

Review

Use of *Spirulina platensis* and *Curcuma longa* as Nutraceuticals in Poultry

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Abstract: Since the banning of antibiotics in animal feeds (2006), there has been an increase in the number of studies looking for alternatives to stimulate the gut immune system. The main objective of our review article is to underline the nutraceutical properties of *Curcuma longa* and *Spirulina platensis* in the broiler chicken industry, and the experimental data were obtained by analyzing literature sources. *Spirulina platensis* is widely recognized as a valuable protein source, containing approximately 55–70% protein, 25% carbohydrates, essential amino acids, and 18% fatty acids. It is also rich in various vitamins like thiamin, riboflavin, pyridoxine, vitamin B12, vitamin C, gamma-linolenic acid, phycocyanins, tocopherols, chlorophyll, beta-carotenes, carotenoids, exhibiting positive effects on growth performance, gut integrity, and immunity. The anti-inflammatory effect of spirulina supplementation at different levels showed a decrease in caspase-3 and the TNF- α immunolabeling index; a reduction in IL-1 β , IL-2 and IFN- γ ; and an increase in the expression of the anti-inflammatory cytokine IL-4. Spirulina inhibits the synthesis of cytokines IL-1, IL-6, and TNF-gamma in addition to the activities of inducible nitric oxide synthase (iNOS) and cyclooxygenase 2 (COX-2) enzymes. Turmeric also positively influences the growth, egg production, and overall health of chickens. Curcumin, the most potent component of turmeric, possesses additional pharmacological activities, including hepatoprotective, immunostimulant, and anticancer effects. Its immunomodulatory properties greatly enhance the immune system response, acting as a natural antibiotic against pathogens and decreasing levels of proinflammatory interleukins IL-1 β , IL-6, IL-2, IL-18, and TNF- α .

Keywords: chickens; spirulina; turmeric; growth promoters; immunomodulators



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1. Introduction

Poultry production, particularly in developing regions, is experiencing rapid growth within the agricultural sector, making a valuable contribution to ensuring food security [1]. The rising demand for alternative feed resources is driven by factors such as intensified competition with other agricultural sectors over land, the impacts of climate change, and the ongoing need to enhance productivity and meat quality. Furthermore, there has been a growing focus on producing innovative functional foods using environmentally friendly sources [2].

Nutraceuticals refer to the essential nutrients or dietary components derived from animals that hold significant nutritional and pharmaceutical value. They exhibit immunomodulatory properties and play a crucial role in preventing diseases, promoting overall health, and subsequently enhancing productivity [3–6]. In addition, these nutraceuticals aid in safeguarding the host from infectious diseases [7], as well as influencing and sustaining essential physiological functions that contribute to the well-being of the host [8].

The term “nutraceutical” was coined in 1989 by Stephen DeFelice, combining the words “nutrition” and “pharmaceutical”. He clarified that a nutraceutical could encompass either a food or a component of food with the potential to prevent and/or treat diseases [9,10]. Since then, the term has been the subject of ongoing global discussions regarding its precise definition and scope.

Nutraceuticals encompass a wide range of substances, including isolated nutrients, such as vitamins, minerals, amino acids, and fatty acids. They also include herbal products, such as polyphenols, herbs, and spices, as well as dietary supplements, such as probiotics, prebiotics, synbiotics, organic acids, antioxidants, and enzymes. Additionally, nutraceuticals can extend to genetically modified foods [8,11,12].

Amino acids [13], minerals [14], and vitamins [15] play a significant role as common components in poultry diets, either individually or in combination [16,17], and can be considered as nutraceuticals with particular importance in poultry feeding. While natural feedstuffs generally provide essential nutrients for poultry, certain crucial amino acids (lysine, methionine, threonine, and tryptophan), vitamins, and minerals are often supplemented synthetically [18]. The refined form of these nutraceutical constituents in the diet can lead to improved digestion, absorption, utilization, and metabolism, ultimately resulting in beneficial health effects compared to conventional forms.

The nutraceutical value and conversion efficiency in poultry are subject to the influence of multiple factors, such as the genetic potential of the birds, environmental conditions, dietary quality, and gut health. Consideration of these factors is crucial for maximizing the productive efficiency of the birds [19–21].

In recent times, nutraceuticals have garnered significant attention in poultry science. This is attributed to the recognition of the nutritional and healthier attributes of feed ingredients, as well as growing concerns regarding the adverse effects associated with chemical pharmaceuticals, such as antibiotic resistance and the presence of drug residues [22,23].

The use of antibiotics in poultry has been known to reduce the microbial load in the gut, thereby increasing nutrient availability for the host [24]. However, concerns regarding the development of antimicrobial resistance and the transfer of antibiotic-resistance genes from animals to human microbiota prompted the European Union to ban the application of antibiotics as growth promoters from 1 January 2006 [25]. The removal of antibiotic growth promoters (AGP) from poultry diets has resulted in challenges related to animal performance and an increase in the occurrence of certain poultry diseases, such as subclinical necrotic enteritis and dysbacteriosis [26]. Consequently, there is a pressing need to find alternatives to AGP.

Ideally, these alternatives should provide similar beneficial effects as AGP. In recent years, there has been a significant increase in nutrition-based research focused on finding alternatives to AGP in various farm animals, including poultry [26].

In this context, nutraceuticals have been discovered to possess numerous beneficial health applications and potential roles in improving production performances in poultry. They serve as antioxidants in promoting health, modulating the composition of gut microbiota, and enhancing poultry immunity [3,11,27–29].

1.1. *Spirulina spp.*

The utilization of microalgae as a feed ingredient offers several advantages in terms of environmental protection and conservation of natural resources, including the prevention of land degradation and water scarcity issues [30]. In the field of poultry nutrition, there is a growing trend toward the incorporation of natural ingredients as alternatives to antibiotics, growth factors, and other chemical substances.

Spirulina platensis (SP), a blue-green filamentous photosynthetic alga, is widely recognized as a valuable protein source, containing approximately 55–70% protein, 25% carbohydrates, essential amino acids, and 18% fatty acids. It is also rich in various vitamins and minerals. Notably, spirulina is known for its high content of thiamin, riboflavin, pyridoxine, vitamin B12, vitamin C, gamma-linolenic acid, phycocyanins, tocopherols, chlorophyll,

beta-carotenes, and carotenoids [31]. Recent studies have demonstrated that spirulina exhibits positive effects on growth performance, gut integrity, and immunity. Additionally, it has shown modulating activity and has been associated with various pharmacological properties.

Several studies have been conducted to investigate the potential benefits of SP in broilers. These studies have explored its use as a growth promoter [32,33], regulator of gut health [34], immune stimulator [35], and enhancer of meat yield and quality [2]. These studies have reported various findings highlighting the positive effects of SP in these different aspects of broiler production.

