Citrus flavonoids: a holistic paradigm in poultry production

Inflammation is the most ubiquitous expression of host defence in response to alterations in bird homeostasis. Under normal conditions, this controlled response is known as physiological inflammation.

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However, any increase in pathogen-specific molecules and/or virulence factors as well as cell debris from tissue injury will transform physiological inflammation into pathological inflammation, which is always accompanied by oxidative stress. During inflammation, several types of immune cells produce free radicals induced by proinflammatory cytokines. In turn, oxidative stress can result in changes in the expression of certain immune-response-related genes (upregulation of proinflammatory molecules), leading to a vicious circle between inflammation and oxidative stress.

In modern poultry production, the duo inflammation and oxidative stress is the basis for the major systemic and intestinal disorders. Given the growing restrictions on the use of medications globally, what the poultry segment in fact needs are not 'stop-gap' solutions but efficient holistic tools to deeply address this underlying issue.

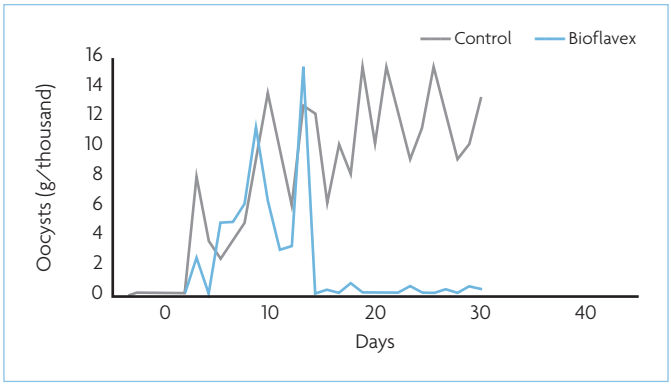


Fig. 2. Eimeria tenella shedding reduction by dietary supplementation of citrus flavonoids in broiler chickens (Laboratorio de Diagnóstico General, 2003).

Citrus flavonoids, a tool of choice

When it comes to facing the aforementioned duo in a profound manner, plant-based polyphenolic compounds have been demonstrated to have potential health and performance benefits in birds. Among those bioactive compounds, citrus flavonoids constitute a large and biologically relevant proportion.

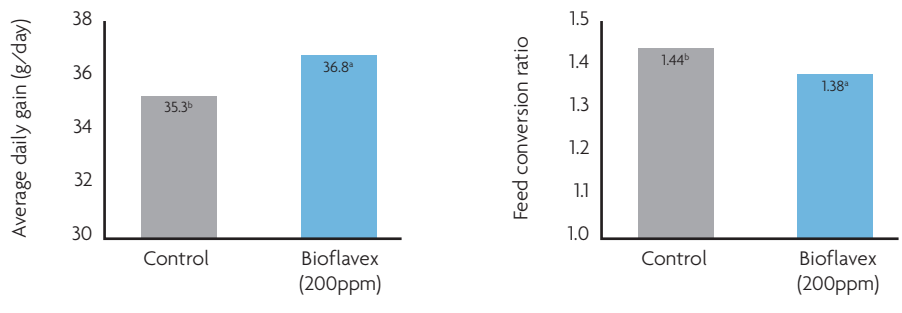
Naringin, naringenin and hesperidin are the most important citrus flavonoids, being found to possess strong antioxidant and anti-inflammatory activities. Furthermore, citrus flavonoids competently perform as immune modulators, lipid- and carbohydrate-metabolism adjustors and microbial regulators in the animal organism.

Adopting this holistic approach, Ferrer HealthTech offers Bioflavex citrus flavonoids products, rich in naringin. How these natural molecules exert each of their wide-ranging activities in birds is hereby briefly reviewed in this article.

Antioxidant activities

The best described property of citrus flavonoids is their antioxidant activity, which can be exercised in several ways:

Fig. 1. Effect of citrus flavonoids on chicken performance at 21 days (extracted from Gracia et al., 2016). Values with different subscript are significantly different ($p<0.05$).



Antiradical actions

Citrus flavonoids are known to scavenge or inhibit the production of several kinds of free radicals and reactive oxygen species, which are the major cause of oxidative stress and inflammatory issues in birds. In particular, naringin and naringenin are both strong scavengers of free radicals.

The phenolic groups of these flavonoids serve as a source of eagerly available 'H' atoms which are incorporated in the radical molecule such that it becomes more stable, less reactive and therefore less hazardous. Furthermore, citrus flavonoids are known to chelate metal catalysts, thereby removing a causal factor for the development of free radicals.

