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Dietary plant flavonoid supplementation for poultry as a potent scavenger of hydroxyl radicals and antioxidants: a review

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ABSTRACT

The poultry industry is paying more attention to plant-based feed additives. Flavonoids are plant secondary metabolites derived from fruits, grains, vegetables, herbs, and medicinal plants. One of the most significant environmental stressors affecting the poultry industry worldwide is heat stress, which lowers the quality and safety of production. An imbalance between the production of free radicals and the body's natural antioxidant defenses leads to oxidative stress in cells. These reactive species can damage proteins, lipids, DNA, and cellular structures. Improving the antioxidant status of poultry bodies by feeding them antioxidant-supplemented feed can increase productivity and health. Plant flavonoid compounds have drawn attention from researchers as possible natural antioxidant sources because of their potential for use as feed additives in poultry production. Numerous studies have demonstrated that dietary flavonoids have strong antioxidant effects and can be utilized as a tonic in poultry to improve health and productivity. Overall, research on the antioxidant capacity of plant flavonoids has generally shown promising results; however, there are still significant issues regarding the detrimental effects of flavonoids to be resolved, and measuring oxidative damage *in vivo* is challenging. This review summarizes the current understanding of dietary plant flavonoid supplementation for poultry as a potent scavenger of hydroxyl radicals and antioxidants.

Subjects Natural Products, Organic Chemistry (other), Organic Compounds
Keywords Flavonoid, Antioxidant, Poultry, Hydroxyl radical, Oxidative stress

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INTRODUCTION

Flavonoids are natural secondary metabolites derived from fruits, grains, vegetables, herbs, and medicinal plants (*Roy et al., 2022*). Flavonoids are essential substances in pharmacological and nutritional applications and have positive health effects on animals (*Mutha, Tatiya & Surana, 2021*). It has been reported that flavonoids have a variety of biological actions, including anti-inflammatory, antioxidant, growth promoter, antiviral, hepatoprotective, antibacterial, antiallergic, anticarcinogenic, antithrombotic, and immunomodulator activities, in various animals and poultry species (*Saeed et al., 2017*; *Ullah et al., 2020*). Poultry diets supplemented with natural plants can strengthen antioxidant defense mechanisms and lessen the intensity of oxidation processes (*Ognik et al., 2016*).

The production of broilers is a crucial element in satisfying the growing need for animal protein in both developed and developing countries (*Greenhalgh et al., 2020*). Maintaining the health of poultry is essential for maximizing production efficiency. However, due to factors such as heat, high stocking density, immunological challenges, handling, transportation, and feed quality, modern large-scale broiler production puts broilers in stressful environmental situations (*Guarino Amato & Castellini, 2022*). Oxidative stress is caused by stressors that increase the production of reactive oxygen species (ROS) and disturb the balance between the oxidant and antioxidant defense systems inside the body, resulting in oxidative stress. In the pathophysiology of many diseases, oxidative stress is a key concept (*Cottrell et al., 2021*; *Donia & Khamis, 2021*). This happens when the cell defense system cannot handle the amount of reactive oxygen species produced. Stress and aging cause an overabundance of free radical production, which damages mitochondrial membranes and causes structural irregularities in cells (*Dumanović et al., 2021*).

One type of reactive oxygen species that is frequently produced *in vivo* is the hydroxyl radical, which may severely damage biomolecules such as proteins, lipids, and nucleic acids. It has an impact on diseases linked to inflammation, such as cancer, neurodegeneration, and chronic inflammation (*Juan et al., 2021*). Scientists strive to combat excessive oxidative stress and find antioxidant molecules, such as those that scavenge hydroxyl radicals or reduce their production in inflammatory tissues, to prevent or stop the progression of related diseases (*Pisoschi et al., 2021*). This can then have an impact on the animals' performance and may even cause the illness to develop. Improving the antioxidant status of animals through feeding optimization (in terms of both quantity and quality) and, in particular, exogenous antioxidant supplementation could be a crucial and very successful way to increase animal productivity and health (*Ponnampalam et al., 2022*).

