

## **New Generation feed Additives**

Livestock populations are undergoing continuous selection to improve the economic efficiency of animal production. Livestock production itself is affected by a number of both external and internal factors that unequivocally include nutrition.

Probiotics are dietary supplements and live microorganisms containing potentially beneficial bacteria or yeasts. According to the currently adopted definition by FAO/WHO, probiotics are: 'Live microorganisms which when administered in adequate amounts confer a health benefit on the host'.

Lactic acid bacteria (LAB) are the most common type of microbes used. LAB have been used in the food industry for many years, because they are able to convert sugars (including lactose) and other carbohydrates into lactic acid. This not only provides the characteristic sour taste of fermented dairy foods such as yogurt, but also by lowering the pH may create fewer opportunities for spoilage organisms to grow, hence creating possible health benefits on preventing gastrointestinal infections. Strains of the genera *Lactobacillus* and *Bifidobacterium*, are the most widely used probiotic bacteria.

### **Non nutritive feed additives**

This class of feedstuffs include ingredients of a non nutritive nature that stimulate growth or other type of performance (such as egg production), improve the efficiency of feed utilisation or are beneficial to the health or metabolism of the animal. Examples of the additives include antibiotics, antibacterial agents, antifungal agents and hormones.

### **Phytogenic feed additives**

Phytogenic additives present a plausible alternative as they enhance a number of important processes in the animal body. Phytogenic feed additives may be included among supplements that are aimed to positively affect feed quality, health of animals as well as animal products by means of their specifically efficacious substances.

They can be classified into several groups:

- 1) Sensory additives (feed additives affecting the sensoric properties of animal products),
- 2) Technological additives (antioxidants, substances decreasing mycotoxin contamination of feeds, etc.),
- 3) Zootechnical additives (immunomodulators, digestive stimulants, growth promoters of non-microbial origin, substances increasing performance or quality of animal products, etc.), and nutritional additives (vitamins, minerals, plant enzymes, etc.).

Phytogenic additives are used mainly in the first three cases, however, a number of phytogenic additives have been demonstrated or are presumed to have more than one positive effect and cannot be strictly classified into the designated groups.

### **Sensory additives**

Traditional sensory additives include substances affecting food odour and palatability, and colourings. Phytogetic additives are commonly used as colourings in laying hens to affect the egg yolk colour. Laying hens cannot synthesize egg yolk pigments; yet, the egg yolk colour is one of the main indicators of egg quality affecting consumer's preference. Pigments of the egg yolk, xanthophylls, are dependent on fat soluble pigments that are present in the feed. The source of these pigments may be natural or synthetic colourings (ethyl ester of  $\beta$ -apo-8'-carotenoic acid and canthaxanthin known as Carophyll Yellow and Carophyll Red) that are more economical but also potentially dangerous to human health (the maximum dose of canthaxanthin should not exceed 8 mg/kg; at higher doses, minute crystal formation may occur in the retina by a reversible deposition process).

Natural colourings are preferred; the most frequently used ones include carotenoids, the source of which are carrot, *Chlorella* algae, marigold (*Tagetes erecta* L.), or lutein, however, natural carotenoids are unstable and their use is also limited by their price. Well known carotenoids include also taxan-thin, which is commonly added to fish feed to provide for a more attractive meat colour. Besides, this substance also has strong antioxidant effects (10× more effective than vitamin E); it is also a subject of recent studies for its effect against reactive oxygen species (ROS), or for its neuroprotective effect in subarachnoid haemorrhage.

