Use of Antioxidants and Nutraceuticals, for the Treatment of Different Gastrointestinal Diseases in Poultry

Maria Asghar[1,*], Ayah Talal Zaidalkilani[2], Ammar AL-Farga[3], Muhammad Uneeb[4], Arhum Maqsood[5], Muti-ur-Rehman Khan[1] and Azka Imran[1]

[1]Department of Pathology, Faculty of Veterinary Sciences, University of Veterinary & Animal Sciences, Lahore, Pakistan
[2]Faculty of Pharmacy and Medical Sciences, Department of Nutrition, University of Petra, Amman, Jordan
[3]Department of Biological Sciences, College of Science, University of Jeddah, Jeddah, Saudi Arabia
[4]Department of Biology, Lahore Garrison University, Lahore, Pakistan
[5]Institute of Microbiology, University of Veterinary and Animal Sciences, Lahore, Pakistan
*Corresponding author: drmariaasghar2001@gmail.com

Abstract

Poultry industry faces substantial economic losses due to severe gastrointestinal diseases, mainly triggered by bacteria and coccidia, and has depended on antibiotics and chemotherapy from years to mitigate these losses. Additionally, the presence of *Salmonella* spp. and *Clostridium perfringens* in poultry- derived products also poses a substantial hazard to public health, as these pathogens can cause serious foodborne illnesses through consumption of contaminated meat, eggs and related products. As antibiotic resistance continues to spread across animal and human population, limiting antibiotic use in livestock and pinpointing essential antimicrobials have become top priorities. That's the reason; research efforts have concentrated towards the discovery of natural products and innovative solutions to combat gastrointestinal diseases in poultry. This chapter provides an overview of the influence of natural compounds on gastrointestinal well-being, host defense and over health status, highlighting their potential as substitutes to antimicrobial agents in commercial poultry farming.

Keywords: Gut health, *Salmonella, Clostridium perfringens,* Nutraceuticals, Phytochemicals, Gastrointestinal diseases

Cite this Article as: Asghar M, Zaidalkilani AT, AL-Farga A, Uneeb M, Maqsood A, Khan MUR and Imran A, 2025. Use of antioxidants and nutraceuticals, for the treatment of different gastrointestinal diseases in poultry. In: Aadil RM, Salman M, Mehmood K and Saeed Z (eds), Gut Microbiota and Holistic Health: The Role of Prebiotics and Probiotics. Unique Scientific Publishers, Faisalabad, Pakistan, pp: 103-109. https://doi.org/10.47278/book.HH/2025.285

A Publication of Unique Scientific Publishers	**Chapter No:** 25-014	**Received:** 14-Feb-2025 **Revised:** 02-Apr-2025 **Accepted:** 30-May-2025

Introduction

For nearly six decades, antibiotics have been administrated to animals with minimal regulatory oversight. These have been used in the chicken business for multiple purposes, prominently growth promotion, avoidance of various diseases, and treatment of such diseases (therapy) (Roth et al., 2019). The development of antibiotic resistance has been greatly aided by the regular use of sub therapeutic antibiotic dosages, which are given in massive quantities to the entire flock. In the light of evidence linking sub therapeutic antibiotic use to the development of resistance across various antibiotic categories, as stated by the WHO (World Health Organization) "it poses an unprecedented risk to public health , food systems and development prospects" today (Cosby et al., 2015). Moreover, scientific consensus confirms that multiple drug resistant microbes, notably Salmonella, linked to use of antibiotic in veterinary field pose substantial threats to human well-being. In 2016, the EU (European Union) took a decisive step by banning antibiotics in animal feed for growth promotion, effectively ending the use of antibiotics for non-medical purpose (Castanon et al., 2007). The output of meat originated from poultry is constantly increasing, reaching a record high of 13.6 million tons in 2020 in Europe, putting much greater emphasis on the investigation of antibiotic substitutes. The three most significant and dangerous gastrointestinal (GI) illnesses that affect chickens will be covered in this chapter: coccidiosis, salmonellosis, and clostridium diseases (also known as necrotic enteritis). Resistance to several antibiotic classes is growing in all of these diseases. In particular, several species of *Salmonella* and *Clostridium* have been accountable for serious foodborne illnesses in humans, aside from coccidiosis. This chapter reviews the primary natural antibiotic substitutes that fall within the categories of phytonutrients and nutraceuticals. With an emphasis on the underlying mechanisms of action, the ability of these drugs to decrease infectious agents and reduce the severity of gastrointestinal diseases in chickens will be examined.

Different Classes of Alternative Compounds

The pathophysiology of various intestinal illnesses depends on gut health. The gut micro biota's function has been extensively clarified, demonstrating how dysbiosis may be a significant risk factor for gastrointestinal disorders (Shehata et al., 2022). The gut microbiota can be affected by a variety of variables, including pathogenic infections, nutrition, and antibiotics. Taking into account clinical presentation and organ damage, the ideal antibiotic substitute should be able to either avoid or lessen the effects of diverse microbial illnesses. An alternative should ideally have the same immunomodulatory and microbiota-modulatory mechanism as antibiotic growth promoters (Huyghebaert et al., 2011). In 1989, Stephen DeFelice combined the concepts "pharmaceutical" and "nutrition" to develop the term "nutraceuticals"(Alagawany et al., 2021). DeFelice defines nutraceuticals as "a feed (or part of a feed) that can be used for prophylactic and therapeutic disease" (Brower, 1998). Natural products notably nutritional fiber, probiotics, prebiotics, organic acids, antioxidants, vitamins, polyphenols, and spices are the numerous kinds of nutraceuticals (Das et al., 2012). The potential to regulate the intestinal microbiota's composition, enhance GI health, the intestinal barrier's functionality, and the host's immune system's activity, all of which have an impact on body weight gain and (FCR) feed conversion ratio, is what motivates their use in the poultry industry (Swaggerty et al., 2022). This category includes probiotics, prebiotics, organic acids, vitamins, enzymes, phytobiotics, and phytochemicals. Usually, feed, water, or in ovo are used to provide all of these substances. The categorization of poultry feed supplements is summarized in table 1. The classification of organic products along with mode of action is given in the table 2

