

# The future of coccidiosis control



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With costs of over 14 billion USD per year (Blake, 2020), coccidiosis is one of the most devastating enteric challenges in the poultry industry. With regard to costs, subclinical forms of coccidiosis account for the majority of production losses, as damage to intestinal cells results in lower body weight, higher feed conversion rates, lack of flock uniformity, and failures in skin pigmentation. This challenge can only be tackled, if we understand the basics of coccidiosis control in poultry and what options producers have to manage coccidiosis risks.

## Current strategies show weak points

Good farm management, litter management, and coccidiosis control programs such as shuttle and rotation programs form the basis for preventing clinical coccidiosis. More successful strategies include disease monitoring, strategic use of coccidiostats, and increasingly coccidiosis vaccines. However, the intrinsic properties of coccidia make these parasites often frustrating to control. Acquired resistance to available coccidiostats is the most difficult and challenging factor to overcome.

Optimally, coccidiosis control programs are developed based on the farm history and the severity of infection. The coccidiostats traditionally used were chemicals and ionophores, with ionophores being polyether antibiotics. To prevent the development of resistance, the coccidiostats were used in shuttle or rotation programs, at which in the rotation program, the anticoccidial changes from flock to flock, and in the shuttle program within one production cycle (Chapman, 1997).

The control strategies, however, are not 100% effective. The reason for that is a lack of diversity in available drug molecules and the overuse of some molecules within programs. An additional lack of sufficient coccidiosis monitoring and rigorous financial optimization often leads to cost-saving but only marginally effective solutions. At first glance, they seem effective, but in reality, they promote resistance, the development of subclinical coccidiosis, expressed in a worsened feed conversion rate, and possibly also clinical coccidiosis.

# Market requests and regulations drive coccidiosis control strategies

Changing coccidiosis control strategies has two main drivers: the global interest in mitigating antimicrobial resistance and the consumer's demand for antibiotic-free meat production.

## Authorities have left ionophores untouched

Already in the late 1990s, due to the fear of growing antimicrobial resistance, the EU withdrew the authorization for Avoparcin, Bacitracin zinc, Spiramycin, Virginiamycin, and Tylosin phosphate, typical growth promoters, to “help decrease resistance to antibiotics used in medical therapy”. However, ionophores, being also antibiotics, were left untouched: The regulation (EC) No 1831/2003 [13] of the European Parliament and the Council of 22 September 2003 clearly distinguished between coccidiostats and antibiotic growth promoters. Unlike the antibiotic growth promoters, whose primary action site is the gut microflora, coccidiostats only have a secondary and residual activity against the gut microflora. Furthermore, the Commission declared in 2022 that the use of coccidiostats would not presently be ruled out “even if of antibiotic origin” (MEMO/02/66, 2022) as “hygienic precautions and adaptive husbandry measures are not sufficient to keep poultry free of coccidiosis” and that “modern poultry husbandry is currently only practicable if coccidiosis can be prevented by inhibiting or killing parasites during their development”. In other words, the Commission acknowledged that ionophores were only still authorized because it believed there were no other means of controlling coccidiosis in profitable poultry production.

## Consumer trends drove research on natural solutions

Due to consumers' demand for antibiotic-reduced or, even better, antibiotic-free meat production, intensified industrial research to fight coccidiosis with natural solutions has shown success. Knowledge, research, and technological developments are now at the stage of offering solutions that can be an effective part of the coccidia control program and open up opportunities to make poultry production even more sustainable by reducing drug dependency.

Producers from other countries have already reacted. Different from the handling of ionophores regime in the EU, where they are allowed as feed additives, in the United States, coccidiostats belonging to the polyether-ionophore class are not permitted in NAE (No Antibiotics Ever) and RWE (Raised Without Antibiotics) programs. Instead of using ionophores, coccidiosis is controlled with a veterinary-led combination of live vaccines, synthetic compounds, phytomolecules, and farm management. This approach can be successful, as demonstrated by the fact that over 50% of broiler meat production in the US is NAE. Another example is Australia, where the two leading retail store chains also exclude chemical coccidiostats from broiler production. In certain European countries, e.g., Norway, the focus is increasingly on banning ionophores.

## The transition to natural solutions needs knowledge and finesse

In the beginning, the transition from conventional to NAE production can be difficult. There is the possibility to leave out the ionophores and manage the control program only with chemicals of different modes of action. More effective, however, is a combination of vaccination and chemicals (bio-shuttle program) or the combination of phytomolecules with vaccination and/or chemicals (Gaydos, 2022).

