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# GROWTH PROMOTER ALTERNATIVES AFTER THE BAN OF ANTIBIOTICS

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## Abstract

Feed additives are used worldwide for many different reasons. Some help to cover the needs of essential nutrients and others to increase animal performance, feed intake and thereby optimize feed utilization. They can positively affect technological properties and quality of feed as well as animal products. In many countries the use of feed additives is more and more questioned by the consumers: Substances such as antibiotics, hormones and β-agonists with expected high risks are banned in animal diets. The consumers' demand trend is for safer and more "organic" food. Environmental aspects and animal management conditions get essential in intensive animal production systems. Therefore, the feed industry is eagerly looking for effective alternatives which are acceptable to the consumer and environmentally sound. Organic acids, enzymes, probiotics, prebiotics and highly available minerals as well as herbs or botanicals can be seen as potential alternatives to metabolic modifiers and antibiotics. The best results can be achieved in the combination of these feed additives and under good environmental conditions.

Key Words : Pigs, feed additives, antibiotics, organic acids, enzymes, probiotics, prebiotics, herbs

## Introduction

In modern society the way of human food production is intensively discussed and questioned. We expect food from plants, farm animals and microorganisms to be of good quality, healthy and inexpensive. In addition, we are increasingly concerned about environmental matters and look for low energy and nutrient input production systems. Arguments for food that is produced as naturally as possible (organic farming) come primarily from consumers organizations. On the other hand, we do not always feel the impact of the steady growth of world population. In twenty-five years from now there will be almost nine billion inhabitants (FAOSTAT, 1998) on earth who expect to get enough food to meet their nutritional needs. The goal to produce sufficient food for everybody can only be achieved in future if the world food production increases by about 2 % per year. It is expected that world animal production will follow this trend. According to IFPRI (1999) world production will grow about 2.0 % for pigs and chicken, respectively, in the next twenty years, mainly in the developing countries with an annual growth between 2.5 and 3 %. World food production must grow without increasing the environmental waste load. This precondition demands the efficient use of all available resources of traditional and modern technologies as well as of feed additives in a responsible way! There is no doubt that today's worldwide agriculture productivity must be increased.

A general ban of antibiotics as antimicrobial performance promoters in animal nutrition is realized since 1986 in Sweden and since 1999 in Switzerland. Today in the European Union only three antibiotics are still permitted (Salinomycin-Na, Flavophospholipol, Avilamycin) and a general ban is foreseen in some years from now. At least for the present time coccidiostats are not included in the list of banned antibiotics for poultry.

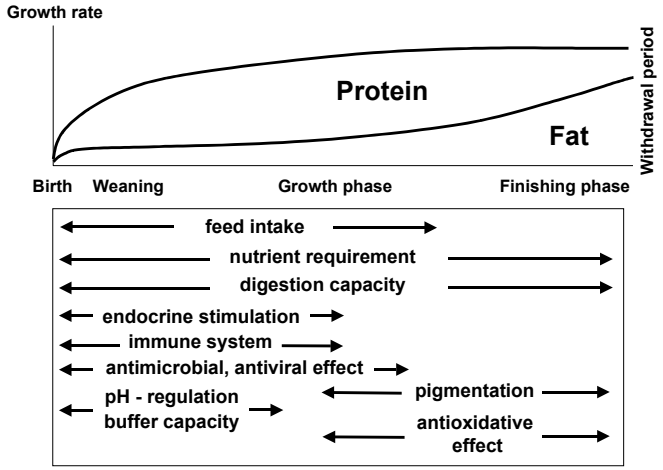


With the restricted use or ban of dietary antimicrobial agents we must explore new ways to improve and protect the health status of farm animals, to guarantee animal performance and to increase nutrient availability. This goal can be attained by good production practicies like housing or climate conditions as well as by the best possible combination of the so called pronutrients (Rosen, 1996) available, including organic acids, enzymes, pro- or prebiotics, specific dietary fibers, highly available nutrients and herbs. The effect of pronutrients on the performance of farm animals can vary over a wide range. Generally, they are more effective in animals with a low performance, with diets of low nutritive value, at low health conditions, in an unfavorable environment, under stress and a bad management of the animals.