A significant and expanding body of research has provided evidence for the immunostimulatory, hepatoprotective, anti-inflammatory, antimicrobial, antiviral, and antioxidative activities of SP [36,37]. These activities are attributed to its ability to enhance disease resistance, stimulate the production of antibodies and cytokines, effectively scavenge free radicals, and inhibit lipid peroxidation. Consequently, the inclusion of SP in poultry production has shown promising results in improving overall production outcomes and attaining greater profitability [38–41].

Spirulina has gained recognition for its diverse biological effects, including the prevention of anemia due to its high iron and vitamin content [42]. It has also shown a potential to inhibit herpes simplex infection [43]. Studies have revealed that the ethanolic extract of SP contains various bioactive compounds, such as alkaloids, flavonoids, glycosides, tannins, phenolic compounds, steroids, and saponins [44].

Numerous studies have indicated the therapeutic effects of spirulina. It has been shown to reduce cholesterol levels and potentially have anticancer properties by enhancing the immune system. Additionally, spirulina has been found to increase the population of beneficial intestinal lactobacilli, reduce nephrotoxicity caused by heavy metals and drugs, and offer radiation protection [45]. Furthermore, spirulina is widely recognized for its antioxidant properties, which can be attributed to molecules such as phycocyanin, beta-carotene, and tocopherol. These antioxidant properties contribute to spirulina's ability to inhibit carcinogenesis and mitigate organ-specific toxicity [46].

Phycocyanin (PC) is a blue pigment found in cyanobacteria and certain red algae of the phycobiliprotein family. It is soluble in water and primarily located in the cytoplasmic membrane. However, it can be released outside the cells when the thylakoid membrane is disrupted by lysozyme enzymes and EDTA-chelated cations [47,48]. PC exhibits a range of beneficial properties, including antioxidant, radical scavenging, anti-inflammatory, anti-arthritic, hepatoprotective, antitumor, and immune-enhancing activities [49,50]. In broiler production, natural antioxidants are preferred due to their health-promoting characteristics [51]. These antioxidants help reduce the production of reactive oxygen species (ROS) and subsequent oxidative stress [52].

In the current global market, there is significant competition between microalgae carotenoids and artificial, synthetic, and unnatural pigments [53]. Despite their relatively high cost, natural algae are used in smaller quantities and have no known side effects [54].

Similar to other animals, the digestive tract of poultry plays a critical role in the utilization and intake of feed while also being important in terms of exposure to environmental pathogens [25]. Any functional disturbances in the digestive tract can pose risks to the health and performance of poultry, as it can disrupt the absorption and digestion of nutrients. The small intestine is particularly crucial for nutrient absorption [55]. The intestinal mucosa plays a vital role in enhancing nutrient absorption and acts as a barrier between the internal tissues of the host and the intestinal contents, thereby serving as an immune defense mechanism [19]. The proper functioning of the mucosal layer is the result of a delicate balance between the mucosal layer, epithelial cells, immune cells, and the microbiota [56].

The intestinal microbiota plays a crucial role in maintaining immune homeostasis and regulating inflammatory responses [57]. Commensal bacteria in the intestine produce short-chain fatty acids (SCFAs), which have anti-inflammatory properties and help protect

against intestinal injury [58]. Modulation of the intestinal microbiota can be achieved by incorporating nutraceuticals into the poultry diet. Nutraceuticals have the potential to promote the growth of beneficial bacteria while suppressing the growth of harmful bacteria [59]. This modulation of the intestinal microbiota can have significant implications for the overall health and well-being of poultry.

The gut microbiota plays crucial roles in the regulation of epithelial cell proliferation in the gut, synthesis of vitamins, and host energy metabolism. In poultry, the gastrointestinal tract (GIT) harbors a complex and dynamic microbiome primarily composed of bacteria, with a lesser presence of fungi, protozoa, bacteriophages, yeast, and viruses. This diverse microbial community has significant impacts on various aspects of poultry health and physiology.

Microbes within the gastrointestinal tract (GIT) interact extensively with the host and the consumed feed. Different regions of the GIT harbor distinct populations of microbes, creating specific niches [21]. In chickens, imbalances in the gut microbiota have been associated with adverse effects on intestinal health [60,61]. It is widely acknowledged that maintaining an appropriate microbial balance, with favorable bacteria comprising about 85% of the total bacterial population, is crucial for the host's well-being [62]. The elimination of antibiotics from feed further compounds bacterial imbalances. Correspondingly, Kabir demonstrated that a balanced gut microbiota is vital for maximizing chicken growth performance and promoting a healthy gut [63].

Fortunately, dietary interventions, in conjunction with promoting the growth of beneficial bacteria in the chicken intestine, can be used to modulate the gut microbial population [59]. Studies by Humphrey and Klasing have shown that changes in the microbiota can impact gut wall morphology, elicit immune responses, and ultimately influence energy expenditure and chicken development [64]. These findings highlight the importance of maintaining a healthy and balanced gut microbiota for optimal poultry growth and overall well-being.

1.2. *Curcuma* spp.

Turmeric (*Curcuma* spp.) is a perennial herb with rhizomatous growth, belonging to the Zingiberaceae family. It is extensively cultivated and utilized in tropical and sub-tropical regions worldwide [65]. Turmeric is highly regarded for its medicinal properties, exhibiting a wide array of pharmacological effects, such as antioxidant, anti-protozoal, antimicrobial, anti-inflammatory, and antitumor activities [66]. The primary active compound in turmeric is curcumin, which demonstrates potent antioxidant capabilities [67,68]. Turmeric belongs to a category of medicinal plants that offer an alternative natural antibiotic approach for poultry farming. Supplementation of turmeric effectively influences the growth, egg production, and overall health of chickens [69]. This medicinal plant possesses rhizomes and subterranean stems resembling roots [70], originally used as a food additive in curries to enhance food storage, appearance, flavor, palatability, and preservation. The addition of turmeric powder and extracts has beneficial effects on the performance of birds and animals [71].

Turmeric contains several active ingredients, namely curcumin, demethoxycurcumin, bisdemethoxycurcumin, and tetrahydro curcuminoids [72]. Among these, curcumin, extracted from turmeric rhizomes, is the primary bioactive compound of *C. longa*, exhibiting antioxidant, antiviral, and antibacterial properties [73]. Curcumin, the most potent component of turmeric, represents 3–5% of the curcuminoids found in the rhizomes and acts as a robust phenolic antioxidant [74]. Turmeric also possesses additional pharmacological activities, including hepatoprotective, immunostimulant, and anticancer effects [75]. Its immunomodulatory properties greatly enhance the immune system's response, acting as a natural antibiotic against pathogens. Turmeric effectively regulates inflammation, playing a crucial role in preventing inflammation-related disorders in poultry [76]. The World Health Organization (WHO) has declared turmeric safe for dietary consumption in humans and animal feed [77].

Curcumin, a polyphenolic compound, possesses various bioactive properties, including antibacterial, anti-inflammatory, anti-carcinogenic, anti-proliferative, and antioxidant effects [78–81]. It has been observed that curcumin affects bile production and lipid metabolism in the liver, leading to the belief that the active constituents in turmeric can enhance liver function by reducing cholesterol levels in the liver and serum. Consequently, they have the potential to regulate cholesterol levels and lipid profiles [82–86].

