Dysbacteriosis and gut health management in poultry

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The growing restrictions on the use of antibiotics growth promoters (AGPs), as well as the development of resistance to some routinely used antimicrobials in the recent past, have increased the incidence of dysbacteriosis within intensive poultry farming. What is the solution to maintaining gut health and animal performance in these circumstances?

What is dysbacteriosis?

Dysbacteriosis has been defined as the presence of a qualitatively and/or quantitatively abnormal microbiota in the proximal parts of the small intestine. This abnormal microbiota produces a cascade of reactions in the gastrointestinal tract, including reduced nutrient digestibility and impaired intestinal barrier function, increasing the risk of bacterial translocation and inflammatory responses (Panneman, 2000; Van der Klis, 2000 and Lensing, 2007). Dysbacteriosis is not a specific disease but a secondary syndrome. Along the entire GI tract, there is a diverse microbial community comprised of bacteria, yeasts, archaea, ciliate protozoa, anaerobic fungi, and bacteriophages, commonly referred to as the intestinal microbiota.

Dysbacteriosis is an imbalance in the gut microbiota as a consequence of an intestinal disruption. The impact of dysbacteriosis can be separated into economic and welfare issues (Bailey, 2010). Dysbacteriosis can lead to very wet litter and caking issues. The prolonged contact of broilers with the caked litter can result in painful ulceration of the feet and hocks (pododermatitis and hock-burn), leading to a serious welfare issue and degradation of the carcass.

Apart from these issues, a major economic impact comes from reduced growth rates, FCR, and increased veterinary treatment costs (Kizerwetter-Świda and Binek, 2008).

Causes of dysbacteriosis

It is believed that both non-infectious and infectious factors can play a role in dysbacteriosis (DeGussem, 2007).

Non-infectious causes are:

- Diet
- Brooding
- Biosecurity
- Risk periods
- Environmental conditions

Diet

Intestinal bacteria derive most of their energy from dietary compounds. Thus, diet has a major influence over the bacterial populations (Apajalahti et al., 2004). Any change in feed and feed raw materials, as well as the physical quality of feed, influence the balance of the gut microbiota. Processing significantly affects the characteristics of the feed as a substrate for the bacterial community. Perhaps the temperature and pressure of the conditioning process give its characteristic signature to the bacterial community structure.

Inappropriate brooding conditions

The provision of optimal brooding conditions is essential for ensuring optimal gut microbiota development. Birds receiving appropriate brooding develop a gut that performs well and has a greater capacity to cope with the challenges of the broiler shed. Early access to feed and water is crucial. One of the most critical factors for the occurrence of dysbacteriosis is the lack of digesta. The microbiota can change in a period of hours when nutrients are not present. The quality of water is also essential to maintain normal intestinal function and digesta pH.

Faulty biosecurity

If clean-out and disinfection procedures are improperly conducted, pathogens will be introduced into the poultry shed, and exposure to these pathogens will influence gut health and development. It has been proven that litter management regimes affect chicken gastrointestinal tract (GIT) and microbiota (Wang et al., 2016)

Risk periods

There are times during poultry production when the bird will be challenged, for example, during feed changeovers, vaccination handling and transportation, overcrowding, or placement in new housing. During these periods, the gut microbiota can fluctuate and, in some cases, if management is sub-optimal, dysbacteriosis can occur.

Environmental conditions

Achieving optimal environmental conditions will promote good gut health. Any perturbation in gastroenteric physiology or immunity of the bird, caused by temperature stress or other environmental discomforts, can cause dysbacteriosis and/or enteritis. These are associated with lower absorption of nutrients by the host. Suzuki et al. 1983 demonstrated that overcrowding and heat stress, very commonly seen in intensive poultry farming, has a significant impact on the microbiota of chickens.

Infectious agents that potentially play a role in dysbacteriosis

- Mycotoxins
- Eimeria spp.
- Clostridium perfringens
- Other bacteria producing toxic metabolites

Mycotoxins

Many mycotoxins can stimulate the secretion of several antimicrobial molecules, which have positive effects on the maintenance of intestinal homeostasis. Fumonisins inhibit the growth of fungi, Fusarium toxins exhibit different antimicrobial defensive mechanisms, and aflatoxins exhibit a moderate antimicrobial activity against Escherichia coli, Bacillus subtilis, and Enterobacter aerogenes [Bevins et al. 1999 and Wan et al.2013]. Mycotoxins such as aflatoxins, trichothecenes, zearalenone, fumonisin, and ochratoxin can alter the normal intestinal functions, such as the barrier function and nutrient absorption. Some mycotoxins, like trichothecenes and ochratoxin, affect the histomorphology of the intestine (Winnie et al., 2018). Mycotoxicosis changes the population equilibrium, which can lead to dysbacteriosis.

Eimeria spp.

Coccidiosis caused by Eimeria spp. in chickens appears to be one of the principal destabilizing agents, causing the destruction of enterocytes and affecting the integrity of the intestinal mucosa and wall. The lesions that it causes, the inflammatory process, the reduced absorption and consequent excess of nutrients in the lumen all contribute to the proliferation of certain groups of bacteria. This situation clearly predisposes birds to intestinal dysbacteriosis and/or bacterial enteritis, and in particular to necrotic enteritis.

Clostridium perfringens

Clostridium perfringens is a natural part of the habitat in the hindgut that is not dangerous under normal circumstances. If it multiplies, the bacterium produces toxic substances that damage the intestinal mucosa and cause a condition called necrotic enteritis. The disease is characterized by necrosis and inflammation of the GIT. Without treatment, this can escalate to perforation of the intestines, hemorrhages, and eventual death from septic shock.

Signs and consequences of dysbacteriosis

Dysbacteriosis can have profound effects on the host. Dysbacteriosis alters the GIT environment and favors the growth of pathogenic bacteria. Pathogenic bacteria produce toxins that increase intestinal motility or cause alterations in the amounts of mucus produced or in its composition. They also result in modifications of gastric acidity, reduction in the production of bacteriostatic peptides in the pancreas, and reduced immunoglobulin (IgA) secretion.

Toxins released by entero-pathogens damage intestinal villi, resulting in focal ulcerations of the mucosa, tissue necrosis, and shifts in gut microorganism numbers and metabolism. The costliest condition for animal production is the chronic inflammatory response of the animal to constant minor dysbacteriosis. These chronic responses can reduce weight gain and cause low feed conversion efficiency. Coccidiosis infections and any other enteric disease can be aggravated when dysbacteriosis is prevalent. Generally, animals with dysbacteriosis have high concentrations of Clostridium that generate more toxins, leading to necrotic enteritis.

In broilers, the syndrome is generally seen between 20 and 30 days of age (Wilson et al., 2005). Clinically, the main signs are:

- pale, glistening or orange droppings with undigested food particles
- wet and greasy droppings and hence dirty feathers
- sometimes foamy caecal droppings
- reduced physical activity
- increased water intake
- decrease in feed intake with a check in weight or reduced gain rates
- increased feed conversion

(Wilson et al., 2005; De Gussem, 2007)

Wet litter is also a general outcome of dysbacteriosis that may affect the air quality of the house, leading to a higher incidence of respiratory problems.

Additionally, foodborne pathogens such as *Salmonella* spp. and *E.coli* proliferate more in the dysbiotic intestine and can become persistent residents of the hindgut.

At necropsy, the main observations are

- a thin, fragile, often translucent intestinal wall
- watery or foamy intestinal contents
- frequent orange mucus and undigested particles in the intestines
- ballooning of the gut
- intestinal inflammation

(Pattison, 2002; De Gussem,2007)

Prevention of dysbacteriosis

The most important factors to prevent dysbacteriosis are

- Minimizing environmental stress
- Maintaining good water quality
- Improving feed digestibility
- Avoiding antinutritional factors, mycotoxins, and rancidity
- Feed additives that could modulate microbial component and avoid dysbacteriosis

Growth-promoting antibiotics are well known for the inhibition of undesired microbiota and the negative effects of their metabolites, and selection for beneficial bacteria. However, the adverse result is that they diminish the natural diversity of the gut microbiota. Antibiotics can also result in animals developing bacterial resistance.