## Need for Alternative Feed Additives

With the restricted use or ban of dietary antimicrobial agents, we must explore new ways to protect and improve the health status of farm animals, to guarantee animal performance and to protect the environment. This target can be attained by good housing or climate conditions along with best possible combination of pronutrients (Rosen, 1996) available as organic acids, dietary fibers, pro- or prebiotics, highly available nutrients or eventually herbs (Fig. 1). Rosen defined the pronutrients as "micro feedingstuffs used orally in a relatively small amount to improve the intrinsic value of the nutrient mix in an animal diet". Comparative observations of the use of alternative additives have been published in the last years (e.g. Flachowsky and Schulz, 1997, Freitag et al., 1999).

Figure 1: Requirements for Feed Additives in Growing Farm Animals




Antibiotic alternative feed additives act in many different ways to influence health status and/or nutrient availability. Such pronutrients produce their activity mainly in the digestive tract. For instance, organic acids help to improve digestive processes especially in monogastric animals. With improved pH regulation, the colonization of undesirable microorganisms in the upper digestive tract can be prevented. Enzymes are used mainly for monogastric animal species to

increase nutrient availability and to allow the use of by-products of the food industry and/or of home grown feeds with reduced risk of digestive problems. Carbohydrases help to alleviate negative effects of dietary fibers. Proteases in optimal combination with carbohydrates increase the digestion processes especially of legumes like soybeans or lupines. Yeast cultures can stimulate microbial activity in ruminants (rumen) and horses (caecum) and help to optimize the digestion processes. Enterococci and lactobacilli are mainly used for pigs and poultry. They stimulate and stabilize the digestion process and help to increase competitive exclusion of undesirable microorganisms in the digestive tract. The main idea of this feed supplementation is a balanced composition of the microflora (eubiosis). Adequate endogenous secretions, an active immune system, improved nutrient supply and utilization by animals are the consequence.

A wide range of other substances are increasingly used to optimize the digestive process and to improve the health of the animal. Oligosaccharides can selectively influence the microflora by enhancing competitive exclusion or by supplying specific nutrients (Gibson and Roberfroid, 1995). Herbs or botanicals may affect feed intake, palatability, product quality through pigmentation, the digestion through certain antimicrobial effects or through a reduction of the oxidation of unsaturated fatty acids in the digestive tract.

## Antimicrobial Agents

Antimicrobial agents that are used as feed additives develop their activity in the digestive tract (in non ruminants mainly in the small intestine). They suppress competitively undesired microorganisms that utilize nutrients and produce undesirable or toxic substances. The consequence is an optimal environment for the intestinal mucosa, which allows an efficient nutrient absorption (François and Michel, 1968). Therefore nutrient utilization, feed conversion ratio and growth rate are in most cases improved. Furthermore, the health status of animals that are reared under sub-optimal conditions become better. With dietary supplementation of antibiotics to healthy piglets even under good housing and hygienic conditions, an increase of body mass gain and of the feed conversion ratio of 10 to 15 % can be expected. The effect of antibiotics is pronounced in young growing animals especially under unfavourable climatic and management conditions. When animals get older, the beneficial effect is reduced and can often not be observed in the finishing period. Pfirter (1998) estimated the effect of the withdrawal of dietary antibiotics on growth and feed conversion efficiency of different farm animals as shown in Table 1.

Table 1 Effect of the Withdrawal of Antibiotics as Performance Promoters on Growth Performance and Feed Conversion Efficiency in different Growing Farm Animals (Pfirter, 1998)

| | Reduction of daily body mass gain | Increase of feed per gain |
|---|---|---|
| Veal calve production | 7 - 8 % | 4 - 5 % |
| Beef production | 4 % | 2 % |
| Weaned piglets | 8 % | 5 % |
| Growing pigs | 5 % | 3 % |
| Fattening pigs | 2 % | 1 % |
| Pig production | 5 % | 2 % |
| Growing chicken | 3 % | 2 % |



In Europe the available antimicrobial substances are clearly categorized under two sub-groups: those for use as feed additives and others for therapeutic applications. As discussed earlier, information on resistance transfer between antibiotics have led several times to an update of the list of antibiotics used in agriculture. Under the pressure of consumer organizations and supermarket chains, the complete ban of all antimicrobial performance promoters in farm animals is presently discussed intensively or an important prerequisite of label programs. Though the risk of antimicrobial resistance transfer from feed additives for farm animals toward human use is not yet epidemiologically clearly confirmed (SCAN, 1996; Bager, 1997), the highest risk occurs in the application and misuse of therapeutic antibiotics in humans. The utilization of antibiotics as feed additives or as medical feed cannot be preciously differentiated. On the other hand, the risks of antibiotics used in the medical care of pet animals are not known. The recent survey of DANMAP (2001) on the use of antibiotics in farm animals in Denmark clearly demonstrates the reduced occurrence of antimicrobial resistance in farm animals and their products with the restriction of the use of antimicrobials. Today it is not yet clear what consequences the ban of antibiotics as growth promoters in farm animals has on the misuse of other substances having an efficient antimicrobial effect such as high dose of ZnO or $CuSO_4$. The ecological consequences of such a misuse can be enormous.