Flavonoids can donate an electron or a hydrogen atom to scavenge free radical species, including superoxide, hydroxyl radicals, and lipid peroxyl radicals. The hydroxyl group in phenol that scavenges these radicals is dissociated to its anionic form based on the pH of the medium (*Parcheta et al., 2021*). Therefore, an increase in the medium pH is associated with an increase in the radical scavenging activity of flavonoids (*Simunkova et al., 2021*). Flavonoids have been shown in numerous studies to have positive effects on meat product color stability, reduce microbial growth, inhibit lipid oxidation, and monitor any pH-dependent deterioration (*Turan & Şimşek, 2021*).

Research indicates that the gut-promoter effects of herbal plants with sufficient flavonoid content have been observed in a variety of farm animal and poultry species. These findings also point to the antioxidant flavonoids as a crucial tool for modifying the small intestine's functional architecture (*Viveros et al., 2011*). These flavonoids are also recognized for enhancing gut health and immunity, which in turn lowers the risk of infectious illnesses and enhances animal performance. Additionally, these might synergize with other synthetic and organic growth promoters as well as with one another. Therefore, these flavonoids both in their purified and phytoextract forms can be beneficial choice to improve the production of poultry (*Kamboh et al., 2015*). Thus far, research on flavonoids in poultry has evaluated their effects on growth performance; other productive traits, such as meat and egg quality parameters; and meat oxidative status.

Rationale of the study

The production of eggs and meat, as well as a major contribution to the food industry as a whole, depend heavily on poultry farming, which is an essential part of modern agriculture. Eggs and poultry meat are very nutritious and beneficial to eat. Owing to their low cost and high nutritional content, eggs are regarded as a crucial component in guaranteeing that everyone has access to a healthy diet (*Dong et al., 2024*). The alleged health advantages of plant-based diets have come to light more and more in recent years. As a result, natural herbal source extracts with antioxidant-producing potential are receiving more and more attention. However, there has been less research on the benefits of feeding dietary supplements containing flavonoids to poultry, particularly those raised for commercial purposes. Research on flavonoids in poultry has so far looked at their impact on growth performance, other productive qualities, and measures related to the quality of the meat and eggs, in addition to the oxidative status of the meat. The objective of the review paper is to summarize the use of different plant flavonoids in poultry supplementation as a potent scavenger of hydroxyl radicals and antioxidants.

SURVEY METHODOLOGY

Studies on recent dietary flavonoid supplementation for poultry feeds as antioxidants were summarized in this review. In this study, the published articles were gathered using the five databases (Scopus, Science Direct, PubMed, Web of Science, and Google Scholar) and searched in December 2023 using terms and phrases such as "plant flavonoid," "supplementation for poultry," and "scavenger of hydroxyl radicals/antioxidants." They were searched in the subject title or in combination with the free term. The selection of research, papers, articles, and other sources for this article was based on their relevancy to poultry antioxidant activity. The full text of the publications that were found was downloaded once the abstract screening process was completed. Any manuscript lacking this information was returned untouched. The only articles that underwent additional screening were those with fully accessible texts for data extraction and analysis.
An all-encompassing picture of the topic was given by the combination of the literature review, research articles, and countermeasures review, which brought to light the main trends and gaps in flavonoid supplements for poultry feed. Overall, this article's survey methodology sought to give readers a thorough understanding by supplementation of flavonoids to poultry diets to reduce oxidative stress, maintain poultry industry standards for quality, and boost output.

Sources of flavonoids

Flavonoids are an important class of natural products. In particular, these compounds are secondary metabolites produced by plants that have a polyphenolic structure and are commonly present in fruits, vegetables, and some drinks (*Mutha, Tatiya & Surana, 2021*;

Shen et al., 2022). Flavonoid compounds are byproducts of plant extraction and are present in various plant parts (Dias, Pinto & Silva, 2021). Among the foods high in natural flavonoids are berries, citrus fruits, grapes, cherries, dock, arugula, onions, artichokes, cocoa, soybeans, cowpeas, black beans, parsley, oregano, and tea (Shen et al., 2022; Roy et al., 2022). Flavonoids are among the most prevalent groups of compounds in higher plants and are crucial for plant growth, pigmentation, and resistance to plaques in the kingdom of plants (Tyagi et al., 2020). Therefore, flavonoids found in animals originate from plants rather than being biosynthesized in animals (Ullah et al., 2020).

