

# Phylogenics can positively influence the efficacy of antibiotics



Many veterinary antibiotics are applied via the waterline, [where they are dosed in combination with other feed additives](#). Amongst those are mixtures of secondary plant compounds with a proven antimicrobial efficacy against veterinary pathogenic bacteria. However, little research has been done to evaluate any effect that antibiotics and phylogenics may have on each other. A possible influence of phylogenics on the efficacy of antibiotics through the combined administration would require a change in application recommendations of antibiotics and phylogenetic feed additives. In the case of no interaction, no changes would be necessary. If they were to interact in a positive way, the dosages could be lowered and if they interact in a negative way, a combined application would be avoided.

## Antibiotics and SPC's in co-incubation

There are different groups of antibiotics depending on the chemical structure and on the pathogen they target. Some impair the cell wall or the cytoplasmic membrane (polymyxins,  $\beta$ -lactam antibiotics) and some affect protein synthesis (macrolides, Chloramphenicol, Lincospectin, tetracyclines, aminoglycosides). Others compromise DNA and RNA synthesis (fluorchinolones, ansamycines) and some disturb the metabolism of e.g. folic acid (Trimethoprim).

The intention of a trial with these different groups of antibiotics was to evaluate possible interactions they may have with a combination of secondary plant compounds. Four ESBL producing *E. coli* field isolates from poultry flocks were experimentally assessed as well as a  $\beta$ -lactamase positive and a  $\beta$ -lactamase negative reference strain as quality control strains for antimicrobial susceptibility testing.

Two-fold serial dilutions of antibiotics and the liquid product based on secondary plant compounds were co-incubated in a checkerboard assay. The highest concentration of the antibiotic was chosen according to CLSI standard recommendations. The control of the serial dilution of SPC's was made without antibiotics and vice versa.

## Lowering the antibiotic dosage by the use of SPC's

In the experiment all field isolates proved resistant against the  $\beta$ -lactam antibiotics, two field isolates and one reference strain were resistant against tetracyclines and macrolides and one field isolate and one reference

strain against aminoglycides.

The results showed that there was no negative influence of the antibiotics on the SPC's and vice versa. Moreover, for several classes of antibiotics an additive to synergistic effect was observed to such an extent that an antibiotic effect could be achieved with half or even one quarter of the former effective dosage. The dosage of the SPC-mixture could also be reduced. Based on the results of this *in vitro* experiment it can be stated that in the case of antibiotic resistance, the option exists to apply a phytogenic product with broad antimicrobial efficacy. Even more, for most combinations between antibiotics and [Activo Liquid](#), a defined mixture of secondary plant compounds, their combined use potentiates the individual efficacy of either compound class against *E.coli* strains *in vitro*. This adds further benefits to the improvements in animal performance and health, for which a number of [phytogenic feed additives have already proven effective](#).

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## Using egg immunoglobulins to enhance piglet survival



**The number of healthy piglets weaned is the most important factor for the calculation of profit in piglet production.**

Losses in the farrowing unit normally occur during the first seven days of life as piglets are born with very little protection in the form of immunity. The intake of immunoglobulins from colostrum is therefore of vital importance. Besides cleanliness and special feeding, piglets can be additionally supported by two strategies that mimick the effect of colostrum:

- a direct one, meaning the feeding of immunoglobulins (IgY from eggs) to piglets that would support the

immune system in the gut or

- an indirect one, meaning a supply of IgY to the sow to keep the pathogenic pressure in the farrowing unit as low as possible.

### **Piglets are born with no immune protection and very low energy reserves**

It is well known that piglets are physiologically immature at birth. Their energy reserves are very low with only 1 – 2% body fat comprising mainly of structural and subcutaneous fat. Therefore, in the first hours of life they rely on the glucose supply from glycogen from the liver as their main energy source. However, this will only cover their needs for a few hours.

Due to the construction of the sow's placenta, a transfer of immunoglobulins (antibodies) within the uterus is not possible. This means that piglets are born with practically no immune protection and depend on the immediate intake of immunoglobulins from colostrum. The immunoglobulins can be absorbed in the [gastrointestinal tract](#) and immediately transferred into the bloodstream – but also only for a short time. The absorption ability of the piglets starts to decrease soon after birth and ends after 24 to 36 hours.