## Organic Acids

The successful use of organic acids or their salts as feed supplements is well known since a long time. The favorable effects on different criteria like feed safety, digestion processes, performance and product quality are appreciated according the different production systems and products used in feed and drinking water.

In the feed, organic acids can suppress the growth of undesired microorganisms by lowering of the pH or a specific antimicrobial effect (Roth and Kirchgessner, 1998). With the change of taste feed intake can be influenced, an effect that is usually less pronounced in poultry compared to young pigs. Organic acids reduce the pH in the digesta and are able to suppress the growth of undesired microorganisms, mainly in the upper part of the digestive tract depending on the place and rate of absorption. The faster the acids are absorbed the smaller is the pH lowering effect. This effect is directly influenced by the acid binding capacity of the diet (Blank et al., 1999). Furthermore, the digestibility of nutrients can be improved by organic acids (Blank et al., 1999; Thacker et al., 1992). Organic acids can be metabolized and represent therefore also an energy source. Finally, they can improve the hygienic quality of meat with the suppression of undesired microorganisms like salmonella or campylobacter (Byrd et al., 2001).

## Enzymes

Biotechnologically produced exogenous enzymes are available to enhance digestive capacity especially of young or ill animals as well as to increase the digestibility of the feed. A variety of carbohydrases are used to enhance digestion of carbohydrates including resistant starch or dietary fibers (Annison and Choct, 1993; Chesson, 1987; Wenk, 1993). Proteases which increase the utilization of vegetable proteins such as soybeans or other legumes (Pugh and Charton, 1995; Schutte and de Jong, 1996) and also lipases (Pluske et al., 1997) are available today. Phytases which increase the availability of phosphorus and other minerals are in use especially in regions with a high animal production intensity to reduce environmental load (Pallauf et al., 1992; Jongbloed et al., 2000; Wenk and Gebert, 2000). Enzymes that increase generally the utilization of organic matter and energy have always a beneficial effect on the environment due to improved feed utilization provided that the dietary nutrient supply is reduced according to the increased availability.

Exogenous enzymes can be utilized successfully if they are well adapted to the secretion of endogenous and microbial enzymes. This is of great importance especially in young, stressed or ill animals. In adult animals, the choice of exogenous enzymes depends mainly on the feed composition.

The use of agro-industrial by-products in animal feeding is very relevant to many countries food an feed industries. In Switzerland in 1993, about 60 % of pig feed consisted of locally available by-products and only about 40 % of the feed derived from directly grown raw materials. With regard to poultry feeds, about 30 % were by-products (Wenk, 1995). Presently, most chicken diets in intensive production systems contain carbohydrases. In piglet diets, carbohydrases and eventually other enzymes are used to optimize the digestion processes with endogenous enzymes (Lindemann et al., 1986; Inborr, 1994). Whole maize plants are commonly used as a major component of diets for ruminants. Experiments conducted by Wenk et al. (1993) revealed that they can also be fed to growing / finishing pigs or to pregnant sows, if they are supplemented with an appropriate enzyme mixture. In their experiments, enzymes increased the energy utilization of the diet containing 50 % whole maize plants by 4 % while increasing the energy digestibility of the maize plant alone by 10 %.

Studies conducted in Sri Lanka on pigs fed with swill and rice bran diets have shown positive responses to carbohydrases and antibiotics. Though the enzyme alone resulted in a small increase in body mass gain, the addition of both enzyme and antibiotic increased the mass gain by about 25 %. Obviously there was a very distinct positive interaction of the enzyme and antibiotic. Birzer et al. (1991), Vukic-Vranjes and Wenk (1995) and Wenk et al. (1997) showed in their studies at least an additive effect of the two supplements. The positive effects of enzymes are well documented today.

## Probiotics and Prebiotics

Many microorganisms are used in the form of probiotics in animal nutrition on different levels. For instance, lactic acid bacteria are used for silage fermentation, other microorganisms serve as protein sources or are utilized to produce amino acids, vitamins, highly available minerals etc.

