

# Consistency in performance: a decisive factor in choosing feed additives



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In practical poultry production, multiple stress factors occur simultaneously: nutrition, management, environment, etc.. The effects of these factors are additive, leading to chronic stress, a condition in which animals cannot regain homeostasis and continuously deviate the use of resources to inflammation and restoring the gut barrier-function (Das et al., 2011). As a result, the gut microbiome is altered and oxidative stress ensues (Mishra et al., 2019). In this situation, health and productivity are compromised.

The feed supplied to production animals is designed to help them express their genetic potential. However, some feed components are also continuous inflammatory triggers. Anti-nutritional factors, oxidized lipids, and mycotoxins induce a low-grade inflammatory response (Cardoso Del Pont et al., 2020). Other factors that trigger gut health issues include the environment, management, and pathogens.

Feed interventions have shown to increase productivity and improve gut-related biomarkers, demonstrating a mitigation effect over the challenge factors (Deminicis et al., 2020; Latek et al., 2022).

# Meta-analysis of broiler studies shows consistent results

As broilers are continuously challenged during the production period, the effects of an in-feed phytogenic (Ventar D – EW Nutrition GmbH) were extensively researched in broiler meat production. 21 trials in different locations (7 in Europe, 6 in the USA, 4 in Japan, 3 in Middle East, and 2 in India), with different production levels (grouped by EPEF) and challenges were analyzed to establish Ventar D's benefits for the broiler production industry in terms of performance and sustainability. In all trials, the treatment group consisted of a supplementation of the basal feed with Ventar D at a dose 100 g/ton. The control groups were not supplemented with any gut health improvement feed additive.

Of these 21 trials, 14 had corn/soybean meal-based diets and 7 had high fiber diets (based on wheat and rye, which constituted a challenge as no NSP-enzymes were included). Reused litter (by 12 to 14 flocks, previous to the trial) also was used as a challenge. 18 trials were performed in research facilities and 3 in commercial farms.

Consistency in the results from Ventar D could be demonstrated as 19 out of 21 trials showed an improvement in FCR, lowering 3.4 points on average; 18 /21 trials showed higher body weight, with an average of 64 grams more; and 17 trials showed lower mortality than the control group, averaging 1.19 percentual points of reduction. The phenolic compounds included in Ventar D, such as thymol, possess antioxidant, anti-inflammatory, and antibacterial activities, which account for improving gut health and thus increasing performance in production animals.

The European Poultry Efficiency Factor (EPEF) was used to establish the performance level of each flock. This index is based on the average daily weight gain, mortality, and feed conversion, and takes in consideration the age of the flock at collection, allowing to make comparisons on performance within and between farms.

Of the 21 trials, 10 control groups had an EPEF lower than 375, and were considered of low performance level, in 8 the EPEF was between 375 and 425 and considered of medium performance, and for 3 the performance was considered high having an EPEF of 425 or more.

Ventar D increased performance at all levels (Figure 1). However, the effects were challenge-dependent: Low performing flocks averaged an 8% increase in EPEF, and high performing flocks increased 4%, indicating that Ventar D can help broilers to overcome challenges commonly found in poultry production, and boost performance even with excellent farm and management conditions. These results concur with a meta-analysis by Valle Polycarpo and collaborators (2022), finding that a microbial challenge can influence the performance of phytogenic feed additives.