Other products have been proposed as alternatives to growth promotion, taking into consideration the increasing bacterial resistance to some antibiotic categories.

Alternate feed additive technologies that have a promising role in controlling dysbacteriosis are:

- Probiotics
- Prebiotics
- Enzymes
- Organic acids
- Essential oils and phytomolecules

Probiotics

The post-hatch period is very critical for the chicks' intestine development. Exposure to the environment in hatchery and farm affects microbial colonization in the intestine tract. The use of selective probiotics in day-old chicks at the hatchery and on the farm immediately after placement in broiler house reduces the risk of dysbacteriosis. Probiotics work by competitive exclusion, thereby prevent the colonization of potentially pathogenic bacteria. Probiotics prevent enteric diseases, improves intestine development and digestion process.

The benefits include enhanced growth and laying performance, improved gut histomorphology, immunity, and an increase in beneficial microbiota (Rajesh Jha et al., 2020)

Prebiotics: Mannan Oligosaccharide

(MOS) mimics the properties of the cells on the gut wall to attract and bind with harmful bacteria. Rather than allowing the bad bacteria to attach to the gut wall, the MOS acts as a sticky sponge, clearing up the harmful bacteria and removing them from the digestive system. MOS play an important role in gut functionality and health, through enhanced nutrient digestibility and improved gut barrier function and local defenses. MOS is also related to long villi and shallow crypts in the intestine, so a larger surface area helped with the absorption of nutrients and improved animal performance (Chand et al., 2016b)

Enzymes

Careful choice of feed enzymes will reduce nutrients available for pathogenic bacterial growth and improve gut health. Bacterial Xylanase is showing promise by digesting both soluble and insoluble arabinoxylans and reducing the viscosity of intestinal content. It maintains gut motility, improves nutrients digestibility, and impairs the growth of pathogenic bacteria in the hindgut.

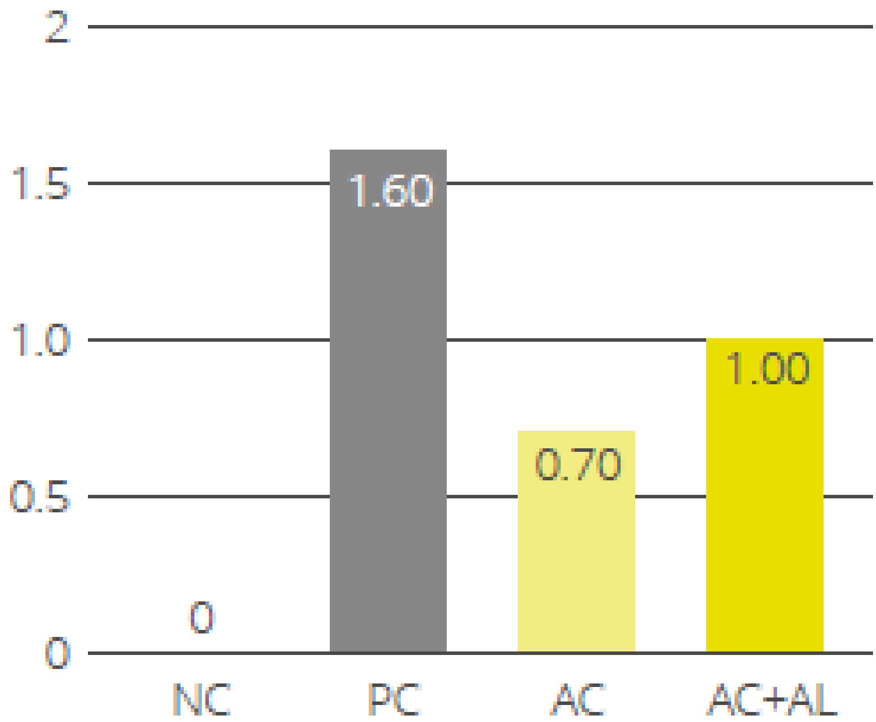
Organic acids

Organic acids ameliorate the conditions of the GIT through the reduction of GIT pH, promoting proteolytic enzyme activity, intensifying pancreatic secretions. They encourage digestive enzyme activity and nutrient digestibility. Organic acids are creating stability of the microbial population by stimulating the growth of beneficial bacteriaPapatisiros et al., 2013).

Phytomolecules

Multiple scientific studies have proven the positive effects of phytomolecules (also known as phytogenics or secondary plant compounds) on the gut health of livestock animals. These substances support digestion and improve the utilization of nutrients. This results in higher daily weight gain and better feed conversion. In addition, phytomolecules have a proven antimicrobial effect, based on different biological modes of action.

EW Nutrition offers standardized phytomolecule-based solutions (Activo and Activo Liquid) that positively influence gut health and subsequent performance parameters in poultry. In scientific studies, the Activo product line has shown a positive effect on gut pathogenic bacteria, reducing necrotic enteritis (Fig 1) and improving production performance.



Conclusion

Dysbacteriosis can have profound effects on the host. Acute dysbacteriosis can result in the proliferation of pathogenic microorganisms that become enteropathogenic. Pathogenic bacteria can produce toxins and metabolites that increase gut motility, increase fermentation with gas production, change gut pH, irritate the mucosa, cause inflammation, and increase mucous secretion. This process reduces the digestibility and absorption of nutrients.

Maintaining the equilibrium of the gut ecosystem is key to avoiding dysbacteriosis. Improving feed digestibility and using feed additives that modulate gut microflora help to maintain more stable gut ecosystems, even during periods of intestinal stress preventing dysbacteriosis. Effective prevention and control of dysbacteriosis help increase poultry operations' economic profitability by way of improved performance, health, and welfare, and reduce foodborne pathogens and environmental impact of poultry production.

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Poultry health and welfare: Phytomolecules for poultry diets

The large majority of poultry specialists in Europe consider phytomolecules as one of the key elements in diets for broilers, broiler breeders, and layers when birds are raised without antibiotics. A quick glance at the market will reveal more commercial products than can possibly be imagined. There are three basic elements you should bear in mind when making your choice:

1. **Most phytomolecules are volatile**. As such, unprotected products will soon evaporate if left exposed to the open air – as it happens, for instance, with feed prepared in commercial farms. Microencapsulation is therefore essential.
2. **There are countless phytomolecules.** Consequently, finding the right mix for the task required is essential, as not all mixtures will get you the desired result. When designing a phytomolecule mix, the manufacturer must have the necessary knowledge and experience to achieve the desired result.
3. **Phytomolecules are powerful.** This is to say that you cannot just keep adding higher quantities to achieve a better result. Finding the exact inclusion rates for the right purpose is a difficult balancing exercise.

In fact, the right protection, the right mix and the right inclusion rates must be combined to ensure that the animals do not refuse the feed (worst case scenario) or just fail to benefit from the inclusion of phytomolecules.

Among the feed additives, phytomolecules (or secondary plant compounds) stand out as a class of active ingredients that may help to improve gut health and thereby reduce the use of antibiotics. Synthesized by plants as a defense mechanism against pathogens, phytomolecules promote the digestion of feed ingredients (Zhai et al. 2018), prevent loss of gut integrity during enteric challenges (Liu et al. 2018), and have antimicrobial properties that hinder the growth of potential pathogens (Chowdhury, 2018). Phytomolecules can prevent the overgrowth of opportunistic pathogens, thereby reducing the frequency of occurrence of diseases such as necrotic enteritis and dysbacteriosis and thus improve performance data such as daily weight gain and feed efficiency.