Depending on the degree of unsaturation and oxidation of the C ring, as well as the carbon of the C ring to which the B ring is attached, flavonoids can be further classified into various subgroups (Chen et al., 2023). Isoflavones are flavonoids in which the B ring is bonded to the C ring at position 3. Those in which the B ring is linked at position 4 are called neoflavonoids, while those in which the B ring is linked at position 2 can be further subdivided into several subgroups based on the structural features of the C ring (de Souza Farias, da Costa & Martins, 2021). These groups of compounds include flavones, flavonols, flavanones, flavanonols, flavanols, catechins, anthocyanins, and chalcones (Liu et al., 2021; Sabah, 2021). The structure of major flavonoids supplemented in poultry feed were expressed in Fig. 1.

Citrus fruits are the main source of flavanones, while herbs, legumes, citrus fruits, anthocyanins, and catechins, as well as all fruits and vegetables, contain flavonols. Nevertheless, a number of variables, including plant genotype, growing environment, soil properties, harvest, and storage, affect the quantity of these compounds (Alam et al., 2022). Green leaves, fruits, and grains are rich in flavonols, which include myricetin, fisetin, isorhamnetin, kaempferol, and quercetin (Dias, Pinto & Silva, 2021; Shen et al., 2022). Quercetin has been shown to have beneficial effects on poultry health and productivity. It can be found in a variety of foods, including onions, apples, wine, tea, and vegetables (Batiha et al., 2020). Dihydroflavones are a significant class of flavonoids that are commonly present in citrus fruits (Alam et al., 2022). Myricetin can be found in nuts, berries, tea, and red wine (Taheri et al., 2020). Acylated anthocyanins are abundant in vegetables such as purple sweet potatoes, red turnips, and red cabbages (Sharma et al., 2021). The increased use of flavonoids as food additives instead of artificial preservatives will help ensure the sustainability of the food industry because they are low-toxicity, naturally occurring compounds found in large quantities in plants and are reasonably priced (Shaker et al., 2022). Numerous studies on poultry diets have verified the beneficial effects of flavonoids on parameters related to productive performance, including oxidative status, meat and egg quality, carcass traits, and growth performance (Omar et al., 2020; Wang et al., 2021).

The antioxidant mechanism of flavonoids

The flavonoid structure provides the antioxidant properties of flavonoids. Because flavonoids have a 2,3-double bond conjugated with a 4-oxo functionality and a hydroxyl group on ring B, they can lower the levels of ROS, such as hydroxyl, peroxyl, and peroxynitrite radicals (Havsteen, 2002; Shah & Smith, 2020; Dias, Pinto & Silva, 2021). This