### **Strategy 1: Making the farrowing unit as safe as possible**

The piglets' environment should be warm to prevent hypoglycaemia. Piglets looking for heat close to the sow can also get crushed. Since the temperature needs of the sow and piglets are different, a piglet nest with a special heat lamp is recommended. Furthermore, the farrowing unit should be clean. Due to their low immune status, piglets are susceptible to common pathogens such as *E. coli*, *Clostridium perfringens*, and rotavirus that can all lead to diarrhoea.

Most pathogens can be traced to those found in the sow's faeces. To keep this amount as low as possible, different measures can be taken:

- A vaccination increases the immune defences of the sow. The antibodies fight against the pathogens so that less "functioning" pathogens are excreted.
- Feeding of probiotics increases the number of good bacteria like Lactobacilli and Bifidobacteria competing with the pathogens for binding sites and nutrients.
- Administration of [egg immunoglobulins](#), which bind to the pathogens within the gastrointestinal tract and make them harmless. These pathogen-immunoglobulin-complexes can be ingested by the piglets without any danger.

### **Strategy 2: Supporting the piglets with immunoglobulins**

The aim here is to strengthen the local [immunity in the gastrointestinal](#) tract by increasing the amount of immunoglobulins (Ig). As already mentioned, the intake of sow colostrum is of vital importance. With the vaccination of the sow, the content of antibodies in the colostrum can even be enhanced.

An additional measure would be to orally supply the piglets with egg immunoglobulins (IgY). Both classes of immunoglobulins (IgG from mammals, and IgY from birds) can bind to pathogens in the gut, preventing them from binding to the intestinal wall and reducing the incidence of diarrhoea. The difference is in the degree of effectiveness and specificity.

### **Conclusion**

To maximize the number of piglets weaned, it is necessary to support their immune system during the first days of life. Besides good hygiene management, the administration of [egg antibodies to the sow](#) will also help reduce the amount of shed pathogens keeping the pathogenic pressure low. The application of egg antibodies directly to the piglets supports their immune system by binding the pathogens in the gut, minimizing the risk of diarrhoea.

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# **A powerful alternative to**

# antibiotics for Aquaculture



Global aquaculture has grown dramatically and shrimp cultivation areas, in particular, have expanded. Unfortunately, the shrimp industry, in particular, faces major problems with bacterial diseases. One of the most important diseases in shrimp is vibriosis. Mortality rates of up to 100 % are possible, so economic losses can be devastating.

## **Characteristics of vibriosis**

Vibriosis generally occurs in all life stages, but mainly in hatcheries. Vibrios are found as normal flora in the hepatopancreas of the healthy crustacean. They can turn from tolerated to pathogenic, if environmental conditions are compromised: e.g. over / underfeeding, overcrowding or decreased levels of oxygen.

The animals can be infected orally, through wounds in the exoskeleton or pores, the gills or the midgut. There are different expressions of the disease depending on which parts of the animal are affected (e.g. appendage and cuticular vibriosis).

## **Negative effects on the ecology**

As antibiotics for shrimps are applied orally together with the feed, not all of them reach their target. An estimated 15-40 % are not ingested due to feeding falling to the bottom. A fraction of the ingested antibiotics is also not absorbed in the body and is excreted. All of these antibiotics stay in the water or sink to the bottom. The number of antibiotics that remain in the water or sediment varies from 1 % (chloramphenicol) up to 90 % (Oxytetracycline).

It is estimated that 70-90 % of antibiotics used in the therapy of farmed organisms end up in the environment and sediment and lead to the development of antibiotic resistance.

## **Secondary Plant Compounds (SPCs) - a good tool to reduce the use of antibiotics?**

SPCs and their components are able to slow down or prevent the growth of molds, viruses, and bacteria. They impair them by acting at different parts/mechanisms of the cells (e.g. cell membrane, transport systems, cell contents, flagella development, quorum sensing...). The best-explained mode of action is one of thymol and carvacrol extracted from thyme and oregano. These substances are able to penetrate the bacterial membrane and disrupt its integrity causing loss of ions or energy equivalents.

Several trials conducted show the high efficacy of secondary plant compounds in aquaculture.

## 1. Scientific Trial (Kasetsart University, Thailand)

### Design

a) 4 groups (6 replicates each) of White Leg Shrimp (*L. vannamei*) were housed in 100 L aquaria with 10 animals each.