Beyond the phytomolecules' proven effects, what works best in supporting the health and welfare of your animals is, in fact, a holistic program (such as those offered by EW Nutrition) that consists of an effective combination of innovative products and consultancy services in the fields of gut health, nutrition, AMR monitoring, and biosecurity management.

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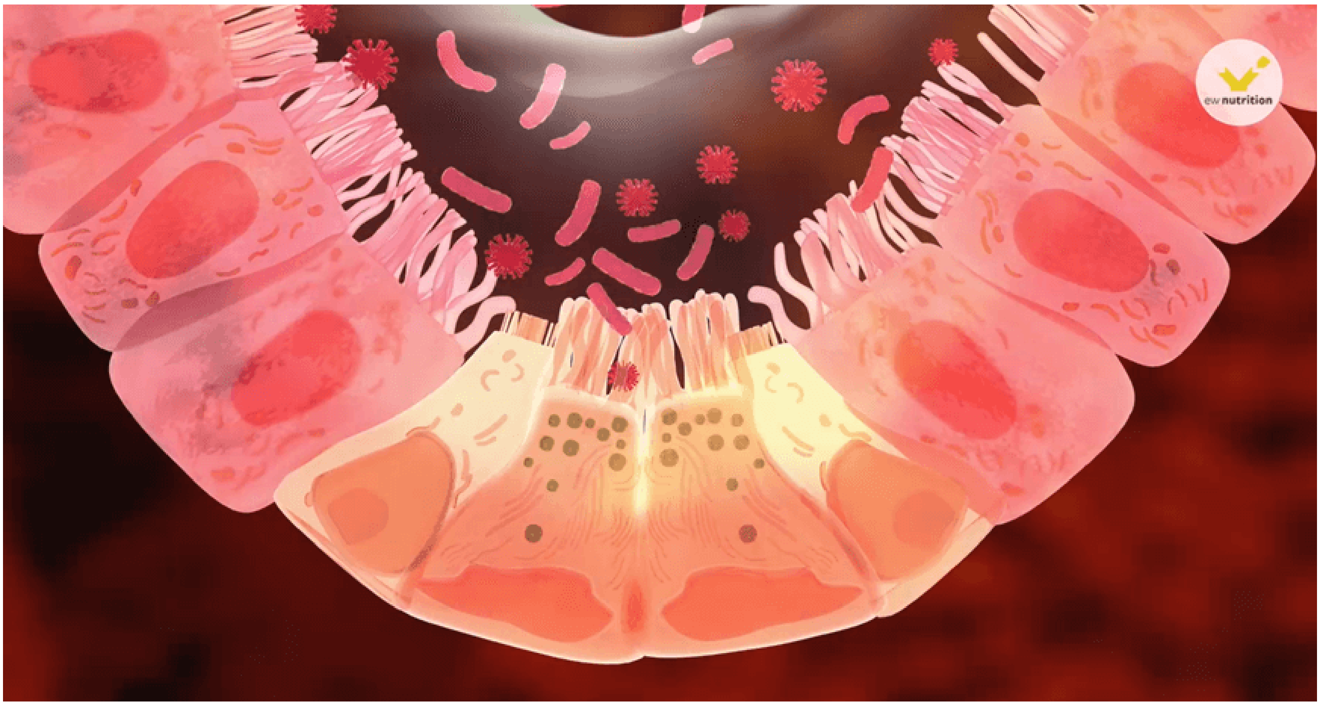


Challenging times for broilers? Phytomolecules, not antibiotics, are the answer

*by **Ajay Bhoyar**, Global Technical Manager, EW Nutrition*

Anyone working with today's fast-growing broiler chicken knows that it is a sensitive creature – and so is its gut health. Thanks to continuous improvements in terms of genetics and breeding, nutrition and feeding, as well as general management strategies, broiler production has tremendously upped performance and efficiency over the past decades. It is estimated that, between 1957 and 2005, the broiler growth rate increased by over 400%, while the feed conversion ratio dropped by 50%.

These impressive improvements, however, have come at the cost of intense pressure on the birds' digestive system, which needs to process large quantities of feed in little time. To achieve optimal growth, a broiler's gastrointestinal tract (GIT) needs to be in perfect health, all the time. Unsurprisingly, enteric diseases such as necrotic enteritis, which severely damages the intestinal mucosa, hamper the intestines' capacity to absorb nutrients and induce an inflammatory immune response.

The modern broiler's gut – a high-performing,

but sensitive system

However, in a system as high performing as the modern broiler's GIT, much less can lead to problems. From when they are day-old chicks up to slaughter, broilers go through several challenging phases during which they are more likely to show impaired gut functionality, e.g. after vaccinations or feed changes. Good management practices go a long way towards eliminating unnecessary stressors for the animals, but some challenging periods are unavoidable.

The transition from starter to grower diets is a classic situation when nutrients are very likely to not be well digested and build up in the gut, fueling the proliferation of harmful microbes. Immunosuppressive stress in combination with an immature intestinal microflora results in disturbances to the bacterial microbiota. At "best", this entails temporarily reduce nutrient absorption, in the worst case the birds will suffer serious intestinal diseases.

Phytomolecules – the intelligent alternative to antibiotics

To safeguard performance during stressful periods, poultry producers need to anticipate them and proactively provide effective gut health support. For many years, this support came in the form of antibiotic growth promoters (AGP): administered prophylactically, they were effective at keeping harmful enteric bacteria in check. However, due to grave concerns about the development of antimicrobial resistance, non-therapeutic antibiotics use has been banned in many countries. Alternatives need to focus on improving feed digestibility and strengthening gut health, attacking the root causes of why the intestinal microflora would become unbalanced in the first place.

Phytomolecules are secondary metabolites active in the defense mechanisms of plants. Studies have found that certain phytomolecules stimulate digestive enzyme activities and stabilize the gut microflora, "leading to improved feed utilization and less exposure to growth-depressing disorders associated with digestion and metabolism" (Zhai et al., 2018). With other trials showing positive effects on broilers' growth performance and feed conversion, the research indicates that phytomolecules might also specifically support chickens during challenging phases.

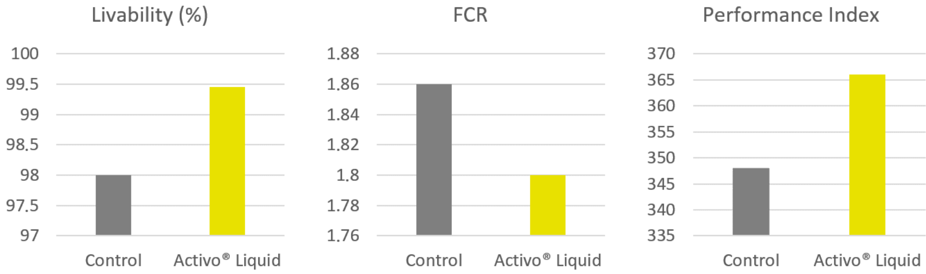
The effect of phytomolecules on broilers during a challenging phase

A study was conducted over a period of 49 days on a commercial broiler farm of an AGP-free integration operation in Japan. The farm reported gut health challenges in the second and third week of the fattening period due to vaccinations and changes to the animals' diets. The trial included 15504 Ross 308 broilers, divided into two groups. The negative control group included a total of 7242 birds, kept in another house.

All the birds were fed the standard feed of the farm. The trial group (8262 birds) received Activo Liquid, which contains a synergistic combination of phytomolecules, administered directly through the drinking water. Activo Liquid was given at an inclusion rate of 200ml per 1000L of water (3.3 US fl oz per gallon of stock solution, diluted at 1:128), from day 8 until day 25, for 8 hours a day.

The results are summarized in Figure 1:

Figure 1: Improved broiler performance for Activo Liquid group (day 49)



The Activo Liquid group clearly showed performance improvements compared to the control group. Livability augmented by 1.5%, while the feed conversion rate improved by 3.2%. This resulted in a more than 5% higher score in terms of the performance index.