With the increasing ban of antimicrobial feed additives, lactobacilli (for monogastric animals) and yeast cultures (for ruminants or horses) are employed more and more as “probiotics”. They are by definition “*microbial food / feed supplements that beneficially affect the host by improving its intestinal microbial balance”* (Gibson and Roberfroid, 1995). Effective probiotics on one hand stimulate beneficial microorganisms in the gastrointestinal tract and on the other hand suppress pathogens by competitive exclusion. In ruminants for instance, yeast cultures stimulate the growth of cellulose degraders and lactic acid utilizers in the rumen (Dawson et al., 1990). The resulting optimal pH regulation can, as a consequence, suppress lactic acid producers.

In monogastric animals a low pH in the upper small intestine helps to suppress pathogens like E. coli or salmonella. Therefore, probiotics for monogastrics should stimulate lactic acid producers. Wenk (1990) observed in experiments with pigs and chickens not only an increased growth rate and better feed efficiency after the supplementation of high fiber diets with lactobacilli and yeast cultures, but also a higher digestibility of energy and some of the fiber fractions.

A new concept is the use of resistant starch or oligosaccharides derived e.g. from inulin as fructose-oligosaccharides, from yeast cell walls such as mannan-oligosaccharides or other oligomers. Again, these additives help to optimize the eubiosis, improve the digestion capacity and increase the health status of the animal. These substances are generally called “prebiotics”. They can be defined as “*nondigestive food / feed substances that beneficially affect the host by*



*selectively stimulating the growth and/or activity of one or a limited number of bacterial species already resident in the digestive tract and thus attempt to improve host health”* (Gibson and Roberfroid, 1995). Prebiotics can be specific nutrient sources for beneficial microorganisms like fructose-oligosaccharides for bifidobacterium spp. (Bornet et al., 1994; Rochat et al., 1994; Bolduan et al., 1993). A main other aspect of the use of prebiotics in diets for young animals is the benefit due to the competitive exclusion of pathogenic microorganisms like E. coli or salmonella (Savage and Zakrzewska, 1995; Spring, 1996). In a meta-analysis with mannan-oligosaccharides as supplement in nursery pig diets Miguel et al. (2002) calculated from 24 experiments a mean improvement of 4.0 % for average daily gain and 2.4 % for feed conversion ratio.

## Highly Available Minerals

Highly available trace minerals in the form of chelates or proteinates can replace those inorganic sources currently in use to meet the nutrient requirements of farm animals. Often a better health status or increased performance can be observed. Due to the higher bio-availability, the use of organic trace elements allows also the reduction in total mineral content in the diet, thus reducing the environmental load.

Organic chromium (Cr) in the form of biologically available glucose tolerance factor supports the carbohydrate metabolism and the activity of insulin. Although Cr affects several physiological mechanisms, only its effect on insulin activity seems to be clearly understood. Recent research gave evidences that the binding of Cr at an oligopeptide, named low-molecular weight chromium binding substance, is responsible for potentiation of insulin's action (Davis and Vincent, 1997). However, partly connected with the insulin metabolism special interest was focused on Cr as a carcass modifier since supplemental Cr decreased fat and increased protein accretion in pigs (Lindemann et al., 1986; Mooney and Cromwell, 1995; Mooney and Cromwell, 1997), and in poultry (Hossain, 1998). In addition, several studies reported beneficial effects of Cr in stressed animals (Chang and Mowat, 1992; Moonsie and Mowat, 1993). Copper-lysine complex (Coffey et al., 1994), chelated iron and zinc proteinate (Wedekind et al., 1994) are further examples for useful application of trace elements in the organic form.

According to Mahan (1995), selenium (Se) when provided as Se-yeast can have specific effects on metabolism and therefore help to increase health status of the animal. An increase of Se in animal products (meat and eggs) has been observed when it was fed as Se-methionine instead of inorganic Se (Mahan, 1999). Selenium is a limiting trace element in human nutrition in many countries worldwide. Because food from animal origin is an important Se source (Zimmerli et al., 1998), the increase of the Se content in these products must be appreciated in the sense of the idea of functional foods.

## Herbs, Spices and Botanicals

Herbs are non-woody, flowering plants valued for their medical properties, flavor or scent. Spices are defined as any of a class of pungent or aromatic substances of vegetable origin as pepper, cinnamon and cloves used as seasonings, preservatives etc. A drug made from a part of a plant as from roots, leaves, bark etc. is called as a botanical. Plant extracts or essential oils possessing a distinct odor are used mainly in the production of perfumes, flavors and pharmaceuticals, but some are also of interest in animal nutrition because of their antimicrobial and antioxidative properties.