Turmeric (*Curcuma longa*) is a widely utilized natural remedy with a plethora of pharmacological properties. In terms of its biochemical composition, turmeric consists of approximately 69.4% carbohydrates, 6.3% protein, 5.1% fat, 3.5% minerals, and 13.1% moisture [78]. It also contains approximately 5% essential oils and 5% curcumin, a bioactive polyphenol [87]. Curcumin, the principal component of turmeric, is insoluble in water and ether but can disperse in ethanol and other organic solvents [88]. Among the noteworthy bioactive constituents in turmeric are curcumin, dimethoxy curcumin, tetrahydro curcuminoids, and bis-methoxy curcumin [87]. The diverse biological activities of turmeric stem from the presence of these various bioactive molecules. Curcumin exhibits specific antimicrobial, anti-inflammatory, antioxidant, and anticancer properties [89]. Moreover, curcumin enhances insulin release, facilitates fatty acid uptake, reduces lipogenesis, and elevates nitric oxide (NO) levels [90]. Turmeric has so far been reported to possess 326 biological activities [64,84,86].

Curcumin possesses a distinctive chemical structure that is primarily responsible for its antioxidant properties. It contains carbon–carbon double bonds, a β -diketo group, and phenyl rings with hydroxyl and methoxy substituents [91]. This unique structure enables curcumin to donate hydrogen atoms (from its phenolic groups) to effectively neutralize free radicals. Aside from curcumin, which is the main polyphenol, turmeric powder also contains dimethoxycurcumin, bis-dimethoxycurcumin, 2,5-xylenol [92], flavonoids, tannins, and ascorbic acid [93]. These compounds can also exhibit neutralizing activity toward free radicals (Figure 1).

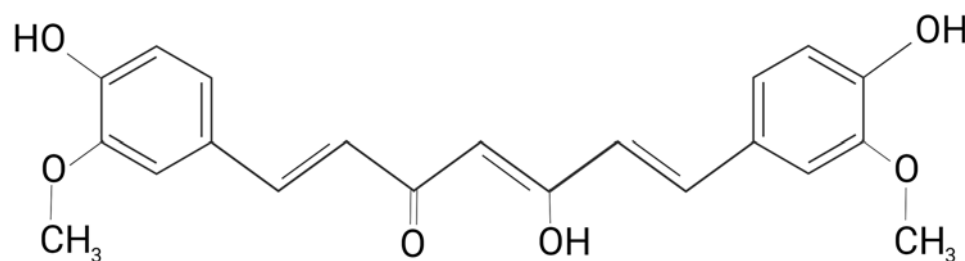


Figure 1. Curcumin chemical structure. The figure was created using [BioRender.com](https://www.biorender.com) accessed on 19 June 2023.

Turmeric is widely used as a treatment for inflammatory conditions and has various applications in traditional Chinese medicine, including its use as a stimulant, aspirant, carminative, emmenagogue, astringent, detergent, and diuretic [94]. Over the past decade, the use of turmeric in poultry feed has become widespread due to its medicinal properties [69]. Curcuminoids, including bisdemethoxycurcumin (BDMC) and demethoxycurcumin (DMC), along with the colorless metabolite tetrahydrocurcumin (THC), act as potent antioxidants [95]. Turmeric powder, which contains approximately 3 to 5 percent curcuminoids, exhibits a broad spectrum of biological activities, including antioxidant, antibacterial, antifungal, antiprotozoal, antiviral, anticoccidial, and anti-inflammatory properties [96]. Turmeric possesses favorable pharmacological properties and can serve as a beneficial natural growth promoter and a safe alternative to antibiotics. However, the dietary supplementation of curcumin is limited due to its low solubility in alkaline pH and its susceptibility to hydrolysis when exposed to light, resulting in poor absorption in animals [97]. Studies conducted on broiler chickens have demonstrated increased weight gain and improved feed conversion ratio (FCR) with turmeric supplementation. Conversely, in

studies by [98–100], no significant effects of turmeric on FCR were observed. The research findings regarding turmeric supplementation in poultry diets are not consistently aligned.

Curcumin, the primary phenolic compound in *Curcuma longa* powder, has been found to possess antioxidant effects [101–103]. Alongside its antioxidant properties, *Curcuma longa* has also been reported to exhibit free radical scavenging abilities [104], hypolipidemic effects [105], protection of biological membranes from peroxidative damage [106], enhancement of immune function [107], and antiviral and antibacterial properties [108]. As a result of its antioxidant properties, *Curcuma longa* suppresses lipid peroxidation [109] while promoting the actions of detoxifying enzymes [110].

Previous studies have additionally highlighted the biological activities of *Curcuma longa*, such as its anticoagulant effects [111] and in improving nutrient digestibility and metabolism [35], enhancing hepatic functions [112], and reducing serum LDL, cholesterol, triglycerides, and blood glucose levels [103]. Recent research has demonstrated that curcumin from *Curcuma longa* can improve the performance of broiler chickens, particularly under thermal stress conditions [101,113].

The supplementation of turmeric in chicken feed as a feed additive has led to significant advancements in chicken performance and economic efficiency [114,115]. As an herbal feed additive, turmeric has been found to enhance the average daily weight gain (DWG) and reduce feed costs in poultry production [114]. It also exhibits positive effects on the DWG, feed conversion ratio (FCR), and carcass characteristics of broiler chickens [115]. Turmeric, a commonly used culinary ingredient in Vietnam, is known for providing artificial color and a distinct aroma to human food. It is readily available in household backyards and local markets. The key active component, curcumin, contributes to its various therapeutic properties, including antibacterial, anticoccidial, antioxidant, hypercholesteremic, and hypolipidemic effects [114–118]. Additionally, turmeric has been found to have substantial levels of crude protein (10.07%), ether extract (6.64%), crude fiber (4.87%), nitrogen-free extract (66.76%), and ash (2.76%) [119,120]. Moreover, turmeric is rich in essential minerals and nutrients crucial for bone and muscle development [120].

The present review focuses on the potential role of nutraceuticals in enhancing the growth performance, immune system, gut microbiota, and health of poultry. In particular, it explores the utilization of *Spirulina* spp. and *Curcuma* spp. as an alternative strategy to reduce the reliance on antibiotic growth promoters (AGP) in poultry diets. To gather relevant information, we conducted a comprehensive search using databases such as Science Direct, Google Scholar, and Web of Science. The keywords “nutraceuticals”, “*Spirulina*”, “*Curcuma*”, and “poultry” were employed to identify relevant articles. The search encompassed papers published between 2000 and 2023, and the selection was based on the content and relevance of the studies. Specifically, articles written in English that addressed the aforementioned topics were included in the review.