Challenging times? Tackle them using phytomolecules

Poultry producers take great care to eliminate unnecessary sources of stress for their birds. Nonetheless, during their lifecycle, broiler chickens face challenging periods during which the balance of the intestinal microflora can easily become disturbed, with consequences ranging from decreased nutrient absorption to full-blown enteric disease.

The trial reviewed here showed that, after receiving Activo Liquid, broilers raised without AGPs showed encouraging performance improvements during a challenging phase of feed changes and vaccinations. Likely thanks to the activation of digestive enzymes and a stabilization of the gut flora, the broilers showed improved livability and feed conversion, thus delivering a much more robust performance during a critical phase of their lives. In times where the non-therapeutic use of antibiotics is no longer an option, phytomolecules allow poultry farmers to effectively support their animals during challenging times.

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Photo Source: Aviagen

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Want antibiotic-free broilers? Raise low-AB breeders

Strong demand by consumers; restaurant chains and wholesalers for antibiotic-free (ABF) meat; the threat of antimicrobial resistance; and stringent regulations on the use of antibiotics – there are many good reasons for poultry producers to strive for antibiotic-free production systems. Crucially, to successfully produce poultry meat without antibiotics requires a paradigm shift that starts right at the parent stock level, with the antibiotic-free production of hatching eggs.

Broiler breeders' gut health is linked to progeny's performance

Broiler breeders' performance is measured in terms of how many saleable day old chicks (DOCs) per hen they produce. However, within a sustainable ABF production system (also known as No Antibiotics Ever or NAE), this parameter is not seen in isolation. Breeder hens' nutritional and health status not only affect the number of DOCs they can produce, but also the transfer of nutrients, antibodies, microbiota and even contaminants, e.g. mycotoxins, to the egg – and therefore, their progeny's long-term health and performance.

This starts with egg formation, which requires several metabolic processes in the hen to function perfectly.

If the hen's intestinal integrity is compromised, for example due to mycotoxins, she will absorb fewer nutrients, which in turn affects egg formation. Mycotoxicosis has particularly insidious effects for egg formation as it can damage the liver whose biosynthetic activities strongly impact on the egg's internal (yolk) and external (eggshell) quality.

Chick embryos depend on the maternal antibodies and nutrients deposited in the yolk, including vitamin D3, carotenoids, and fatty acids, to develop normally. Eggshell quality, among other things, affects the embryo's access to oxygen, which is especially important when it develops body tissues.

Hens' ability to form healthy eggs depends on their diet and health. Research indicates that, via the impact on egg formation, broiler breeders' feeding program quantifiably influences their progeny's immune system and intestinal health. There is indeed a direct relationship between parent and offspring's gut health because the chick's microbiome is in part also inherited from the hen. The impact on DOC quality is thus one of many dimensions to consider when calibrating one's broiler breeders feeding approach.

The challenge of feeding an ABF broiler breeder

Just as their offspring, breeder hens are genetically predisposed for rapid growth and muscle development. From rearing right through to the laying period, poultry nutritionists need to carefully balance their diets and moderate weight gain in order for hens to reach their reproductive potential.

Different stages of a breeder's life cycle come with different objectives – for example, good flock uniformity in the rearing period versus egg size and hatchability in the laying phase – and thus different requirements in terms of calories, amino acids, vitamins, and minerals. What remains constant is that the actual nutrient intake depends on intestinal health, determining both the breeders' performance and, via the impact on egg characteristics, its progeny's performance.

The feeding regimes adopted to avoid hens becoming overweight can have a negative effect on their gut flora. Without antibiotics as a tool to maintain or recover optimal gut function, even mild intestinal disorders can quickly become chronical impairments that negatively impact breeders' productivity. In ABF production systems, intestinal health therefore needs to be a central focus for the feeding strategy.

Can phytomolecules improve broiler breeders' performance?

Among the plethora of feed additives, phytomolecules, or secondary plant compounds, stand out as a class of active ingredients that may help to improve gut health and thereby reduce the use of antibiotics. Synthesized by plants as a defense mechanism against pathogens, phytomolecules combine digestive, antimicrobial and antioxidant properties.

Some studies have shown that phytomolecules-based products can increase broilers' body weight gain and improve laying hens' laying rate, egg mass and egg weight. Both broilers and laying hens responded to the inclusion of phytomolecules in their diet with inclusion rate-dependent improvements in feed conversion. To evaluate if phytomolecules could similarly improve broiler breeders' performance, two trials were conducted.

Study I: Effect of phytomolecules on laying performance during peak production

The first study was set up on a farm in Thailand. In total, 40000 Cobb broiler breeders (85% female, 15% male) were divided into two groups with 8500 hens (one house) in the control and 25500 (three houses) in the trial group. Both groups were fed standard feed. The trial group additionally received a phytomolecules-based liquid complementary feed (Activo Liquid, EW Nutrition GmbH) via the waterline from week 24 to week 32 at a rate of 200ml/1000L during 5 days per week.

Activo Liquid was found to have a positive influence on laying performance (Figure 1). The average laying rate increased by 7.2% during the trial period, resulting in almost 3 additional hatching eggs per hen housed. A further indication of the beneficial influence that this particular combination of phytomolecules had on gut health was a 0.2% lower mortality.

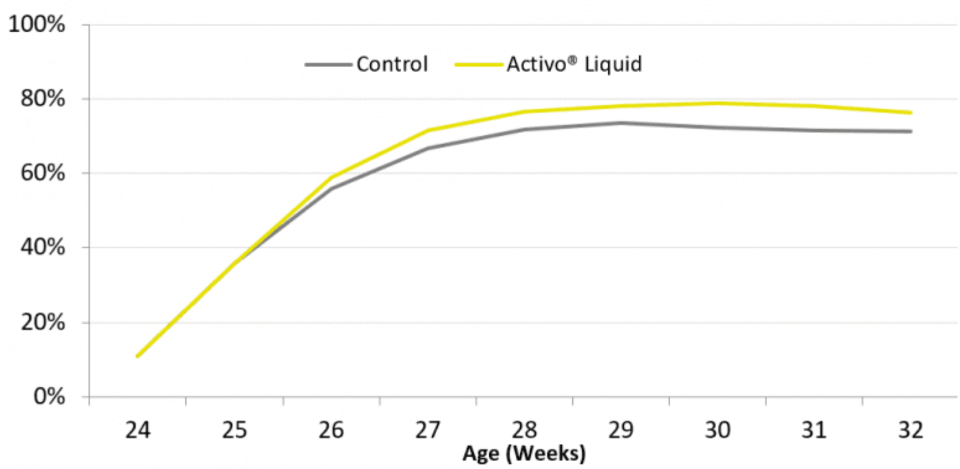

Figure 1: Laying rate (%) of breeder hens during first 9 weeks of production

Study II: Effect of phytomolecules on laying performance after peak production

For a second study, conducted in the Czech Republic, 800 female and 80 male Hubbard breeders (JA57 and M77, respectively) were divided into 2 groups with 5 replicate pens and 80 female and 8 male breeders per pen. The experiment started after the peak-production period, at 34 weeks of age and ended at 62 weeks of age. All animals received a standard mash diet. For one group a phytogenic premix (Activo, EW Nutrition GmbH) was added to the diet at a rate of 100g/MT.

The results indicate that Activo helped maintain the breeder hens' egg laying performance close to the breed's genetic potential (Figure 2). In the course of the experiment, Activo supplemented birds produced 3.6 more eggs than control birds, while consuming a similar amount of feed. As a result, feed consumption per egg produced was lower for birds receiving phytomolecules than for the control birds (169.9 versus 173.6g/d, respectively).

