Memories of the Agricultural and Livestock Area of the VI CCIUTM, Ecuador

Anthocyanins, Intestinal Health and Productive Response in Broiler Chickens

José Arteaga[1,2], Juan José Toro-Letelier[3] and Sixto Reyna[2*]

[1]Maestría en Agroecología, Universidad Politécnica Salesiana, Código postal 170517, Quito, Ecuador; [2]Departamento de Veterinaria, Facultad de Ciencias Veterinarias, Universidad Técnica de Manabí, Manabí, Ecuador; [3]Dirección de Extensión y vinculación con el medio, Facultad de Ciencias Veterinarias y Pecuarias, Universidad de Chile, Código postal 8820000.

Abstract | Broilers are the main source of animal protein for human consumption, and since the mid-twentieth century, their productive efficiency has been supported by the inclusion of sub-therapeutic doses of antibiotics as growth promoters (AGPs) in their diets. However, concerns regarding the environmental impact of AGPs and their contribution to bacterial resistance have led to increased interest in evaluating alternative strategies to sustain productivity under intensive rearing conditions without the adverse effects associated with AGPs. In this context, various plant species and their extracts contain bioactive compounds, such as flavonoids, particularly anthocyanins. Due to their antioxidant, anti-inflammatory and antimicrobial properties, anthocyanins positively influence the morphology and physiology of the intestinal mucosa while modulating the composition of its microbiota. These effects further contribute to intestinal health through the production of short-chain fatty acids or anthocyanin -derived metabolites, ultimately impacting the bird's overall health and productive performance. Based on this, the present review explores several mechanisms of action underlying the potential of anthocyanins as an alternative to AGPs, as recently described.

Received | Sepctember 22, 2023; **Accepted** | April 12, 2025; **Published** | May 13, 2025
***Correspondence** | Sixto Reyna, Departamento de Veterinaria, Facultad de Ciencias Veterinarias, Universidad Técnica de Manabí, Manabí, Ecuador; **Email:** sixto.reyna@utm.edu.ec
Citation | Arteaga, J., J.J.T. Letelier and S. Reyna. 2025. Anthocyanins, intestinal health and productive response in broiler chickens. *Sarhad Journal of Agriculture*, 39(Special issue 2): 173-188.
DOI | https://dx.doi.org/10.17582/journal.sja/2023/39/s2.173.188
Keywords | Microbiota. Anthocyanins. Antibiotic alternatives. Broilers. Poultry production

Introduction

Due to their high growth rate and productivity, broiler chickens have become the most important and efficient source of animal protein for human nutrition (Paul *et al*., 2022), driving the poultry industry to adopt intensive rearing systems. Unfortunately, these systems increase the likelihood of infectious outbreaks in flocks (Diaz *et al*., 2019). In this context, the gastrointestinal tract (GIT) of broilers is continuously exposed to pathogens and environmental factors that disrupt intestinal homeostasis, compromising their health and productivity (Yegani and Korver, 2008; Akinyemi and Adewole, 2021).

Antibiotics, owing to their ability to inhibit or

eliminate microbial growth, have been widely used to treat infectious diseases-primarily intestinal infections-and, at subtherapeutic doses, as antibiotic growth promoters (AGPs) (Díaz-Sánchez *et al.*, 2015; Lauridsen, 2019; Rahman *et al.*, 2022). AGPs modify the gut microbiota, reduce bacterial toxin production, lower the incidence of subclinical enteric infections, stimulate the immune system, and enhance nutrient absorption and bioavailability, thereby improving the birds' productive performance (Paul *et al.*, 2022; Fernández Miyakawa *et al.*, 2024).

However, the growing demand for AGP-free animal products (Ghimpețeanu *et al.*, 2022), environmental concerns over antibiotic residues in livestock and their ecotoxicological effects (O'Neill, 2016; Tian *et al.*, 2021) and the global threat of antibiotic resistance-linked to an estimated 1.27 million deaths in 2019 and projected to reach 10 million by 2050-have driven the progressive elimination of AGPs from the poultry industry in developed countries (O'Neill, 2016; Rahman *et al.*, 2022).

In contrast, in less developed countries where AGPs are still in use, rising demand for animal protein is expected to increase antibiotic consumption from 63,151 tons in 2010 to over 105,000 tons by 2030 (Van Boeckel *et al.*, 2015; Ghimpețeanu *et al.*, 2022). Furthermore, the removal of AGPs from poultry diets has significantly increased the incidence of enteric diseases leading to greater reliance on therapeutic antibiotics (Redondo *et al.*, 2014; Hasted *et al.*, 2021).

In this context, investigating the effects of different nutritional strategies on intestinal morphology, gut health, and productive performance is essential for developing viable alternatives to AGPs (Amer *et al.*, 2022). Among these alternatives, phytogenics (also referred to as phytobiotics or phytochemicals) have gained interest. These compounds are classified into terpenoids, organosulfur compounds, phytosterols, alkaloids, and polyphenols (Lillehoj *et al.*, 2018; Al-Mnaser *et al.*, 2022), the latter being secondary plant metabolites characterized by an aromatic ring with at least one hydroxyl group. Of the 8,000 phenolic compounds identified, at least half belong to the flavonoid group (Lillehoj *et al.*, 2018; Tungmunnithum *et al.*, 2018; Hasted *et al.*, 2021; Salamon *et al.*, 2021). Through their antimicrobial, anti-inflammatory, and antioxidant properties-along with their ability to modulate the immune system and intestinal microbiota- flavonoids inhibit pathogen colonization in the GIT, thereby promoting intestinal health and enhancing nutrient absorption capacity (Lillehoj *et al.*, 2018; Ayalew *et al.*, 2022; Pliego *et al.*, 2022).