2. Growth-Promoting Effects on Broiler Chicken

2.1. Growth-Promoting Effects of *Spirulina*

The primary objectives of poultry farming are to achieve rapid growth and maximize feed efficiency. To attain optimal performance in livestock, several factors need to be taken into account, including the genetic potential of the animals, feed quality, environmental conditions, and disease management [19]. These factors play crucial roles in determining the overall productivity and health of poultry. By considering these aspects and implementing appropriate strategies, farmers can enhance growth rates and improve feed utilization, leading to better outcomes in poultry production.

The supplementation of algae has shown beneficial effects on broiler performance. A study conducted by [121] found that the inclusion of supplemental algae in broiler diets improved feed intake and body weight gain. This indicates that algae can contribute to enhancing growth performance in broilers (Figure 2).

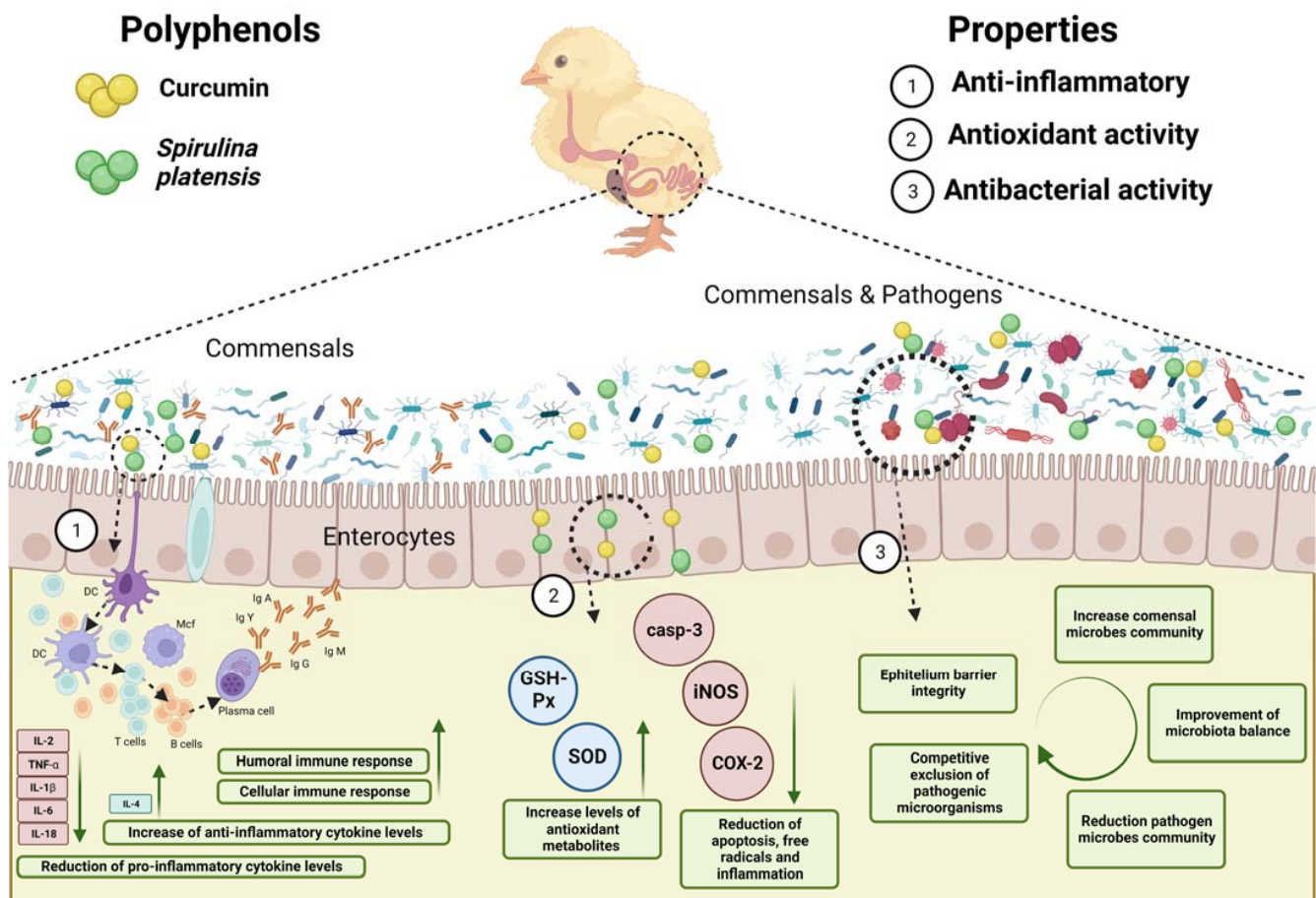


Figure 2. Anti-inflammatory properties and antioxidant and antibacterial activity of curcumin and *Spirulina platensis* on GALT in chickens. IL-2 (interleukin-2), TNF- α (tumor necrosis factor- α), IL-1 β (interleukin-1 beta), IL-6 (interleukin-6), IL-18 (interleukin-18), IL-4 (interleukin-4), GSH-Px (glutathione peroxidase), SOD (superoxide dismutase), casp-3 (caspase-3), iNOS (nitric oxide synthases), and COX-2 (cytochrome c oxidase subunit 2). The figure was created using [BioRender.com](https://www.biorender.com) accessed on 19 June 2023.

Additionally, research [122] suggests that the nutrient composition and physiological functions of spirulina may have positive effects on the metabolic systems associated with broiler growth performance. This indicates that spirulina, with its specific composition and properties, can potentially support the growth and development of broilers.

These findings highlight the potential of incorporating algae, such as spirulina, into broiler diets as a means to optimize growth performance and maximize productivity in the poultry industry. The studies by [123–126] provide evidence of the positive impacts of spirulina supplementation on the productive performance of broilers, indicating that the inclusion of SP in broiler diets improves body weight gain (BWG) and feed conversion (FC). Spirulina supplementation at different levels, such as 0.9 g/kg, has been shown to promote BWG in broilers, which may be attributed to the absorption of minerals and vitamins present in SP. Furthermore, the studies highlight that SP supplementation enhances feed utilization efficiency, leading to improved feed conversion. This improvement in feed conversion is associated with the balanced microbial population in the gastrointestinal tract, which enhances the absorbability of dietary vitamins and minerals. This, in turn, contributes to the overall performance and health of broilers. Overall, the findings suggest that the inclusion of SP in broiler diets can have positive effects on body weight gain, feed conversion, and overall productivity. The study by [123] found that the inclusion of feed containing 1% SP led to a decrease in abdominal fat in broilers compared to the control

group and other supplemented groups. This suggests that spirulina supplementation may have a positive impact on reducing abdominal fat deposition in broilers.

Additionally, ref. [127] reported that dietary supplementation with spirulina significantly improved the carcass parameters of broilers in terms of factors such as meat yield and composition. Furthermore, ref. [128] observed that feeding birds with spirulina at levels of 40 and 80 g/kg in broiler diets resulted in significant differences ($p < 0.01$) in the meat color of chick muscles. This suggests that spirulina supplementation may influence the color of meat in broilers, potentially enhancing its visual appeal and quality.