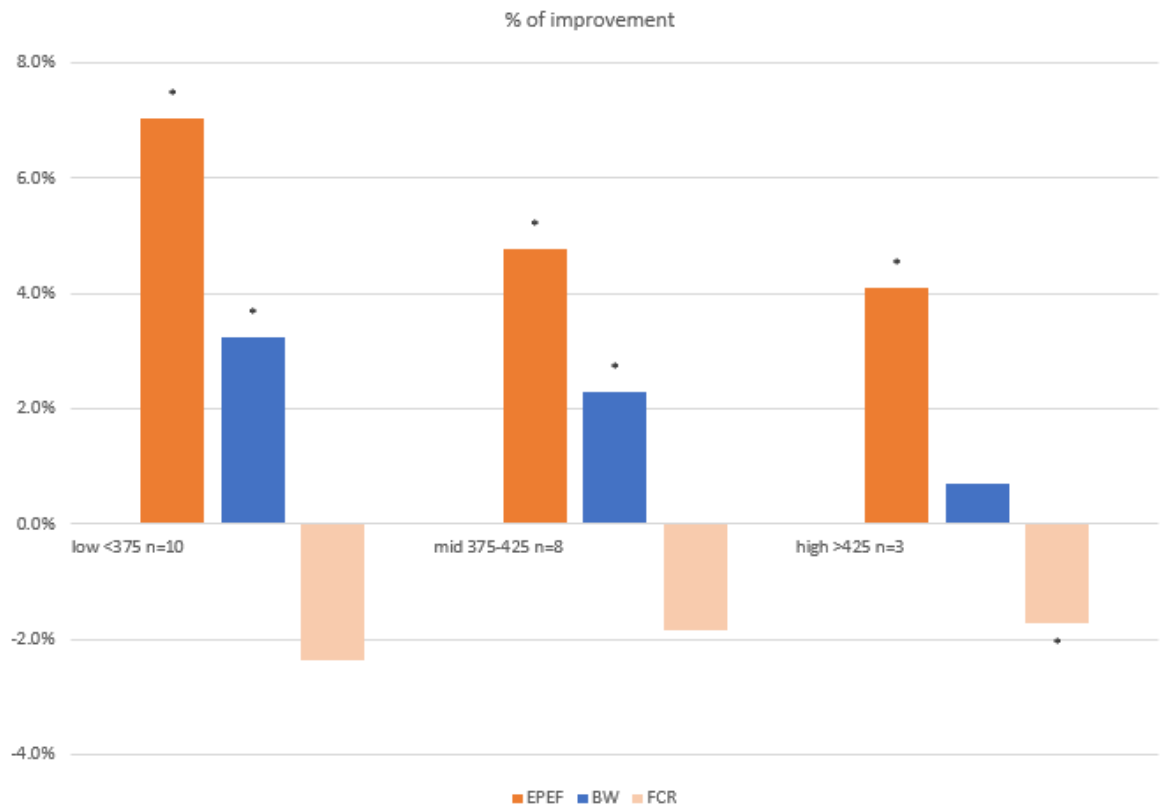


Figure 1: % of improvement in EPEF, body weight (BW) and Feed Conversion Rate (FCR) against a non-supplemented control group of IFI supplemented flocks with low (<400), mid (400 – 450) and high (>450) EPEF levels. Significant differences ( $p<0.05$ ) against a control group (not shown as the improvements against it are depicted) are indicated by (\*).

Overall, this analysis demonstrates that effective nutritional interventions can give consistent results and constitute effective tools to help production animals overcome stress and enhance productivity.

## Managing gut health - a key challenge in ABF broiler production





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Gut health is a critical challenge in antibiotics-free (ABF) production as it plays a vital role in the overall health and well-being of animals. Antibiotics have long been used as a means of preventing and treating diseases in animals, but their overuse has led to the development of antibiotic-resistant bacteria. As a result, many farmers and producers are shifting towards antibiotics-free production methods. This shift presents a significant challenge as maintaining gut health without antibiotics can be difficult. It is, however, not impossible.

One of the main challenges in antibiotics-free production is the prevention of bacterial infections in the gut. The gut microbiome plays a crucial role in the immune system and overall health of animals. When the balance of microbes in the gut is disrupted (dysbiosis), it can lead to poor nutrient absorption which subsequently results in reduced live bird performance including feed efficiency and weight gain in broiler chicken. In the absence of antibiotics, farmers and producers must rely on other methods to maintain a healthy gut microbiome.



## Antibiotic reduction - a major global trend

The trend in recent years has been for poultry producers to reduce their use of antibiotics to promote public health and improve the sustainability of their operations. This has been driven by concerns about the development of antibiotic-resistant bacteria and the potential impact on human health, as well as by consumer demand for meat produced without antibiotics. Many countries now have regulations in place that limit the use of antibiotics in food and animal production.

### Challenges to antibiotics-free poultry (ABF) production

1. **Disease control.** Antibiotic-free poultry production requires farmers to rely on alternative methods for controlling and preventing diseases, such as stepped-up biosecurity practices. This can be more labor-intensive and costly.
2. **Higher mortality rates.** Without antibiotics, poultry farmers may experience higher mortality rates due to disease outbreaks and other health issues. This can lead to financial losses for the farmer and a reduced supply of poultry products for consumers.
3. **Feeding challenges.** Antibiotic growth promoters (AGPs) are often used in feed to promote growth and prevent intestinal disease in poultry. Without AGPs, poultry producers can find alternative ways to ensure expected production performance.
4. **Increased cost.** Antibiotic-free poultry production can be more expensive than conventional production methods, as farmers must invest in additional housing, equipment, labor, etc.

Phasing out AGPs will likely lead to changes in the microbial profile of the intestinal tract. It is hoped that strategies such as infectious disease prevention programs and using non-antibiotic alternatives minimize possible negative consequences of antibiotic removal on poultry flocks (Yegani and Korver, 2008).

# Gut health is key to overall health

A healthy gastrointestinal system is important for poultry to achieve its maximum production potential. Gut health in poultry refers to the overall well-being and functioning of the gastrointestinal tract in birds. This includes the balance of beneficial bacteria, the integrity of the gut lining, and the ability to digest and absorb nutrients. Gut health is important for maintaining the overall health and well-being of the birds. A healthy gut helps to improve feed efficiency, nutrient absorption, and the overall immunity of the birds.