**Control:** Standard feed, no additive

AB-Group: Standard feed + 10 ppm Enrofloxacin

**Activo Group 1:** Standard feed + 100 g Activo/t of feed

**Activo Group 2:** Standard feed + 200 g Activo/t of feed

Evaluation of mortality and specific growth

a) End of the feeding trial: stressing of the shrimp (high water temperature, 33°C for 1 hour), then challenge with *Vibrio parahaemolyticus* ( $7,6 \times 10^6$  cfu/ml) by subcutaneous injection.

Evaluation of mortality

a) Survival rates in the AB-Group (93,3 %) and in the Activo Group 2 (90,0 %) were similar. The specific growth rate of the AB-Group (2,32 %/day) and the Activo Group 2 (2,22 %/day) were higher than the control (1,94 %/day). The Activo Group 1 (2,18 %/day) ranged performance-wise between the control and AB-Group.

b) After the challenge, mortality in the control group (43,3%) was approximately twice as high as in the AB-Group (20 %) and in the two Activo groups (both 23,3%).

## 2. Field Trial (Shrimp farm Ecuador)

### Design

Two ponds with 80.000 shrimps/ha

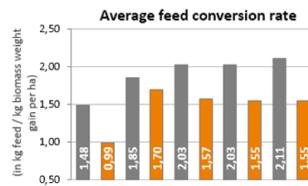
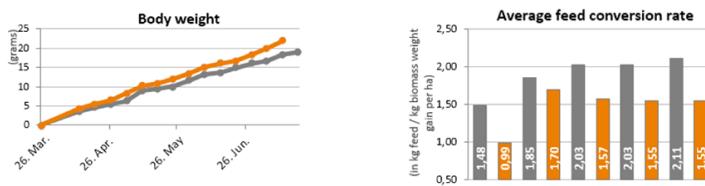
**Control** (3 ha): standard feed

**Activo Aqua Group** (5 ha): standard feed + 2 kg Activo Aqua (Activo upgraded by immune system stimulating- mannan-oligosaccharides) /t of feed on top