It is important to note that not all studies investigating the addition of SP or other microalgae to broiler diets have reported positive effects on growth performance. Some studies have found no significant effect or even adverse effects on growth parameters [2,129]. El-Bahr et al. [130] reported that the inclusion of a 1 g SP/kg diet did not influence feed intake (FI), feed conversion ratio (FCR), or BWG in broilers. Similarly, Altmann et al. [129] found no noticeable effect on live weight or carcass weight when SP replaced half of the soy protein in broiler diets.

These contrasting results may be attributed to various factors, including the dosage and duration of microalgae supplementation, variations in experimental conditions, differences in bird strains, and variations in the composition and quality of the microalgae used. Additionally, the presence of anti-nutritional factors or interactions with other dietary components may also contribute to the observed effects.

Overall, the effects of microalgae supplementation on broiler growth performance can vary depending on the specific conditions and experimental setups. Further research is needed to better understand the optimal dosage, duration, and potential interactions of microalgae supplementation in broiler diets to achieve consistent and positive growth outcomes.

In this regard, ref. [32] highlights a potential negative effect of spirulina supplementation on broiler performance. The addition of spirulina to broiler diets led to a 15% lower performance compared to non-supplemented birds during a specific two-week period (21–35 days old). The researchers attributed this negative effect to the high digesta viscosity caused by the gelation of indigestible proteins present in spirulina.

Interestingly, even the addition of exogenous enzymes, such as lysozyme or Rovabio Excel AP, did not improve upon the negative findings. Although lysozyme was able to break down the cell walls of spirulina, it did not prevent the harmful gelation of the microalga proteins. The researchers suggested that combining lysozyme with a specialized exogenous peptidase could potentially enhance the digestion of spirulina proteins and prevent gelation.

This study emphasizes the importance of considering factors such as digestibility and interactions with other dietary components when evaluating the effects of microalgae supplementation in broiler diets. The gelation of proteins and subsequent increase in digesta viscosity can negatively impact nutrient utilization and performance in broiler chickens. Further research is needed to explore potential strategies to overcome these challenges and optimize the use of spirulina or other microalgae as feed additives in broiler production.

Indeed, the contradictory findings among studies regarding the effects of spirulina supplementation in broiler diets can be attributed to various factors. Here are some possible factors that may contribute to the inconsistencies.

1. Levels of spirulina: The concentration or inclusion level of spirulina in diets can vary among studies. Different levels of supplementation may have different effects on broiler performance.
2. Broiler hybrids: Different broiler strains or hybrids may respond differently to spirulina supplementation. Genetic variations among broiler breeds can influence their ability to utilize nutrients and respond to dietary interventions.

3. Broiler age: The age of broilers at the time of spirulina supplementation can influence the outcomes. The physiological and metabolic status of broilers change as they grow, which can affect their response to dietary interventions.
4. Housing conditions: Variances in housing conditions, such as temperature, humidity, and ventilation, can impact broiler performance. Environmental stressors may interact with spirulina supplementation and influence the results.
5. Feed preparation: The processing and formulation of broiler diets, including the method of spirulina incorporation, can affect the availability and digestibility of nutrients. Differences in feed preparation techniques among studies may contribute to variations in the results.
6. Administration method: The way spirulina is administered to broilers can vary. It could be mixed directly into the diet, offered as a separate supplement, or administered via drinking water. The mode of administration may influence the interaction between spirulina and the birds' digestive system.

Considering these factors, it is important to interpret the findings of individual studies within the context of the specific experimental conditions and methodology used. Further research with standardized protocols and larger sample sizes may help to establish more consistent conclusions regarding the effects of spirulina supplementation on broiler performance.

2.2. Growth-Promoting Effects of Curcuma

Nouzarian et al. [131] also found no significant effect on daily feed intake and body weight gain in chickens. Kumari et al. [99] observed that supplementation with 7.5 g/kg turmeric powder in feed resulted in the highest weight gain in birds. The variations in body weight values could be attributed to differences in agroclimatic conditions [100]. Ahlawat et al. [132] reported that supplementation of 3.3, 6.6, and 10 g/kg turmeric powder in broiler chicken improved feed efficiency, which is consistent with the findings supported by Kafi et al. [72].

Arslan et al. [132] found that turmeric supplementation at different rates improved feed conversion efficiency, with the best result observed at a supplementation rate of 1.5 percent. Shohe et al. [133] also observed that feed conversion efficiency was lowest in the group supplemented with 7.5 g turmeric powder/kg feed, followed by groups supplemented with 5, 2.5, and 1.5 g/kg turmeric powder.

It is important to note that the dietary supplementation of curcumin (Figures 1 and 2), the main active component in turmeric, is limited due to its low solubility in alkaline pH and susceptibility to hydrolysis when exposed to sunlight, resulting in poor absorption in animals [97]. However, studies on broiler chickens have shown that dietary supplementation of turmeric can lead to increased weight gain and improved feed conversion ratio [64].

Curcumin was found to have the potential to reduce stomach acid production, leading to an increase in blood sugar released from body cells. This decrease in sugar levels in body cells can induce hunger in chickens, resulting in a significantly higher feed intake and an increase in carcass weight within a shorter period of time. Additionally, since turmeric is readily available at a lower cost, incorporating it into the feed can help reduce overall feed expenses [134]. Durrani et al. [135] observed better feed efficiency in broiler chickens when turmeric was included in their diet at lower concentrations, specifically at 0.5%. This suggests that even at lower levels of supplementation, turmeric can positively impact feed efficiency in broiler chickens.

Turmeric powder (TRP) has shown positive effects on growth performance, as well as in reducing oxidative stress and improving the gut health of poultry [136,137]. Furthermore, the presence of curcumin, the active component in turmeric, in the chicken's diet may have potential health benefits for humans consuming the meat, including anti-inflammatory and antioxidant effects [138].

Therefore, incorporating turmeric powder into the diet of chickens can enhance the efficiency, health, and quality of the produced meat [139]. This also provides valuable insights into the potential impact of turmeric on human health.

Supplementing the basal diet with TRP in the range of 5 to 10 g per kilogram led to a significant reduction in abdominal fat in birds compared to the control group ($p < 0.05$). A study by Hosseini-Vashan et al. [140] demonstrated that supplementation of turmeric powder at 0.4 to 0.8 percent significantly reduced belly fat in birds during 28-day and 42-day fat sampling periods. Similarly, a study conducted in China showed that supplementation of 100 to 300 mg/kg of feeds significantly reduced the abdominal fat ratio ($p < 0.05$) compared to the control group [73]. Furthermore, adding 0.25, 0.5, and 0.75 percent of TRP to the diet of broiler chickens slaughtered at 49 days old resulted in a significant reduction in abdominal fat [141]. The mechanism behind fat reduction with TRP ingestion is attributed to its inhibitory effect on reactive oxygen species of enzymes, such as lipoxygenases, which play a role in adipogenesis processes [142]. The lipoxygenase pathway is known to contribute to adipose tissue inflammation in obesity-related animal models. Lipoxygenase isoforms are primarily produced by non-adipose cells and exhibit distinct translation patterns in subcutaneous and omental fatty tissues in humans [143].