The gut is host to more than 640 different species of bacteria and 20+ different hormones. It digests and absorbs the vast majority of nutrients and makes up for nearly a quarter of body energy expenditure. It is also the largest immune organ in the body (Kraehenbuhl and Neutra, 1992). Consequently, 'gut health' is highly complex and encompasses the macro and micro-structural integrity of the gut, the balance of the microflora, and the status of the immune system (Chot, 2009).

## Poultry immunity is mediated by the gut

The gut is a critical component of the immune system, as it is the first line of defense against pathogens that enter the body through the digestive system. Chickens have a specialized immune system in the gut, known as gut-associated lymphoid tissue (GALT), which helps to identify and respond to potential pathogens. The GALT includes Peyer's Patches, which are clusters of immune cells located in the gut wall, as well as the gut-associated lymphocytes (GALs) that are found throughout the gut. These immune cells are responsible for recognizing and responding to pathogens that enter the gut.

The gut-mediated immune response in chickens involves several different mechanisms, including the activation of immune cells, the production of antibodies, and the release of inflammatory mediators. The GALT and GALs play a crucial role in this response by identifying and responding to pathogens, as well as activating other immune cells to help fight off the infection.

The gut microbiome also plays a critical role in gut-mediated immunity in chickens. The gut microbiome is made up of a highly varied community of microorganisms, and these microorganisms can have a significant impact on the immune response. For example, certain beneficial bacteria can help to stimulate the immune response and protect the gut from pathogens.

Overall, the gut microbiome, GALT, and GALs all work together to create an environment that is hostile to pathogens while supporting the growth and health of beneficial microorganisms.

## Dysbiosis/Dysbacteriosis impacts performance

Dysbiosis is an imbalance in the gut microbiota because of an intestinal disruption. Dysbacteriosis can lead to wet litter and caking issues. Prolonged contact with the caked litter can lead to pododermatitis (feet ulceration) and hock-burn, resulting in welfare issues as well as degradation of the carcass (Bailey, 2010). Apart from these issues, the major economic impact comes from reduced growth rates, FCR, and increased veterinary treatment costs. Coccidiosis infection and other enteric diseases can be aggravated when dysbiosis is prevalent. Generally, animals with dysbiosis have high concentrations of *Clostridium* that generate more toxins, leading to necrotic enteritis.

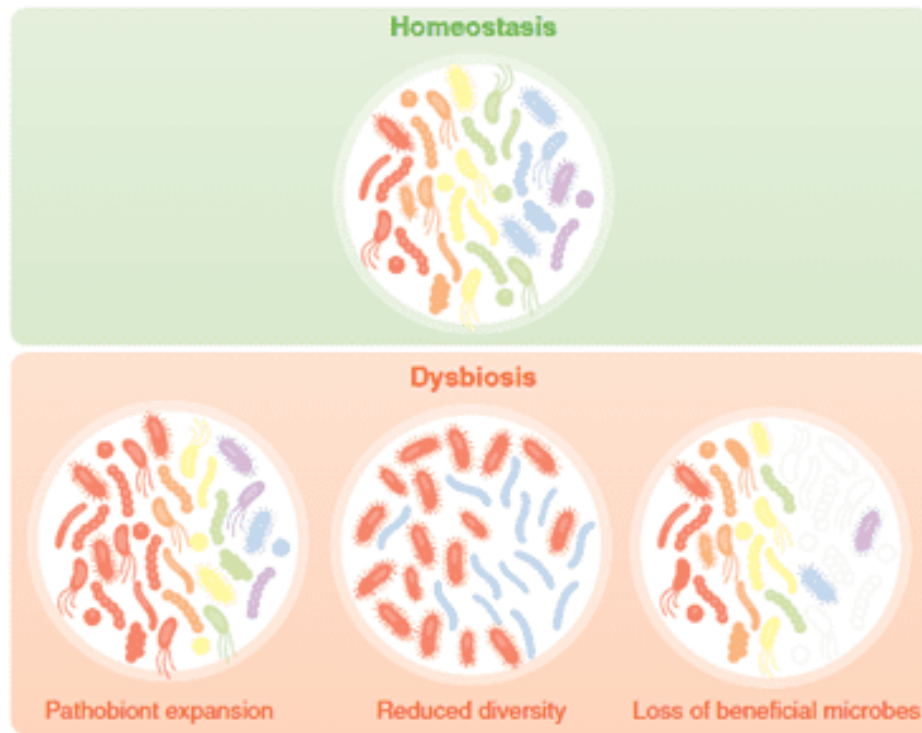


Fig.1: Dysbiosis – a result of challenging animal’s microbiome. Source: Charisse Petersen and June L. Round. 2014

It is believed that both non-infectious and infectious factors can play a role in dysbacteriosis (DeGussem, 2007). Any changes in feed and feed raw materials, as well as the physical quality of feed, influence the balance of the gut microbiota. There are some risk periods during poultry production when the bird will be challenged, for example during feed change, vaccination, handling, transportation, etc. During these periods, the gut microbiota can fluctuate and, in some cases, if management is sub-optimal, dysbacteriosis can occur.

