Eubiotics: Definition and different concepts

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Introduction

About 20 years ago, the use of feed antibiotics and some other antimicrobial compounds, used as performance enhancers became the target of increasing public criticism and a topic of political controversy (particularly in the EU countries). As the first country in Europe, Sweden banned the use of antimicrobial growth promoters as early as 1986. The use of avoparcin as a growth promoter was banned first in Denmark (May 1995), subsequently in Germany (January 1996) and finally in the remaining EU countries by April 1997. Based on various safety concerns and partly as a precautionary measure, the EU Council of Ministers suspended the authorization of four other feed antibiotics (spiramycin, tylosin, virginiamycin, Zn-bacitracin) by July 1999, and two quinoloxaline derivatives (carbadox, olaquindox) by September 1999.

By January 2006, an EU ban on the use of the four remaining feed antibiotics, namely flavophospholipol, avilamycin, salinomycin-Na and monensin-Na (for beef cattle only) became effective. This total ban on the use of antibiotics as growth promoters has been integrated into a new EU regulation concerning feed additives (No. 1831/2003). Before the implementation of this complete ban on the use of antibiotic growth promoters (AGP), some experts attempted to assess possible effects on growth rate and feed conversion efficiency and discussed possible alternatives after the ban (Brufau, 2000; Versteegen & Scharfsm, 1999; Wenk, 2003; Witte et al., 2000).

Serious problems were expected, particularly in early weaned piglets, with an average reduction in daily weight gain of 8% and a 5% increase in feed consumption per gain. In addition, a dramatic deterioration in the general health status of piglets was expected, resulting in a marked increase in prophylactic use of various therapeutic antibiotics. This trend has indeed been observed in many countries after the implementation of this general ban.

Eubiotics: Alternative products for replacement of AGP

Before discussing which currently approved feed additives might be used as effective alternatives for replacement of AGP, it would be helpful to approach this topic from a scientific point of view, taking into account their principal mode of action. There is currently no doubt that their efficacy is primarily based on antimicrobial effects and their ability to influence and partly modify the composition and overall concentration of intestinal microflora. Taking this into consideration, we can see how various new and some traditional feed additives claim to affect the composition or activity of intestinal microbiota, such as organic acids, probiotics, prebiotics, essential oil compounds, and Zn and Cu compounds. In recent years, some of those products have been described by the general term ‘Eubiotics’, which is related to the Greek term ‘Eubiosis’, referring to an optimal balance of microflora in the gastrointestinal tract. The main purpose of using such eubiotics is to maintain the intestinal eubiosis, which will result in an improved health status and performance in farm animals.

Organic acids

Organic acids and some of their salts have been added to compound feeds, for many years, in particular for early weaned piglets. The potential of diet acidification in order to overcome digestive insufficiency and post-weaning problems in piglets has been studied for a long time. The efficacy of fumaric acid, citric acid, formic acid, lactic acid, sorbic acid and also of some salts (Ca-formate, Na-formate) has been demonstrated. However, all these compounds are officially approved in the EU as feed preservatives, however, some of them are used primarily for the stabilization of health status and performance enhancement at the dietary inclusion levels of 0.5 to 2.0% (Gabert & Sauer, 1994; Partanen & Mroz, 1999). In order to reduce dietary inclusion levels and enhance their efficacy at economically feasible costs, either blends of organic acids or coated forms have appeared on the market in recent years. Various hypotheses regarding the mode of action and beneficial effects of organic acids have been described in the literature, such as:

- Improvement of palatability and reduction of diet pH;
- Antimicrobial and preservative effects in the feed;
- Reduction of gastric pH and enhancement of pepsin activity;
- Effects on microflora in the gastro-intestinal tract, reduction of coliforms and diarrhea;
- Increased digestibility of nutrients.

Since July 2001, potassium diformate has been approved as a feed additive in the EU and included in the zootechnical additive group. In May 2003, benzoic acid has been approved as a feed additive for growing-finishing pigs at the inclusion levels of 0.5 to 1.0% and included in the acidity regulator group. Due to its specific metabolism, this organic acid shows multiple beneficial effects (Broz, 2004). Dietary supplementation results in a decrease in urinary pH accompanied by a reduction in ammonia emission and improved growth performance. Since November 2006, benzoic acid at the inclusion level of 0.5% has also been approved for use in weaned piglets, as a zootechnical additive. Due to its antibacterial activity and slower absorption, dietary benzoic acid is also capable of significantly reducing the density and metabolic activity of intestinal microflora in piglets (Kluge et al., 2006; Broz & Paulus, 2006). Balance trials have confirmed significant beneficial effects on the apparent ileal digestibility of dietary energy and nitrogen, as well as a significant increase in nitrogen retention. In a series of performance trials, benzoic acid at 0.5% has repeatedly resulted in significant improvements in piglet growth rates after weaning.