Regulating effect on gut health can be attributed to curcumin's action on adipocyte death or glucose uptake from the blood [73,144]. The aforementioned mechanisms explain the significant decrease in abdominal fat observed with turmeric supplementation in broiler chickens' diets.

The effect of turmeric supplementation on liver weight in broiler chickens appears to be variable across different studies. Some studies have reported a slight but insignificant increase in liver weight with turmeric supplementation compared to the control group [68]. On the other hand, there are studies that have shown a significant reduction in liver weight with curcumin supplementation [15]. However, it is worth noting that the study by Yarru et al. [145] indicated that supplementation of TRP to aflatoxin-treated feeds improved liver weights in broiler chickens.

Turmeric, specifically its active compound curcumin, has been demonstrated to have hepatoprotective effects against various toxicants in mice, rats, and ducks, including carbon tetrachloride, aflatoxin B, and cyclophosphamide [146]. Curcuminoids have also shown a protective effect against aflatoxin B1.

The inconsistencies in the effect of turmeric on liver weight observed in different studies may be attributed to several factors, including variations in experimental conditions, turmeric dosage, duration of supplementation, and the presence of other variables that were not controlled or accounted for in the statistical analysis. It is important to consider these factors and conduct further research to better understand the impact of turmeric supplementation on liver weight in broiler chickens.

In previous research, turmeric has been extensively utilized in commercial broiler chickens and laying hens, yielding significant outcomes. Adding 0.75% turmeric to the feed increased BWG and enhanced the FCR of commercial broiler chickens, ultimately leading to increased gross profit [144]. Furthermore, incorporating turmeric into the diet has been shown to enhance the growth performance and egg production of poultry due to its natural antibiotic effects [68]. Moreover, turmeric supplementation improves antioxidant capacity, FCR, and carcass characteristics in broiler chickens [135]. Additionally, including 3% TRP in broiler chicken feed resulted in the lowest feed intake while simultaneously improving other performance measures [147]. All of the studies presented so far are summarized in Table 1.

Table 1. List of sources showing growth-promoting effects of spirulina and curcuma in broilers.

Drug Form	Dose	Effect	Source
Turmeric powder	1000 g of turmeric/kg	Enhanced feed utilization and improved weight gain	[118]
<i>Spirulina platensis</i>	1%	Increased body weight, decreased feed consumption ratios, improved blood parameters	[124]
Curcumin	200 mg/kg	Enhanced bird growth performance, behavioral patterns, and immunity	[137]
Turmeric powder	0.6 g/kg	Improved broiler performance index and net profit per bird	[148]
<i>Spirulina platensis</i>	0.5–1%	Improved broiler production performance and balancing of the redox status	[149]
<i>Spirulina platensis</i> phycocyanin	0, 0.25, 0.5, 0.75, and 1 g kg ^{−1} diet	Enhanced growth-promoting, antioxidant, and anti-inflammatory properties	[150]
<i>Spirulina plantesis</i>	0.7–0.9 g/kg	Improved growth performance, blood parameters, and biochemical changes in serum and microbial load	[151]

3. Intestinal Morphology, Microbiota Modulation, and Immunomodulation

3.1. Effects of *Spirulina* on Intestinal Morphology, Microbiota Modulation, and Immunomodulation

The improvement in growth parameters observed in broilers may be attributed to the enhanced health of the birds, as evidenced by positive changes in the morphology of the small intestine. This includes increased villus length, higher numbers of goblet cells, and an enhanced absorption surface area, leading to improved nutrient digestibility and absorption. The phycocyanin component (PC) of spirulina has been shown to boost antioxidant enzyme activity and reduce the production of pro-inflammatory cytokines (IFN- γ and IL1 β), contributing to a healthier gastrointestinal environment.

Spirulina has a beneficial impact on the gastrointestinal flora, promoting a healthier balance of microorganisms, and it also enhances the activities of digestive enzymes, leading to improved overall digestion of dry matter and nitrogen [122]. Additionally, it enhances the digestibility of nutrients, specifically amino acids, as well as protein synthesis [152], in addition to improving the utilization of apparent metabolizable energy [153]. Moreover, spirulina positively influences the composition of the intestinal microbial population by reducing the presence of harmful bacteria, such as *E. coli* and increasing the levels of beneficial lactic acid bacteria [154,155]. The presence of phycocyanin (PC) in spirulina stimulates the production of short-chain fatty acids and helps to reduce the presence of harmful pathogens in the intestines, thereby improving gut health [147].

The abundant essential amino acids found in spirulina play a crucial role in enhancing overall health status and body weight while also mitigating health disorders and mitigating the effects of heat stress. Additionally, phycocyanin (PC), a hydrophilic protein present in spirulina, helps regulate vascular colloidal osmotic pressure to maintain a balance with bodily fluids and promote optimal physiological functioning [156,157].

Phycocyanin (PC) exhibits antioxidant, anti-inflammatory, and immune-boosting activities [147,158]. Extracts derived from spirulina demonstrate antimicrobial effects that hinder the growth of various pathogens, including *Staphylococcus aureus*, *Escherichia coli*, *Salmonella typhi*, and *Klebsiella pneumonia* [159]. Moreover, spirulina possesses immunostimulant properties that enhance the secondary humoral response to SRBC antigens in broilers [160,161].

The supplementation of *Spirulina platensis* phycocyanin (SPC) led to a linear and quadratic increase in the activity of serum antioxidant enzymes, including catalase (CAT), superoxide dismutase (SOD), and total antioxidant capacity (TAC) [45,162,163]. Furthermore, SPC supplementation linearly reduces the levels of malondialdehyde (MDA), which can be attributed to its strong antioxidant activity [45,162,163]. This antioxidant activity is

believed to stem from the ability of spirulina extract to scavenge free radicals and chelate metal ions [164]. Mirzaie et al. [160] and Moustafa et al. [149] demonstrated that broilers fed diets containing spirulina exhibited higher activities of SOD and total antioxidant capacity, as well as lower levels of MDA, compared to those fed basal diets. Similarly, Park et al. [165] observed a linear increase in the enzyme activities of SOD and glutathione peroxidase (GPx) with increases in the spirulina supplementation levels (0.25%, 0.5%, 0.75%, and 1%) in broiler diets.

In the context of pro-inflammatory cytokines, one study showed that spirulina supplementation did not affect levels of IL1 β , a potent pro-inflammatory cytokine involved in response to disease and infection [166]. The anti-inflammatory properties of spirulina may be attributed to its ability to inhibit the synthesis of proinflammatory cytokines, such as TNF- γ , IL-6, and IL-1, as well as the activities of cyclooxygenase 2 (COX-2) enzymes and inducible nitric oxide synthase (iNOS) [167]. Additionally, SPC is present in spirulina and exhibits a strong anti-inflammatory effect [168].

