

Newsletter

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> EDITORIAL

In January 2012 BIOMIN finalized the takeover and integration of the German-based Phytogenics and feed flavorings company MICRO-PLUS. This acquisition adds to our proven expertise in Phytogenics an additional 27 years of know-how, along with an experienced team of professionals working to provide the best possible solutions for our customers. Building on the existing strengths of the two companies, BIOMIN is setting the pace in the field of Phytogenics. BIOMIN's strong research and development comes together with the broad knowhow in functional plant ingredients, classical aromas and sweeteners. In addition, BIOMIN's global network will allow better access to market and an extended technical support for Phytogenics to customers worldwide. MICRO-PLUS was founded in 1984 in Holzminden, Lower Saxony, and has a long-standing expertise in the development of sensory feed ingredients, i.e. classical aromas and feed flavorings. Focusing on this product segment in the 1980s, the company's focus was extended towards phytogenic feed additives with the development of the first Digestarom® products in the 1990s. Today, the brand of Digestarom® is regarded as a pioneer product in phytogenic feed additives. BIOMIN has now two strong phytogenic product lines, i.e. Biomin® P.E.P. and Digestarom®. In order to bundle this expertise and facilitate the global communication of the Phytogenics portfolio, these product lines will be merged into one. Digestarom® will then be the global umbrella brand, standing for expertise in Phytogenics, as well as for proven and effective products. Digestarom® does not only provide a portfolio of new, effective products, but also adds to our knowledge in understanding how our phytogenic additives work. Recent research results are presented in this newsletter, highlighting significant improvements in digestibility and anti-inflammatory mechanisms supporting proper digestion on the genetic level.



Tobias Steiner & Ahmed Aufy



Digestarom® product line

Kingdom Plantae is such an impressive kingdom, not only because of its incredible biodiversity, but also because of the secrets that each leaf on a single plant carries. Day after day, we discover that animal feed materials originating from plants contain the solutions for many expected or unexpected challenges in commercial farming.

Phytogenic feed additives (PFAs) are a group of plant-derived substances which have been used to an increasing extent under the pressure of banning antibiotic growth promoters (AGPs). The ban in AGPs becomes a worldwide trend where many countries outside the European Union are on their way to restrict or stop the use of AGPs in animal feed. Therefore, the importance of PFAs is supposed to further grow strongly in the years to come.

Phytogenic substances have been known and used for thousands of years. Every day, we are using herbs and spices as food flavorings. For more than 5000 years, Egyptians and Chinese were using these functional compounds in therapeutics and for other purposes as well.

Phytogenics – New Benefits of a Proven Approach

Understanding Phytogenics

Phytogenics exert pronounced flavoring properties, hence having an impact on the palatability of commercial diets. Moreover, their secondary metabolites, such as bitter or pungent substances, saponins, essential oils, alkaloids or flavonoids, are considered the plants' secrets holders. The effects and economic impact of PFAs under commercial

conditions, where consistent improvements in feed intake, growth rate and feed conversion were reported, confirm positive results from an ever growing number of scientific publications.

In fact, the effectiveness of plant active ingredients has often been underestimated in recent years and not seldom their mode of action is misunderstood even by companies offering such products. It is often postulated that PFAs are antimicrobial. In deed many secondary plant ingredients and extracts do have such properties. The *in vitro* antimicrobial activity of plant active ingredients is well documented through scientific findings and plants themselves can respond to bacterial or viral attack for example by producing “phytoalexins”. However, it would be inappropriate to limit the value of phytogetic substances to an antimicrobial effect only. The complexity of plant secondary metabolites has far more to offer: Stimulation of saliva and gastric juices, support of liver function, anti-inflammatory and anti-oxidant effects are among those properties that are highly important for *in vivo* efficacy of PFAs, as recent research shows.

Formulating phytogetic feed additives

The fine art of formulating PFAs lies in a suitable combination of the right plant materials. This requires a deep understanding of the flavoring properties, as well as the biological effects of plant compounds in the animal organism. Only the combination of different plant materials, including e.g. herbs and spices in complete and finely ground form, essential oils and non-volatile extracts allows for making use of the full potential that plants offer. An interaction of all constituents working harmoniously together makes a well-formulated PFA more potent than the sum of its individual parts. In this context, PFAs must be clearly distinguished from products based solely on nature-identical compounds.