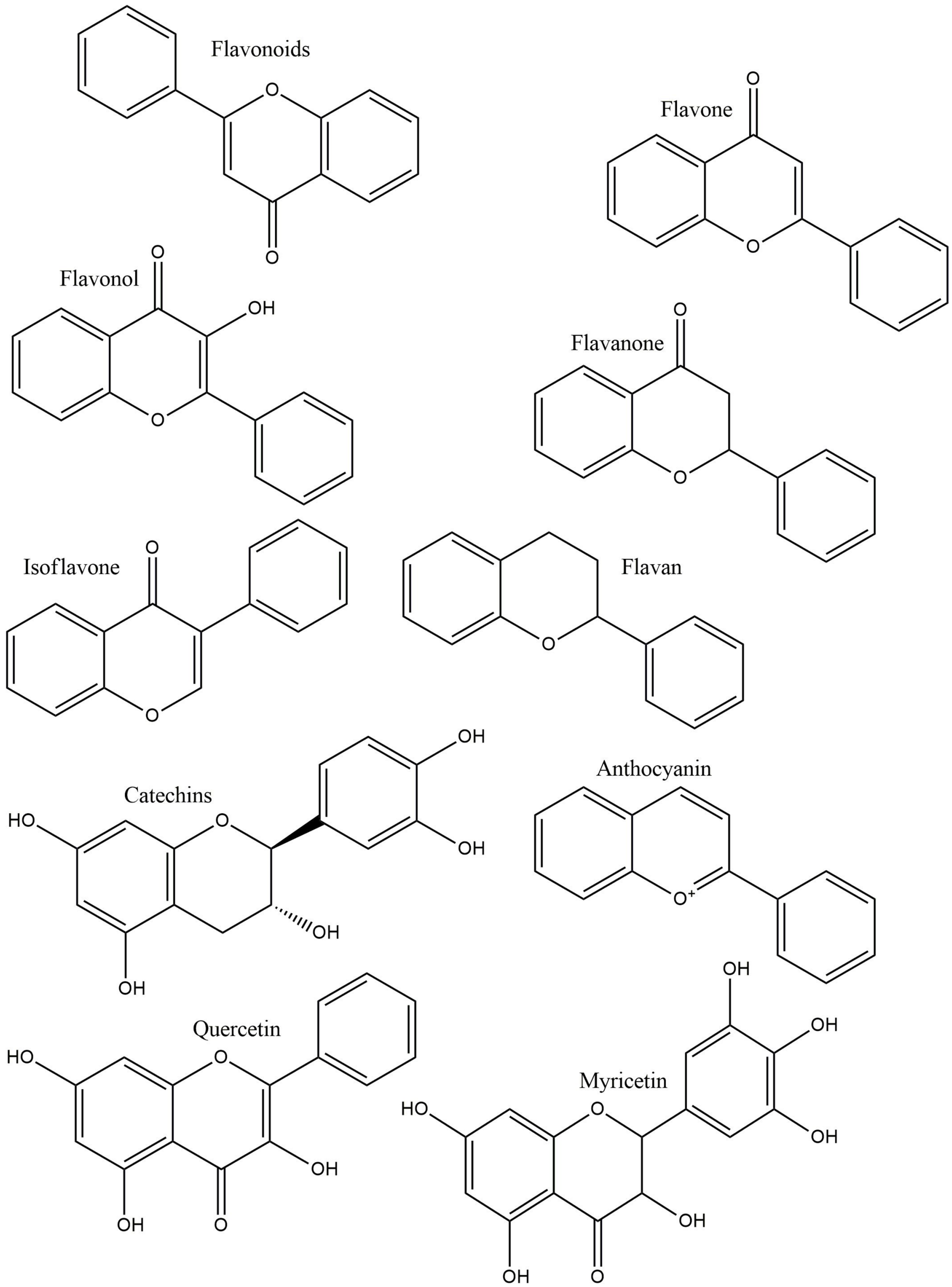

Figure 1 **The structure of major flavonoids supplemented in poultry feed.**
Full-size DOI: 10.7717/peerj-ochem.9/fig-1

happens through the flavonoid hydroxyl group donating an electron and a hydrogen atom, which results in the production of a relatively stable flavonoid radical (*Treml & Šmejkal, 2016*). As a result, the 3′–4′ catechol structure of ring B and the 3-position hydroxyl group of ring C both serve as potent indicators of antioxidant capacity. The flavonoid molecule becomes planar as a result of the catechol moieties, which create hydrogen bonds with 3-OH (*Slika et al., 2022*) (Fig. 2). Due to the unsaturated double bond on carbons 2 and 3 conjugating with the 4-oxo group, this planarity facilitates conjugation and electron delocalization (*Shah & Smith, 2020*; *Slika et al., 2022*).

Reducing *in vitro* radicals does not guarantee that a substance will act as an antioxidant in an *in vivo* setting. This is a result of the easy diffusion and spread of free radicals (*Speisky et al., 2022*). It has been reported that flavonoids act as antioxidants by activating antioxidant enzymes, scavenging reactive oxygen species (ROS) (Fig. 3) and reactive nitrogen species (RNS), and, in certain cases, chelating transition metal ions in a structure-dependent manner (*Kejík et al., 2021*). ROS are free radicals that serve as messengers within cells but can potentially cause damage to proteins, RNA, and DNA at high concentrations (*Lobo et al., 2010*). Flavonoids possess strong antioxidant and chelating properties *in vitro* due to their conjugated double bonds and carbonyl groups, which, together with multiple hydroxyl groups, enable stable electron delocalization. By preventing low-density lipoprotein (LDL) oxidation, phenolic compounds can chelate metal ions such as iron and copper or function as hydrogen donors (*Parcheta et al., 2021*).