The small intestine of broilers, especially the duodenum and jejunum, play a crucial role in the digestion and absorption of nutrients. A well-developed small intestine is associated with improved nutrient utilization and enhanced growth performance [165]. The development of the small intestine can be evaluated using morphometric measurements, such as villus height (VH) and crypt depth (CD), where longer villi and shallower crypts indicate the improvement of digestive efficiency via increased mucosal surface [165,169]. Additionally, the count of goblet cells is indicative of the condition of the small intestine [170].

The study demonstrated that supplementation with spirulina led to an increase in villus height, villus width, VH:CD ratio, and goblet cell count in the small intestine. These findings suggest a positive effect of SPC on gut health, nutrient utilization, and growth. These results are consistent with previous research conducted on broilers, in which it was also reported that SPC supplementation positively influences villus height, crypt depth, and goblet cell numbers in the intestine, ultimately improving nutrient absorption, FCR, and BWG [123,171]. Spirulina, when supplemented at different levels, exhibits an anti-inflammatory effect, as indicated by the decreased immunolabeling of caspase-3 and TNF- α . Interferon- α is an inflammatory cytokine produced during acute inflammation and plays a crucial role in the body's defense against cancer and infection. Caspase-3 is a lysosomal enzyme involved in protein degradation and is necessary for efficient cell apoptosis.

The anti-inflammatory properties of *Spirulina* spp., specifically SPC, may be attributed to its ability to downregulate the expression of pro-inflammatory cytokines, such as interleukin-2 (IL-2), IL-1 β , interferon- γ (TNF- γ), and interferon- α (TNF- α) while increasing the expression of the anti-inflammatory cytokine IL-4 [172]. SPC acts as a COX-2 inhibitor and possesses hepatoprotective and anti-inflammatory activities [173]. Its hepatoprotective effect is linked to inhibited production of hepatocyte growth factor and TGF- β 1, which prevent inflammatory infiltration [75]. Research conducted by Martinez et al. [174] demonstrated that SPC preparation can suppress TNF- α , IL-6, iNOS, COX-2, and neutrophil infiltration at the site of inflammation [175].

3.2. Effects of Curcuma on Intestinal Morphology, Microbiota Modulation, and Immunomodulation

Emadi et al. [176] conducted a study on broiler chickens and found that the inclusion of TRP at levels of 0.25%, 0.5%, and 0.75% in the diet did not have a significant effect on total protein and albumin concentrations at 21 days of age. Kumari et al. [99] reported no changes in the activity of liver enzymes, such as ALT, AST, and ALP, in the treatment group with TRP in broiler chickens. However, it is important to consider that factors such as chicken breed, level of turmeric inclusion, duration of the experiment, and environmental factors may have contributed to variations in results. Ekine et al. [117] observed an increase in AST and ALT levels with the inclusion of 250 g of TRP per 25 kg of feed, but this increase did not negatively impact the liver or muscle of broiler birds. Significant hepatic damage is typically indicated by AST and ALT levels exceeding 275 and 800 μ L, respectively. In this

study, AST and ALT levels were not statistically influenced by dietary turmeric inclusion. Regarding alkaline phosphatase (ALP), it was observed to increase in the treatment groups (T2 and T3) compared to the control group (TC), which contrasts with the findings of Kumari et al. [99] and Mehala and Moorthy [100], where no changes in liver enzyme activities, including ALP, were observed with turmeric inclusion in the broiler chicken diet. However, ALP levels were lower in the treatment group T1, which aligns with the results of Emadi and Kermanshahi [176], where decreased ALT and ALP enzyme activities were observed in broiler birds fed turmeric at varying levels. The discrepancies between these studies may be attributed to factors such as different levels of turmeric inclusion and variations in the bioactive substances present in the turmeric plant, which depend on factors such as plant species, soil type, harvest season, and the preparation process. In avian species, an increase in ALP levels has been associated with increased osteoblast activity and various disease states, including traumatic, neoplastic, and infectious diseases.

Curcumin (Figure 1), a highly pleiotropic component found in turmeric, has been found to have significant effects on inflammatory responses. It exerts its anti-inflammatory effects by downregulating the activities of enzymes, such as lipoxygenase, cyclooxygenase-2, and inducible nitric oxide synthase [177]. Furthermore, curcumin can interact with various molecular targets involved in inflammation, leading to inhibitory effects on cytokines [79].

Studies have shown that curcumin has the ability to decrease the levels of inflammatory cytokines, including tumor necrosis factor-alpha (TNF- α) and various interleukins (IL-1, IL-1 β , IL-6, and IL-8) [178]. It also inhibits the activation of nuclear factor-kappa B (NF- κ B), a transcription factor involved in the regulation of inflammatory responses and reduces cell proliferation [84,177]. Overall, curcumin's anti-inflammatory properties are attributed to its ability to modulate various inflammatory mediators and signaling pathways, providing a potential therapeutic approach for managing inflammatory conditions.

Locally sourced turmeric is indeed known for its antioxidant properties. Antioxidants play a crucial role in protecting cells and tissues from oxidative damage caused by free radicals and reactive oxygen species. In the context of chicken eggs, maintaining oxidative stability is important to prevent lipid oxidation and preserve their quality. Turmeric, with its antioxidant function, has been found to help in this regard. A study by Laganá et al. [139] demonstrated that antioxidant diets containing turmeric can effectively inhibit yolk lipid oxidation and contribute to the preservation of egg quality.

Curcumin, the main bioactive compound in turmeric, was shown to have the ability to neutralize superoxide anion and hydroxyl radicals, which are highly reactive and can cause oxidative damage [73]. Moreover, the supplementation of broiler chickens with dietary turmeric rhizome extracts was found to significantly enhance the activity of SOD, an important antioxidant enzyme that helps neutralize superoxide radicals [73,179].

Curcumin exhibits antiviral properties against various viruses, including influenza. It demonstrated effectiveness against influenza viruses, altering cellular metabolism and serving multiple functions to hinder viral invasion. By binding to the viral envelope, curcumin renders the viral pathogens inactive, preventing them from infecting cells and causing harm. This suggests that curcumin has the potential to neutralize viruses before they can initiate infection and cause subsequent damage to cells [180].

Numerous studies have demonstrated the immunomodulatory properties of turmeric, highlighting its ability to enhance the body's defense against disease-causing microorganisms. Turmeric exhibits immediate antimicrobial effects against pathogens, acting as a natural antibiotic. Moreover, the bioactive compounds present in turmeric contribute to the reduction of infection-induced inflammation and stimulate an immune response in chickens. Turmeric, when incorporated as a phytobiotic, facilitates the healing of lymphocytes in lymphoid organs, thus providing a mechanism for cellular repair [78,84].

Furthermore, research has shown that the inclusion of TRP in broiler chicken feed can elevate the levels of immunoglobulins, such as IgM, IgA, and IgG, while significantly reducing the monocyte ratio [176]. Mehala and Moorthy [100] also reported an enhanced

immune response in broiler chickens with the dietary inclusion of turmeric. Additionally, when used as a natural feed additive, *Curcuma longa* has been found to serve as an immune enhancer for broilers against *Pasteurella multocida* infection [181].