Evaluation of average shrimp weight at regular intervals

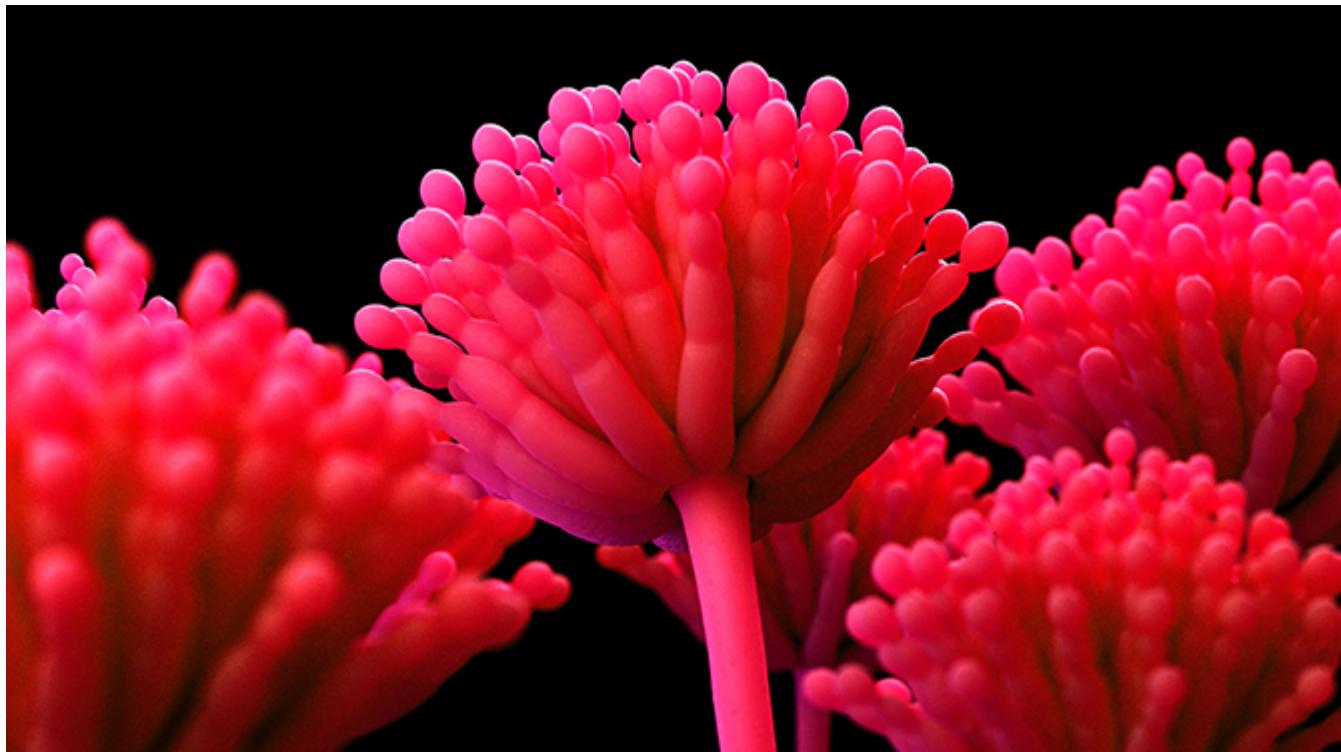
### Results

Activo Aqua Group showed a consistently better development of body weight compared to the control, resulting in a shorter cultivation period until harvesting (112 compared to 123) and therefore a higher turnover of animals. Feed conversion in the Activo Aqua group was better in every growth stage.



**Both trials present secondary plant compounds as a good alternative to antibiotic growth promoters. In the case of disease, they decrease mortality. Under standard conditions, the improved development shortens time to harvest and increases the turnover. The improved feed conversion lowers feeding costs.**

# Using milk thistle to reduce liver damage from mycotoxins



**Mycotoxins not only reduce animal performance, but they also cause significant liver damage.**

**The seeds of the herb plant milk thistle contain a mixture of flavonolignans known as [silymarin](#) and can help in [reducing liver damage](#) when animals get in contact with mycotoxin contaminated feed.**

Mycotoxins are a constant problem in cereals causing economic losses to the global animal industry. Mycotoxins are produced by filamentous fungi varying widely in their chemical and biological characteristics and effects on animals. Among the various mycotoxins, aflatoxins, and more specifically aflatoxin B1, is one of the most problematic because it affects maize, one of the major staple ingredients in animal diets worldwide. Of course, in nature, mycotoxins mostly occur in combinations, but even with singly contaminated ingredients, the nature of animal feeds leads to the concurrent presence of multiple mycotoxins, coming from the different ingredients. The separation of mycotoxins in polar and non-polar, however, simplifies their management. For example, aflatoxins (polar) are easily addressed by the inclusion of an adsorbent (like bentonite, for example). The same ingredient adsorbs not only aflatoxins, but also other mycotoxins, like zearalenone, ochratoxin A, and T-2 toxin, albeit at reduced efficiency.

## **Products limited to work in gut**

Certainly, anti-mycotoxin agents are effective only while the feed is being

digested, that is, while the feed remains in the lumen of the [gastrointestinal tract](#). Anti-mycotoxin agents are not absorbed by the animal, whereas non-adsorbed mycotoxins are; leading to the need for further detoxification within the organism. Parts of mycotoxins might enter the organism despite the use of an anti-mycotoxin agent in feed due to the fact that no product is 100% effective, not all mycotoxins are affected similarly by a single product, non-polar mycotoxins might not be inactivated if only a polar agent is used, and vice versa and lastly, high contamination might render the normal dosage inadequate. This is often seen as being the most common cause, In other words, part of mycotoxins in the feed can still enter the animal. The exact effects on animal health and performance will depend, of course, on the initial contamination levels in the feed and on the constitution of the liver.

### **Mycotoxins and liver damage**

Even short-term exposure to mycotoxins suffices to cause significant liver damage and loss of performance. In a study (Meissonnier, 2007), pigs were given 385, 867, or 1807 µg aflatoxin B1/kg feed for four weeks. Pigs receiving the highest level of aflatoxin developed clear signs of aflatoxicosis: hepatic dysfunction and decrease in weight gain. Also, the pigs exposed to the lower levels of mycotoxins showed clear signs of impaired metabolism and biotransformation. Additionally, mycotoxins and particularly aflatoxins inhibit the major hepatic biotransformation enzymes. This has significant consequences in veterinary medication applications as animals become unable to clear medications from their system – and of course, other toxins.

Read [Using milk thistle to reduce liver damage from mycotoxins](#) the full article  
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