Table 1: Categorization of Poultry Feed Supplements.

No.	Compounds	Source	Definition
1.	Nutraceuticals	Plant/animal	A part of feed that can be used for both treatment and prevention of a disease (Chauhan et al., 2013).
2.	Phytochemicals	Plant	Compounds derived from plants that have anti-inflammatory, anti-mutagenic, and antioxidant properties (Yan et al., 2019).
3.	Bioactive Compounds	Plant/animal	Non-essential nutrients found in feed and dietary supplements that provide health benefits beyond basic nutritional requirements, affecting health condition (El-Sherbiny et al., 2016).
4.	Antioxidant	Plant/animal	Substances that are either synthetic or natural, added to feed to prevent the deterioration of food (Shahidi, 2000).

Table 2: Categorization of products for the regulation of gut microbiota in Poultry with their mode of action

No.	Products	Definition	Mode of Action
1.	Probiotics	Live bacteria or yeast, when administer in sufficient amount provide the benefits to the host body especially to gastrointestinal tract of host (Division, 2006)	• Suppression of pathogenic bacterial growth through microbial competition, • Regulation of immune response, • Change in gut integrity, • Restore dysbiosis (Asghar et al., 2023)
2.	Prebiotics	Health promoting dietary fibers that modulate the gut microbiota to benefit the host (Pourabedin et al., 2015)	• Inhibit colonization of pathogenic bacteria • Immune system modulation • Improves the villus height of small intestine (Asgharet al., 2023)
3.	Phytobiotics	Plant based products added to animal feed for the removal of harmful pathogens , to improve the nutrient absorption and digestibility (Kholif & Olafadehan, 2021)	• Improvement in Feed conversion ratio(FCR) • Increase in nutrient absorption and digestibility • Destruction of pathogens by entering into their cell membrane • Change in gut integrity (Abdelli et al., 2021)
4.	Vitamins	Vital nutrients required for development, growth and metabolism of cells (Shojadoost et al., 2021)	• Have antioxidant properties • Reduce the formation of free radicals • Boost up the mucosal and cellular immunity (Shojadoost et al., 2021)

Salmonellosis

The three species of Salmonella; *S. enterica*, *S. bongori*, and *S. subterranean*, are members of the Enterobacteriaceae family. Only *S. enterica* subspecies enterica, out of the six subspecies of the species, is linked to the onset of disease in mammals and birds. Enteritidis and Typhimurium are the most common serovars in humans and poultry within the subspecies *S. enterica* (Gast et al., 2019). *Salmonella enterica* serovar *enteritidis* is frequently linked to poultry and its byproducts, however, serovar Typhimurium affects a diverse array of species, including poultry, cattle, and pigs (Antunes et al., 2016). The chicken industry suffers significant losses due to this bacterium, which is found all over the world. Anorexia, weakness, anxiety, drooping wings, ruffled feathers, and profuse diarrhea are typically the sole signs and symptoms of a Salmonella infection in young birds. Weight loss or growth retardation is typically seen during the first two to three weeks of life, when morbidity and death are at their highest. In older birds, clinical symptoms are uncommon (Gast et al., 2019). Considering that *S. enterica* is the second most prevalent foodborne illness in Europe, it also has significant implications for human health (EFSA & ECD, 2019). Antibiotics are widely used to treat this disease, and their misuse has encouraged the development of multi-drug resistant strains.

Resistance initially developed to earlier antibiotics (trimetoprim-sulfamethoxazole, ampicillin, and chloramphenicol), then spread to fluoroquinolones (ciprofloxacin) and extended-spectrum cephalosporins. Emergence of resistance to medically important antibiotics is a problem that has prompted calls for novel therapeutic compounds, such as carbapenems (Antunes et al., 2016).

Probiotics and Prebiotics

Numerous researches discuss the application of various probiotic strains to strengthen poultry's resistance against salmonellosis (El-Shall et al., 2020). The notion that a healthy micro flora can cause suppression of pathogenic bacterial growth through microbial competition, in which the probiotics compete with harmful bacteria for gut space, lowering the likelihood of microbial invasion, is connected to the idea of utilizing probiotics to achieve microbial control (Fuller, 1989). As far as other infections that will be covered later are concerned, this idea applies to *Salmonella* spp. Yet, probiotics also have other benefits, like lowering intraluminal pH through the synthesis of volatile fatty acids, producing host defense peptides, improving gastrointestinal function, and stimulating the immune system. Investigations have evaluated the anti-Salmonella potential of single or multi-strain probiotics incorporating *Lactobacillus*, *Enterococcus* and *Bacillus* species in chicken model, yielding encouraging outcomes (Neveling et al., 2020).