Probiotics

Probiotics are viable microorganisms that are used as feed additives in monogastric animals. The probiotic concept is primarily based on the assumption that direct feeding of microbial cultures may affect the composition of intestinal microbiota. Selected strains of microorganisms, believed to possess beneficial effects on digestive processes or animal health are used. Enterococcus faecium and spore-forming Bacillus spp. are the most frequently utilized probiotic microorganisms for swine. Probiotics were established as a new category of feed additives in the EU about twenty years ago and at present, there are more than 40 preparations approved for animal nutrition. In the US, such products are usually marketed as direct-fed microbials.
The modes of action of probiotics are not well characterized and therefore various hypotheses have been suggested in the literature (Kelly, 1998; Simon et al, 2003):

- Competitive adhesion of probiotic microorganisms to epithelial receptors may prevent the attachment of pathogenic bacteria (rational behind “competitive exclusion”);
- Aggregation of probiotics and pathogenic bacteria;
- Competition for nutrients between probiotic and undesired bacteria;
- Increased synthesis of lactic acid and reduction of intestinal pH;
- Production of specific antibacterial substances;
- Reduced production of toxic amines and decrease of ammonia level in the gastro-intestinal tract.
- Beneficial effects on the intestinal immune system, an improved intestinal defense against viral infections.

Several beneficial claims have been established for microbial probiotics, but it is not always possible to provide sufficient scientific evidence to back up these claims. They usually show usually only limited and variable growth-promoting effects and in general, the “probiotic effect” is not as consistent as in case of AGP.

**Prebiotics**

The concept of prebiotics was first developed and introduced by Gibson and Roberfroid (1995) in human nutrition. It is based on the feeding of certain non-digestible oligosaccharides in order to control or manipulate microbial composition and/or activity, thereby assisting to maintain a beneficial microflora (Zimmermann et al, 2001). Initially, various oligosaccharides, which are natural constituents of plants were considered as potential probiotic products for animal nutrition, such as fructo-oligosaccharides, xylo-oligosaccharides, isomalto-oligosaccharides, trans-galactooligosaccharides (TOS), mannan-oligosaccharides and some fructans (inulin, lactulose). Dietary inclusion levels of potential prebiotics are usually 0.1 to 0.5% and many suppliers intend to market them as feed ingredients, claiming selective regulation of intestinal microflora, reduction of pathogens and promotion of beneficial microorganisms (e.g. Bifidobacteria, Lactobacilli). Roberfroid (2007) revisited this concept in human nutrition and concluded, that only 2 dietary non-digestible oligosaccharides, namely inulin and TOS (mixture of oligosaccharides derived from lactulose by enzymatic transglycosylation) fulfill all the criteria necessary for prebiotic classification. They include resistance to gastric acidity, to hydrolysis by digestive enzymes and to gastrointestinal absorption, fermentation by intestinal microflora and selective stimulation of the growth and/or activity of those intestinal bacteria that contribute to health and well-being. Unfortunately, the effects of such ingredients on performance of farm animals such as poultry and swine are not consistent.

**Future innovative concepts**

Substantial research has been conducted over the past few years to evaluate the potential of alternative antimicrobial agents for replacement of AGP. Some natural compounds such as lactoferrin, lysozyme, bacteriocins and antimicrobial peptides appear to result in beneficial effects. Lactoferrin, isolated from bovine milk was evaluated as a potential feed additive in early weaned piglets and significant positive effects on performance parameters were observed at a 2000ppm inclusion level. However, due to its relatively high production costs, practical use in animal nutrition is currently not feasible. Lysozyme (1,4-beta-N-acetylmuramidase) is an enzyme exhibiting antibacterial properties. It is present at low concentrations in animal products such as milk, hen eggs and also in many tissues. Recently published results confirmed that dietary addition of lysozyme improved growth performance of young piglets and it could also be considered as an alternative to AGP. Bacteriocins and antimicrobial proteins have also attracted attention as potential substitutes, but some regulatory issues, particularly in the EU, in addition to their high production costs are factors that might prevent their practical application in the near future.

**Summary**

The total ban on antibiotic growth promoters in the European Union since January 2006 has had a serious impact on both performance and health status of early weaned piglets. Recent developments concerning possible replacement of AGP by effective alternative products referred to as eubiotics are reviewed in this contribution, with the main emphasis on organic acids, probiotics, prebiotics and essential oils. Some innovative concepts, in particular the potential use of lactoferrin, lysozyme and bacteriocins are also discussed.

- References are available upon request