Anthocyanins are water-soluble pigments belonging to the flavonoid family, widely distributed throughout the plant kingdom, and responsible for the red, purple, or blue coloration of various fruits (Sun *et al.*, 2018; Csernus *et al.*, 2020; Luo *et al.*, 2022). Although antioxidant, anti-inflammatory, and antimicrobial properties of anthocyanins have been documented in various animal species-improving intestinal health by promoting mucosal integrity and modulating the microbiota-information on their use as feed additives in broiler chickens remains limited. In particular, few studies have evaluated their specific effects on intestinal health and productive responses in birds reared without AGPs (Changxing *et al.*, 2018; Amer *et al.*, 2022).

Since intestinal health depends a balanced gut microbiota composition, proper intestinal barrier functionality, and equilibrium between pro- and anti-inflammatory responses (Ducatelle *et al.*, 2018; Wickramasuriya *et al.*, 2022), this review will examine the effects of anthocyanins on the intestinal morphology and physiology of broiler chickens. Additionally, it will explore their potential impact on gut microbiota composition, implications for productive performance, and the underlying mechanisms of action.

Morphology, Physiology and Gut Health in Broilers

The GIT of broilers consists of the esophagus, crop, glandular stomach (proventriculus), gizzard, small intestine (duodenum, jejunum, and ileum), cecum, colon, and cloaca (Pan and Yu, 2014; Alshamy *et al.*, 2018). Compared to mammals, broilers have a relatively shorter small intestine, which reduces food retention time and digestive capacity (Pan and Yu, 2014; Wickramasuriya *et al.*, 2022). Beyond its primary role in nutrient absorption, the intestine functions as a protective barrier against pathogens and toxins and hosts a complex microbiota (Mishra and Jha, 2019; Alyileili *et al.*, 2020). In the small intestine, dietary components are enzymatically hydrolyzed into simpler molecules such as peptides, amino acids, fatty acids, and monosaccharides. These nutrients are efficiently transported from the intestinal lumen to various tissues due to the extensive intestinal absorption surface (Alshamy *et al.*, 2018; Bedford and

Apajalahti, 2022).

Structurally, the intestine comprises four interrelated barriers (Figure 1): (1) the microbiological barrier, formed by commensal microorganisms that prevent pathogen colonization; (2) the chemical barrier, consisting of a mucus layer primarily composed of mucins (high -molecular- weight glycoproteins) produced by goblet cells, which protects against pathogen invasion and inhibits bacterial proliferation; (3) the mechanical barrier, maintained by intestinal permeability regulated by stem cells, epithelial cells, goblet cells, and Paneth cells; and (4) the immunological barrier, located beneath and between epithelial cells and composed of dendritic cells, B cells, T cells, and macrophages. These barriers collectively ensure intestinal homeostasis and defense (Duangnumsawang *et al.*, 2021; Liu *et al.*, 2021; Wickramasuriya *et al.*, 2022).

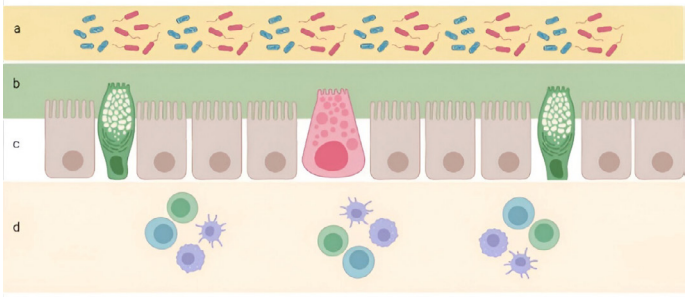

Figure 1: *Intestinal barriers.*
a) *Microbial barrier;* ***b)*** *Chemical barrier;* ***c)*** *Mechanical barrier;* ***d)*** *Immunological barrier.*

Dysbiosis, defined as an alteration in gut microbiota composition, can be triggered by factors such as microbial activity, environmental and nutritional influences, and a high metabolic rate. This imbalance leads to an increase in opportunistic pathogens, which has been associated with inflammatory processes, intestinal barrier deterioration, and oxidative stress-caused by an excess of reactive oxygen species (ROS) and reactive nitrogen species (RNS)-in the GIT of birds (Awad *et al.*, 2017; Ducatelle *et al.*, 2018; Mishra and Jha, 2019; Fancher *et al.*, 2020).

Oxidative stress arises when the overproduction of ROS exceeds the capacity of the endogenous antioxidant system (Mishra and Jha, 2019). This system includes key enzymes such as superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT), which are responsible for neutralizing free radicals in early stages (Mishra and Jha, 2019). Under physiological conditions, these systems regulate ROS levels and prevent oxidative damage (Lauridsen, 2019). However, during oxidative stress, the resulting imbalance promotes cellular damage and intestinal dysbiosis. ROS modulate transcription factors such as Nuclear Factor Kappa beta (NF-κB), Activator Protein 1 (AP-1), and Peroxisome Proliferator-Activated Receptor gamma (PPAR-γ) -this latter has a different role depending on the cell context-. Although Hypoxia-Inducible Factor 1-alpha (HIF-1α) is primarily activated under hypoxic conditions, its stabilization can be indirectly enhanced by ROS through the inhibition of prolyl hydroxylases (PHDs) (Chatterjee, 2016; Zheng *et al.*, 2022; Hu *et al.*, 2023).

