Controlling Coccidiosis Infection with plant extracts

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ABSTRACT Coccidiosis is recognized as the costliest parasitic disease for the poultry industry worldwide. In recent years, the development of resistance to coccidiostats, elevated costs of systematic vaccination and increasing consumer demand for "natural" food products has fuelled the development of natural, plant-based alternatives for coccidia control in poultry farming.

INTRODUCTION

Coccidiosis is recognized as the costliest parasitic disease for the poultry industry worldwide. Williams (1998) estimated its annual worldwide cost at $800 million in total[1], encompassing the costs of prophylaxis, medications and losses of productivity due to mortality, morbidity, and lowered feed conversion. Other sources estimate the global cost of its sole prevention in chicken at $300 million a year[2]. Among the multiple species of this intracellular parasite, the two most common types affecting poultry production worldwide are *Eimeria acervulina*, which causes upper intestinal coccidiosis, and *Eimeria tenella* (caecal coccidiosis), whose morbidity is 10-40% and mortality up to 50%. Because coccidia damage the intestinal epithelium, feed digestion is impaired, resulting in losses of performance (reduced weight gain, feed efficiency and temporary reduction of egg production in layers).

Why the need for alternative solutions?

An outbreak of coccidiosis in a flock will depend on several factors which can be more or less controlled: it usually is the result of a breakdown in the balance between three elements: the parasite, the host (chickens selected for their zootechnical performances are particularly sensitive to coccidia), and the environment (intensive rearing is more vulnerable to coccidiosis). A coccidia control program should take into account all these elements, starting with hygiene and housing management practices. Much work has also been done on the role of dietary factors: the influence of the nutrients, micronutrients (Vitamin K, A, Selenium…) has been largely studied, but also of the feed form and origin (maize could be more favorable than wheat). However, these are not sufficient and additional coccidia control solutions are often necessary in commercial poultry rearing.

For decades, their multi-species activity and cost-effectiveness have made anticoccidians (ionophores or synthetic molecules) the method of choice to fight coccidiosis. Their widespread use has lead to drug-resistant species. Moreover, tissue residue of ionophorous antibiotics may be found in meat products. The rapid development of multi-drug resistant pathogens, increasing consumer pressure for natural food, as well as regulatory trends (since 2006 antibiotic growth promoters have been banned in the European Union), have all put an end to the development of new drugs and triggered the search for alternative solutions.

Much research has been done on immunization and vaccination with live attenuated Eimeria is proven to be effective. Recombinant vaccines are still in development. However, unlike anticoccidian, immunization is species-specific and often associated with transient loss of performance. And it remains costly. In recent years, scientific publications and various production trials have gathered that explore the potential of certain plant based alternatives for coccidia control, some of which issued from ancient pharmacopeia. The initial selection of natural compounds is often empiric. But the good understanding of Eimeria biology (with around 90 years of intensive research, avian coccidia is one of the most advanced field of microbiology!) associated to research into the plant extracts biological activity allow to identify various modes of action, with either direct or indirect antiparasitic activity.

Direct antiparasitic effects

This will be the case of certain essential oils which are documented for their broad anti-microbial activity. For example, Giannenas et al.[3] has shown that oregano oil was effective against *E. tenella*. Another study shows

the effect of an essential oils blend on *E. acervulina* infection[4]. Essential oils contain known active ingredients, such as phenols, aldehydes, terpenes, oxides, which have a direct anti-parasitic effect. One of their key modes of action is targeted against microbial membranes and cell walls, which are then disrupted. This specificity confers them a large spectrum of activity, targeting gram + and gram – bacteria, yeast or fungus, as well as free coccidia, the form present in the intestine lumen. It has been demonstrated that the supplementation of chicken feed with certain plant extracts prior to pathogen challenge (*E. acervulina* and *E. tenella*), reduces the detrimental effect of the parasite on weight gain and reduces lesion scores, six days after the challenge[5].
Tipu et al.[6] have shown that neem fruit extract could be more effective than ionophore in reducing mortality and fecal oocyst count following multi species Eimeria challenge. Other effective plant extracts have also been reported even though their modes of action have not been elucidated, but could consist of a combination of various pathways.

Indirect antiparasitic activity

This will concern compounds able to help the host's organism to resist or fight infection or recover from tissue damages. Two main types of biological activity can be distinguished:

i) Immunostimulation. Certain plant based polysaccharides, in particular, exert an immunostimulating effect. By mimicking an infectious agent, certain polysaccharides are able to trigger the non specific immune response. For example, Guo et al.[7] has shown that immunoactive polysaccharides from mushrooms and plants have a synergistic action with vaccination.

ii) Immunomodulation. Certain plant extract with antioxidant or anti-inflammatory properties can have an immunomodulating effect.

- **Antioxidants:** an infection such as coccidiosis leads to the production and release of nitric oxide radicals (NO•) by macrophages. If there is a disequilibrium between the body's endogenous anti-oxidant defenses and the production of free radicals, the animal is subject to oxidative stress. This leads to reduced performances and can also limit the response against infections in the case where immune cells are damaged (vicious circle). Indeed, the acute phase of primary coccidian infection, (5-7 days post infection) which corresponds to oocysts shedding is usually a period of important tissue damages: this is known to be associated with important oxidative stress. In this case, an intake of plant-based exogenous antioxidant capable of scavenging free radicals can help limiting oxidative stress and preventing the damages caused by free radicals on cells lipid and protein constituents, but also on genetic material.
  Various natural compounds, known for their antioxidant properties have shown beneficial in the fight against coccidia: grape seed proanthocyanidins protect against *E. tenella*, with positive effects on body weight, mortality and lesion scores[8]. Certain antioxidant vitamins and minerals have also shown benefits against Emeiria infection: Selenium, Vitamin A and E. A Korean study has shown that green tea extract reduced oocysts shedding in *E. maxima* infected broilers but did not improve body weight[9]. An experimental pathogen challenge study (*E. tenella* and *E. maxima*) has shown that chicken feed supplementation with a natural antioxidant alone had a positive effect on weight gain, lesion scores as well as NO synthase activity[10].

