## The big challenge: Keeping sows healthy and productive - Part 2 Nutritional interventions -Phytomolecules



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The first of the two articles focused on general aspects to be observed to achieve a particular stock of healthy and well-performing sows, as well as high productivity on the farm. In addition to general measures, feed supplements can be used to further support the sows. Phytomolecules with characteristics supporting gut and overall health are effective for this purpose.

## Phytomolecules - how can they help?

Phytogenics, also known as phytomolecules, are plant-derived, natural bioactive compounds that promote livestock health and well-being, as well as improve growth performance and production efficiency. Phytomolecules encompass a diverse range of compounds, including terpenes, phenols, glycosides, saccharides, aldehydes, esters, and alcohols.

The literature describes some of their effects, including stimulation of digestive secretions, immune stimulation and anti-inflammatory activity, intestinal microflora modulation, and antioxidant effects

(Durmic and Blanche, 2012; Ehrlinger, 2007; Zhao et al., 2023), as well as estrogenic and hyperprolactinemic properties (Farmer, 2018) and effects on colostrum and milk porcine sensory profiles (Val-Laillet et al., 2018). They represent exciting antibiotic alternatives in swine production (Omonijo et al., 2018).

## **1. Phytomolecules modulate intestinal** microbiota

Phytomolecules are microbiome modulators through different mechanisms. They can directly impact pathogenic bacteria by damaging the cell membrane, cell wall, or cytoplasm, interrupting the anion exchange, resulting in changes to cellular pH, and inhibiting the cell's energy production system. Additionally, phytomolecules interfere with the virulence capacity of pathogenic bacteria through the indirect quorum quenching mechanism. (Rutherford and Bassler, 2012).

The favorable consequence of this differential microbial modulation is maintaining gut microbiome diversity, shifting it to a bacterial population with reduced pathogenic and increased beneficial microbes.

### Proof of Ventar D's pathogen-inhibiting effect

An in vitro study evaluated the effect of Ventar D on pathogenic *Clostridium perfringens* and beneficial *Lactobacillus spp*.

#### Process

To test the effect of Ventar D on four different beneficial *Lactobacillus spp.*, and pathogenic *Clostridium perfringens*, the phytogenic formulation (Ventar D) was added to the respective culture medium in the following concentrations:  $0 \mu g/mL$  – control, 500  $\mu g/mL$  (only *C. perfr.*), 750  $\mu g/mL$ , 1000 mg/mL (only *C. perfr.*), and 1250  $\mu g/mL$ .

After cultivating the bacteria in the culture medium, the colony-forming units (CFU) were counted.

#### **Results and discussion**

The study demonstrated a dose-dependent decrease in the Clostridium perfringens population. At the lowest tested concentration (500  $\mu$ g/mL), Ventar D's antimicrobial effect was already detectable; at 750  $\mu$ g/mL, scarce colonies were observed; and at 1000  $\mu$ g/mL, *C. perfringens* could no longer grow.



Figure 1: Effect of Ventar D on Clostridium perfringens

In contrast, even at higher concentrations of Ventar D, the beneficial *L. agilis* S73 and *L. agilis* S1 populations were only mildly affected, and *L. casei* and *L. plantarum* were unaffected.



Figure 2: Effect of Ventar D on Lactobacillus spp.

These findings confirm the differential antimicrobial activity of Ventar D's formulation, specifically a bactericidal effect on pathogenic C. perfringens populations and a mild to no inhibition of beneficial *Lactobacillus spp*.

## 2. Phytomolecules improve intestinal integrity

The gut barrier is semipermeable and is responsible for immune sensing and regulating the movement of nutrients and undesirable microbes and substances.

The "gatekeepers" are tight junctions (TJ), adherent junctions (AJ), and desmosomes situated between the intestinal enteric cells (IEC). The tight junctions regulate the transport of small molecules and ions. The adherent junctions and desmosomes maintain the integrity of the intestinal barrier by keeping the IECs together through cell-adhesion bonds.

Oxidative stress resulting from factors such as heat stress or fat oxidation in the feed, as well as dysbacteriosis caused by changes in diet, out-of-feed events, poor dietary formulation, or bacterial contamination, can compromise the integrity of these critical adhesions and junctions between enterocytes.

The support of these tight junctions prevents bacteria and toxins from passing into the organism. Besides reducing disease occurrence, it also reduces the activation of the immune system and inflammatory processes. Ingested nutrients can be used for growth and need not be spent for the defense of the organism.

#### **Proof of Ventar D's gut barrier-stabilizing effect**

An experiment was conducted to determine the level of tight junction gene expression biomarkers closely related to gut integrity.

#### Process

The experiment was conducted in broilers. They were fed 100 g of Ventar D/ t of feed, and the gene expression of Claudin and Occludin was measured (the higher the gene expression, the higher the level of gut barrier damage).



Figure 3: Effect of Ventar D on gut barrier function

#### Results

The lower levels of both gut tight junction gene expression biomarkers, Claudin and Occludin, in Ventar Dsupplemented birds support a lower level of damage and a more robust gut barrier function (Figure 3).