The inflammatory response is initiated when Toll-like receptors (TLRs) recognize pathogen-associated molecular patterns (PAMPs) or damage-associated molecular patterns (DAMPs), triggering signaling cascades that include mitogen-activated protein kinase (MAPK), NF-κB, and (AP-1. These pathways stimulate the transcription of proinflammatory cytokines, such as IL-6 and IL-8/CXCL8, and antimicrobial peptides, promoting the recruitment of immune cells-including neutrophils, monocytes, and lymphocytes—to the site of inflammation. This response contributing to tissue damage through the release of enzymes and chemical mediators. Concurrently, the inflammatory processes promote the generation of ROS, triggering oxidative stress, lipid peroxidation, mitochondrial dysfunction, and alterations in cellular signaling (Biswas, 2016; Chen *et al.*, 2018; Mishra and Jha, 2019; Surai *et al.*, 2019; Tarradas *et al.*, 2020).

In birds, intestinal dysbiosis, closely linked to oxidative stress, exacerbates this inflammatory cascade, intensifying tissue damage (Li *et al.*, 2024; Wickramasuriya *et al.*, 2022). Thus, inflammation and oxidative stress are intimately connected and can negatively affect productivity, as prolonged inflammatory leads to tissue damage and diverts nutrients away from growth and production (Chatterjee, 2016; Broom and Kogut, 2018).

Additionally, various pathogenic bacteria and their toxins have been reported to alter the structure and function of tight junction proteins, thereby increasing intestinal permeability (Awad *et al.*, 2017), leading to GIT hyperpermeability, facilitating the translocation of microorganisms and toxins, from the intestinal lumen into the circulatory system, ultimately causing

systemic conditions that impair the productive performance of birds (Akbarian *et al*., 2016; Lillehoj *et al*., 2018; Mishra and Jha, 2019; Luo *et al*., 2022).

Anthocyanins

Structure and Sources

In nature, anthocyanins exist as O-glycosides, in which the anthocyanidin (aglycone) is bound to a sugar via a β-glycosidic bond. Anthocyanidins contain a flavylium cation, whose structure can exhibit hydroxylations primarily on carbons C3, C5, C7 of ring A and C3', C4', C5' of ring B (Mattioli *et al*., 2020), giving rise to different types of anthocyanidins (Figure 2). To date, 17 types of anthocyanidins have been identified, although the most abundant are delphinidin, cyanidin, peonidin, petunidin, pelargonidin, and malvidin (Mattioli *et al*., 2020; Salamon *et al*., 2021). The biological activities of anthocyanins depend on their bioavailability, chemical structure, stability, origin of the food matrix, interaction with other phytonutrients, and intrinsic factors of the organism (Changxing *et al*., 2018; Garg *et al*., 2019).

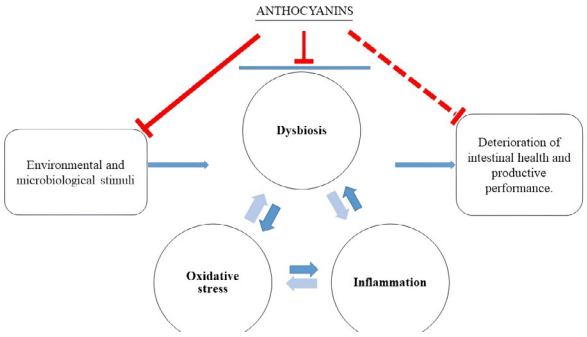

Figure 2: *General structure of anthocyanins (Kalt, 2019).*

Anthocyanins are widely distributed in nature, with major dietary sources including berries, purple corn, red cabbage, black rice, and *Hibiscus sabdariffa*, among others. These natural pigments contribute to the coloration of plant tissues and have been extensively studied for their health benefits (Mattioli *et al*., 2020; Verediano *et al*., 2021; Zhang *et al*., 2023). A detailed summary of the main anthocyanin-rich sources and their respective compositions is presented in Table 1.

Digestion, Absorption, and Metabolism of Anthocyanins

In the oral cavity, non-acetylated anthocyanins are hydrolyzed into aglycones primarily by the β-glucosidase activity of the oral microbiota (e.g., *Streptococcus spp*.) (Tian *et al*., 2019; Jokioja *et al*., 2021). In the stomach, the acidic pH induces partial degradation- more pronounced in non-acetylated anthocyanins. Although their absorption is limited at this stage, most anthocyanins reach the small intestine (Tian *et al*., 2019).

In the small intestine, anthocyanins absorption- particularly that of non-acetylated compounds-occurs mainly in the jejunum, followed by the duodenum (Chen *et al*., 2022). Non-acetylated glycosides enter enterocytes via transporters such as GLUT2 and SGLT1, while acetylated anthocyanins are metabolized by gut microbiota, specifically by *Bifidobacterium* and *Lactobacillus* strains with β-glucosidase activity (Tian *et al*., 2019; Jokioja *et al*., 2021). Absorption efficiency depends on physicochemical properties such as polarity, molecular size, and hydrophobicity, favoring small, polar molecules (Chen *et al*., 2022).

Once absorbed, anthocyanins undergo metabolism in the intestinal epithelium, liver, and kidneys, leading to the formation of glucuronides, sulfates, and methylated derivatives. In the GIT, they may undergo enterohepatic recycling via the bile duct to the jejunum due to their enterohepatic persistence (Fang, 2014; Changxing *et al*., 2018; Tian *et al*., 2019) or enter systemic circulation, appearing rapidly in the bloodstream. Undigested anthocyanins are excreted via urine, feces, and breath (Jokioja *et al*., 2021).

Approximately 65% of anthocyanins are not absorbed and reach the colon, where microbiota-mediated β-glucosidase activity-particularly from *Bifidobacterium* spp. and *Lactobacillus* spp.-facilitates their degradation, generating bioactive metabolites. In humans, the primary metabolites derived from pelargonidin, cyanidin, delphinidin, peonidin, and malvidin are 4-hidroxybenzoic acid, protocatechuic acid (PCA), gallic acid, vanillic acid, and syringic acid, respectively (Tian *et al*., 2019; Csernus *et al*., 2020; Hasted *et al*., 2021; Luo *et al*., 2022).