- **Anti-inflammatory properties:** Inflammation is a physiological mechanism which enables the recruitment of immune cells to the infection site. But, as it is also the case with free radical production, if there is an over-reaction, it can lead to tissue damage at the site of infection. For example, curcumin, one of the key active ingredients in turmeric has been largely documented for both its antioxidant and anti-inflammatory properties[11]. It represents a very potent natural ingredient in the fight against the consequences of infectious agents.

In practice…

In order to combine potential direct and indirect anti-parasitic effects for a synergistic action against digestive parasites such as coccidia and cryptosporidium, scientists have developed a specific blend of selected essential oils and natural antioxidants (spice extracts) (Oleobiotec®, Phodé Laboratories, France). Zootechnical trials performed in broiler chickens indicate that such solution could represent an interesting tool as part of a coccidia control program.

A pathogen challenge trial was performed in a French research station on broiler chickens (strain ROSS, 3 birds per cage). The pathogens used in this trial were *Eimeria acervulina* and *Eimeria tenella*. For each of the three treatments (Control, Challenged, and Oleobiotec®/pathogen challenged), six replicates were

performed corresponding to six cages with three birds per cage.

All birds received the same starter feed, supplemented with the natural feed additive (Oleobiotec® LX 221 P2, Phodé Laboratories, France) at 500g/Ton of feed for the treated group.
At 20 days of age (Day 0), the two Pathogen Challenged groups were inoculated orally with 100 000 oocysts of *E. acervulina* and 20 000 oocysts of *E. tenella*.
Both zootechnical parameters (weight gain, feed consumption) and pathogenic criteria were measured up to slaughtering, which occurred at 28 days of age (Day 8 post-pathogen challenge). Pathogenic criteria included: coccidiosis-induced mortality, morbidity assessed as prostration state in chickens (ranked from 0: normal behaviour to 4: extreme prostration), feces score (form 0: normal aspect to 4: diarrheas), oocysts shedding in the feces (standardized on a feces sample), and finally, gut lesion score at slaughter for both *E. acervulina* (upper intestine) and *E. tenella* (caecum) - from 0 to 4, according to the Johnson- Reid Lesion Score System-.
Results are summarised in Table 1.

Tableau 1. Summary of pathological results, average data for each group (36 chickens/group).

	Control	Challenged	Challenged + Oleobiotec®
Average morbidity	0	2	1.75
Average feces score	0	1.75	1.5
Excreted oocysts	6500	**12 997 000**	**4 089 000**
Average *E. acervulina* lesion score	0	3.00	2.39
Average *E. tenella* lesion score	0	2.78	3.22

First of all, the number of oocysts excreted in feces of infected chickens was lower during the prepatent period (day 4-7), when the birds had received Oleobiotec®, indicating a less severe infection but also a diminished risk of contamination in the poultry house.

Morbidity in challenged chickens is slightly improved with the supplement. Feces score is improved with the supplement when compared to control (less diarrheas).

The supplementation seemed to have an effect in reducing the risks of Coccidiosis contamination: on average oocyst shedding by treated chickens was lowered.

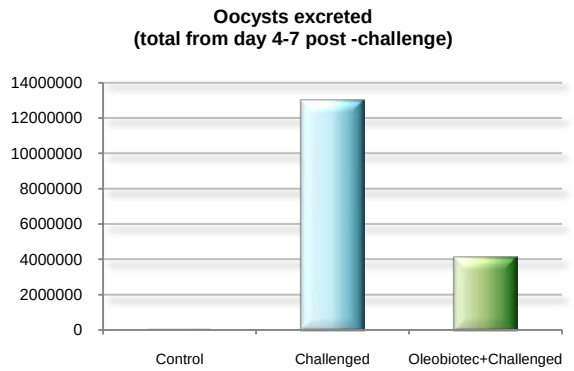

Figure 1: The average number of oocysts excreted in feces decreased by 31.46% over the seven days post-challenge when the chickens had received Oleobiotec® in the diet.

The treated chickens were also less affected by the infection: the severity of infectious symptoms is lowered. These results were matched with post-mortem pathological analysis: *E. acervulina* lesion score was significantly lower in the Oleobiotec® group as compared to the control, pathogen challenged group.

Another experimental challenge trial was performed to compare the effects of Oleobiotec® to those of a herbal product which is already on the market. Chickens were challenged at 16 days of age with both *Eimeria acervulina* and *Eimeria tenella*. This new trial showed that both products give similar zootechnical and pathological results (low mortality and lesion scores - between 1.5-2), except for a tendency to lower oocysts excretion in the feces of Oleobiotec® treated chickens. This trial showed that Oleobiotec® efficacy was comparable to those of a commercial herbal preparation and confirmed its interest for the industry.

CONCLUSION

When it comes to plant extracts vs. isolated compounds such as vitamins or antioxidant it is not a clear-cut picture and authors rarely advance a possible mode of action. The vegetal world is extremely rich and many of the plants with known health benefits are diverse in bioactive compounds (e.g. more than 140 compounds have been isolated from neem tree!). They could possibly associate various modes of action to fight against Eimeria. In a practical approach, as shown in the reported trial, it could be interesting to associate compounds with known anti-parasitic action such as essential oils to antioxidant or immune-acting ingredients for a synergistic effect.

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