### **Technological additives**

Phytogetic additives are newly studied also in terms of decreasing the production of harmful gases in pigs. In vitro study reported that adding 0.1% various additives (red ginseng barn powder, persimmon leaf powder, ginkgo leaf powder, and oregano lippia seed oil extract) during anaerobic incubation of swine faecal slurries for a period of 12 to 24 h led in all groups to a significant decrease ( $P < 0.05$ ) in propionate production, to higher production of volatile fatty acids ( $P < 0.05$ ), and, with the exception of the group with the addition of oregano, to higher pH. In the group with the addition of oregano, they noted in contrast a decrease of pH and different bacterial population (uncultured bacterium clone PF6641 and *Streptococcus lutetiensis* (CIP 106849T)), and the dangerous gases ammonia-nitrogen ( $\text{NH}_3\text{-N}$ ) and hydrogen sulfide ( $\text{H}_2\text{S}$ ) were not detected in this group; compared to control and other additives tested, they noted lower amounts of "odorous compounds", and recommended the use of this additive in the grower category of pigs. Various phytogetic substances or mixtures have the potential to reduce  $\text{CH}_4$  emissions from ruminants. Methane is the second most important greenhouse gas, and a large part of it originates in animal production. *Artemisiae annuae* extract and a herbal mixture (60 g/kg diet; *Dryopteris crassirhizoma* Nakai, *Astragalus membranaceus* (Fisch.) Bge., *Crataegus pinnatifida* Bge., *Mentha haplocalyx* Briq.) significantly ( $P < 0.05$ ) lowered the methane production.

### **Zootechnical additives**

Immunomodulators. One of the main aims of using phytogetic additives is their potential effect on the immune system. Important immunomodulators include oligosaccharides, in particular  $\beta$ -glucans. These substances are obtained mainly from fungi, Basidiomycetes and

yeast of the genus *Saccharomyces cerevisiae*; their effects are studied in a number of animal species, e.g. in cattle, sheep or pigs.

Beta-glucans can be found in plant components, too, traditionally in the aleuronic layer of barley and oat bran, or seaweed. Extraction of  $\beta$ -glucans from plant components is demanding not only financially; nevertheless, bamboo leaf extracts appear to be a new and promising source of  $\beta$ -glucans. The authors found mainly higher activity of CD8+ T lymphocytes, i.e. cells that are crucial for the immune response to a number of viral infections. Beta-glucans are present also in the cell walls of pathogenic fungi, and plants themselves (*Nicotiana benthamiana*) have recently started to be used for the production of the so called therapeutic antibodies attacking  $\beta$ -glucans, thus providing important protection against *Candida albicans*, *Aspergillus fumigatus*, or *Cryptococcus neoformans* in animal models.

### **Substances increasing production performance or animal product quality:**

In most European countries, the trend is to increase poultry meat consumption, where especially broiler meat is of satisfactory nutritive quality and acceptable to most consumers with respect to price and its organoleptic traits. Improvement of the nutritive quality of broiler meat as a functional product is the aim of many studies. A whole range of phytogetic additives have been studied in broiler chickens with the aim to enhance their growth performance, to achieve more effective feed utilization, or just to enhance meat quality.

Phytogetic feed additives are plant-derived products used in animal feeding to improve the performance of agricultural livestock. This appears to be strongly driven by the ban on most of the antibiotic feed additives within the European Union in 1999, a complete ban enforced in 2006, and ongoing discussions to restrict their use outside the European Union because of speculated risk for generating antibiotic resistance in pathogenic microbiota. In this context, phytogetic feed additives are discussed possibly to add to the set of non-antibiotic growth promoters, such as organic acids and probiotics, which are already well established in animal nutrition. Phytogetics, however, are a relatively new class of feed additives and our knowledge is still rather limited regarding their modes of action and aspects of their application. Further complications arise because phytogetic feed additives may vary widely with respect to botanical origin, processing, and composition. Most studies investigate blends of various active compounds and report the effects on production performance rather than the physiological impacts. In this context, the following provides an overview of recent knowledge on the use of phytogetic feed additives in piglet and poultry diets, possible modes of action, and safety implications.

### **General aspects of phytogetic feed additives**

Phytogetic feed additives (often also called phytoiotics or botanicals) are commonly defined as plant-derived compounds incorporated into diets to improve the productivity of livestock through amelioration of feed properties, promotion of the animals' production performance, and improving the quality of food derived from those animals. Although this definition is driven by the purpose of use, other terms are commonly used to classify the vast variety of

phytogenic compounds, mainly with respect to origin and processing, such as herbs (flowering, nonwoody, and nonpersistent plants), spices (herbs with an intensive smell or taste commonly added to human food), essential oils (volatile lipophilic compounds derived by cold expression or by steam or alcohol distillation), or oleoresins (extracts derived by nonaqueous solvents). Within phytogenic feed additives, the content of active substances in products may vary widely, depending on the plant part used (e.g., seeds, leaf, root, or bark), harvesting season, and geographical origin.