Infectious agents that potentially play a role in dysbacteriosis include mycotoxins, *Eimeria* spp., *Clostridium perfringens*, and other bacteria producing toxic metabolites.

## Factors affecting gut health

The factors affecting broiler gut health can be summarized as follows:

1. **Feed and water quality:** The form, type, and quality of feed provided to broilers can significantly impact their gut health. Consistent availability of cool and hygienic drinking water is crucial for optimum production performance.
2. **Stress:** Stressful conditions, such as high environmental temperatures or poor ventilation, can lead to an imbalance in the gut microbiome and an increased risk of disease.
3. **Microbial exposure:** Exposure to pathogens or other harmful bacteria can disrupt the gut microbiome and lead to gut health issues.
4. **Immune system:** A robust immune system is important for maintaining gut health, as it helps to prevent the overgrowth of harmful bacteria and promote the growth of beneficial bacteria.
5. **Sanitation:** Keeping the broiler environment clean and free of pathogens is crucial for maintaining gut health, as bacteria and other pathogens can easily spread and disrupt the gut microbiome.
6. **Management practices:** Proper management practices, such as proper feeding and watering, and litter management can help to maintain gut health and prevent gut-related issues.





*Fig. 2. Key factors affecting broilers' gut health*

## Key approaches for managing gut health without antibiotics

Two key approaches for managing gut health in poultry without the use of antibiotics are outstandingly successful.

### Proper nutrition and management practices

Ensuring the birds have access to clean water, high-quality feed, and a stress-free environment is crucial for ABF poultry production. A balanced diet in terms of protein, energy, and essential vitamins and minerals is essential for maintaining gut health.

The environment in which birds have kept plays a major role in maintaining gut health. Proper sanitation and ventilation, as well as the right temperature and humidity, are crucial to prevent the spread of disease and infection. There is no alternative to the strict implementation of stringent biosecurity measures to prevent the spread of disease.

Early detection and treatment of diseases can help to prevent them from becoming more serious problems affecting the profitability of ABF production. It is important to keep a close eye on birds for signs of disease, such as diarrhea, reduced water, and feed consumption.

### Gut health-promoting feed additives

Another approach to maintaining gut health in antibiotics-free poultry production is using gut health-supporting feed additives. A variety of gut health-supporting feed additives including phytochemicals/essential oils, organic acids, probiotics, prebiotics, exogenous enzymes, etc. in combination or alone are used in animal production. Particularly, phytogenic feed additives (PFAs) have gained interest as cost-effective feed additives with already well-established effects on improving broiler chickens' intestinal health.

Plant secondary metabolites and essential oils (generically called phytogenics, phytochemicals, or phytomolecules) are biologically active compounds that have recently garnered interest as feed additives in poultry production, due to their capacity to improve feed efficiency by enhancing the production of digestive secretions and nutrient absorption. This helps reduce the pathogenic load in the gut, exert antioxidant properties and decrease the microbial burden on the animal's immune status (Abdelli et al.



2021).

## Plant extracts - Essential oils (EOs) /Phytomolecules

Phytochemicals are naturally occurring compounds found in plants. Many phytomolecules have been found to have antimicrobial properties, meaning they can inhibit the growth or kill microorganisms such as bacteria, viruses, and fungi. Examples of phytomolecules with antimicrobial properties include compounds found in garlic, thyme, and tea tree oil. Essential oils (EOs) are raw plant extracts (flowers, leaves, roots, fruit, etc.) whereas phytomolecules are active ingredients of essential oils or other plant materials. A phytomolecule is clearly defined as one active compound. Essential oils (EOs) are important aromatic components of herbs and spices and are used as natural alternatives for replacing antibiotic growth promoters (AGPs) in poultry feed. The beneficial effects of EOs include appetite stimulation, improvement of enzyme secretion related to food digestion, and immune response activation (Krishan and Narang, 2014).

A wide variety of herbs and spices (thyme, oregano, cinnamon, rosemary, marjoram, yarrow, garlic, ginger, green tea, black cumin, and coriander, among others), as well as EOs (from thyme, oregano, cinnamon, garlic, anise, rosemary, citrus, clove, ginger), have been used in poultry, individually or mixed, for their potential application as AGP alternatives (Gadde et al., 2017).