Anthocyanins and Gut Health

Anthocyanins, Antimicrobial Activity, and Microbiota Modulation

The GIT of broiler chickens hosts a complex microbiota composed of symbiotic and pathogenic microorganisms, including bacteria, fungi, archaea, protozoa, and viruses, with bacteria being the most abundant components. Colonization begins at hatching, primarily through the ingestion of bedding material, a process crucial for nutrient absorption, intestinal

Table 1: *Sources of Anthocyanins and Representative Examples.*

Category	Source	Scientific Name
Fruits		
	Grapes	*Vitis vinifera*
	Apples	*Malus domestica*
	Plums	*Prunus domestica*
	Aronia (chokeberry)	*Aronia melanocarpa*
	Blackberry	*Rubus fruticosus*
	Blueberry	*Vaccinium corymbosum*
	Cranberry	*Vaccinium macrocarpon*
	Raspberry	*Rubus idaeus*
	Black mulberry	*Morus nigra*
	Cornelian cherry	*Cornus mas*
	Black currant	*Ribes nigrum*
	Plum	*Prunus domestica*
	Maqui	*Aristotelia chilensis*
	Açai	*Euterpe oleracea*
	Eggplant	*Solanum melongena*
	Cherry	*Prunus avium*
	Strawberry	*Fragaria × ananassa*
	Jabuticaba	*Myrciaria jaboticaba*
	Bilberry	*Vaccinium myrtillus*
	Blood orange	*Citrus × sinensis*
Vegetables	Purple cabbage	*Brassica oleracea var. capitata f. rubra*
	Radish	*Raphanus sativus*
	Black carrot	*Daucus carota subsp. sativus var. atrorubens*
Tubers and root crops	Red potato	*Solanum tuberosum*
	Purple sweet potato	*Ipomoea batatas*
	Beetroot	*Beta vulgaris*
Legumes	Black beans	*Phaseolus vulgaris*
	Black soybean	*Glycine max* (L.) Merr.
Grains	Purple corn	*Zea mays*
	Black rice	*Oryza sativa*
By-products	Grape skins	*Vitis vinifera*
Flowers/calyxes	Roselle	*Hibiscus sabdariffa*

health, and productivity (Iqbal *et al.*, 2020; Vera *et al.*, 2023). At the taxonomic level, Firmicutes and Bacteroidetes are the dominant phyla, followed by Proteobacteria and Actinobacteria, collectively accounting for over 90% of the gut microbiota. The most prevalent genera include *Lactobacillus*, *Enterococcus*, *Bacteroides*, *Clostridium*, *Ruminococcus*, and *Bifidobacterium*, with relative abundances varying according to intestinal region, diet, and environmental factors (Ding *et al.*, 2023; Vera *et al.*, 2023).

Microbial composition differs across GIT regions. In the small intestine (duodenum, jejunum, and ileum), *Firmicutes* and *Lactobacillus*-facultative and acid-tolerant bacteria-predominate. In contrast, the cecum exhibits greater diversity, dominated by Bacteroidetes and strict anaerobic genera such as *Clostridium*, *Ruminococcus*, and *Bacteroides*. In

healthy birds, a dynamic equilibrium is maintained, where Gram-positive bacteria (e.g., *Firmicutes*) comprising over 85% of the population. This balance is essential for digestion, nutrient absorption, immune system development, and disease resistance. However, environmental factors, heat stress, and housing conditions can disrupt this equilibrium, leading to dysbiosis. This condition is characterized by microbial imbalances, inflammation, and impaired intestinal functions, which compromise mucosal barrier integrity, promote pathogen translocation, and ultimately reduce productive efficiency (Iqbal *et al*., 2020; Fang *et al*., 2023; Vera *et al*., 2023).

In addition to their antioxidant and anti-inflammatory properties, anthocyanins exhibit antimicrobial activity against *Salmonella* spp., *Escherichia coli*, *Staphylococcus aureus*, *Listeria monocytogenes*, *Vibrio parahaemolyticus*, and other bacteria (Sun *et al*., 2018; Ma *et al*., 2019; Dong *et al*., 2022). Although the precise mechanisms underlying bacterial inhibition remain unclear, anthocyanins have been reported to increase the hydrophobicity of the bacterial cell surface (Sun *et al*., 2018; Dong *et al*., 2022), thereby affecting both cell-cell and cell-surface interactions (Danchik and Casadevall, 2021). This increase in hydrophobicity has been associated to lipopolysaccharide (LPS) neutralization, membrane permeabilization, and enhanced bacterial susceptibility to antimicrobial peptides (Zhang *et al*., 2023). Additionally, anthocyanins disrupt the bacterial cell wall, leading to leakage of intracellular ions and cytoplasmic content. They also reduce the activity of alkaline phosphatase, adenosine triphosphatase (ATPase), and SOD in various pathogenic bacteria, inducing metabolic alterations (Sun *et al*., 2018; Ma *et al*., 2019).

Beyond their antimicrobial effects, anthocyanins modulate the intestinal microbiota. Although their mechanisms of action are not fully elucidated, most anthocyanins reach the colon, where they are metabolized by bacteria such as *Bifidobacterium* spp. and *Lactobacillus* spp., promoting their proliferation (Tian *et al*., 2019). For instance, supplementation with black corn anthocyanin extract in broiler chickens has been shown to favorably alter the cecal microbiome by increasing *Bifidobacterium* and *Clostridium* populations while reducing *E. coli* abundance. It has been proposed that *Bifidobacterium*, through β-glucosidase activity, hydrolyzes anthocyanins into aglycones and phenolic compounds that support its growth. Likewise, several *Lactobacillus* strains ferment phenolic compounds, utilizing them as carbon sources (Verediano *et al*., 2022).