However, studies on the capacity of flavonoids and phenolic acids to scavenge reactive nitrogen species are limited. One such species is NO, which is created by endothelial cells, neurons, *etc*., using nitric oxide synthase. Additionally, iNOS is induced, and NO synthesis is activated at sites of inflammation (*Ferreira et al., 2018*). Moreover, peroxynitrite is produced at these sites during chronic inflammation when nitric oxide and superoxide radicals are simultaneously produced. Superoxide radicals and nitric oxide react quickly to form peroxynitrite, a hazardous oxidizing and nitrating species (*Pacher, Beckman & Liaudet, 2007*). Quercetin is a flavonoid that reduces ischemia-reperfusion injury by blocking the activity of inducible nitric oxide synthase. Numerous cell types, such as macrophages and endothelial cells, produce nitric oxide (*Abou Baker, 2022*; *Zhang et al., 2023*).

A higher concentration of nitric oxide produced by inducible nitric oxide synthase in macrophages can cause oxidative damage, even though the early release of nitric oxide through the activity of constitutive nitric oxide synthase is important for maintaining the dilation of blood vessels (*Zhang et al., 2023*). Under these conditions, activated macrophages produce a significant amount of superoxide anion and nitric oxide simultaneously. When free radicals and nitric oxide combine, the extremely harmful compound peroxynitrite is created (*Förstermann & Sessa, 2012*). Peroxynitrite is primarily responsible for nitric oxide injury because it can directly oxidize LDLs and cause irreparable damage to the cell membrane (*Sharifi-Rad et al., 2020*). Free radicals are scavenged when flavonoids are utilized as antioxidants; as a result, they are unable to react with nitric oxide and cause as much harm (*Zhang et al., 2023*). Interestingly, nitric oxide can be thought of as a radical in and of itself. It has been shown that flavonoids directly scavenge nitric oxide molecules (*Nijveldt et al., 2001*).

Flavonoids may also exert their effects through interactions with other enzyme systems. One source of oxygen-free radicals is xanthine oxidase. Superoxide-free radicals are produced through the reaction of xanthine oxidase with molecular oxygen. Quercetin and