The use of feed additives is usually subject to restrictive regulations. In general, they are considered as products applied by the farmer to healthy animals for a nutritional purpose on a permanent basis (i.e., during the entire production period of the respective species and category), in contrast to veterinary drugs (applied for prophylaxis and therapy of diagnosed health problems under veterinarian control for a limited time period, partially associated with a waiting period). In the European Union, for example, feed additives need to demonstrate the identity and traceability of the entire commercial product, the efficacy of the claimed nutritional effects, including the absence of possible interactions with other feed additives, and the safety to the animal (e.g., tolerance), to the user (e.g., farmer, worker in feed mills), to the consumer of animal-derived products, and to the environment (for further details, refer

### **Antioxidative action of phytogenic feed additives**

Antioxidative properties are well described for herbs and spices. Among a variety of plants bearing antioxidative constituents, the volatile oils from the Labiatae family (mint plants) have been attracting the greatest interest, especially products from rosemary. Their antioxidative activity arises from phenolic terpenes, such as rosmarinic acid and rosmarol. Other Labiatae species with significant antioxidative properties are thyme and oregano, which contain large amounts of the monoterpenes thymol and carvacrol.

Plant species from the families of Zingiberaceae (e.g., ginger and curcuma) and Umbelliferae (e.g., anise and coriander), as well as plants rich in flavonoids (e.g., green tea) and anthocyanins (e.g., many fruits), are also described as exerting antioxidative properties. Furthermore, pepper (*Piper nigrum*), red pepper (*Capsicum annuum* L.), and chili (*Capsicum frutescens*) contain antioxidative components. In many of these plants, parts of the active substances are highly odorous or may taste hot or pungent, which may restrict their use for animal feeding purposes.

The antioxidant property of many phytogenic compounds may be assumed to contribute to protection of feed lipids from oxidative damage, such as the antioxidants usually added to diets (e.g.,  $\alpha$ -tocopheryl acetate or butylated hydroxytoluene). Although this aspect has not been explicitly investigated for piglet and poultry feeds, there is a wide practice of successfully using essential oils, especially those from the Labiatae plant family, as natural antioxidants in human food, as well as in the feed of companion animals.

The principal potential of feed additives from the Labiatae plant family containing herbal phenolic compounds to improve the oxidative stability of animal-derived products has been

demonstrated for poultry meat rabbit meat. Oxidative stability was also shown to be improved with other herbal products

### **Specific impact on dietary palatability and gut functions**

Phytogenic feed additives are often claimed to improve the flavor and palatability of feed, thus enhancing production performance. However, the number of studies having tested the specific effect of phytogenic products on palatability by applying a choice-feeding design is quite limited. They show dose-related depressions of palatability in pigs fed essential oils from fennel and caraway, as well as from the herbs thyme and oregano. On the other hand, there are numerous reports on improved feed intake through phytogenic feed additives in swine (see the subsequent section on growth-promoting efficiency).

### **Antimicrobial actions**

Herbs and spices are well known to exert antimicrobial actions in vitro against important pathogens, including fungi. The active substances are largely the same as mentioned previously for antioxidative properties, with phenolic compounds being the principal active components. Again, the plant family of Labiatae has received the greatest interest, with thyme, oregano, and sage as the most popular representatives. The antimicrobial mode of action is considered to arise mainly from the potential of the hydrophobic essential oils to intrude into the bacterial cell membrane, disintegrate membrane structures, and cause ion leakage.