As hatchability was not influenced by the dietary treatment in this study (P>0.5), the 3.6 extra eggs resulted in 2.9 extra day old chicks per hen produced, during the post-peak period alone.

The microencapsulated, selected phytomolecules contained in Activo are likely to have improved gut health and feed digestibility, and thereby enhanced the animals' feed efficiency.

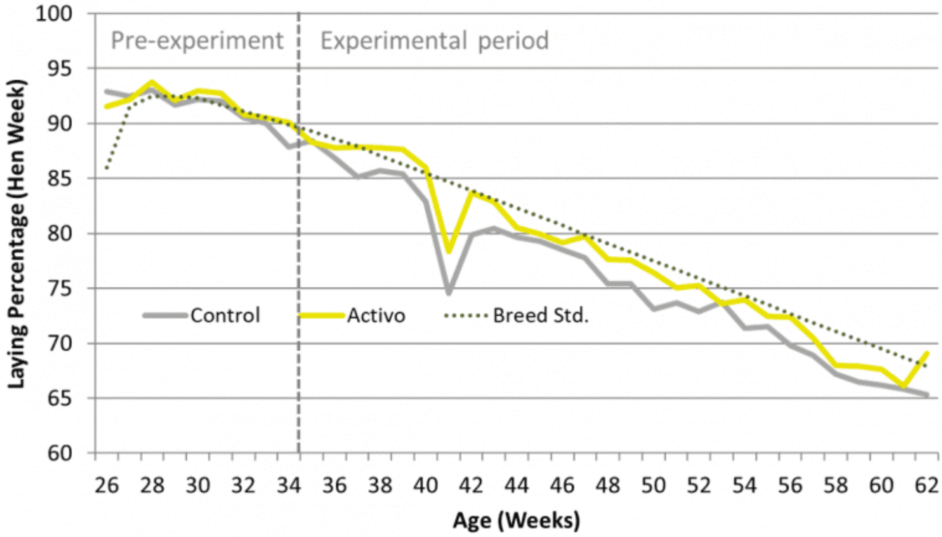

Figure 2: Laying rate (%) of breeder hens week 35 till 62

Chicken or egg? Antibiotic-free poultry production looks at the bigger picture

To successfully produce antibiotic-free poultry meat requires a systematic re-think of each component of the production process. Broiler breeders' lay the foundation for their progeny's health and performance via the egg. Breeder hens need to be in optimal health to consistently deliver optimal eggs. Without recourse to antibiotics for maintaining or recovering intestinal functionality, an effective ABF production needs to make gut health central to its feeding approach.

The trials reviewed demonstrate that selected phytomolecules quantifiably boost breeders' laying performance, increasing the number of hatching eggs and DOCs, while reducing mortality and feed consumption per egg produced. As part of an intelligent antibiotic reduction strategy, the right phytogenic products can be potent tools to help poultry producers achieve their NAE objectives.

by Technical Team, EW Nutrition

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Phytomolecules: Boosting Poultry Performance without Antibiotics

Antimicrobial resistance (AMR) is a major threat to global public health. It is largely caused by the overuse of antibiotics in human medicine and agriculture. In intensive poultry production most antibiotics are used as antimicrobial growth promoters and/or used as prophylactic and metaphylactic treatments to healthy animals. Reducing such antibiotic interventions is crucial to lowering the incidence of AMR. However, antibiotic reduction often results in undesirable performance losses. Hence alternative solutions are needed to boost poultry performance. Phytomolecules have antimicrobial, digestive, anti-inflammatory and antioxidant properties, which could make them key to closing the performance gap.

Poultry performance depends on intestinal health

Poultry performance is to a large extent a function of intestinal health. The intestines process nutrients, electrolytes and water, produce mucin, secrete immunoglobulins and create a barrier against antigens and pathogens.

In addition, it is an important component of the body's immune defense system. The intestine has to identify pathogens and reject them, but also has to tolerate harmless and beneficial microorganisms. If the intestines do not function properly this can lead to food intolerance, dysbiosis, infections and diseases. All of these are detrimental to feed conversion and therefore also to animal performance.

Antibiotics reduce the number of microorganisms in the intestinal tract. From a performance point of view this has two benefits: first, the number of pathogens is reduced and therefore also the likelihood of diseases; second, bacteria are eliminated as competitors for the available nutrients. However, the overuse of antibiotics not only engenders AMR: antibiotics also eliminate probiotic bacteria, which negatively impacts the digestive tracts' microflora.

Products to boost poultry performance may be added to their feed or water. They range from pre- and probiotics to medium chain fatty acids and organic acids to plant extracts or phytomolecules. Especially the latter have the potential to substantially reduce the use of antibiotics in poultry farming.

Phytomolecules are promising tools for antibiotic reduction

Plants produce phytomolecules to fend off pathogens such as moulds, yeasts and bacteria. Their antimicrobial effect is achieved through a variety of complex mechanisms. Terpenoids and phenols, for example, disturb or destroy the pathogens' cell wall. Other phytomolecules inhibit their growth by influencing their genetic material. Studies on broilers show that certain phytomolecules reduce the adhesion of pathogens such as to the wall of the intestine. Carvacrol and thymol were found to be effective against different species of *Salmonella* and *Clostridium perfringens*.

There is even evidence that secondary plant compounds also possess antimicrobial characteristics against antibiotic resistant pathogens. In-vitro trials with cinnamon oil, for example, showed antimicrobial effects against methicillin resistant Staphylococcus aureus, as well as against multiresistant E. coli, Klebsiella pneumoniae and Candida albicans.

Importantly, there are no known cases to date of bacteria developing resistances to phytomolecules. Moreover, phytomolecules increase the production and activity of digestive enzymes, they suppress the metabolism of pro-inflammatory prostaglandins and they act as antioxidants. Their properties thus make them a promising alternative to the non-therapeutic use of antibiotics.

Study design and results

In order to evaluate the effect of phytomolecules on poultry performance, multiple feeding studies were conducted on broilers and laying hens. They were given a phytogenic premix (Activo, EW Nutrition GmbH) that contains standardized amounts of selected phytomolecules.

To achieve thermal stability during the feed processing and a targeted release in the birds' gastrointestinal tract, the product is microencapsulated. For each , the studies evaluated both the tolerance of the premix and the efficacy of different dosages.

Study I: Evaluation of the dose dependent efficacy and tolerance of Activo for broilers
Animals: 400 broilers; age: 1-35 days of age
Feed: Basal starter and grower diets
Treatments:
– No supplement (negative control)
– 100 mg of Activo /kg of feed

– 1.000 mg of Activo /kg of feed
– 10.000 mg of Activo /kg of feed
Parameters: weight gain, feed intake, feed conversion ratio, health status, and blood parameters

Results: The trial group given the diet supplemented with 100 mg/kg Activo showed significant improvements in body weight gain during the starter period (+4%) compared to the control group. Additional significant improvements in feed conversion ratio (FCR) in the growing period (+4%) resulted in an overall improvement in FCR of 3%. At a 1.000 mg/kg supplementation, a significant improvement in FCR of 6% was observed over the entire feeding period. Hematological parameters were within the reference range of healthy birds when feeding up to 10,000 Activo/ kg of feed.