A key bacterial metabolite of anthocyanins, PCA, may contribute to intestinal health in broilers. Supplementation with 300 mg/kg of PCA has been shown to reduce jejunal inflammation, improve intestinal barrier integrity, and modulate microbiota composition (Wang *et al*., 2019). Additionally, in broilers challenged with LPS, PCA supplementation enhanced antioxidant status, mitigated LPS-induced intestinal barrier damage, and restored plasma levels of immunoglobulins A, M, and γ (Jiang *et al*., 2023).

Both anthocyanins and PCA also modulate the intestinal microbiota, promoting the growth of bacteria that produce short-chain fatty acids (SCFAs) (Tian *et al*., 2019; Wang *et al*., 2019; Verediano *et al*., 2022). These SCFAs serve as energy substrates for enterocytes and acidify the intestinal environment, thereby reducing the risk of pathogen colonization (Liu *et al*., 2021). Additionally, polyphenols exhibit prebiotic activity by enhancing *Lactobacillus* populations. In turn, *Lactobacillus* exerts probiotic effects through immunomodulatory and anti-inflammatory actions, inhibition of bacterial toxins, and competitive exclusion of pathogens (Verediano *et al*., 2022).

Anti-inflammatory and antioxidant effects of anthocyanins

The excessive production of ROS, triggered by various stimuli that disrupt redox homeostasis, leads to the activation of multiple transcription factors (NF-κB, AP-1, HIF-1α, and PPAR-γ). Upon translocation to the nucleus, these factors induce the expression of genes involved in the inflammatory response, further contributing to ROS generation (Chatterjee, 2016; Rahman *et al*., 2021). In this context, polyphenols in general-and anthocyanins in particular-exert antioxidant activity by scavenging free radicals through the formation of ionic metal complexes and inhibiting singlet oxygen formation. This process is mediated by hydrogen atoms from hydroxyl groups located in the aromatic rings of anthocyanins, thereby preventing oxidative damage to biomolecules, inhibiting oxidase enzymes, and activating antioxidant enzymes (Cásedas *et al*., 2017; Bendokas *et al*., 2020; Amer *et al*., 2022; Luo *et al*., 2022).

Additionally, anthocyanins have the potential to

modulate ROS-regulated transcription factors. In humans with metabolic syndrome, a daily supplementation with 320 mg of anthocyanins for four weeks reduced the expression of NF-κB- dependent genes, including those encoding tumor necrosis factor-alpha (TNF-α), interleukin 1A (IL-1A), IL-6, and cyclooxygenase 2 (COX-2) (Aboonabi and Aboonabi, 2020). Likewise, *in vitro* and *in vivo* studies have demonstrated that cyanidin-3-glycoside inhibits NF-κB signaling while promoting the expression and translocation to the nucleus of nuclear factor erythroid 2-related factor 2 (Nrf2), a transcription factor that mediates the antioxidant response by upregulating the expression of CAT, GPx, and SOD (Aboonabi and Aboonabi, 2020; Rahman *et al*., 2021). In broiler chickens challenged with *Salmonella typhimuriumγ*, anthocyanin supplementation attenuated the inflammatory response by reducing the production of ileal cytokines, including interleukin-1 beta (IL-1β), IL-6, IL-8, TNF-α, interferon beta (IFN-β) and IFN- γ (Zhang *et al*., 2023).

At the systemic level, the anti-inflammatory and antioxidant effects of anthocyanins have also been demonstrated. For instance, supplementation with purple corn as a source of anthocyanins increased the expression and activity of SOD, GPx, and CAT, as well as the total antioxidant capacity in the plasma of Chishui chickens (Luo *et al*., 2022). Similarly, supplementation with a *Hibiscus sabdariffa* (Jamaica flower) extract enhanced serum CAT and SOD levels, reduced malondialdehyde concentrations, and improved oxidative stress defense mechanisms in Ross 308 chickens. Additionally, this extract exhibited anti-inflammatory and immunomodulatory properties by increasing serum interleukin-10 (IL-10) and enhancing Ig γ in the spleen (Amer *et al*., 2022).

Furthermore, supplementation with anthocyanins from Hungarian cherries reduced IL-1β concentrations in the spleen, although it did not significantly alter IL-6, IFN-α, IFN-γ, TLR-4, or TLR-5 levels (Csernus *et al*., 2020). In broiler chickens challenged with *Salmonella typhimurium*, anthocyanin supplementation reduced plasma nitric oxide (NO) levels-a molecule involved in inflammatory responses, lipid peroxidation of cell membrane, and DNA damage-suggesting anthocyanins may attenuate immune responses induced by this pathogen (Zhang *et al*., 2023).

Intestinal Morphology and Integrity

Anthocyanins also have the potential to improve intestinal morphology. For instance, in Ross 308 broiler chickens, supplementation with varying doses (50, 100, 200, and 400 mg/kg) of *Hibiscus sabdariffa* L. extract as a source of anthocyanins for 35 days enhanced small intestinal villus height, reduced crypt depth, and increased the villus height-to-crypt depth (VH:CD) ratio. Additionally, it elevated the number of goblet cells in the small intestine (Amer *et al*., 2022). Notably, villus height and the VH:CD ratio are key indicators of intestinal health (Ducatelle *et al*., 2018), while a higher number of goblet cells promotes mucin production, which in turn inhibits intestinal pathogen colonization (Duangnumsawang *et al*., 2021).