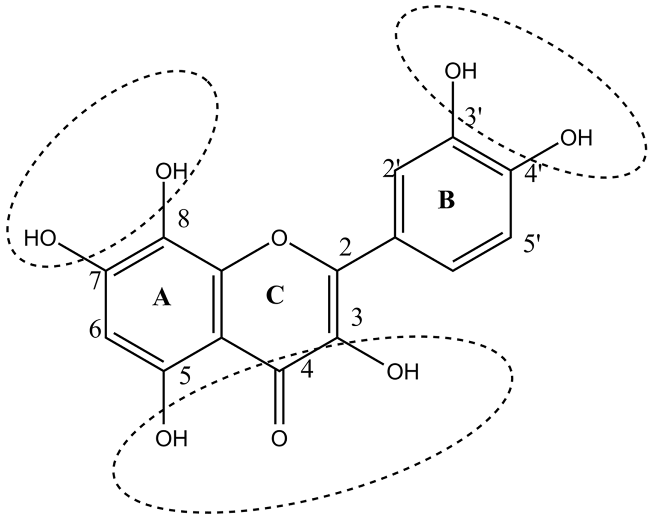

Figure 2 **The features of flavonoids with strong radical scavenging activity.**
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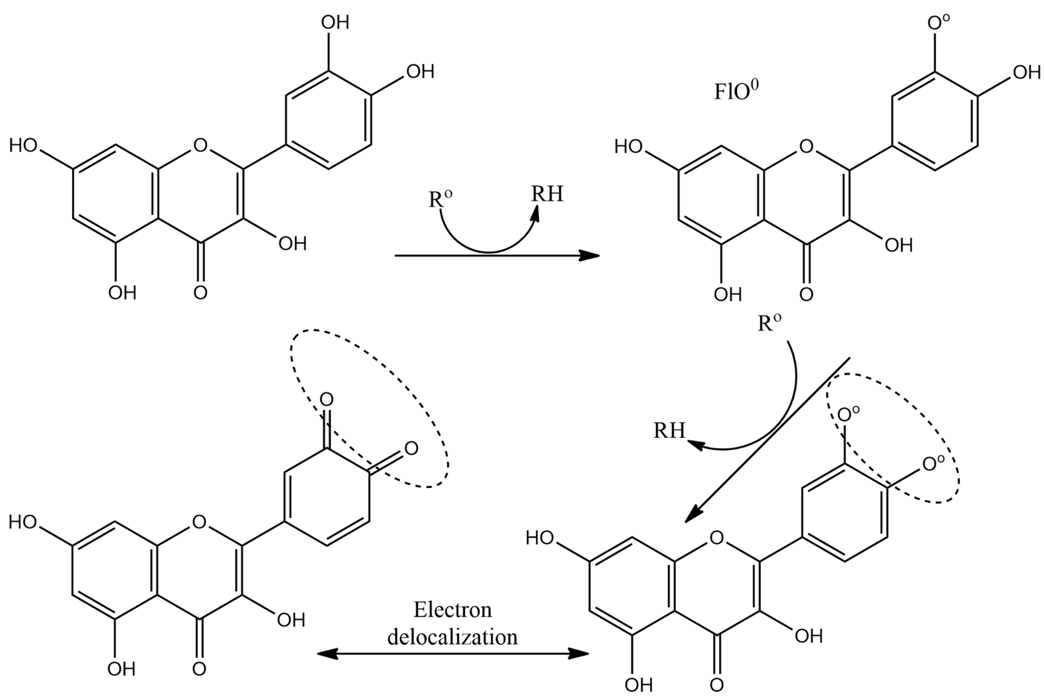

Figure 3 **Scavenging of ROS (R°) by flavonoids.** Full-size DOI: 10.7717/peerj-ochem.9/fig-3

silibin are two flavonoids that at least partially suppress the action of xanthine oxidase, which reduces oxidative damage (*Mohamed Isa, Ablat & Mohamad, 2018*). Reduced peroxidase release is another characteristic of flavonoids. Disruption of the activation of α1-antitrypsin prevents neutrophils from producing reactive oxygen species (*Hussain et al., 2016*). In neutrophils, gradual inactivation of proteolytic enzymes has been reported. Flavonoids also inhibit arachidonic acid metabolism through enzymatic systems (*Panche, Diwan & Chandra, 2016*). Flavonoids have antithrombogenic and anti-inflammatory qualities because of these characteristics (*Maleki, Crespo & Cabanillas, 2019*). In general, inflammatory reactions begin with the release of arachidonic acid. Arachidonic acid is converted into chemotactic chemicals by neutrophils *via* the action of lipoxygenase. They also cause cytokines to be released (*Panche, Diwan & Chandra, 2016*).

Effect of dietary supplementation with flavonoids as antioxidants on poultry production

Several environmental issues linked to the commercial production of poultry meat put hens at risk for oxidative stress. Challenges such as oxidative stress and infections have a number of detrimental effects on poultry welfare and productivity. Oxidative stress negatively affects the health and productivity of chickens, according to prior research (*Onagbesan et al., 2023*; *Oluwagbenga & Fraley, 2023*). Heat stress increases the production of ROS, which can lead to lipid peroxidation and oxidative damage to proteins and DNA (*Belhadj Slimen et al., 2014*).

Because of their potent anti-inflammatory and antioxidant qualities, flavonoids may be utilized as dietary supplements to produce higher-quality chicken meat products.
In conditions outside of the comfort zone, birds experience reductions in food intake depending on the severity of the food intake, cellular malfunction, and lipid peroxidation, leading to related diseases (*Abd El-Hack et al., 2023*; *Maleki, Crespo & Cabanillas, 2019*).

The meat industry is currently looking into natural compounds that can be used in place of synthetic antioxidants due to various health concerns over the industry's use of artificial antioxidants (*Ponnampalam et al., 2022*). The potential of flavonoids to mitigate the harmful consequences of oxidative stress has been piqued by their biological activities. *Peña et al. (2008)* studied the effects of flavonoids (quercetin and rutin) coupled with ascorbic acid (AA) on the performance and meat quality attributes of broilers under heat stress over 32 days. The beneficial mechanism is believed to involve the upregulation of antioxidant enzymes and stress response proteins, which balance the generation of reactive oxygen species (ROS). To increase antioxidant capacity and lessen the effects of heat stress, treatment with certain flavonoids, such as epigallocatechin gallate (EGCG), elevates the expression of superoxide dismutase (*Hu et al., 2019*).