The importance of flavor

A very important property of PFAs is their influence on feed flavor, particularly in young animals. Perception of flavor is a complex physiological response. It is a combination of taste, which stimulates receptors in the mouth, and odor or aroma, which stimulates receptors in the nasal cavity. To be perceived as aroma, molecules must be volatile, but both volatile and non-volatile molecules may have a taste. There are several types of flavor which can be added to feed to enhance or mask the natural flavor characteristics of feed and thus improve palatability. However, there are differences between animal species. The susceptibility to taste, for example, differs depending on the number of taste buds (Table 1).

Table 1. Susceptibility of different animals to taste

Animal	No. of taste buds
Chicken	24
Bat	800
Dog	1'700
Human	9'000
Pig	15'000
Goat	15'000
Rabbit	17'000
Cattle	25'000
Catfish	100'000

A versatile mode of action

Phytogetic compounds have a versatile mode of action, which had been a big myth for those who used these substances as additives in animal feed. Therefore, a major objective of research and development in the last few years was to understand the role of PFAs in improving animal performance (Hippenstiehl *et al.*, 2011; Windisch *et al.*, 2008). However, the vast number of phytogetic compounds and the differences in composition of PFAs makes it impossible to postulate a general mode of action that is applicable to all commercial PFAs in the market.

Improving digestibility – optimizing efficiency

Recently, more scientific data was generated, which enables us to put the right blocks together and understand better how our phytogetic additives contribute to productivity in animal production. An improvement in digestibility is a main effect ultimately leading to better growth performance and feed efficiency. Such improvements were reported for proximate nutrients and amino acids in pigs (e.g. Maenner *et al.*, 2011, Figure 1) and poultry (e.g. Mountzouris *et al.*, 2011).

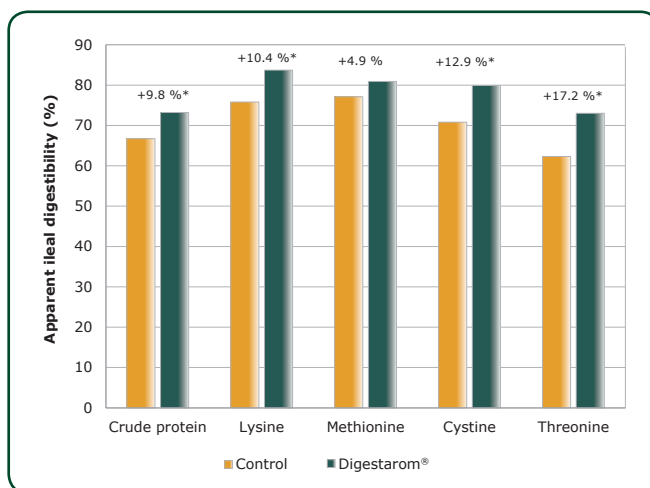


Figure 1. Digestarom® increases ileal digestibility (meta-analysis of 2 trials with weaning piglets; Maenner *et al.*, 2011)

Improved digestibility is a consequence of different effects:

- Stimulated gastric and intestinal secretions
- Optimization of the intestinal microbiota
- Reduction of microbial toxic metabolites in the intestine
- Relief from immune stress, including a reduction in sub-clinical intestinal inflammation processes

Phytogenics can inhibit cellular inflammation

Recent scientific work points out that a potent anti-inflammatory efficacy plays a major role in the mode of action of Digestarom®. Experts in livestock production are aware of the importance of controlling subclinical intestinal inflammation processes in the herd or flock because of the losses that occur due to this incidence. As such, anti-inflammatory effects of Digestarom® can largely contribute to animal performance. In order to understand how Digestarom® exerts its anti-inflammatory effect, we had to dig very deeply at sub-cellular level to elucidate the exact mechanisms involved. In an experiment carried out at the University of Gießen (Germany), the anti-inflammatory activity of Digestarom® was examined in a test model with inflammation-induced intestinal cells. The inflammation was induced by treating the cells with tumor necrosis factor α (TNF α). These cells were incubated or not with an extract of Digestarom®. The first element to study was the nuclear factor κ B (NF- κ B). This is a protein complex and a very important transcriptional factor that controls the expression of different genes [interleukin 8 (IL-8), intracellular adhesion molecule (ICAM-1) and monocyte chemoattractant protein 1 (MCP-1)] that are involved in the regulation of the pro-inflammatory response. The experiment revealed excellent inhibitory effects of Digestarom® on IL-8, ICAM-1 and MCP-1 (Figure 2). Thus, Digestarom® exerted a highly positive effect on the cellular inflammatory status by down regulation of NF- κ B.