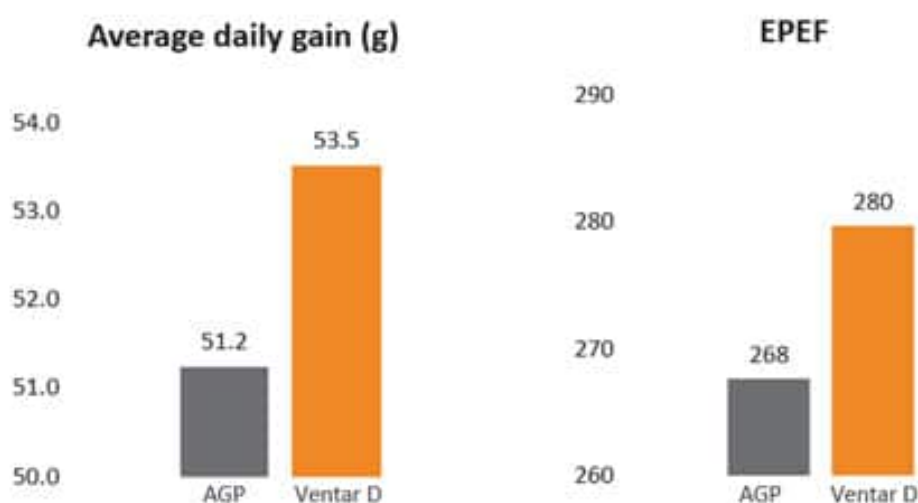


Fig. 3: Phytomolecule-based feed additive outperforms AGPs with improved broiler performance (42 Days field study)

One of the primary modes of action of EOs is related to their antimicrobial effects which allow for controlling potential pathogens (Mohammadi and Kim, 2018).

Phytomolecule blend	<i>Clostridium perfringens</i>	<i>Enterococcus caecorum</i>	<i>Enterococcus hirae</i>	<i>Escherichia coli</i>	<i>Salmonella typhimurium</i>	<i>Staphylococcus aureus</i>
Ventar D	1250	2500	5000	2500	5000	2500

Fig. 4: Effectivity of phytomolecule-based feed additive (Ventar D) against enteropathogenic bacteria (MIC value in PPM)

Phytomolecules have been shown to have anti-inflammatory properties. These compounds include flavonoids, polyphenols, carotenoids, and terpenes, among others. One of the ways in which phytomolecules exhibit anti-inflammatory effects is through their ability to inhibit the activity of pro-inflammatory enzymes and molecules. For example, polyphenols have been shown to inhibit the activity of nuclear factor-kappa B (NF- $\kappa$ B), a transcription factor that plays a key role in regulating inflammation.

Phytomolecules also have antioxidant properties, which can help to protect cells from damage caused by reactive oxygen species (ROS) and other reactive molecules that can contribute to inflammation. Plant extracts are also proposed to be used as antioxidants in animal feed, protecting animals from oxidative

damage caused by free radicals. The presence of phenolic OH groups in thymol, carvacrol, and other plant extracts act as hydrogen donors to the peroxy radicals produced during the first step in lipid oxidation, thus retarding the hydroxyl peroxide formation (Farag et al., 1989, Djeridane et al., 2006). Thymol and carvacrol are reported to inhibit lipid peroxidation (Hashemipour et al. 2013) and have strong antioxidant activity (Yanishlieva et al., 1999).

Overall, the anti-inflammatory effects of phytomolecules are thought to be due to a combination of their ability to inhibit the activity of pro-inflammatory enzymes and molecules, their antioxidant properties, and their ability to modulate the immune system. Plant extracts (i.e. carvacrol, cinnamaldehyde, eugenol. etc.) inhibit the production of pro-inflammatory cytokines and chemokines from endotoxin-stimulated immune cells and epithelial cells (Lang et al., 2004, Lee et al., 2005, Liu et al., 2020). It has been indicated that anti-inflammatory activities may be partially mediated by blocking the NF- $\kappa$ B activation pathway (Lee et al., 2005).

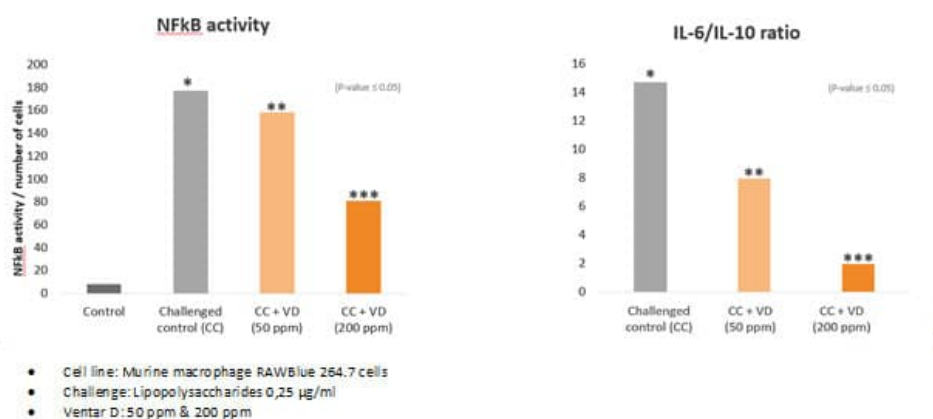


Fig. 5: Anti-inflammatory effect of phytomolecule-based feed additive (Ventar D) - the reduced activity of inflammatory cytokines

