malic acid) and a mix of formic and propionic acids were compared to oregano essential oil, spice extracts of turmeric and capsicum in different diets. The authors evaluated gastrointestinal tract development and metabolism, growth performance, and carcass characteristics. Some of the supplements showed a decrease in the pH of the crop content, and all supplements increased body weight, with the observation that this increase was only significant at the age of 84 days. Feed conversion ratio decreased compared to the control, and no effect was seen in the carcass weights.

Dried oregano leaves (*Origanum vulgare* subsp. *hirtum*) were tested on early maturing female turkeys to observe the effect in different diets and evaluate body weight, feed intake, feed conversion efficiency, carcass characteristics, and serum cholesterol concentration (Bampidis et al., 2005). The results in this study proved that dried oregano leaves could be used as natural growth and health promoter for early female maturing turkeys.

### Yeast extracts

Previous studies have shown that yeast extracts can have several effects on turkeys. Some of these effects might be influenced by other characteristics such as the age of the hens that produced the poults (Huff et al., 2007), sex of the turkeys (Huff et al., 2011), and environmental conditions (Huff et al., 2014). For example, yeast extracts supplemented to poult diets can cause immunostimulation, improve body weight and feed-to-gain ratio (Huff et al., 2007). However, the same study found that overstimulation of the immune system (in case of poults from older hens) can lead to unwanted effects such as lower weight gain and higher mortality, especially if the birds are being challenged by pathogenic bacteria or environmental stress (Huff et al., 2007). Yeast extract supplementation was also found to decrease mortality and pathogen isolation from female turkeys (Huff et al., 2011), and to be protective against clostridial dermatitis (Huff et al., 2014).

#### Conclusions

The addition of antibiotics and other antimicrobials in turkey feed and water is currently under criticism due to increasing consumer awareness and the demand for antibiotic-free products; therefore, the search for new alternative replacements to be used in animal production will only continue to grow. In addition, the need for alternative approaches to antibiotic use has gained interest because of the stricter regulations regarding their use as growth promoters and the increased consumer demand for poultry products with

Alternative	Effect	Reference
Probiotics	Competitive exclusion, production of bacteriocins	Torres-Rodriguez et al. (2007)
	or other antimicrobial or inhibitory compounds,	Russell and Grimes (2009)
	improved growth and market body weight, ben-	Ezema (2013); Bajagai et al
	eficial to intestinal cytokine production, increase	(2016); Gadde et al. (2017); The
	in digestion and absorption of nutrients, alteration	Pew Charitable Trusts (2017)
	in gene expression in pathogenic microorganisms,	Pineda-Quiroga et al. (2019)
	immunomodulation	Żbikowski et al. (2020)
Prebiotics	Stimulate the growth of probiotic bacteria, regula-	Charalampopoulos and Rastal
	tion of intestinal immunity, improve performance	(2009); Ricke (2018); The Per
		Charitable Trusts (2017)
Essential oils and	Improve performance and organ weight, decrease	Mikulski et al. (2008); Al
plant extracts	crop and ileal digesta pH, increase -glucosidase	Shuwaili et al. (2015); Aky
	activity in the ileal digesta, in vitro antibacterial	ildiz and Denli (2016); The Pew
	effect, improve digestive enzymes secretion	Charitable Trusts (2017)
Organic acids	Eliminate acid-sensitive pathogenic bacteria, in-	Mikulski et al. (2008); The Pev
	crease body weight, lower feed conversion rate,	Charitable Trusts (2017)
	reduce digesta pH, increase pancreatic secretion,	
	reduce in cecal pH, decrease ileal viscosity and	
	amount of digesta, increase the activity of micro-	
	bial enzymes in the cecal digesta	
Yeast extract	Protection against stress and clostridial dermati-	Huff et al. (2007, 2011, 2014)
	tis, immunostimulation, improved body weight	
	and feed-to-gain ratio	

 Table 2: Types and possible effects of alternatives to antimicrobials used in turkey production

the "Raised Without Antibiotics" or "No Antibiotics Ever" labels (Gadde et al., 2017). Given that food labeling, packaging, and different ways of production affect the consumer's eye and their confidence in poultry products, there should be more solutions as to how to be efficient while maintaining food quality and safety and the animals' health.

As regulations become more stringent and consumers more demanding, the need for research focusing on "natural" alternatives to antibiotics, especially probiotics, prebiotics, plant-derived bioactive compounds, organic acids, and other compounds such as yeast extracts, has increased. Additionally, these research projects must focus on incorporating these alternative products into animal feed to enhance productivity. Fortunately, many of these attempts have been successful, and many products are now available to growers. Therefore, considering the low cost and high availability of some of these alternatives, the poultry industry should support more research to find alternatives for antibiotics and antimicrobials consistently.

Several alternative approaches to the use of antibiotics were investigated in the present article, and their effects on several production markers were considered. A summary of the most common alternative approaches can be found in Table 2. Some of the production markers found to be affected by these alternative products include, but are not limited to, performance, carcass traits, meat quality, hypocholesterolemic impact, antioxidant activity, and effect on immunity. Certainly, other alternatives are being studied. The goals for their usage remain the same; the production of safe and high-quality poultry products without using synthetic antimicrobials and considering the animal's health and well-being.

In addition to the individual alternative approaches, combining these approaches can also be beneficial and have a better response in the bird compared to when they are used separately. Therefore, probiotics and prebiotics alone might not be sufficient to completely eradicate a problem from a farm; however, the use of probiotics, prebiotics, and organic acid might eradicate certain pathogens from a flock. Unfortunately, there are not enough research trials that have investigated the use of these products simultaneously.

The turkey industry is growing, and consumers tend to purchase more turkey meat during special holidays, such as Thanksgiving and Christmas. Nonetheless, according to the Agricultural Marketing Resource Center (2021), consumer demand for turkey products is increasing, which is probably because these products are a lean alternative to beef and pork. This emphasizes the need for more research that focuses specifically on turkey production, which is longer and more complex than chicken production is. In addition, there are different production systems and phases of production, so more studies are needed to support the grower in producing healthy turkeys, resulting in high quality and safe turkey meat available to consumers. Furthermore, there are several options of feed additives that can be adjusted to be used in turkey production, but which product would be the best choice and the ideal dosage should be studied in detail. The world population is increasing, and producing affordable, high quality, safe, and nutritious turkey meat is of utmost importance.

#### **Article Information**

Funding. This research received no external funding. Conflict of Interest. The authors declare no conflict of interest.

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