Researchers are now interested in quercetin's potential as a chicken feed additive due to its extraordinarily strong antioxidant qualities. This is because antioxidant mediators improve the organoleptic qualities and nutritional value of animal-derived eggs or meat by reducing the peroxidation of feed lipids (*Fernandes, Trindade & de Melo, 2018*). Several biological benefits, including growth stimulation and antioxidant and antiviral properties, have been linked to quercetin in poultry species (*Saeed et al., 2017*). Importantly, quercetin has anti-obesity effects by reducing the accumulation of fat *via* a variety of mechanisms (*Oliveira et al., 2022*). According to *Bhutto et al. (2018)*, quercetin boosts P-glycoprotein overexpression and absorption in broilers in a dose-dependent manner.

Quercetin is currently used in chicken feed as a photogenic supplement to enhance growth performance and meat quality. It does this by directly inhibiting the oxidation of low-density lipoproteins and shielding erythrocytes from certain environmental elements that can harm them (*Goliomytis et al., 2014*). There is currently no standard for the use of

Table 1 Summary of flavonoids used in poultry production as antioxidants.

Source	Flavonoid types	Concentration	Finding	Reference
Soybean isoflavone	Isoflavone	10, 20, 40, and 80 mg/kg in	Increased total antioxidant and elevated total superoxide dismutase activity	*Jiang et al. (2007)*
Genistein (98% pure)	Genistein	5 mg/kg in diet	Downregulated heat shock protein 70 mRNA in breast muscle.	*Kamboh et al. (2013)*
Hesperidin (98% pure)	Hesperidin	20 mg/kg in diet	Downregulated heat shock protein 70 mRNA in breast muscle	*Kamboh et al. (2013)*
Hesperidin and naringin	Hesperidin and naringin	0.75, 1.5 g/kg diet	Malondialdehyde values decreased in tissue samples	*Goliomytis et al. (2015)*
Baicalin (98% pure)	Baicalein	450 mg/kg in diet	effectively prevents oxidative stress and apoptosis in the splenocytes	*Ishfaq et al. (2019)*
Root of *Scutellaria baicalensis* Georgi,	Baicalein	100 and 200 mg/kg in diet	Low-density lipoprotein cholesterol were decreased. Increased serum superoxide dismutase, catalase, and glutathione peroxidase	*Zhou, Mao & Zhou (2019)*
Bamboo leaf extract	Flavonoids	1, 2, 3, 4, and 5 g/kg in diet BLE	Total antioxidant capacity and glutathione peroxidase activity were increased. lipid oxidation and antioxidant capacity of breast meat increased	*Shen et al. (2019)*
Hawthorn flavonoid extract	Flavonoids	0.1, and 0.2 ml/L in drinking water	Reduced pulmonary hypertension syndrome	*Ahmadipour et al. (2020)*
Curcumin 98%	Curcumin	50, 100, and 200 mg/kg of diet	Increase the resistance of broilers to heat stress by reversing the FC and activating the antioxidant defense mechanism of liver.	*Zhang et al. (2018)*
Quercetin (97% purity)	Quercetin	0.2, 0.4, and 0.6 g of quercetin/kg of diet	Improve performance, Cu-Zn-superoxide dismutase increased.	*Liu et al. (2014)*
Quercetin	Quercetin	250, 500, and 1,000 mg quercetin/kg	Increased the content of total superoxide dismutase and total antioxidant capacity linearly increased	*Zhang & Kim (2020)*
Rutin (95% purity)	Rutin	500 and 1,000 mg rutin/kg	Increased activities of total superoxide dismutase and total antioxidant capacity in jejunal mucosa	*Chen et al. (2022)*
Scutellaria baicalensis Georgi	Flavonoids	120, 180 or 240 mg SBGFN/kg	Increased activities of total superoxide dismutase and promoted antioxidative ability of broilers	*Liao et al. (2018)*
Artemisia ordosica	Flavonoids	500, 750, and 1000 mg/kg	Decreased total superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and total antioxidant capacity	*Shi et al. (2022)*
Moringa flavonoiod meal	Flavonoids	Basal diet + 0.2% MFM; basal diet + 0.4% MFM.	Increase serum superoxide dismutases and glutathione peroxidase levels	*Yang et al. (2023)*
Bamboo leaf flavonoids	Flavonoids	Basal diet with 50 mg BLF/kg, and basal diet with 250 mg BLF/kg	Enhanced the serum antioxidant capacity and immune responses.	*Cao et al. (2022)*
Hawthorn-leaves flavonoids	Flavonoids	30 mg/kg, 60 mg/kg.	Improved the activity of antioxidant enzymes (T-AOC, GSH-Pχ)	*Dai et al. (2021)*