Thus, it has been confirmed in studies with chickens that citrus flavonoids improve the plasma antioxidant status and also modify the biomarkers of heat-stress in a positive way; improving the performance of birds.

This positive effect on performance was clearly observed in a broiler chicken trial undertaken in southern Spain, in which the dietary supplementation of 200ppm of Bioflavex resulted in a significant increase in the average daily gain and a four-point reduction in feed conversion ratio at 21 days of life (Fig. 1).

Oxidase inhibition and increase of antioxidant enzymes' activity

Another effective anti-oxidation mechanism of citrus flavonoids is the inhibition of oxidases, contributing to the decrease of oxidative injury.

In this sense, naringin has been found to significantly inhibit the xanthine oxidase activity in vitro and in vivo.

An additional protective effect of naringin is the increase of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) when supplemented in the diet of broiler chickens and laying hens.

Cellular antioxidant actions

Certain citrus flavonoids also have

Continued on page 9

Continued from page 7
antioxidant effects at the cellular level due to their scavenging activity and lipid peroxidation prevention on the cell phospholipid membranes, in addition to their interactions with specific proteins that are essential in some intracellular signalling cascades, resulting in a decrease in the production of intracellular pro-oxidants.

The antioxidant action of citrus flavonoids in the cells results in positive effects on the quality of the meat in poultry. Thus, it is recognised that the dietary administration of naringin retards the rate of lipid oxidation in broiler breast and thigh meat.

Immunomodulatory and anti-inflammatory activities

The above referred efficacy of citrus flavonoids against oxidative stress is surely the foundation of their effect on inflammation and immune response. In consequence, citrus flavonoids are indeed strong anti-inflammatory compounds.

For instance, there is evidence that naringin shows noticeable anti-inflammatory effects, significantly reducing the concentrations of pro-inflammatory cytokines and regulating inflammatory cell infiltration into the tissues.

In addition, biomarkers of heat stress in breast muscle are positively changed by dietary supplementation with citrus flavonoids.

Furthermore, it has been observed that citrus flavonoids also contribute to the amelioration of birds under heat stress by decreasing the heterophil-to-lymphocyte ratios, as well as by the quenching action on oxygen radicals generated by heat stress. Hence, these compounds may offer a good nutritional strategy to overcome the negative impacts of heat stress. Likewise, citrus flavonoids deserve to be considered within programs against poultry metabolic diseases (for example, pulmonary hypertension syndrome, cardiopulmonary disorders and sudden death syndrome), since this type of disease is strongly related to an inflammatory background.

In this way, citrus flavonoids might contribute to reducing cost in modern poultry production since metabolic diseases are the major cause of mortality in broiler chickens.

On the other hand, new research with broiler chickens has shown that dietary supplementation with citrus flavonoids improves antibody production in response to Newcastle disease, avian influenza, infectious bursal disease and infectious bronchitis virus vaccines.

The improved humoral immunity is possibly due to the improvement of the activity of the B lymphocytes, which are prone to oxidative damage. In recent years, the availability of new vaccines has increased worldwide and their use has expanded tremendously within the poultry industry.

The effectiveness of vaccines depends to a large extent on the good condition of the cells of the bird's immune system. Thus, the use of citrus flavonoids in poultry feed could be an interesting 'dietary adjuvant' that enhances the response to vaccines.

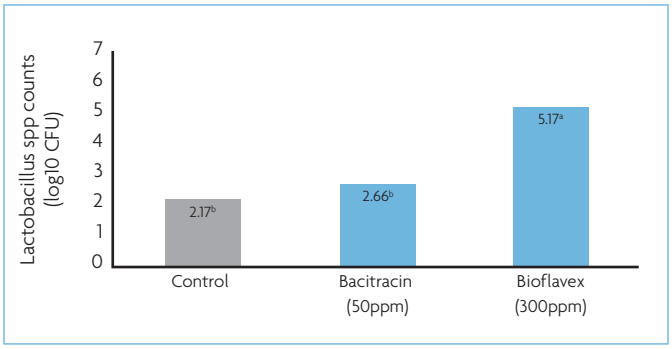


Fig 3. Effect of dietary supplementation of citrus flavonoids on the Lactobacillus spp counts in excreta of chickens (37 days of life). Values with different subscript are significantly different (p<0.05).