The supplementation of turmeric in broiler chicken diets has been shown to have regulatory effects on their hematological parameters, as reported by Dono [78]. In Ross male broiler chickens, the addition of TRP to their feed resulted in an increase in hemoglobin, total cholesterol, and HDL cholesterol levels. Conversely, LDL cholesterol, VLDL cholesterol, and red blood cell counts were decreased. A significant decrease in blood albumin levels was also observed in the study [176].

Additionally, a study on Fayoumi broilers demonstrated that incorporating turmeric in their diets improved their ingestive behavior (drinking and feeding) and growth. Furthermore, it led to an increase in total serum protein, globulins, calcium, and phosphorus levels [182].

Curcumin has been demonstrated to have various positive effects on gut architecture and gut bacteria. It stimulates the release of enzymes, such as amylase, protease, and bile acids, in the stomach, promoting digestion and nutrient absorption [183] (Rajput et al., 2013). The gastrointestinal system of chickens, which houses diverse and complex microbiota, can benefit from adjustments in feed composition to include turmeric. Studies have shown that feeding broiler chicks phenolic compounds, such as curcumin, reduces gastrointestinal inflammation and enhances nutrient absorption [184]. In fact, supplementation with curcumin at a dosage of 200 mg/kg feed has been shown to improve overall metabolic efficiency, increase the absorption area of the small intestine through increased villus height, and reduce abdominal fat deposition [183].

Moreover, an increase in the height of intestinal villi and the villus height to crypt depth ratio has been linked to improved nutrient absorption rates [185]. The addition of TRP to the diet of hens was found to increase the abundance of the beneficial bacteria *Lactobacillus* spp. in their intestines [83]. However, it should be noted that in vitro studies have shown that high doses of turmeric extracts can inhibit the growth of *Lactobacillus*, while whole TRP at certain concentrations can completely suppress lactobacilli [186].

Supplementation of TRP has a significant impact on the length and weight of the small intestine ($p < 0.05$) [187]. The length of the small intestine increased significantly in broilers provided with 5–10 g compared with 0 or 2.5 g of TRP per kilogram in their basal diet. However, the weight of the small intestine decreased significantly with higher levels of TRP supplementation. It is noteworthy that while the length of the small intestine increased, its weight decreased with increasing TRP levels. This longer small intestine offers advantages, such as enhanced efficiency of fluid and nutrient absorption, as well as improved breakdown of ingested feed. The presence of villi and microvilli in the intestinal wall increases the surface area for absorption, which could contribute to the favorable growth of broiler chickens at an early age in addition to their recognized role as growth promoters. This finding was observed in a study conducted in 2023 [187].

The weight of the bursa of Fabricius in broiler chickens showed a significant increase with the supplementation of TRP in the basal diet compared to the control group ($p < 0.05$) [187]. The bursa of Fabricius plays a crucial role in the development of B-cells, which are responsible for producing antibodies. This finding is supported by the results of the study conducted by Naderi et al. [188], where the bursa of Fabricius exhibited a numerically larger mass in the turmeric and cinnamon-supplemented groups compared to the control and avilamycin-supplemented groups.

The supplementation of TRP in the basal diets did not have a significant effect on the weights of the pancreas, gall bladder, heart, and spleen in broiler chickens ($p > 0.05$) [187], which is consistent with the findings of previous studies. Mondal et al. [68] reported that supplementation of TRP at 0.5 to 1.5 percent did not have a significant impact on the heart weight of broiler chickens. Similarly, Hussein et al. [64] found that TRP did not significantly affect the relative weight of the pancreas in broiler chickens when supplemented at a rate of 0.25 to 0.5 percent. Qasem et al. [74] also reported that supplementation of TRP in the diet

of broiler chickens at a rate of 10–20 g per kilogram of basal feed did not have a significant effect on the relative weight of the pancreas. [147]. All of the studies presented so far are summarized in Tables 2 and 3.

Table 2. List of sources showing microbiota modulation effects of spirulina and curcuma in broilers.

Drug Form	Dose	Effect	Source
<i>Spirulina platensis</i>	1%	Decreased the numbers of coliform in the ileum and the caecum	[34]
Turmeric powder	1%	Increased the abundance of <i>Lactobacillus</i> spp. in the chicken intestines	[83]
<i>Spirulina platensis</i> powder	10 g/kg	Increased the levels of beneficial lactic acid bacteria	[155]
<i>Spirulina platensis</i>	1–2 g/kg	Increased the <i>Lactobacillus</i> spp. count	[189]

Table 3. List of sources showing antibacterial, antioxidant, and anti-inflammatory properties of spirulina and curcuma in broilers.

Drug Form	Dose	Effect	Source
Turmeric rhizome extract	300 mg/kg	Enhanced antioxidant capability, growth performance, and breast muscle weight ratio and reduced abdominal fat ratio	[73]
Turmeric rhizome extract	50 and 100 mg/kg curcumin	Improved antioxidant capability, high growth performance, increased breast muscle weight ratio, reduction in the abdominal fat ratio	[104]
<i>Curcuma</i> spp.		Increased anti-inflammatory activity and weight index of lymphoid	[117]
<i>Curcuma longa</i> (Turmeric)	0.5 and 1.0%	Increased both erythrocytic and total leukocytic counts in addition to bursa, thymus, and spleen weight	[138]
Curcumin powder	2.000 mg/kg	Significantly decreased absolute and relative abdominal fat weight and markedly decreased concentrations of plasma low-density lipoprotein cholesterol and plasma and hepatic triglyceride	[147]
Curcumin		Enhanced anti-inflammatory properties	[177]
<i>Curcuma longa</i> powder	1%	Immune enhancer	[181]
Spirulina powder	2 g Spirulina/kg feed	Improved gut integrity and immunity in broiler production	[171]
<i>Spirulina platensis</i> phycocyanin	0, 0.25, 0.5, 0.75, and 1 g kg ⁻¹ diet	Enhanced antioxidant and anti-inflammatory properties	[150]

4. Conclusions

Given the ban on growth-promoting antibiotics, research on gut mucosa-associated lymphoid tissue has been ongoing in order to develop pre- and probiotics that are best suited for stimulating the gut immune system. Following our review of literature sources, we can state that the addition of *Spirulina platensis* or curcumin positively influences both productive performances and immunity in broiler chickens, improving humoral and cellular immune responses and lymphoid organ development. The anti-inflammatory

effect of *Spirulina platensis* supplementation at different levels has been shown to decrease caspase-3 and TNF- α immunolabeling; reduce IL-1 β , IL-2, and IL-4 interferon- γ expression; reduce IL-1 β , IL-2, and IFN- γ ; and increase the expression of anti-inflammatory cytokine IL-4. *Spirulina* inhibits the synthesis of cytokines IL-1, IL-6, and TNF- γ and the activities of inducible nitric oxide synthase (iNOS) and cyclooxygenase 2 (COX-2) enzymes. Curcumin supplementation decreases the levels of TNF- α and IL-1 β , IL-6, IL-2, and IL-18.

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