Study II: Evaluation of the dose depending efficacy and tolerance of Activo for laying hens

Animals: 200 hens; age: 20 to 43 weeks
Feed: basal diet for laying hens
Treatments:
– No supplement (negative control)
– 100 mg of Activo/ kg of feed
– 250 mg of Activo/ kg of feed
– 500 mg of Activo/ kg of feed
– 5.000 mg of Activo/ kg of feed
Parameters: weight gain, feed intake, feed conversion ratio, health status, and blood parameters

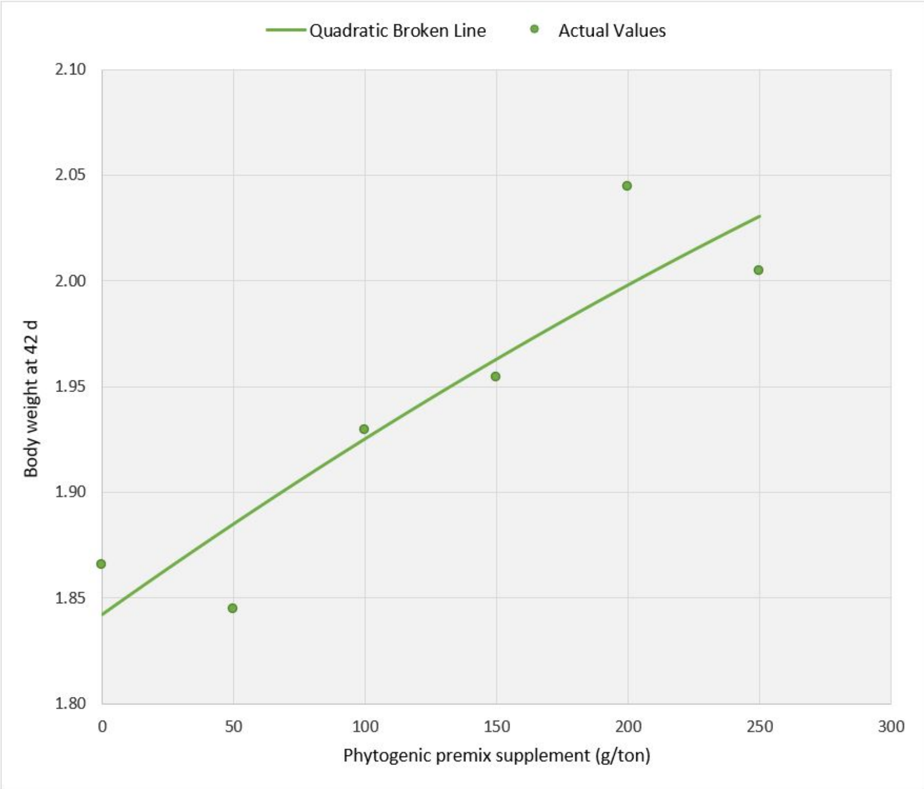
Results: Inclusion levels from 100 mg/kg of Activo onwards improved laying performance, egg mass and egg weight and reduced FCR compared to the control group. Results recorded for hematological parameters were within the reference range of healthy birds when feeding up to 5.000 mg Activo/ kg of feed.

Study III: Evaluation of the dose-dependent effects of Activo for coccidiosis vaccinated broilers

Animals: 960 broiler chickens; age: 42 days
Feed: Standard starter and finisher feed
Treatments:
– No supplement (negative control)
– 50 g of Activo /US ton of feed
– 100 g of Activo /US ton of feed
– 150 g of Activo /US ton of feed
– 200 g of Activo /US ton of feed
– 250 g of Activo /US ton of feed
– Antibiotic growth promoter (AGP)(positive control)
Parameters: weight gain, feed efficiency
Specific: In order to represent field conditions, the birds were challenged with used, homogenized litter.

Results: A clear dose response for both body weight gain and feed efficiency was observed (see Figure 1): the more phytogenic premix given, the better the birds' performance. The group with 200g of Activo /US ton of feed showed similar performance levels than the positive control group supplemented with AGP.

Figure 1: Dose-dependent effects of for coccidiosis vaccinated broilers



Study IV: Evaluation of the dose-dependent effects of Activo for laying hens

Animals: 40 hens; age: week 20 to 43
Feed: basal diet for laying hens
Treatments:
– No supplement (negative control)
– 100 mg of Activo/ kg of feed
– 250 mg of Activo/ kg of feed
– 500 mg of Activo/ kg of feed
– 5.000 mg of Activo/ kg of feed
Parameters: weight gain, feed intake, egg production, feed conversion ratio, health status
Duration: 168 days of feeding period

Results: The laying hens showed a higher laying rate when fed with a higher concentration of phytomolecules (Figure 2). Similarly improved results were observed for the feed efficiency. The more phytogenic premix added to their diet the better feed efficiency (Figure 3).

Figure 2: Dose-dependent effects of Activo on laying rate in laying hens

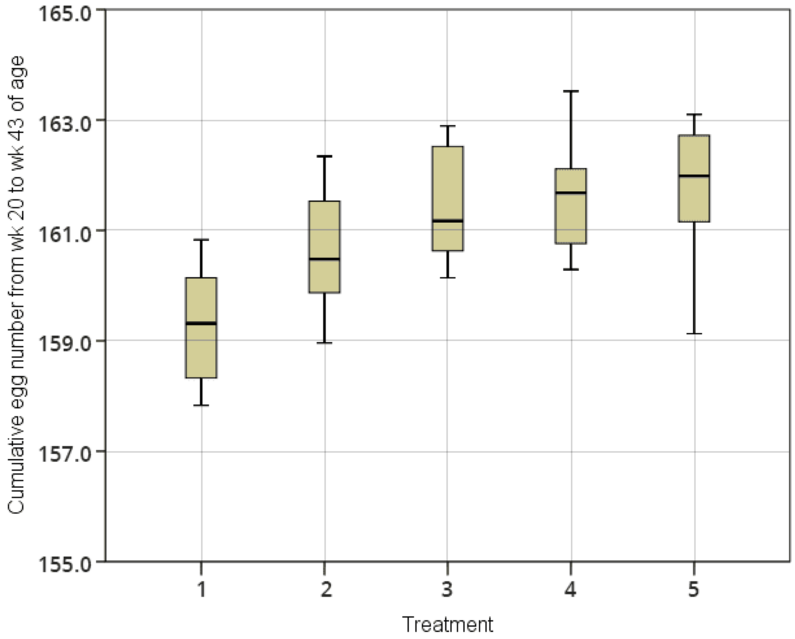
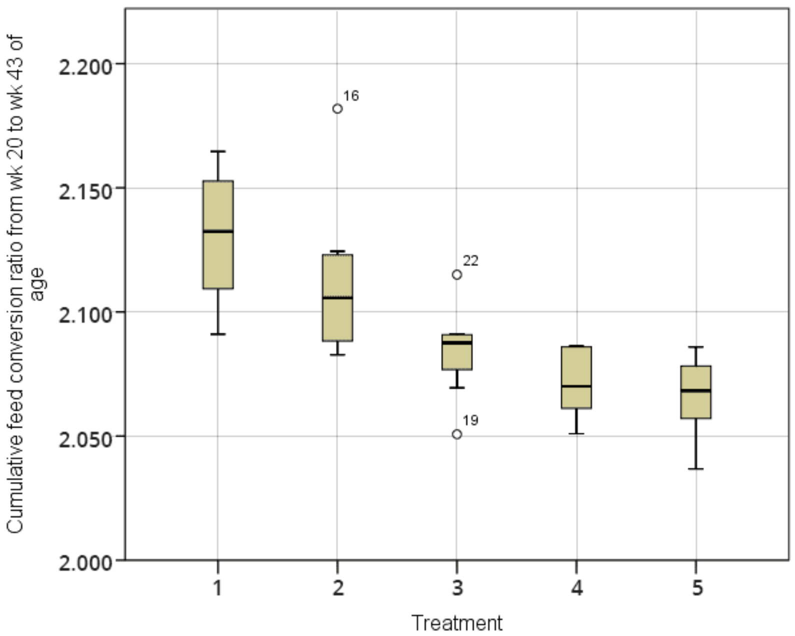


Figure 3: Dose-dependent effects of Activo on feed efficiency in laying hens



In conclusion, all four studies indicate that the inclusion of phytomolecules in broilers' and laying hens' diet improves their performance. Increasing levels of a phytogenic premix (Activo) significantly increased the production parameters for both groups. These improvements might bring performance in antibiotic-free poultry production on par with previous performance figures achieved with antimicrobial growth promoters.