However, under inflammatory conditions-as in broilers intramuscularly inoculated with LPS-the relative expression of genes encoding intestinal tight junction proteins-occludin (OCLN), Zonula Occludens-1 (ZO-1), junctional adhesion molecule-2 (JAM-2), as well as mucin-2 (MUC-2), decreased, while malondialdehyde levels (a lipid peroxidation marker) increased. Simultaneously, total superoxide dismutase (T-SOD) activity and the expression of T-SOD, CAT, and GPx in the jejunal mucosa were reduced. However, dietary supplementation with 100 and 400 mg/kg of anthocyanins upregulated the relative expression of ZO-1, JAM-2, and OCLN, counteracted the LPS-induced suppression of antioxidant enzymes, and mitigated jejunal mucosal damage, thereby improving absorptive capacity and intestinal integrity (Wang *et al*., 2023).

Similarly, in broiler chickens challenged with *Salmonella Typhimurium*, a reduction in intestinal villus height, an increase in crypt depth, and a deteriorated VH:CD ratio were observed, compromising intestinal barrier integrity. However, after 60 days of supplementation with blueberry anthocyanins (100 and 400 mg/kg), these effects were reversed. This improvement was attributed to their antimicrobial activity-including LPS degradation in Gram-negative pathogens-and the upregulation of tight junction proteins (ZO-1, claudin-1, and OCLN) (Zhang *et al*., 2023). Additionally, in birds intraperitoneally inoculated with *E. coli* LPS, supplementation with Hungarian cherry anthocyanins not only reduced inflammatory responses but also increased ileal villus height and improved the VH:CD ratio, ultimately enhancing nutrient absorption (Csernus *et al*., 2020). These

findings highlight the critical role of anthocyanins in avian intestinal health, as summarized in Figure 3.

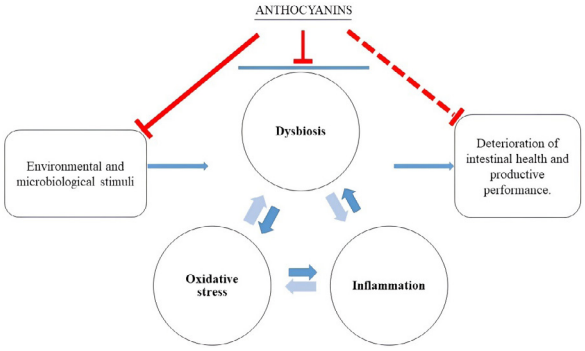

Figure 3: *Effect of anthocyanins on gut health. Anthocyanins help counteract the effects of environmental and microbiological stimuli by reducing dysbiosis, oxidative stress, and inflammatory responses, ultimately promoting intestinal health and overall performance in broiler chickens. Blue arrows indicate the influence of environmental and microbiological stimuli, while the red inhibition line represents the direct suppressive effects of anthocyanins on dysbiosis, oxidative stress, inflammation, and their underlying triggers. The dotted line illustrates the potential indirect effects of anthocyanins on gut health in broilers.*

Anthocyanins and Productive Performance in Broilers

The majority of evidence suggests that the inclusion of flavonoids, including anthocyanins, exerts positive effects on both the health and productive performance of broiler chickens (Changxing *et al.*, 2018; Kamboh *et al.*, 2019). These benefits are attributed to various mechanisms of action, such as their antioxidant and anti-inflammatory activities, which contribute to improved intestinal morphology and integrity, modulation of gut microbiota, reduced peristalsis, and slower chyme transit time. These effects enhance nutrient absorption, leading to increased weight gain and improved feed conversion efficiency (Csernus *et al.*, 2020; Luo *et al.*, 2022; Tan *et al.*, 2022; Li *et al.*, 2023).

At the systemic level, anthocyanins have been shown to reduce the activity of cyclooxygenases (COX-1 and COX-2), inhibit the production of pro-inflammatory cytokines such as IL-1β, IL-6 and TNF-α, and increase the activity of antioxidant enzymes like SOD and GPx. These anti-inflammatory and antioxidant properties help maintain cellular integrity and optimize metabolic function, increasing energy availability and, consequently, improving productive performance (Changxing *et al.*, 2018; Verediano *et al.*, 2021; Saltos *et al.*, 2021; Tan *et al.*, 2022; Li *et al.*, 2023).

Furthermore, anthocyanins have been reported to stimulate thyroid function by increasing serum thyroxine (T4) concentrations and growth hormone secretion (GH), which may positively influence metabolism and, thereby, growth parameters in broilers (Amer *et al.*, 2022). On the other hand, the anti-adipogenic activity of anthocyanins-through inhibition of lipogenesis and stimulation of hepatic β-oxidation-may support liver health and enhance metabolic efficiency (Amnueysit *et al.*, 2010; Reyna *et al.*, 2018; Saltos *et al.*, 2021).

Regarding the beneficial effects of anthocyanins on the productive performance, supplementation with 0.15% and 0.75% purple corn extract (equivalent to 66 and 330.8 mg anthocyanins/kg diet, respectively) significantly improved final weight in Cobb 500 chickens raised under tropical conditions, while also reducing hepatic steatosis (Saltos *et al.*, 2021). Additionally, supplementation with PCA enhanced feed intake, feed efficiency, and final weight in broilers (Wang *et al.*, 2019). In LPS-inoculated chickens, an ethanolic blueberry extract rich in anthocyanins mitigated declines in final weight and feed intake, an effect linked to improved intestinal antioxidant status and upregulated expression of intestinal tight junction proteins (Wang *et al.*, 2023).