## 3. Phytomolecules act as antioxidants

As mentioned, oxidative stress can disrupt gut barrier function and negatively impact the health of sows and piglets. Therefore, it is vital to scavenge reactive oxygen species (ROS) to reduce the damage these free radicals can cause to enterocytes and tight junctions.

#### Proof of Ventar D's antioxidant effect in vitro

In this case, an in vitro trial was conducted to show Ventar D's antioxidant effects.

#### Process

Ventar D's antioxidant activity was tested in vitro using the ORAC (Oxygen Radical Absorbent Capacity) test. The ORAC test measures the antioxidant activity of a compound compared to that of the Vitamin E analog Trolox.

#### Result

The components in Ventar D demonstrated its capacity as an antioxidant, with a more substantial effect than the Vitamin E analog Trolox (see Figure 4).



Figure 4: Antioxidant capacity of Ventar D compared to Vit. E analogue (AUC – Area under curve)

## 4. Phytomolecules decrease inflammation

In intensive production, animals face daily inflammation associated with various stressors, including gut incidents and intestinal dysbiosis, social hierarchy-associated fighting resulting in musculoskeletal or skin injuries, farrowing and lactation trauma to reproductive organs, and diseases affecting any system in the pig.

Animals with high-performance expectations, such as gestating, farrowing, and lactating sows, are particularly susceptible to high nutrient diversion, which can lead to inflammation and activation of the immune system. To mitigate the excessive continuation of inflammatory processes, phytomolecules with anti-inflammatory effects can be utilized.

#### Proof of Ventar D's anti-inflammatory effect in vitro

The anti-inflammatory effect of Ventar D was shown in an in vitro trial conducted in the Netherlands.

#### **Process**

For the trial, cells from mice (Murine macrophages, RAW264.7) were stressed with lipopolysaccharides (LPS, Endotoxin) from E. coli O111:B4 (0.25  $\mu$ g/ml) to provoke an immune response. To evaluate the effects of Ventar D, two different concentrations (50 and 200 ppm) were tested, and the levels of NF- $\kappa$ B, IL-6, and IL-10 were determined. IL-6 and IL-10 could be measured directly using specific ELISA kits, whereas, in the case of NF- $\kappa$ B activity, an enzyme induced by NF- $\kappa$ B (secreted embryonic alkaline phosphatase – SEAP) was used for measurement. The trial design was as follows (Figure 5):

## **Trial design**





#### Results

The trial results showed a dose-dependent reduction of NF- $\kappa$ B activity in LPS-stimulated mouse cells, with 11% and 54% reductions at 50 and 200 ppm Ventar D, respectively. The pro-inflammatory cytokine IL-6 was downregulated, and the anti-inflammatory cytokine IL-10 was upregulated by 84% and 20%, respectively, resulting in a decrease in the IL-6 to IL-10 ratio. This ratio is essential in balancing the pro-and anti-inflammatory outcomes of cellular signaling.



Figure 6: Activity of NFkB



Figure 7: IL-6/IL-10 ratio

## **5. Phytomolecules improve production performance and efficiency**

The intensive production systems of today encompass many factors that create stress in the animals. Phytomolecules exhibiting the positive characteristics mentioned in points 1 to 4 result in better performance in animals.

In pigs in suboptimal conditions, the antimicrobial effect of phytomolecules is the most important. However, in pigs held under optimal conditions and with extraordinary growth, the antioxidant and antiinflammatory effects are most relevant. Anabolic processes, driven by strong growth, increase oxidative stress, while non-infectious inflammations burden the immune system.

#### Proof of Ventar D's performance-promoting effect in pigs

To evaluate growth-promoting effects in pigs, a study was conducted on a commercial farm in the United States.

#### Process

A total of 532 approx. 24-day-old weaned piglets were housed in 28 pens, each containing 19 noncastrated males or gilts. Piglets were blocked by body weight and fed a three-phase feeding program (Table 1). Phase 1 and 2 diets were pellets, and phase 3 was mash. Diets were based on corn and soybeans, and a concentrate including soy protein concentrate, whey permeate, and fish meal was added in phases 1 and 2, at a ratio of 50% of the total feed in phase 1 and 25% in phase 2. No feed medication was used in this trial.

Trial groups	Feeding Phase 1 (day1 - day 14)	Feeding Phase 2 (day 15 - day 24)	Feeding Phase 3
Control	No additive	No additive	No additive
Ventar D	Ventar D 200 g/MT	Ventar D 200 g/MT	Ventar D 200 g/MT

Table 1: Feeding scheme and product application

#### Results

Adding Ventar D increased final body weight and improved FCR (see Figures 8 to 10). Furthermore, the addition of Ventar D to the feed reduced mortality.





Figures 8-10: Performance of piglets fed Ventar D in comparison to a negative control

# Phytomolecules can help to keep sows healthy and productive

Intensive animal production places a significant strain on animal organisms. High stocking density often accompanies high pathogenic pressure and stress, and high growth performance can lead to increased oxidative stress and inflammation. It isn't easy to keep all challenges under control. However, phytomolecules can be a solution as their modes of action cover different relevant topics.

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