## Proper protection of EOs/Phytomolecules is key to optimum results

Several phytogenic compounds have also been shown to be largely absorbed in the upper GIT, meaning that without proper protection, the majority would not reach the lower gut where they would exert their major functions (Abdelli et al. 2021). The benefits of supplementing the broiler diet with a mixture of encapsulated EOs were higher than the tested PFA in powdered, non-protected form (Hafeez et al. 2016). Novel delivery technologies have been developed to protect PFAs from the degradation and oxidation process during feed processing and storage, ease the handling, allow a slower release, and target the lower GIT (Starčević et al. 2014). The specific protection techniques used during the commercial production of an EO/phytomolecule blend are crucial in delivering on all the objectives with remarkable consistency.

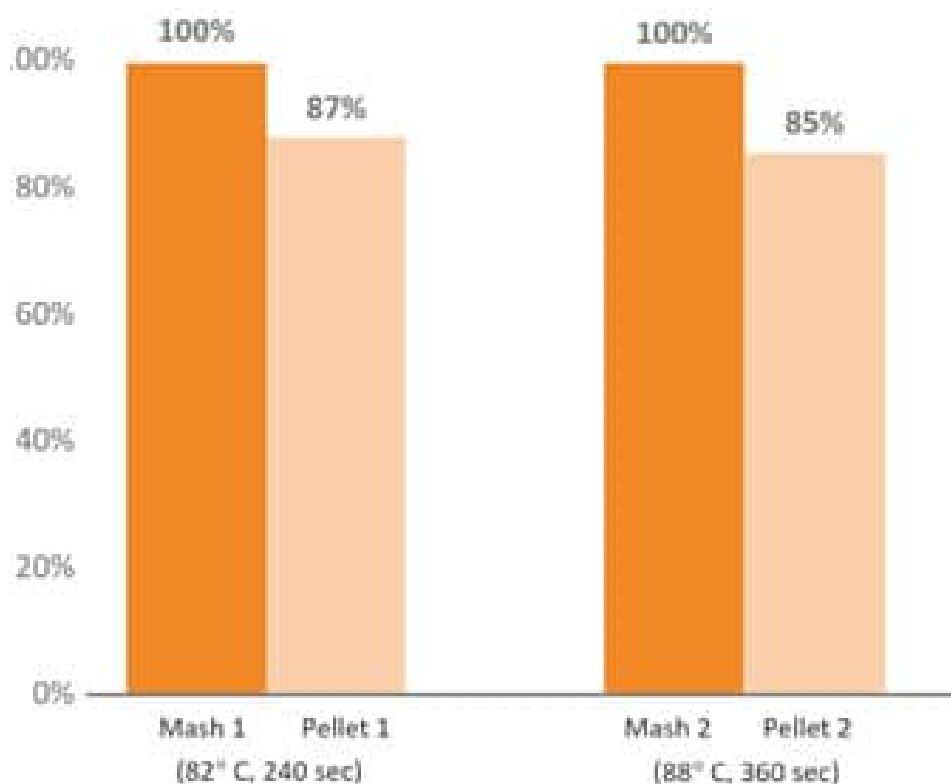


Fig. 6: Pelleting stability of phytomolecule – based feed additive (Ventar D) at high temperature and longer conditioning time

## Phytomolecule blend optimizes production performance

Removal of antibiotics in poultry production can be challenging for controlling mortality and maintaining the production performance of the birds. Phytogenic feed additives have been shown to [improve production performance](#) of chicken due to their antimicrobial, anti-inflammatory, antioxidant, and digestive properties. Possible mechanisms behind improved nutrient digestibility by phytogenic feed additives (PFAs) supplementation could be attributed to the ability of these feed additives to stimulate appetite, saliva secretion, intestinal mucus production, bile acid secretion, and activity of digestive enzymes such as trypsin and amylase as well as to positively affect the intestinal morphology (Oso et al. 2019). EOs are perceived as growth promoters in poultry diets, with strong antimicrobial and anticoccidial activities (Zahi et al., 2018). PFAs have positive effects on body weight gain and FCR in chickens (Khattak et al. 2014, Zhang et al. 2009).