Concerning carcass traits in broilers, the partial replacement of yellow corn with anthocyanin-rich purple corn significantly reduced abdominal fat (Amnueysit *et al.*, 2010). Additionally, supplementation with 80 mg/kg of purple corn extract enriched in anthocyanins improved the amino acid profile and increased polyunsaturated fatty acid (PUFA) content in the muscle tissue of Chishui chickens, while also enhancing productive performance at doses of 80 and 160 mg/kg feed. These effects may be attributed to the antioxidant properties of anthocyanins, which, at low doses, prevent oxidative peroxidation and mitigate free radical damage in tissues, thereby increasing energy availability and improving productive outcomes. However, the lack of effects with 240 mg/kg of purple corn extract is likely due to the pro-oxidant effects of these compounds at high doses (Luo *et al.*, 2022). Similarly, other studies have reported improvements in meat quality and muscle composition, including elevated n-3 PUFA levels and antioxidant capacity (Wang *et al.*, 2021; Amer *et al.*, 2022).

Table 2: *Summary of the effects of various anthocyanin sources on the productive performance of broiler chickens.*

Author/year	Study objective	Effects	Conclusions
Amnueysit (2010)	To assess partial replacement of yellow corn with 20, 30, 40 and 60% purple corn (anthocyanin source) on carcass yield, visceral organ weight, and abdominal fat in 42-day-old broilers	The substitution of yellow corn with purple corn did not significantly alter the relative weight of visceral organs, though it reduced that of abdominal fat and the heart	The use of purple corn reduced the relative weight of abdominal fat and heart in poultry, which may indicate improved overall health
Csernus *et al* (2020)	To evaluate bioactive compounds, including anthocyanins (dietary supplementation of sour cherry; 0.5%), on growth, immunity, and gut morphology in *E. coli* LPS-challenged Ross 308 broilers.	Anthocyanins in LPS-challenged broilers: No beneficial effects on productive parameters, but reduced splenic IL-1β (↓inflammation), ↑villus height/crypt depth ratio, and thickened mucosa → enhanced intestinal absorption	Anthocyanins may benefit broilers under immune challenge by reducing inflammation and enhancing gut morphology for nutrient absorption
Saltos *et al* (2021)	To evaluate of dietary purple corn extract supplementation (0.05%, 0.15%, 0.75%; 22, 66 and 330.8 mg anthocyanins/kg feed) on productive performance and lipid metabolism in 56-day-old Cobb 500 broilers.	↑BW (0.15-0.75% PCE vs control/0.05%). No diff. in feed intake, FCR, mortality, carcass/organ metrics. PCE ↓hepatic steatosis. Serum lipids (TAG, TC, LDL-C, HDL-C) similar. CV risk ratios (TC/HDL-C, LDL-C/HDL-C) ↓in PCE groups.	PCE has the potential to reduce atherogenic risk and hepatic steatosis in broiler chickens (used as models of these diseases) while improving final body weight, without compromising other productive performance metrics
Tolnai *et al* (2021)	To assess the interaction between bioactive compounds-including anthocyanins (Hungarian sour cherry, 0.5%)-and the gut microbiota of Ross 308 broiler chickens, as well as their relationship with productive performance	Anthocyanin supplementation altered gut microbiota: ↓*Lactobacillus* (prestarter), ↑*Subdoligranulum* (butyrate-producing), *Blautia*, *Ruminococcus* (finisher). ↓*Firmicutes*/*Bacteroidetes*, ↑*Campylobacter* (no adverse effects). microbial interaction modulation. By end cycle, ↓ body weight (non-significant) vs. control.	Anthocyanins modulate the intestinal microbiota of broiler chickens by altering bacterial quantity, the *Firmicutes/Bacteroidetes* ratio, and taxonomic interactions. These phase-dependent changes promote intestinal health and support their use as an additive in sustainable poultry production.
Wang *et al* (2021)	To explore the effects of bilberry extract (BBE, 100-400 mg/kg) on growth performance, immune function, antioxidant capacity, and meat quality in broiler chickens	BBE supplementation (100-400 mg/kg) did not affect growth/survival, enhanced immunity (↑bursa of Fabricius weight at 21 days) and antioxidant capacity (↑GSH-Px-/T-SOD activity, ↓MDA levels in plasma/tissues). In meat, it reduced post-mortem oxidation (↓MDA) and improved pH/water retention, without altering color or intramuscular fat	Bilberry extract (400 mg/kg) enhances immunity and antioxidant capacity in chickens without affecting growth. It reduces meat oxidation and improves its quality, serving as a natural additive for sustainable poultry production.
Amer *et al* (2022)	Analysis of *H. sabdariffa* anthocyanin supplementation (50, 100, 200 and 400 mg/kg diet) on growth parameters, intestinal health and immunity in Ross 308 broilers.	ARRE enhanced antioxidant (↑TAC/SOD, ↓MDA), immune (↑IL-10/lysozyme/IgG), and intestinal functions, increased n-3 PUFAs in breast muscle, without affecting broiler growth.	ARRE supplementation showed no significant effects on productive performance. However, it improved immune function, intestinal health, and the lipid profile of breast muscle, with an optimal dose of 280 mg/kg
Luo *et al* (2022)	To assess the effect of purple corn pigment supplementation (80, 160 and 240 mg/kg anthocyanins) on productive performance, antioxidant capacity, immunity, and cecal microbiota in *Chishui blackbone* chickens.	Supplementation with PCP (80–160 mg/kg) ↑ ADFI, ADG, BWC, and final weight ↑ SOD, GPx and CAT levels, ↓ MDA. It optimized amino acids/PUFAs profile in breast muscle. ↑ serum albumin, ↓ reduced water/drip loss; FCR and initial weight remained unaffected.	Purple corn meal supplementation (anthocyanins) improves growth performance, enhances antioxidant capacity, modulates, and benefits cecal microbiota in broilers