The usage of oligosaccharides, including mannanoligosaccharides (MOS), galactooligosaccharides (GOS), fructooligosaccharides (FOS), and inulin, is the primary focus of prebiotic research. Because mannose is present in the lumen, the use of MOS can reduce the adherence to intestinal epithelium and decrease the activity of *Salmonella* spp. It can also boost the immune response against *S. enteritidis* by increasing the infiltration of T lymphocytes in the mucosal layer of intestine (Lourenço et al., 2015).

Phytogenic Feed Additives (PFAs)

Researchers are exploring the potential of PAFs to contribute to a balanced gut micro-biome. According to the findings, essential oils from herbs and spices can play a crucial role in maintaining the health and productivity of birds by promoting feed intake, endogenous enzyme secretion, antioxidant generation, and antibacterial activity (Abudabos et al., 2016). This group includes plant extracts and its active components, such as carvacrol, thymol, capsaicin, cineole, and others, whose health benefits are associated with certain bioactive compounds (Murugesan et al., 2015). Interesting findings are shown in the contrasting impact of antibiotics and other PFAs, including anise, thymol essential oil, thyme essential oil, and other components, on broilers challenged with *S. Typhimurium* (Abudabos et al., 2016).

Vitamins

Vitamins C and E are potential supplements for preventing Salmonella infections in broiler chickens. Vitamin C, either by itself or in combination with other substances like curcumin, can help animals cope with a variety of stresses and lower the number of *Salmonella* spp. (Ghosh et al., 2019) and an enhancement of gut health (Gan et al., 2020). While there is no reduction in the cecal colonization of *S. typhimurium*, vitamin E and Arginine synergistically enhance immune defense against bacterial colonization by decreasing oxidative and immunological stress (Liu et al., 2014).

Necrotizing Enteritis

Necrotic enteritis (NE) induced by Clostridium perfringens strains (type A, C, G), is a significant economic burden on the chicken industry. Anorexia, sadness, diarrhea, ruffled feathers, and dehydration are just a few of the vague symptoms of NE. Animals death in acute forms may occur without any symptoms. More often, the only effects of subclinical forms of NE are weight and feed intake reduction.

The presence of gas causes the small intestine to become dilated, fragile, and hyperaemic, which are typical macroscopic lesions seen during autopsy. Light brown pseudo-membranes and sporadic bleeding are visible on the mucosal surfaces. Healthy hens typically include *C. perfringens* in their GI content, and predisposing conditions including coccidiosis, decreased feed quality, or the presence of another immunosuppressive disease are linked to onset of clinical manifestations. The potential of *C. perfringens* to create enterotoxins during sporulation, which can cause foodborne illnesses in humans (subtype A causes diarrhea, while subtype C induces NE), makes it a public health concern as well (Boulianne et al., 2020). Prevention and immediate treatment in the context of clinical manifestation are the cornerstones of traditional NE management techniques. Antibiotics, particularly bacitracin, tylosin, and lincomycin, have been utilized extensively. Yet, achieving the greatest possible reduction in predisposing variables, mainly coccidiosis, is the first essential component to restrict the spread and clinical manifestations of NE. New strategies to combat this infection are therefore required.

Probiotics and Prebiotics

Probiotics, prebiotics, and symbiotics are important because they can improve intestinal health, limit dysfunctions caused by lesions of the intestinal tight junction, and change bacterial translocation and/or nutrient absorption in addition to reducing *C. perfringens* infection. When *Bacillus subtilis* PB6 is used on infected hens, intestinal morphology is greatly improved, resulting in enhanced villus morphology characterized by increased villus length and villus to crypt ratio (Jayaraman et al., 2013). Due to the synthesis of host defense peptides, several strains of *Bacillus* species shown agonistic activity against *C. perfringes*, significantly reducing its symptoms (Hussein et al., 2020). The pathogenic impact of *C. perfringens* is diminished by the presence of specific Lactobacillus strains (Wang et al., 2017)

Phytogenic Feed Additives (PFAs)

Significant research has investigated the implications of PFAs on intestinal gross lesions and intestinal burden in *C. perfringens*. Phenolic chemicals including thymol, carvacrol, and eugenol, which have been shown to have potent antibacterial properties, are a significant component of essential oils (EOs) (Pham et al., 2020). Thymol, carvacrol, and eugenol, which are constituents of essential extracts from *Origanum vulgare, Piper nigrum, Syzygium aromaticum*, and *Thymus vulgaris*, have been studied for their ability to suppress *C. perfringens*. In some cases, a direct inhibitory impact on the pathogen or an action against its toxins is documented; however, the precise mechanism of action of these compounds is yet unknown (Diaz Carrasco et al., 2016). Tests of the effects of lysozyme and the essential oils thymol and carvacrol revealed that while each have benefits, but their combination does not enhance them (Du and Guo, 2021). Furthermore, extracts from quebracho (*Schinopsis lorentzii*) and chestnut (*Castanea sativa*), two common sources of tannins, have a significant effect on *C. perfringens* and its toxins, decreasing the number of bacteria and the extent of intestinal damage while shielding infected gastrointestinal tissue from oxidative injury (Tosi et al., 2013).