quercetin or other polyphenolic supplements in chicken nutrition, despite the encouraging findings of several studies. The inconsistent outcomes from various dietary trials could be attributed in part to this lack of clear uniformity (*Sierżant et al., 2023*). Due to their antioxidant properties, flavonoids can help maintain a healthy cellular environment in several tissues, including the mucosal layer of the gut, and shield other nutrients from oxidation. The addition of hesperidin can lower serum and yolk cholesterol levels in laying hens; enhance antioxidant capacity, health, and egg production (*Ting, Yeh & Lien, 2011*); and improve the fatty acid profile by reducing SFAs and increasing polyunsaturated fatty acid (PUFA) content in broilers (*Hager-Theodorides et al., 2021*). In addition to accelerating growth, myricetin served as a strong antioxidant to prevent the oxidation of postmortem tissue and lipids in the body in chickens (*King, Griffin & Roslan, 2014*).

The anti-inflammatory, antioxidant, and antiobesity properties of catechins—including large amounts of green tea—such as epicatechin (EC), epicatechin gallate (ECG), and epigallocatechin gallate (EGCG)—have been extensively researched (*Ntamo et al., 2024*). Catechins have been demonstrated to suppress adipocyte differentiation and proliferation, lipogenesis, and fat deposition in studies using animal obesity models and mammalian cell culture (*Neyrinck et al., 2017*). *Goliomytis et al. (2014)* incorporated quercetin at 0.5 and 1 g/kg in broiler feeds and reported a prolonged meat shelf life through a reduced rate of lipid peroxidation. Grape pomace (*Vitis vinifera*) contains high levels of anthocyanins, flavanols, flavonols, and flavanones and can be considered a natural source of antioxidants. When grape pomace (30 and 60 g/kg) was used in broiler diets containing PUFAs, the content of MDA, a marker of oxidative stress, decreased in thigh meat (*Turcu et al., 2020*). The summary of flavonoid supplement in poultry feeds is summarized in Table 1.

CONCLUSION AND FUTURE DIRECTION

In recent years, commercial poultry have been subjected to several stressors, such as heat stress, excessive stocking density, and infections, which can negatively impact birds and lead to various alterations. Recently, many bioactive compounds for chickens have been derived from plants used in feed. Dietary supplementation with plant flavonoids has shown potential for reducing oxidative stress in poultry farms. It has been revealed that adding flavonoids to feed can improve bird health, productivity, and reproduction. The fact that numerous studies provide contradictory findings on the consistent effects of flavonoids on development and production metrics presents a practical application difficulty for the research's findings. To take full advantage of the use of flavonoids in the poultry production industry, additional research is required to determine the availability and absorption of these compounds in poultry from various plant and feed sources. It is crucial to remember that studies vary in terms of the flavonoid supplements used, the diet's dosages, the length of the study, the bird's genetic background, and how the ingredients are processed and combined with the diet. These variations can have an impact on the molecular structure, bioavailability, bioactivity, and other nutrients in the diet. Moreover, there is a lack of adequate research techniques for quantifying oxidative damage *in vivo*, and measuring objective endpoints is still challenging. However, further research is needed to fully understand the detrimental effects of flavonoids, which include the inhibition of certain enzymes and interference with the absorption of certain minerals.

ADDITIONAL INFORMATION AND DECLARATIONS

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Competing Interests
The authors declare that they have no competing interests.

Author Contributions
- Jiregna Gari Negasa conceived and designed the experiments, performed the experiments, analyzed the data, performed the computation work, prepared figures and/or tables, authored or reviewed drafts of the article, and approved the final draft.

Data Availability
The following information was supplied regarding data availability:

This is a literature review.

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