In the past few years, the western world has been learning what many Asians and native Americans have known for centuries that plant extracts and spices can play a significant role in health and nutrition (Bye and Linares, 1999). Herbs and botanicals can beneficially affect feed

intake, secretion of digestive juices and the immune system of animals. They may have antibacterial, coccidiostatic, anthelmintic, antiviral or anti-inflammatory activity and particularly antioxidant properties. Most of these active secondary plant metabolites belong to the classes of isoprine derivatives, flavonoides and glucosinolates and a large number of these compounds has been suggested to act as antibiotics or as antioxidants *in vivo* and in food. Several authors have reported on these substances (Rhodes, 1996; Wenk, 2000) and their antioxidative properties (Halliwell et al., 1995).

Spring, Wang and Ding (1998) reported the occurrence of antimicrobial activity of a number of Chinese herbs. Oils of spices usually contain natural antioxidants which can be used to improve the oxidative stability of animal products. These antioxidants are mainly tocopherols or phenoles (Baldioli et al., 1996). While a number of herbs and spices are reported to contain antioxidative properties, some of the herbs and spices can have no such activity or even pro-oxidative effects (Deans et al., 1993). Therefore, when herbs and spices are used as alternatives to traditional antibiotics, coccidiostats or antioxidants, a proper screening of such materials is very important to assure the expected results.

## Conclusions

The beneficial effect on health status, performance as well as nutrient and energy utilization and some times environmental issues are the main reasons as to why animal feed additives are widely used. With the todays trend towards more “natural” or “organic” animal production systems, antimicrobial agents and other growth promoters are banned by special labeled programs or at the national level (e.g. Sweden and Switzerland). Discussions about the possibility of the transfer of resistance against antibiotics from animal products to humans fortify that development. Therefore, agriculture is looking for more consumer friendly additives. Whether pro- or prebiotics, enzymes, herbs, highly available minerals or other feed additives are appropriate has to be considered in each practical application. Only the best combination of the possible alternatives can be recommended.

Pro- and prebiotics show the best activity in young animals when the digestive system is still in development. While metabolic modifiers are influencing the intermediate metabolism, antimicrobial agents, enzymes or pro- and prebiotics affect the digestive processes in different modes of action. They can partly replace each other. Enzymes increase the digestion capacity in young animals and help to decrease the risk of digestive problems and therefore increase the health status. In adult animals, enzymes can be used successfully to increase the use of (homegrown) feedstuffs rich in dietary fibers or other components with a low digestibility (by-products from food industry) and to reduce environmental load with nutrients.

Most feed additives discussed develop their activity in the digestive tract or have a special form that allows a high availability (minerals in organic form). A higher absorption rate of the nutrients and changes in the microflora are the consequences. Furthermore, nutrient and energy requirements are met efficiently. This increases the health status and the performance of animals.



With the ban of antibiotics in Europe, and eventually soon also in other countries, strategies of alternatives are often discussed, especially in production of veal calf and of young pigs. The strategies must be based primarily on optimal management and housing conditions. The main aspects are:

- adapted temperature (microclimate of the calves and piglets)
- fresh air, no draft
- adapted space and appropriate floor
- if possible bedding with straw (no mycotoxins!)
- low humidity and minimal dust
- good rotation system

The animals should primarily be supplied with all essential nutrients and energy in adequate amounts. In large groups, adequate feed troughs must allow all animals getting sufficient amounts of food. On the other hand overeating of the heavier animals should be avoided so that digestive disorders do not occur. With the following measures the risks of digestion problems mainly in the young pig can be minimized:

- low acid binding capacity
  - reduced mineral content (< 6 g Ca and < 5 g P per kg feed)
  - reduced protein content (but essential amino acids according to requirement)
  - use of organic acids (mainly fumaric and lactic acid)
- use of enzymes, prebiotics and dietary fibers
  - use of mainly phytases and carbohydrases
  - use of fructose and mannose oligosaccharides
  - use of pectins or other soluble dietary fibers
- liquid feeding systems with the possibility of fermentation before feeding
- use of herbs, botanicals, spices or essential oils
- use of probiotics (lactobacilli)
- supply of sufficient amounts of special amino acids (glutamine and alanin)
- prevention of anti-nutritional factors (ANF)

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