Vitamins

Despite the lack of research in this area, vitamins may have a preventative effect on chicken with NE. When broilers were treated with beta-carotene, their intestinal *C. perfringens* count and lesion score from infection decreased (Kang et al., 2018).

Coccidiosis

One poultry disease of global significance is coccidiosis. The causative agent of coccidiosis is Eimeria. Seven species of *Eimeria* (*E. acervuline, E. maxima, E. brunetti, E. praecox, E. mitis, E. tenella,* and *E. necatrix*) can infect poultry, with the most serious conditions being linked to infections with *E. tenella* and *E. necatrix*. Dehydration, a compromised digestive process, a diminished capacity to absorb nutrients, and heightened vulnerability to other pathogens are all symptoms of intestinal damage caused by *Eimeria* spp. Severe consequences are linked to bloody diarrhea and extremely high death rates (McDougald et al., 2020). *Eimeria* spp. infections are currently primarily linked to subclinical symptoms due to the decrease in severe clinical signs brought about by the use of anticoccidial medications, primarily sulphonamides. Yet, it continues to result in significant financial losses for the poultry sector. Additionally, *Eimeria* species alter the intestinal mucosa's permeability and functionality, which makes them a major risk factor for bacterial infections (Williams, 2005). Since the parasite is common and resistant, the best course of action in chicken production is prevention. Additionally, anticoccidial medications also experienced tolerance and widespread resistance, similar to antibiotics. Although the immunization against a number of *Eimeria* species showed great promise, but adverse consequences such mild infection after vaccination and decreased feed conversion and weight increase are deterring this approach (McDougald et al., 2020).

Probiotics and Prebiotics

Numerous products contain blend of beneficial bacteria, including *Bacillus* species, *Lactobacillus* species, *Enterococcus* species, *Pedicoccus* species, and *Bifidobacterium*, have been investigated in recent years with extremely encouraging results. By attaching themselves to the intestinal mucosa, probiotic bacteria limit the availability of receptors during *Eimeria* spp. infection, preventing Eimeria invasion. This prevents the intestinal mucosa from rupturing and secreting sporozoites, which in turn prevents the oocysts from proliferating and spreading (Madlala et al., 2021). Additionally, probiotic bacteria improve intestinal function and health by boosting GI microbiota balance and having an immuno-modulating and protective effect (Mohsin et al., 2021).

Furthermore, certain prebiotics, including inulin, fructo-oligosaccharides, mannan-oligosaccharides (MOS), and xylooligosaccharides, have been studied for the treatment of chicken coccidiosis (Adhikari et al., 2020). Both probiotic (*Bacillus subtilis*) and a prebiotic (mannan-oligosaccharides and β-glucans) can raise the feed conversion ratio without interfering negatively with the coccidiosis vaccination (Wang et al., 2019). MOS has been found to promote growth performance and reduce *E. tenella* related lesions in broilers, with efficacy comparable to that of Amprolium, a conventional anticoccidial agent (Chand et al., 2016).

Phytogenic Feed Additives (PFAs)

The most intriguing natural options for treating coccidiosis are PFAs and probiotics. El-shall et al. studied the majority of plants and their bioactive compounds utilized to combat *Eimeria* spp. infection. With so many articles on the subject, it is evident from this thorough analysis that the poultry sector is very interested in and has great potential for phytochemicals. Most of the time, it has been demonstrated that both herbs and herbal mixes are beneficial in preventing avian coccidiosis. A few anticoccidial actions have been observed, although the precise mode of action is not always clear. These include preventing invasion, inhibiting the growth of several *Eimeria* species, enhancing the immune system, preventing sporulation, preventing oocyst shedding, and lowering the oocyst score. Cell death results from the herbal extracts' phenolic components are reacting with the *Eimeria* cell membrane. Additionally, these extracts improve the healing of damaged epithelium, raise intestinal lipid peroxidation, and reduce intestinal cell permeability brought on by *Eimeria* species with a greater cellular turnover (El-Shall et al., 2022).