# Coccidiosis vaccination essentials

When it is decided that natural solutions shall be used to control coccidiosis, some things about vaccination must be known:

1. There are different strains of vaccines, natural ones selected from the field and attenuated strains. The formers show medium pathogenicity and enable a controlled infection of the flock. The latter, being early mature lower pathogenicity strains, usually cause only low or no post-vaccinal reactions.
2. A coccidiosis program that includes vaccination should cover the period from the hatchery till the end of the production cycle. Perfect application of the vaccines and effective recirculation of vaccine strains amongst the broilers are only two examples of preconditions that must be fulfilled for striking success and, therefore, early and homogenous immunity of the flock.
3. Perfect handling of the vaccines is of vital importance. For that purpose, the personnel conducting the vaccinations in the hatchery or on the farms must be trained. In some situations, consistent high-quality application at the farm has shown to be challenging. As a result, interest in vaccine application at the hatchery is growing.

## Phytochemicals are a perfect tool to complement coccidiosis control programs

As the availability of vaccines is limited and the application costs are relatively high, the industry has been researching supportive measures or products and discovered phytochemicals as the best choice. Effective phytochemical substances have antimicrobial and antiparasitic properties and enhance protective immunity in poultry infected by coccidiosis. They can be used in rotation with vaccination, to curtail vaccination reactions of (non-attenuated) wild strain vaccines, or in combination with chemical coccidiostats in a shuttle program.

In a recent review paper (El-Shall et al., 2022), natural herbal products and their extracts have been described to effectively reduce oocyst output by inhibiting *Eimeria* species' invasion, replication, and development in chicken gut tissues. Phenolic compounds in herbal extracts cause coccidia cell death and lower oocyst counts. Additionally, herbal additives offer benefits such as reducing intestinal lipid peroxidation, facilitating epithelial repair, and decreasing *Eimeria*-induced intestinal permeability.

Various phytochemical remedies are shown in this simplified adaptation of a table from El-Shall et al. (2022), indicating the effects exerted on poultry in connection to coccidia infection.

Bioactive compound	Effect
Saponins	<p><i>Inhibition of coccidia:</i> By binding to membrane cholesterol, the saponins disturb the lipids in the parasite cell membrane. The impact on the enzymatic activity and metabolism leads to cell death, which then induces a toxic effect in mature enterocytes in the intestinal mucosa. As a result, sporozoite-infected cells are released before the protozoa reach the merozoite phase.</p> <p><i>Support for the chicken:</i> Saponins enhance non-specific immunity and increase productive performance (higher daily gain and improved FCR, lower mortality rate). They decrease fecal oocyst shedding and reduce ammonia production.</p>
Tannins	<p><i>Inhibition of coccidia:</i> Tannins penetrate the coccidia oocyst wall and inactivate the endogenous enzymes responsible for sporulation.</p> <p><i>Support for the chicken:</i> Additionally, they enhance anticoccidial antibodies' activity by increasing cellular and humoral immunity.</p>

Flavonoids and terpenoids	<p style="text-align: center;"><i>Inhibition of coccidia:</i></p> <p>They inhibit the invasion and replication of different species of coccidia.<i>Support for the chicken:</i></p> <p>They bind to the mannose receptor on macrophages and stimulate them to produce inflammatory cytokines such as IL-1 through IL-6 and TNF. Higher weight gain and lower fecal oocyst output are an indication of suppression of coccidiosis.</p>
Artemisinin	<p style="text-align: center;"><i>Inhibition of coccidia:</i></p> <p>Its impact on calcium homeostasis compromises the oocyst wall formation and leads to a defective cell wall and, in the end, to the death of the oocyst. Enhancing the production of ROS directly inhibits sporulation and also wall formation and, therefore, affects the Eimeria life cycle.<i>Support for the chicken:</i></p> <p style="text-align: center;">Reduction of oocyst shedding</p>
Leaf powder of Artemisia annua	<p style="text-align: center;"><i>Support for the chicken:</i></p> <p>Protection from pathological symptoms and mortality associated with Eimeria tenella infection. Reduced lesion score and fecal oocyst output.</p> <p>The leaf powder was more efficient than the essential oil, which could be due to a lack of Artemisinin in the oil, and to the greater antioxidant ability of A. annua leaves than the oil.</p>
Phenols	<p style="text-align: center;"><i>Inhibition of coccidia:</i></p> <p>Phenols change the cytoplasmic membrane's permeability for cations (H<sup>+</sup> and K<sup>+</sup>), impairing essential processes in the cell. The resulting leakage of cellular constituents leads to water unbalance, collapse of the membrane potential, inhibition of ATP synthesis, and, finally, cell death. Due to their toxic effect on the upper layer of mature enterocytes of the intestinal mucosa, they accelerate the natural renewal process, and, therefore, sporozoite-infected cells are shed before the coccidia reaches the merozoite phase.</p>

Table 1: Bioactive compounds and their anticoccidial effect exerted in poultry

## Consumers vote for natural - phytochemicals are the solution

Due to still rising antimicrobial resistance, consumers push for meat production without antimicrobial usage. Phytomolecules, as a natural solution, create opportunities to make poultry production more sustainable by reducing dependency on harmful drugs. With their advent, there is hope that antibiotic resistance can be held in check without affecting the profitability of poultry farming.