

# Phytogenics 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 phytogenics may have on each other. A possible influence of phytogenics on the efficacy of antibiotics through the combined administration would require a change in application recommendations of antibiotics and phytogenic 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 (fluorquinolones, 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 aminoglycosides.

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 phytogetic 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 [phytogetic feed additives have already proven effective](#).

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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

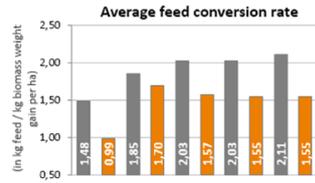
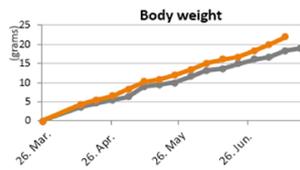
**Control** (3 ha): standard feed

**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.**