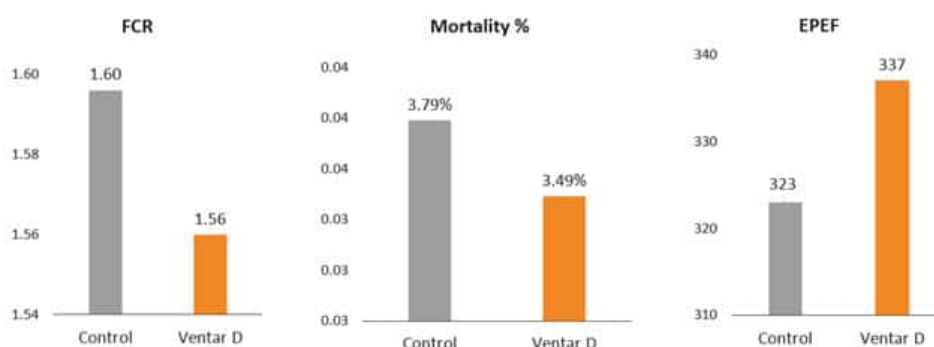


Fig. 7: Phytomolecule-based feed additive improved broiler FCR and mortality in field trial

# Conclusion

In conclusion, managing gut health is a significant challenge in ABF broiler production that must be addressed to achieve optimal performance and welfare of the birds. The use of antibiotics as a preventative measure in broiler production has been widely used, but with the increasing demand for antibiotic-free products, alternative methods to maintain gut health must be implemented. These include using gut health-supporting feed additives, and proper management practices such as implementing biosecurity measures, maintaining optimal environmental conditions, providing adequate space and ventilation, and reducing stress. However, it is essential to note that there is no one-size-fits-all solution for gut health management in ABF broiler production. It is important to continuously monitor and assess their flock's gut health and make adjustments as necessary. Additionally, research and development in this field should be encouraged to identify new and innovative ways to maintain gut health in ABF broiler production.

Overall, managing gut health is a critical challenge that requires a multi-faceted approach and ongoing monitoring and management. By implementing the appropriate strategies and utilizing new technologies, poultry operators can ensure the health and well-being of their flocks while meeting the growing demand for antibiotic-free products sustainably.

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## How to develop phytogenic feed

# additives



by *EW Nutrition Phytogenics* team

**Modern feed additives are now commonly used as a critical tool to improve animal health. Among these, phytogenic feed additives are increasingly widely adopted. Consequently, more and more products are entering the market, leaving producers to wonder how these products differ from one another and which product performs best. To better understand the benefits that phytogenic feed additives can bring to operations, one must understand the development process feed additives undergo.**





## Not all feed additives are born equal

Feed additives are products that are added into an animal feed to improve its value. They are typically used to improve animal performance and welfare and consequently to optimize profitability for livestock producers.

Their purpose should not be confused with that of veterinary drugs. Feed additives provide additional benefits *beyond* the physiological needs of the animals and should be combined with other measures to improve production efficiency. Those measures include improvements in management, selection of genetics, and a constant review of biosecurity measures.

Several categories of feed additives exist. They all have in common that they are mixed into the feed or premix or the drinking water in relatively low inclusion rates to serve a *specific* purpose. Examples of feed additives are organic acids, pre- and probiotics, short and medium chained fatty acids, functional yeast products, and phytogenic feed additives. Modern feed additives also blend those different additives into combination products, increasing the value of the final products.

Phytogenic feed additives are a sub-category of additives containing phytomolecules, active ingredients which originate from plants and provide a unique set of characteristics. These molecules are produced by plants to protect themselves from molds, yeasts, bacteria, and other harmful organisms. Depending on the type of molecule, phytomolecules have different properties, ranging from antimicrobial to antioxidant and anti-inflammatory.

# EW Nutrition's approach to developing Ventar D: 6 steps

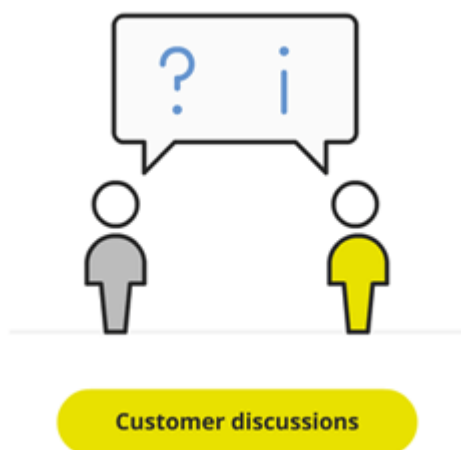
The development of best-in-class phytogenic feed additives is a complex process. For [Ventar D](#), EW Nutrition divided the process into the following steps, which can serve as a template for a successful development process:

1. Reviewing customer needs
2. Active ingredient selection
3. Technical formulation
4. Application development and scale-up
5. Performance tests
6. Safety and regulatory validation

## Understanding customer needs

The most important point in developing a feed additive is customer-centricity. Understanding the challenges and needs of producers is crucial to developing feed additive solutions.