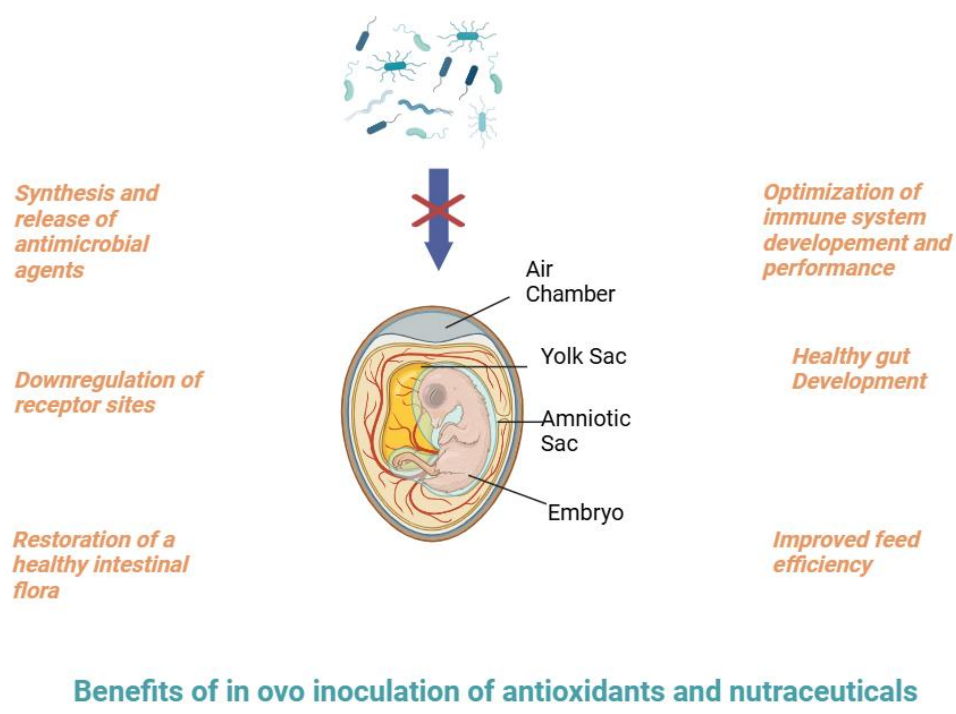

Fig. 1: Benefits of in ovo inoculation of antioxidants and nutraceuticals

Antioxidants

One method to lessen the effects of an *Eimeria* spp. infection is to add vitamins to the broiler's diet because this can lower the amount of Vitamin C and Vitamin E in the host cells. Furthermore, several anticoccidial compounds, including toltrazuril and salinomycin, work by limiting peroxidation (Khater et al., 2020). Selenium, zinc, vitamin E, copper, and manganese supplements can lessen the disease's effects and the coccidian load can be reduced by using a combination of curcumin (*Curcuma longa*) and microencapsulated phytogenics that contain thymol, cinnamon aldehyde, and carvacrol (Galli et al., 2020). Additionally, providing chickens with higher-than-recommended levels of vitamin E and arginine can enhance their innate and humoral responses to animals challenged by *Eimeria spp.* (Perez-Carbajal et al., 2010). Antioxidant enzyme levels can also be raised by curcumin and cinnamon aldehyde, which protects the cells of intestine from oxidative stress induced by *E. tenella* (Khan et al., 2012).

In Ovo Technique

During the incubation period, we can directly administer chemicals to the chicken embryo using a technique called in ovo inoculation. It was initially intended to provide early and efficient immunization for the Marek's Disease (MD) vaccination (Sharma and Burmester, 1984). The in ovo technique was employed to investigate supplementary substances. The notion of feeding embryos in ovo was introduced in 2003, which involves delivering essential nutrients and other natural bio substances into the embryonic amnion to regulate the hatchling's intestinal development (Uni and Ferket, 2003). Since the intestinal system of chickens is still developing when they hatch, the time between hatching and the first feeding is crucial. As a result, administering drugs in ovo gives us significant impacts on the future growth of the animal. Air chamber, allantoid sac, amniotic sac are different sites that can be used for injections during incubation days (12–19 days). The amniotic sac is the recommended site for inoculation, where the vaccine of MD is also given. The injected materials are consumed by the chicken prior to hatching, making direct contact with the respiratory and digestive systems (Jha et al., 2019).

The benefits of in ovo technique are described in the figure 1, which include synthesis and release of antimicrobial agents, down regulation of receptor sites, restoration of a healthy intestinal flora, optimization of immune system, development of healthy gut, improved FCR.

In Ovo inoculation Technique against Gastrointestinal Pathogens

Salmonella spp. from the environment is frequently encountered before the chicken has eaten its first meal. A healthy gastrointestinal tract can lessen the impact of low level Salmonella spp. infection, and probiotic bacteria can stop pathogens from colonizing through the mechanism of competitive exclusion (De Oliveira et al., 2014). The amniotic sac is the preferable location of administration in this situation because the inoculum comes into direct touch with the gastrointestinal system, and in ovo probiotic and prebiotic administration can decrease Salmonella colonization and fecal shedding (Hosseini-Mansoub et al., 2011).

In hens challenged with Eimeria maxima at 14 days posthatch and then with *C. perfringens* at 18 days posthatch, selenium, a non-metallic important micronutrient, can alter the immunological response. Compared to non-intervention group, the treated groups, which received 10 and 20 μg of selenium per egg, exhibited lower level of intestinal damage and oocyst shedding as well as higher serum antibody levels against *C. perfringens* α-toxin and NetB toxin, indicating an improved immune response during the post-hatching phase (Hosseini-Mansoub et al., 2011). A raffinose family oligosaccharide (RFO) isolated from *Lupinus luteus* seeds was injected in ovo after 12 days of incubation, resulting in a 2.5 log reduction in *C. perfringens* count and an 89% reduction in *Eimeria* spp. oocyst shedding (Stadnicka et al., 2020). In ovo probiotic delivery on day 18 of incubation substantially decreases the severity of *Eimeria* induced microscopic lesions in intestines. This treatment also improves zootechnical performance, offering a promising strategy for enhancing poultry health and productivity (Pender et al., 2016).

Conclusion

Due to increase in the antimicrobial resistance, antioxidants and nutraceuticals has gain importance as possible alternative to antimicrobials. Any replacement for antibiotics should ideally match their ability to improve growth rates, optimize FCR and mitigate the risk of pathogenic infections. A wide range of natural products has been identified as better alternative to antibiotics, with dual benefit of boosting immune system as well as defense system of animal body against the infections. Numerous studies have been undertaken to demonstrate the potential of antioxidants and nutraceuticals for the prevention and control of gastrointestinal infections with a focus on their efficacy and safety. The existing literature generally supports the efficacy of antioxidants and nutraceuticals in promoting gut integrity and boosting immune system; however, some studies have raised conflicting findings in the data highlight the need for continued research in this area. The in ovo inoculation approach offer a promising strategy , enabling early intervention that shapes the development of gut and immune systems, thereby enhancing the chicken’s defenses against gastrointestinal infection and promoting the overall health status.