The studies also showed that microencapsulated phytogenic premixes are safe when used in dose ranges recommended by the suppliers. No negative effects on animal health could be observed even at a 100 fold / 50 fold of the recommended inclusion rate in diets for broiler or laying hens, respectively. Thanks to their positive influence on intestinal health, phytomolecules thus boost poultry performance in a safe and effective way.

By Technical Team, EW Nutrition

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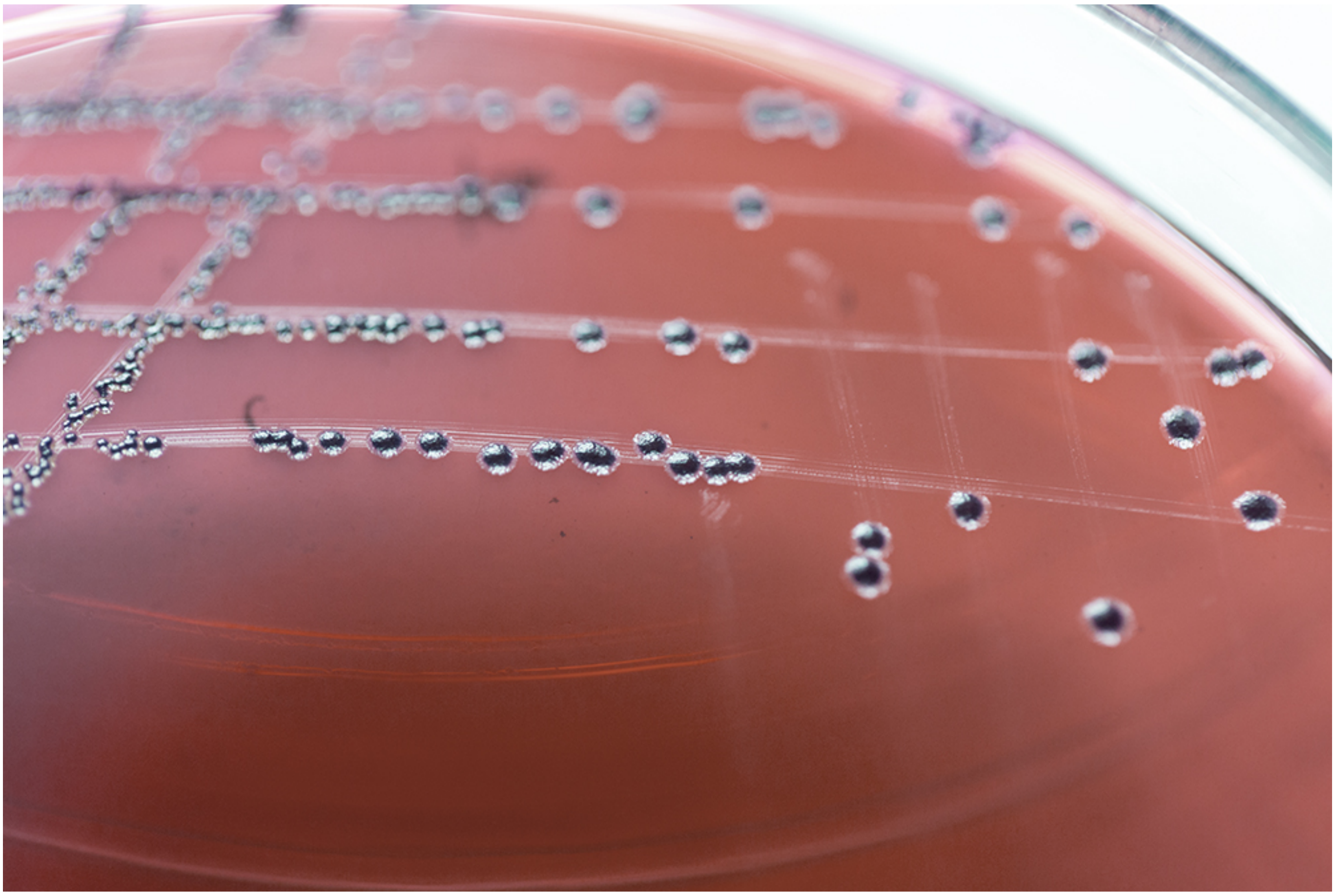
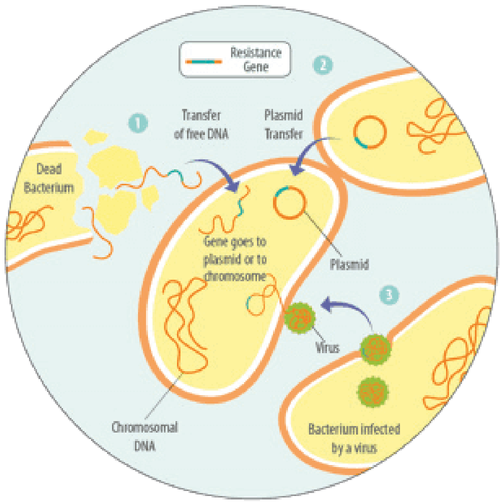
Photo source: Aviagen

Secondary Plant Compounds (SPC's) to reduce the use of antibiotics?



Initial in vitro trials give reason for hope

Antibiotic Resistance



Some bacteria, due to mutations, are less sensitive to certain antibiotics than others. This means that if certain antibiotics are used, the insensitive ones survive. Because their competitors have been eliminated, they are able to reproduce better. This resistance can be transferred to daughter cells by means of „resistance genes“. Other possibilities are the intake of free DNA and therefore these resistance genes from dead bacteria 1, through a transfer of these resistance genes by viruses 2 or from other bacteria by means of horizontal gene transfer 3 (see figure 1). Every application of antibiotics causes a selection of resistant bacteria. A short-term use or an application at a low dosage will give the bacteria a better chance to adapt, promoting the generation of resistance (Levy, 1998).

Antibiotics are promoting the development of resistance:

- Pathogenic bacteria possessing resistance genes are conserved and competitors that do not

possess these genes are killed
- Useful bacteria possessing the resistance genes are conserved and serve as a gene pool of antibiotic resistance for others
- Useful bacteria without resistance, which probably could keep the pathogens under control, are killed

Reducing the use of antibiotics

	Activo Liquid		
Central Poultry Diagnostic Laboratory, Kondapur, Hyderabad (India)	**10%**	**2%**	**1%**
E. coli (reference strains)	++	+	+
Proteus vulgaris (reference strains)	+	+	+
Pseudomonas fluorescens	++	+	-
Salmonella pulmorum	++	++	+
Salmonella gallinarum	++	++	+
Staphylococcus aureus (reference strains)	+++	++	++
- *no effect* + *growth inhibiting* ++ *bactericidal*			

Table 1: Effect of Activo Liquid against standard pathogens

Ingredients from herbs and spices have been used for centuries in human medicine and are now also used in modern animal husbandry. Many SPC's have antimicrobial characteristics, e.g. Carvacrol and Cinnamon aldehyde. They effectively act against Salmonella, *E. coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, Entero– and *Staphylococcus,* and *Candida albicans*. Some compounds influence digestion, others act as antioxidants. Comprehensive knowledge about the single ingredients, their possible negative but also positive interaction (synergies) is essential for developing solutions. Granulated or microencapsulated products are suitable for addition to feed, liquid products would be more appropriate for an immediate application in the waterline in acute situations.

SPC's (Activo Liquid) against livestock pathogens in vitro

In "agar diffusion tests", the sensitivity of different strains of farm-specific pathogens was evaluated with different concentrations of Activo Liquid. The effectiveness was determined by the extent to which they prevented the development of bacterial overgrowth. The larger the bacteria-free zone, the higher the antimicrobial effect.