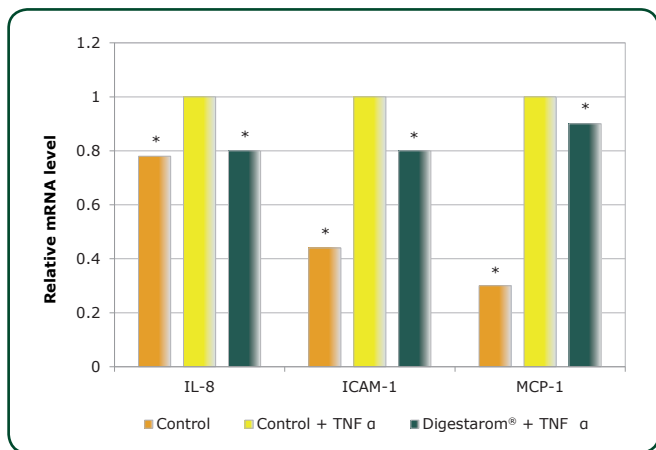


Figure 2. Intestinal protection: Anti-inflammatory effect of Digestarom® (down-regulation of NF- κ B target genes)

*Significant difference vs. induced inflammation (Control + TNF α) ($P < 0.05$)

Another very important cellular element is the transcription factor Nrf-2, which is responsible for anti-oxidative activity. Activation of the Nrf-2 pathway leads to the induction of genes responsible for cellular defense against reactive oxygen species and detoxification of xenobiotics. Nrf-2 is located in the cytoplasm in a protein complex. Digestarom® was found to up-regulate Nrf-2 target genes, i.e. cytochrome P450 isoform 1A1 (CYP1A1), heme oxygenase-1 (HO-1) and UDP glucuronosyltransferase isoform 1A1 (UGT1A1) (Figure 3).

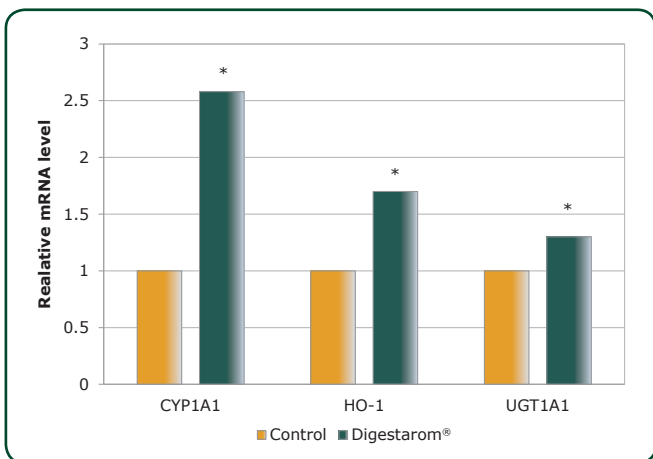


Figure 3. Intestinal protection: Anti-oxidative effect of Digestarom® (up-regulation of Nrf-2 target genes)

*Significant difference vs. Control ($P < 0.05$)

Regular supplementation of Digestarom® in the diet acts as a prophylactic against inflammatory reactions in the gastrointestinal tract by inhibiting the NF- κ B factor and stimulating the anti-oxidative factor Nrf-2. This activity interrupts the damaging circle of the release of inflammatory mediators that otherwise would provoke intensive inflammation and the resulting necrosis and performance depression (Syed, 2011).

Conclusion

The classical view of Phytogenics must be changed and specialists should regard these substances as necessity rather than additives. It is true that Phytogenics enhance digestibility and can represent very powerful alternatives to AGPs. However, if we focus all the time on only these effects, we will run forever in a closed circle.

Feed is not solely a source of protein, energy, minerals and vitamins; feed (plants) can offer very sophisticated solutions to critical challenges that animals undergo during their productive life. Digestarom® is a smart feed additive that can increase the value of the diet not only by making more protein and energy accessible to the animal, but also by decreasing the severity of intestinal inflammation.

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