References

Abdelli, N., Solà-Oriol, D., & Pérez, J. F. (2021). Phytogenic feed additives in poultry: achievements, prospective and challenges. *Animals*, *11*(12), 3471.

Abudabos, A. M., Alyemni, A. H., Dafalla, Y. M., & Khan, R. U. (2016). The effect of phytogenic feed additives to substitute in-feed antibiotics on growth traits and blood biochemical parameters in broiler chicks challenged with Salmonella typhimurium. *Environmental Science and Pollution Research*, *23*, 24151-24157.

Adhikari, P., Kiess, A., Adhikari, R., & Jha, R. (2020). An approach to alternative strategies to control avian coccidiosis and necrotic enteritis. *Journal of Applied Poultry Research*, *29*(2), 515-534.

Alagawany, M., Elnesr, S. S., Farag, M. R., Abd El-Hack, M. E., Barkat, R. A., Gabr, A. A., & El-Sabrout, K. (2021). Potential role of important nutraceuticals in poultry performance and health-A comprehensive review. *Research in Veterinary Science*, *137*, 9-29.

Antunes, P., Mourão, J., Campos, J., & Peixe, L. (2016). Salmonellosis: the role of poultry meat. *Clinical Microbiology and Infection*, *22*(2), 110-

121.

Asghar, M,, Khan, M.U.R., Shah, S.M.Q.A., Naseem, M.F., Bibi, N., Dastageer, H., Farooq, I., Imran, A., Ameen, A., and Wazir, N., 2024. Use of probiotics and prebiotics against clostridial diseases in poultry. In: Liu P (ed), *Gut Heath, Microbiota and Animal Diseases, 1,* (pp. 58-66). Unique Scientific Publishers, Faisalabad, Pakistan.

Boulianne, M., Uzal, F. A., & Opengart, K. (2020). Clostridial diseases. *Diseases of Poultry*, 966-994

Brower, V. (1998). Nutraceuticals: poised for a healthy slice of the healthcare market? *Nature Biotechnology*, *16*(8), 728-731.

Castanon, J. (2007). History of the use of antibiotic as growth promoters in European poultry feeds. *Poultry Science*, *86*(11), 2466-2471.

Chand, N., Faheem, H., Khan, R. U., Qureshi, M. S., Alhidary, I. A., & Abudabos, A. M. (2016). Anticoccidial effect of mananoligosacharide against experimentally induced coccidiosis in broiler. *Environmental Science and Pollution Research*, *23*, 14414-14421.

Chauhan, B., Kumar, G., Kalam, N., & Ansari, S. H. (2013). Current concepts and prospects of herbal nutraceutical: A review. *Journal of Advanced Pharmaceutical Technology & Research*, *4*(1), 4-8.

Cosby, D. E., Cox, N. A., Harrison, M. A., Wilson, J. L., Buhr, R. J., & Fedorka-Cray, P. J. (2015). Salmonella and antimicrobial resistance in broilers: A review. *Journal of Applied Poultry Research*, *24*(3), 408-426.

Das, L., Bhaumik, E., Raychaudhuri, U., & Chakraborty, R. (2012). Role of nutraceuticals in human health. *Journal of Food Science and Technology*, *49*, 173-183.

De Oliveira, J., Van der Hoeven-Hangoor, E., Van de Linde, I., Montijn, R., & Van der Vossen, J. (2014). In ovo inoculation of chicken embryos with probiotic bacteria and its effect on posthatch Salmonella susceptibility. *Poultry Science*, *93*(4), 818-829.

Díaz Carrasco, J. M., Redondo, L. M., Redondo, E. A., Dominguez, J. E., Chacana, A., & Fernandez Miyakawa, M. E. (2016). Use of plant extracts as an effective manner to control Clostridium perfringens induced necrotic enteritis in poultry. *BioMed Research International*, *2016*(1), 3278359.

Division, N. (2006). Health and Nutritional Properties and Guidelines for Evaluation—Report of a Joint FAO/WHO Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food including Powder Milk with Live Lactic Acid Bacteria. In: FAO/WHO.

Du, E., & Guo, Y. (2021). Dietary supplementation of essential oils and lysozyme reduces mortality and improves intestinal integrity of broiler chickens with necrotic enteritis. *Animal Science Journal*, *92*(1), e13499.

El-Shall, N. A., Awad, A. M., El-Hack, M. E. A., Naiel, M. A., Othman, S. I., Allam, A. A., & Sedeik, M. E. (2019). The simultaneous administration of a probiotic or prebiotic with live Salmonella vaccine improves growth performance and reduces fecal shedding of the bacterium in Salmonella-challenged broilers. *Animals*, *10*(1), 70.

El-Sherbiny, I. M., El-Baz, N., & Hefnawy, A. (2016). Potential of nanotechnology in nutraceuticals delivery for the prevention and treatment of cancer. *Nanotechnology in the Agri-Food Industry*, *4*, 117-152.

European Food Safety Authority and European Centre for Disease Prevention and Control (EFSA and ECDC). (2019). The European Union one health 2018 zoonoses report. *EFSA Journal*, *17*(12), e05926.