Regulation of lipid and carbohydrate metabolism

Citrus flavonoids are capable of lowering increased plasma lipid concentrations. Several studies have shown that naringin and naringenin lower plasma lipids in experimental models with laboratory animals.

Recent investigations have also shown that naringin supplementation in high-fat/high-carbohydrate-diet fed animals ameliorates the increase in plasma cholesterol, triglycerides and circulating fatty acids.

Similarly, the hypoglycaemic effect of naringin and naringenin is well documented and seems to be mediated via uptake of glucose in the skeletal muscle.

In modern broiler breeds, the drive toward improved productivity and carcase conformity may lead to a persistent nutrient excess (mostly fatty acids and carbohydrates) resulting in chronic low-grade inflammation and metabolic disorders such as wooden breast syndrome.

It could be wise to consider whether the addition of citrus flavonoids to feed could help to mitigate this type of disorder, since, in addition to being powerful anti-inflammatory compounds, they reduce the lipid and glycaemic levels in the birds' plasma.

Flavonoids can also play a crucial role in the liver. A hepatoprotective action of naringin has been reported by several investigators. In addition, it has been demonstrated that naringenin significantly reduces lipid peroxidation and restores the levels of SOD, CAT, GPx and glutathione S-transferase in liver.

Furthermore, it is known that the dietary supplementation of citrus flavonoids also reduces hepatic lipogenesis. Thus, the potential mitigating effect of these compounds on fatty liver syndrome in chickens deserves to be the subject of new scientific studies.

Antimicrobial properties

Nowadays, there is an increasing interest in using plant bioactive substances with antimicrobial properties. Citrus flavonoids have also proved to be a good choice in this regard. Available literature on coccidial infections appears to confirm anticoccidial activity of flavonoids and their protective role in the gut, with a consequent decline in oocyst shedding.

Accordingly, dietary administration of Bioflavex has shown a significant reduction of Eimeria tenella oocyst faecal excretion in broiler chickens (Fig. 2).

The potent antioxidant effect of citrus flavonoids may also contribute to limit Eimeria-induced damage to the intestinal wall during pro-inflammatory reaction and thus improve nutrient absorption and ultimately improve performance of birds.

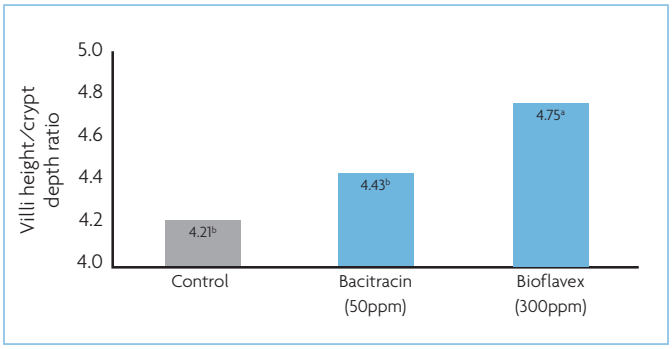
Furthermore, both naringin and naringenin are well known to have antibacterial ability. Therefore, their dietary supplementation may contribute to the regulation of the intestinal microbiota in chickens, reducing the growth of pathogenic bacteria and consequently facilitating the development of beneficial bacterial populations.

This positive effect on the intestinal microbiota has recently been confirmed by a trial undertaken at Kasetsart University in Thailand, in which the supplementation of Bioflavex promoted higher numbers of Lactobacillus spp. when compared to the other experimental treatments (Fig. 3).

As is well known, gut microbiota interacts with the development of the gut system of the host. This interaction is very complex and, depending on the composition and activity of the gut microbiota, it can have either positive or negative effects.

In this sense, in the above referred Thai study, the supplementation of Bioflavex significantly increased the villi height/crypt depth ratio of jejunum in chickens, indicating an improvement in gut functionality (Fig. 4).

Fig. 4. Effect of citrus flavonoids (300ppm in feed) on the villi height/crypt depth ratio of jejunum in chickens (37 days of life). Values with different subscript are significantly different (p<0.05).



Conclusion

The wide spectrum of activities of citrus flavonoids makes them a key tool in the approach to the main systemic and intestinal disorders in poultry, both of metabolic and infectious origin.

These activities are supported by numerous scientific studies, which make these compounds worthy of the trust of the most demanding poultry nutritionists and veterinarians in the face of the growing demand for meat and eggs from antibiotic-free production systems. ■

References are available from the author on request