Fang *et al* (2023)	To assess the impact of purple sweet potato anthocyanins (PSPA, 8, 16 and 32 mg/kg BW/day) on growth, meat quality, oxidative balance, and gut health in heat-stressed Wenchang chickens.	PSPA reversed heat stress effects on growth and meat/carcass quality. ↑Digestive enzymes, ↑GSH-Px and SOD, ↓MDA (serum/liver). Cytokine regulation (↑IL-10, ↓IL-1β/IL-6/TNF-α). ↑Intestinal villi length/goblet cells. ↓Serum lipids, ↑lipase activity. Microbiota modulation: ↑beneficial bacteria, ↓harmful taxa, correlating with health/performance improvements.	PSPA enhances growth performance, meat/carcass quality, and reduces oxidative stress, dyslipidemia, intestinal damage, and dysbiosis in heat-stressed Wenchang chickens. A promising additive for heat stress management in poultry.
Zhang *et al* (2023)	To evaluated of cranberry anthocyanins (100 and 400 mg/kg) on production and intestinal health of slow-growing male Lingnan chickens challenged by *S. Typhimurium*.	Mitigated weight loss, improved FCR; reduced *Salmonella* CFUs in liver/spleen, preserved ileal morphometry, lowered ileal cytokines, enhanced gut barrier, and restored cecal microbiota	Blueberry anthocyanins counteracted *S. Typhimurium*'s impact on broiler growth, enhanced gut health (structure, tight junctions, cecal microbiota balance), and reduced inflammation

Abbreviations. ADFI: *Average Daily Feed Intake;* **ADG:** *Average Daily Gain;* **BWC:** *Body Weight Change;* **SOD:** *Superoxide Dismutase;* **GPx:** *Glutathione Peroxidase;* **CAT:** *Catalase;* **MDA:** *Malondialdehyde;* **PUFAs:** *Polyunsaturated Fatty Acids;* **FCR***: Feed Conversion Ratio;* **PCE:** *Purple Corn Extract;* **BW:** *Body Weight;* **PCE:** *Purple Corn Extract;* **FCR:** *Feed Conversion Ratio;* **TAG:** *Triacylglycerols;* **TC:** *Total Cholesterol;* **LDL-c:** *Low-Density Lipoprotein Cholesterol;* **HDL-c:** *High-Density Lipoprotein Cholesterol;* **ARRE:** *Anthocyanin-Rich Roselle Extract;* **TAC:** *total antioxidant capacity;* **FCUs:** *Forming Colony Units.*

Current evidence suggests that anthocyanins exert predominantly beneficial effects on broiler chicken health. In *in vitro* studies and animal models, minimal or no adverse effects have been reported (Alam 2021). wever, in broilers, some studies have shown variable outcomes, including increased feed intake without proportional weight gain, alterations in gut microbiota-such as reduced *Lactobacillus* and increased *Campylobacter jejuni* and a tendency toward lower body weight, albeit without adverse clinical manifestations (Csernus *et al*., 2020; Saltos *et al*., 2021; Tolnai *et al*., 2021).

These variations do not result from intrinsic side effects of anthocyanins but rather from factors such as the botanical source of extraction, the concentration used, the presence of co-occurring bioactive compounds in the plant matrix, and interactions with dietary or environmental components (Changxing *et al*., 2018; Saltos *et al*., 2021; Tolnai *et al*., 2021; Predescu *et al*., 2024). Therefore, these differences represent practical limitations for their application, rather than inherent side effects associated with consumption. However, few studies address the potential toxicity or side effects of prolonged or high-dose exposure to these herbal bioactive compounds in vivo (Li *et al*., 2024). The following table summarizes key findings from the literature on the use of various anthocyanin sources in broiler chicken nutrition, (Table 2).

Conclusions and Recommendations

Following the ban on antibiotic growth promoters (AGPs) in animal production, various alternatives have been explored to maintain productivity. In this context, anthocyanins-flavonoids with antioxidant, anti-inflammatory, and antimicrobial properties-enhance intestinal absorption, strengthen the mucosal barrier, modulate the gut microbiota, and promote the production of metabolites that inhibit pathogenic bacteria while supporting intestinal health.

At a systemic level, anthocyanins prevent bacterial and toxin translocation, enhance immune function, and contribute to poultry productivity. However, despite their health benefits, their effects on growth performance remain inconsistent, underscoring the need to select sources based on composition, bioavailability, and interactions with other dietary components.

Further research is needed to elucidate the molecular mechanisms underlying anthocyanins' effects, their interactions with the gut microbiota, the formation of bioactive metabolites, and their synergy with intestinal mucosal pathways. A deeper understanding of these aspects would enable the optimization of supplementation strategies through precise combinations, dosages, and co-administration with other phytogenic compounds. Additionally, evaluating

the efficacy of microencapsulated anthocyanins and their activity at the cecal level, as well as characterizing anthocyanin-rich plant sources and food industry byproducts, could further advance their use as a sustainable alternative to AGPs.

Acknowledgements

The authors thank Dra. María Elena Villanueva Espinoza, Faculty of Zootechnics, Universidad Nacional Agraria la Molina-Peru, for his valuable review and insights.

Novelty Statement

The manuscript examines the effect of anthocyanins on the intestinal health of broiler chickens and their subsequent impact on productive performance. It also explores the potential mechanisms of action that make these bioactive compounds a promising alternative to growth-promoting antibiotics.

Authors' Contribution

José Arteaga; Participated in drafting and critical revision of the paper.
Juan José Toro-Letelier; Participated in literature search, and critical revision of the data.
Sixto Reyna; Conceived and drafted the manuscript.

Conflict of interest
The author(s) declare(s) that there is no conflict of interests regarding the publication of this article".

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