Fuller, R. (1989). Probiotics in man and animals. *The Journal of Applied Bacteriology*, *66*(5), 365-378.

Galli, G. M., Gerbet, R. R., Griss, L. G., Fortuoso, B. F., Petrolli, T. G., Boiago, M. M., & Wagner, R. (2020). Combination of herbal components (curcumin, carvacrol, thymol, cinnamaldehyde) in broiler chicken feed: Impacts on response parameters, performance, fatty acid profiles, meat quality and control of coccidia and bacteria. *Microbial Pathogenesis*, *139*, 103916.

Gan, L., Fan, H., Mahmood, T., & Guo, Y. (2020). Dietary supplementation with vitamin C ameliorates the adverse effects of Salmonella Enteritidis-challenge in broilers by shaping intestinal microbiota. *Poultry Science*, *99*(7), 3663-3674.

Gast, R. K., & Porter Jr, R. E. (2019). Salmonella infections. In D. E. Swayne, M. Boulianne, C. M. Logue, L. R. McDougald, V. Nair, D. L. Suarez, S. de Wit, T. Grimes, D. Johnson, M. Kromm, T. Y. Prajitno, I. Rubinoff, G. Zavala (Eds.), *Diseases of Poultry, 1*, (pp. 717-753). John Wiley & Sons.

Ghosh, T., Srivastava, S. K., Gaurav, A., Kumar, A., Kumar, P., Yadav, A. S., & Navani, N. K. (2019). A combination of linalool, vitamin C, and copper synergistically triggers reactive oxygen species and DNA damage and inhibits Salmonella enterica subsp. enterica Serovar Typhi and Vibrio fluvialis. *Applied and Environmental Microbiology*, *85*(4), e02487-02418.

Hosseini-Mansoub, N., Vahdatpour, T., Arjomandi, M., & Vahdatpour, S. (2011). Comparison of different methods of probiotic prescription against Salmonella infection in hatchery broiler chickens. *Advances in Environmental Biology, 5*(7), 1857-1860.

Hussein, E. O., Ahmed, S. H., Abudabos, A. M., Suliman, G. M., Abd El-Hack, M. E., Swelum, A. A., & N. Alowaimer, A. (2020). Ameliorative effects of antibiotic-, probiotic-and phytobiotic-supplemented diets on the performance, intestinal health, carcass traits, and meat quality of Clostridium perfringens-infected broilers. *Animals*, *10*(4), 669.

Huyghebaert, G., Ducatelle, R., & Van Immerseel, F. (2011). An update on alternatives to antimicrobial growth promoters for broilers. *The Veterinary Journal*, *187*(2), 182-188.

Jayaraman, S., Thangavel, G., Kurian, H., Mani, R., Mukkalil, R., & Chirakkal, H. (2013). Bacillus subtilis PB6 improves intestinal health of broiler chickens challenged with Clostridium perfringens-induced necrotic enteritis. *Poultry Science*, *92*(2), 370-374.

Jha, R., Singh, A. K., Yadav, S., Berrocoso, J. F. D., & Mishra, B. (2019). Early nutrition programming (in ovo and post-hatch feeding) as a strategy to modulate gut health of poultry. *Frontiers in Veterinary Science*, *6*, 82.

Kang, M., Oh, J., Cha, S., Kim, W., Cho, H., & Jang, H. (2018). Efficacy of polymers from spontaneous carotenoid oxidation in reducing necrotic enteritis in broilers. *Poultry Science*, *97*(9), 3058-3062.

Khan, R. U., Naz, S., Javdani, M., Nikousefat, Z., Selvaggi, M., Tufarelli, V., & Laudadio, V. (2012). The use of turmeric (Curcuma longa) in poultry feed. *World's Poultry Science Journal*, *68*(1), 97-103.

Khater, H. F., Ziam, H., Abbas, A., Abbas, R. Z., Raza, M. A., Hussain, K., & Selim, A. (2020). Avian coccidiosis: Recent advances in alternative control strategies and vaccine development. *Agrobiological Records*, *1*, 11-25.

Kholif, A. E., & Olafadehan, O. A. (2021). Essential oils and phytogenic feed additives in ruminant diet: Chemistry, ruminal microbiota and fermentation, feed utilization and productive performance. *Phytochemistry Reviews*, *20*(6), 1087-1108.

Liu, X., Byrd, J., Farnell, M., & Ruiz-Feria, C. (2014). Arginine and vitamin E improve the immune response after a Salmonella challenge in broiler chicks. *Poultry Science*, *93*(4), 882-890.

Lourenço, M., Kuritza, L., Hayashi, R., Miglino, L., Durau, J., Pickler, L., & Santin, E. (2015). Effect of a mannanoligosaccharide-supplemented diet on intestinal mucosa T lymphocyte populations in chickens challenged withSalmonella Enteritidis. *Journal of Applied Poultry Research*, *24*(1), 15-22.

Madlala, T., Okpeku, M., & Adeleke, M. A. (2021). Understanding the interactions between Eimeria infection and gut microbiota, towards the control of chicken coccidiosis: a review. *Parasite*, *28*.

McDougald, L. R., Cervantes, H. M., Jenkins, M. C., Hess, M., & Beckstead, R. (2020). Protozoal infections. *Diseases of Poultry*, 1192-1254.