High antibacterial activities are also reported from a variety of nonphenolic substances, for example, limonene and compounds from *Sanguinaria Canadensis*. Microbiological analysis of minimum inhibitory concentrations (MIC) of plant extracts from spices and herbs, as well as of pure active substances, revealed levels that considerably exceeded the dietary doses when used as phytogenic feed additives. This may indicate that the antimicrobial action of phytogenics should not contribute significantly to the overall efficacy of this class of feed additives. On the other hand, some studies with broilers demonstrated in vivo antimicrobial efficacy of essential oils against *Escherichia coli* and *Clostridium perfringens*

Another implication of the antimicrobial action of another implication of the antimicrobial action of phytogenic feed additives may be improving the microbial hygiene of carcasses. Indeed, there are isolated reports on the beneficial effects of essential oils from oregano on the microbial load of total viable bacteria, as well as of specific pathogens (e.g., *Salmonella*) on broiler carcasses. However, available data are still too limited to allow reliable conclusions on the possible efficacy of certain phytogenic feed additives to improve carcass hygiene.

### **Growth-promoting efficacy**

In recent years, phytogenic feed additives have attracted increasing interest as an alternative feeding strategy to replace antibiotic growth promoters. This has occurred especially in the European Union, where antibiotics have been banned completely from use as additives in

livestock feed since 2006 because of a suspected risk of generating microbiota with increased re-sistance to the antibiotics used for therapy in humans and animals.

The primary mode of action of growth-promoting feed additives arises from stabilizing feed hygiene (e.g., through organic acids), and even more from beneficially affecting the ecosystem of gastrointestinal microbiota through controlling potential pathogens. This applies especially to critical phases of an animal's production cycle characterized by high susceptibility to digestive disorders, such as the weaning phase of piglets or early in the life of poultry. Because of a more stabilized intestinal health, animals are less exposed to microbial toxins and other undesired microbial metabolites, such as ammonia and biogenic amines. Consequently, growth-promoting feed additives relieve the host animals from immune defense stress during critical situations and increase the intestinal availability of essential nutrients for absorption, thereby helping animals to grow better within the framework of their genetic potential.

### **Further considerations on the use of phytogenic feed additives**

Besides efficacy, application of phytogenic feed additives to livestock also has to be safe to the animal, the user, the consumer of the animal product, and the environment. Regarding exposed animals, adverse health effects cannot generally be excluded in the case of an accidental overdose. For the user (e.g., feed manufacturer, farmer), the handling of pure formulations of such feed additives usually requires protective measures because they are potentially irritating and can cause allergic contact dermatitis. With respect to consumer safety, the phytogenic feed additives cannot be relieved from determination of possible undesired residues in products derived from animals fed those products. However, metabolic activity (e.g., absorption, potential to accumulate in edible tissues) differs widely among phytogenic compounds, and thus safety needs to be assessed separately for each individual phytogenic feed additive.

Another consideration when using phytogenic feed additives is possible interactions with other feed additives. Many of the feeding trials investigating the efficacy of phytogenic feed additives included other growth promoters (e.g., antibiotics, organic acids, and probiotics), as well as combinations with them, without showing antagonistic interaction among these feed additives.

On the other hand, studies on interactions of phytogenic feed additives with enzyme preparations (e.g., phytase, enzymes degrading nonstarch polysaccharides, etc.) are very limited. Phytogenic feed additives containing components with astringent properties, however, were reported to interact negatively with proteinaceous feed additives through partial denaturation.

In conclusion, phytogenic feed additives are claimed to exert anti-oxidative, antimicrobial, and growth-promoting effects in livestock, actions that are partially associated with enhanced feed consumption. Whereas available results do not support a specific amelioration of palatability, the anti-oxidative efficacy of some phytogenic compounds to protect the quality of feed, as well as that of food derived from animals fed those substances, cannot be ruled out. With respect to antimicrobial action, some observations in vivo support the assumption that the general potential of phytogenic feed additives is to contribute to a final reduction of intestinal pathogen pressure. When compared with antimicrobial feed additives and organic acids, the phytogenic substances currently used in practice similarly seem to modulate relevant gastrointestinal variables, such as microbial colony counts, fermentation products (including undesirable or toxic substances), digestibility of nutrients, gut tissue morphology, and reactions of the gut-associated lymphatic system. Furthermore, some isolated observations seem to support the claimed enhancements of digestive enzyme activity and absorption capacity through phytogenic compounds. In addition, phytogenic products may stimulate intestinal mucus production, which may further contribute to relief from pathogen pressure through inhibition of adherence to the mucosa.