In this trial, Activo Liquid showed an antimicrobial effect on all bacteria tested. The degree of growth inhibition positively correlated with its concentration.

Table 1: Inhibition of field isolated standard pathogens by different concentrations of Activo Liquid

Activo Liquid against antibiotic resistant field pathogens in vitro

	Activo Liquid			
Laboratory: Vaxxinova, Münster, Germany	**0.1%**	**0.2%**	**0.4%**	**1%**
E.coli Reference ATCC25922	+	++	++	++
ESBL 1 (Pig)	-	++	++	++
ESBL 2 (Pig)	±	++	++	++
ESBL 3 (Poultry)	±	++	++	++
ESBL 4 (Poultry)	-	++	++	++
S. aureus Referenz ATCC29213	-	+	++	++
MRSA 1 (Pig)	-	+	++	++
MRSA 2 (Pig)	-	+	+	++
- no effect ± bacteriostatic	+ growth inhibiting ++ bactericidal			

Table 2: Effect of Activo Liquid against field-isolated standard pathogens

It cannot be excluded that resistant pathogens not only acquired effective weapons to render antibiotics harmless to them but also developed general mechanisms to rid themselves of otherwise harmful substances. In a follow-up laboratory trial, we evaluated whether the Activo Liquid composition is as effective against ESBL producing E. coli and Methicillin resistant S. aureus (MRSA) as to non-resistant members of the same species.

Trial Design: Farm isolates of four ESBL producing E. coli and two MRSA strains were compared to nonresistant reference strains of the same species with respect to their sensitivity against Activo Liquid. In a Minimal Inhibitory Concentration Assay (MIC) under approved experimental conditions (Vaxxinova Diagnostic, Muenster, Germany) the antimicrobial efficacy of Activo Liquid in different concentrations was evaluated.

The efficacy of SPC's (Activo Liquid) against the tested strains could be demonstrated in a concentration-dependent manner with antimicrobial impact at higher concentrations and bacteriostatic efficacy in dilutions up to 0,1% (ESBL) and 0,2% (MRSA)(table 2).

Conclusion:
To contain the emergence and spread of newly formed resistance mechanisms it is of vital importance to reduce the use of antibiotics. SPC's are a possibility to decrease antibiotic use especially in pro- and metaphylaxis, as they show good efficacy against the common pathogens found in poultry, even against resistant ones.

I. Heinzl

Necrotic enteritis in poultry

Enteric diseases cause significant economic losses due to decreased weight gain, higher mortality, higher feed conversion, higher veterinary costs and medicine and a higher risk of contamination by poultry products in food production. The losses due to necrotic enteritis mainly occurring in broilers and fattening turkeys in intensive floor or free-range management are put at 2 billion US$ per year.

After the ban of antibiotic growth promoters, the relevance of this formerly well controllable disease reappeared and increased.

Necrotic enteritis is a disease of the gut
It is caused by specific gram-positive, anaerobic bacteria – *Clostridium perfringens,* mostly Type A. Clostridia are found in litter, faeces, soil, dust and in healthy animals' guts. These spore forming bacteria are extremely resistant against environmental influences and can survive in soil, feed, and litter for several years and even reproduce.
Clostridium perfringens is a component of the normal gut flora. It occurs in a mixture of diverse strains in a concentration of up to 10^5 CFU / g intestinal content. In animals suffering from necrotic enteritis particularly one strain of *Clostridium perfringens* is found in a much more higher concentration of 10^6-10^8 CFU / g.
Necrotic enteritis affects chickens and turkeys at the age of 2-16 weeks, proliferating at the age of 3-6 weeks. There is an acute clinical, and a subclinical form.
Birds suffering from the clinical form clearly show symptoms like a poor general state of health and diarrhoea. Mortality rates up to 50 % can occur. Subclinical necrotic enteritis cannot be diagnosed easily, as there are no clear symptoms. This form, however, stays within the flock and causes losses due to decreased growth.

Factors promoting an infection with necrotic enteritis should be avoided!
In general, factors have to be cited that create an intestinal environment favourable for the facultative anaerobic *Clostridium perfringens* or weaken the immune status of the host:

1. **Feed:**
   Here **NSP's** have to be mentioned. Undigested NSP's serve as substrate and some of them cause higher production of mucus also serving as substrate and providing ideal anaerobic conditions. Undigested **proteins** due to high contents in the diet also serve as substrates. **Animal protein** and **fat** are worse than vegetable variants and a homogeneous size of particles in the diet is better than an **inhomogeneous mixture**.
2. **Stress**
   Stresses such as feed change or high stocking density favour NE
3. **Diseases**
   Immunosuppressive diseases such as infective chicken anaemia, Gumboro or Marek's decrease resistance against intestinal infections and facilitate their colonisation. Some pathogens exert pressure on the gut and prepare the way for clostridia. Here Cryptosporidia and salmonella have to be mentioned.

New approaches
Secondary plant compounds show good results against the two microorganisms just mentioned. In a trial conducted with free range broilers in France, a combination of a vaccination against coccidia and a mixture of secondary plant compounds (Activo liquid) resulted in a reduced occurrence of necrotic enteritis in the trial group compared to the control. Additionally due to an improved feed conversion, the margin per animal in the trial group was 5 Cent higher than in the control (1,44 € vs 1,39 €).
In an *in vitro* test, Activo liquid also showed bactericidal efficacy against field isolated *Salmonella pulmorum* and *Salmonella gallinarum* at a 2 % concentration.
The trials show that combined with a good feeding and stress management, secondary plant compounds, could be a good tool to eliminate predisposing factors for necrotic enteritis and could therefore help control this economically important disease.

Secondary plant compounds are the new frontier in poultry nutrition

Why should you read another story about phytogenics? Or, is it botanicals, spices, herbs, and extracts? No matter what we call them, scientists have named them “secondary plant compounds”, and if we are to follow the American tradition we can call them SPC. Then, here is the first interesting thing we can discuss about this plant-derived class of active compounds. They are “secondary” in nature, but not insignificant. They play no role in normal metabolism, but they help plants (and now animals) survive under adverse conditions. Perhaps, this is why some experts consider them as the next frontier in poultry nutrition. With poultry that are raised in less than ideal conditions, especially when we consider the movement towards antibiotic reduction (for growth promoting reasons, not complete removal of all medicines), we understand that such natural compounds can be of significant help.

As it happens, the majority of poultry specialists in Europe and increasingly in the Americas consider SPC as an almost-essential element in diets for broilers and layers (and turkeys, ducks, and all poultry for that matter) when birds are raised without antibiotics. Some go even further and use them along with antibiotics because, as we all know, antibiotics are never 100% efficient as bacteria sooner or later develop some form of resistance. Such resistance has not yet been observed with SPC. So if one is to use SPC in poultry feds, which ones to buy? A quick glance at the market will reveal more commercial products than can possibly be imagined. Some must be better than the rest, but how can we separate the wheat from the chaff? Price alone is not always a good indicator. A high quality product must be expensive – for there is no such thing as a free lunch – but all expensive products are not always of the highest possible quality!

There are three basic criteria, which we can mention briefly here:

1. **SPC are volatile** – at least most of them. As such, unprotected products will soon evaporate if left in the open air as it happens with feed prepared in commercial farms. So, some form of protecting SPC is essential.
2. **SPC are innumerable** – so finding the right mix for the job required is important. You cannot get the same results with any kind of mix. So, in designing an SPC mix, the manufacturer must declare and have knowledge of the target to be accomplished.
3. **SPC are powerful** – meaning you cannot just keep adding as much as possible. Here finding the exact dosage for the right purpose is a difficult balancing exercise. So, the right mix and the right dosage must be combined, otherwise animals will refuse the feed (worst case scenario) or just fail to benefit from SPC inclusion.

There is so much more to learn about this exciting class of compounds that can replace the growth promoting action of antibiotics that it is worth spending time learning more about them.