Mohsin, M., Abbas, R. Z., Yin, G., Sindhu, Z.-U.-D., Abbas, A., Huang, Z., & Ejaz, A. (2021). Probiotics as therapeutic, antioxidant and immunomodulatory agents against poultry coccidiosis. *World's Poultry Science Journal*, *77*(2), 331-345.

Murugesan, G. R., Syed, B., Haldar, S., & Pender, C. (2015). Phytogenic feed additives as an alternative to antibiotic growth promoters in broiler chickens. *Frontiers in Veterinary Science*, *2*, 21.

Neveling, D. P., van Emmenes, L., Ahire, J., Pieterse, E., Smith, C., & Dicks, L. (2020). Effect of a multi-species probiotic on the colonisation of Salmonella in broilers. *Probiotics and Antimicrobial Proteins*, *12*, 896-905.

Perez-Carbajal, C., Caldwell, D., Farnell, M., Stringfellow, K., Pohl, S., Casco, G., & Ruiz-Feria, C. (2010). Immune response of broiler chickens fed different levels of arginine and vitamin E to a coccidiosis vaccine and Eimeria challenge. *Poultry Science*, *89*(9), 1870-1877.

Pender, C., Kim, S., Potter, T., Ritzi, M., Young, M., & Dalloul, R. (2016). Effects of in ovo supplementation of probiotics on performance and immunocompetence of broiler chicks to an Eimeria challenge. *Beneficial Microbes*, *7*(5), 699-706.

Pham, V. H., Kan, L., Huang, J., Geng, Y., Zhen, W., Guo, Y., & Wang, Z. (2020). Dietary encapsulated essential oils and organic acids mixture improves gut health in broiler chickens challenged with necrotic enteritis. *Journal of Animal Science and Biotechnology*, *11*, 1-18.

Pourabedin, M., & Zhao, X. (2015). Prebiotics and gut microbiota in chickens. *FEMS Microbiology Letters*, *362*(15), fnv122.

Roth, N., Käsbohrer, A., Mayrhofer, S., Zitz, U., Hofacre, C., & Domig, K. J. (2019). The application of antibiotics in broiler production and the resulting antibiotic resistance in Escherichia coli: A global overview. *Poultry Science*, *98*(4), 1791-1804.

Shahidi, F. (2000). Antioxidants in food and food antioxidants. *Food/nahrung*, *44*(3), 158-163.

Shehata, A. A., Yalçın, S., Latorre, J. D., Basiouni, S., Attia, Y. A., Abd El-Wahab, A., & Hafez, H. M. (2022). Probiotics, prebiotics, and phytogenic substances for optimizing gut health in poultry. *Microorganisms*, *10*(2), 395.

Sharma, J. M., & Burmester, B. R. (1984). *U.S. Patent No. 4,458,630*. Washington, DC: U.S. Patent and Trademark Office.

Shojadoost, B., Yitbarek, A., Alizadeh, M., Kulkarni, R. R., Astill, J., Boodhoo, N., & Sharif, S. (2021). Centennial Review: Effects of vitamins A, D, E, and C on the chicken immune system. *Poultry Science*, *100*(4), 100930.

Stadnicka, K., Bogucka, J., Stanek, M., Graczyk, R., Krajewski, K., Maiorano, G., & Bednarczyk, M. (2020). Injection of raffinose family oligosaccharides at 12 days of egg incubation modulates the gut development and resistance to opportunistic pathogens in broiler chickens. *Animals*, *10*(4), 592.

Swaggerty, C. L., Bortoluzzi, C., Lee, A., Eyng, C., Pont, G. D., & Kogut, M. H. (2022). Potential replacements for antibiotic growth promoters in poultry: interactions at the gut level and their impact on host immunity. *Recent Advances in Animal Nutrition and Metabolism*, 145-159.

Tosi, G., Massi, P., Antongiovanni, M., Buccioni, A., Minieri, S., Marenchino, L., & Mele, M. (2013). Efficacy test of a hydrolysable tannin extract against necrotic enteritis in challenged broiler chickens. *Italian Journal of Animal Science*, *12*(3), e62.

Uni, Z., & Ferket, P. R. (2003). Enhancement of development of oviparous species by in ovo feeding. In: Google Patents.

Wang, H., Ni, X., Liu, L., Zeng, D., Lai, J., Qing, X., & Jing, B. (2017). Controlling of growth performance, lipid deposits and fatty acid composition of chicken meat through a probiotic, Lactobacillus johnsonii during subclinical Clostridium perfringens infection. *Lipids in health and disease*, *16*, 1-10.

Wang, X., Peebles, E. D., Kiess, A. S., Wamsley, K. G., & Zhai, W. (2019). Effects of coccidial vaccination and dietary antimicrobial alternatives on the growth performance, internal organ development, and intestinal morphology of Eimeria-challenged male broilers. *Poultry science*, *98*(5), 2054-2065.

Williams, R. (2005). Intercurrent coccidiosis and necrotic enteritis of chickens: rational, integrated disease management by maintenance of gut integrity. *Avian Pathology*, *34*(3), 159-180.

Yan, L., An, S., Lv, Z., Wang, Z., Wu, Y., Zhu, Y., & Zhu, Z. (2019). Effects of phytonutrients on growth performance, antioxidative status, and energy utilization of broilers fed low energy diets. *Animal Nutrition*, *5*(3), 270-277.