In a first step, additive producers need to evaluate and *quantify* customer needs wherever possible. This is achieved through communication and literature review: Producers, key opinion leaders, and research partners are interviewed, and their challenges are listed. In the next step, those challenges are further analyzed using scientific literature. In a final step, the customer needs are ranked according to their impact on the customer's profitability.



Subsequently, the *minimum requirements* for the new feed additive are derived. For phytogenic feed additives, this might be, for instance, something like “Improving animal performance and reducing antibiotic use while increasing profitability”. The selected key performance parameters might be, for example, feed efficiency improvements in broilers.





Market research

## Meeting unmet needs

Once the customer needs have been understood, the next phase of the development starts. Based on the intended mode of action, certain phytomolecules are chosen based on their described properties. In our example, this might be an antimicrobial mode of action that targets enteropathogenic bacteria in broilers, supporting gut health.



Laboratory research

In this *in-vitro* process, the selected individual compounds will be tested for their respective antimicrobial efficacy using MIC and MBC testing. Those tests are run using high-purity compounds.



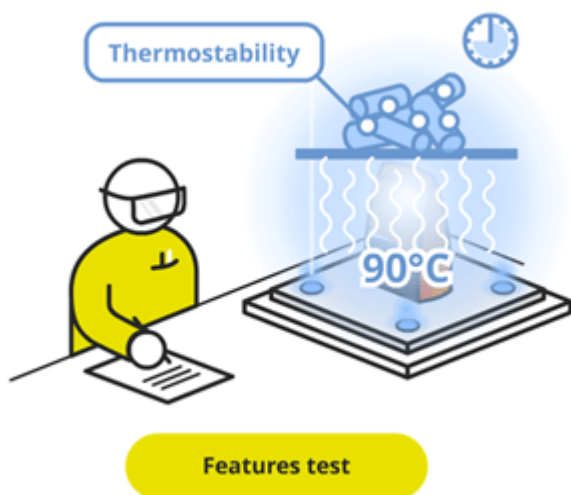
Features test

The tests will be conducted using various relevant field strains like *E. Coli*, *S. enterica* or *C. perfringens*. In the next step, the testing will be repeated with commercially available ingredients. The most promising compounds will be tested in more complex mixtures.

Modern phytogetic feed additives are based on the concept of combining different phytochemicals to attack bacteria in diverse ways, with their antimicrobial effects being multi-modal. This mode of action is crucial because it makes it very unlikely that bacteria can develop resistance to combinations of phytochemicals, as they do to antibiotics.

## Selecting the right form of application

Feed processing is often a challenge for additives. Many phytochemicals are highly volatile and prone to volatilization and high temperatures. Especially non-protected phytogetic products are negatively affected by high pelleting temperatures and long retention times of the feed in the conditioner. The results are losses in activity.



Therefore, the [development of appropriate delivery systems](#) is a preemptive method to ensure the release of the effective compounds where they should be released – in the gut of the animals. Those delivery systems can utilize emulsifiers when applying the additive via the water for drinking, or encapsulation technologies when the new additive is administered via feed.

Due to the importance of mixability, flowability, and pelleting stability for the performance of the feed additives, the exact types of emulsifiers, carrier, and technologies used in their production is often considered corporate intellectual property.

## The importance of *in-vivo* evaluations

In one of the last steps of the development, the newly developed feed additive prototype needs to prove its safety and efficacy in the animal. Hence the need to run evaluation studies to confirm the mode of action chosen in the initial lab phase. Typically, the additive will be tested in the target species in in-house and external research institutes.



Farm test

For a phytogenic feed additive, that might entail comparing its effect on body weight gain, feed efficacy, and gut health against different control groups. Additionally, the newly developed feed additive might be compared to existing additives to get a better understanding of its capabilities.



Safety test

Dose-finding studies are conducted to verify the chosen dose recommendation and additional overdosing studies are conducted to prove the safety of the additive for both animals and consumers. In certain markets or regulatory environments, additional studies might be required. Those can contain environmental safety assessments or proof that the new additive does not create residues in animal products.

## Case study: Ventar D

For Ventar D, the process followed these steps meticulously, in agile iterative development loops that went from the customer need to formulation, testing, scale-up, in-house and external trials, and finally production.

These steps ensured that the final product that reaches the customer's doorstep [delivers on the expectations – and more](#).



Scale-up & Distribution

## Choose your phytogenic products wisely

The plethora of (phytogenic) feed additives in the market leaves producers with many options to choose from. However, only scientifically developed feed additives can be relied upon to optimize both animal health and production profitability. It is important to select reliable feed additive producers who developed their phytogenic product with the customers' challenges in mind and went through all the steps necessary to create a high-performing and safe additive.