Feed Additives and Feeding Strategies to Replace Antibiotics

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Introduction

Piglets are highly susceptible to enteric disorders immediately after weaning. Piglets have then an immature digestive system, whose capacity for nutrient digestion is impaired by the transition from high quality liquid milk to a solid diet. Diarrhea is common post-weaning and is characterised by reduced digestive capacity in young pigs leading to poor growth performance (Pluske et al., 1997). Because of an immature intestinal immune system, proliferation of enteropathogenic bacteria has a high incidence that further predisposes piglets to enteric infections. To mitigate these effects, weaned pigs are fed complex diets based on costly ingredients like processed blood proteins and milk by-products. Pig starter diets are also routinely supplemented with sub-therapeutic levels of antibiotics as growth promoters (de Lange et al., 2010). However, public pressure is increasing to eliminate animal by-products and antibiotics from swine diets for fear of risks to human health and, in case of antibiotics transfer of antibiotic-resistant bacteria to humans. These concerns have sparked considerable interest in identifying alternative nutritional strategies for managing newly-weaned pigs fed antibiotic-free diets. Non-use of antibiotics in swine feeding programs has an added advantage as a marketing tool as several major international markets continue to demand pork products originating from pigs raised under such production systems.

Therefore, the goal of this paper is to review the application of available feed additives and feeding strategies that might be used to effectively manage weaned piglets in antibiotic-free feeding regimens.

Feed Additives

A considerable number of feed additives have been suggested as alternatives to in-feed antibiotics in nursery pig diets (de Lange et al., 2010). These
includes spray dried porcine plasma, acidifiers, high levels of zinc and copper salts, probiotics, prebiotics, nucleotides and nucleotide-rich products, essential oils, egg yolk antibodies, lysozyme, and herbs and spices. Whereas there is evidence that some of these additives may positively influence weaning transition, response to their application varies considerably and majority of them have elicited some concerns which have hampered wider application. For example, studies have shown that organic acids or high levels of zinc oxide may be used as alternatives to antibiotics, but questions regarding safety of organic acids and environmental pollution of zinc oxide make these additives problematic. Similarly, there have questions related to the use of blood plasma in piglet diets and its potential implications for human health.

Despite the concerns and the variable nature of the responses to the use of some of the additives, there is ample evidence that many of these products have a role to play in the nutritional management of piglets raised in antibiotic-free feeding systems. Therefore, the use of selected additives is discussed briefly.

**Zinc Oxide**

In many studies and in practice, pharmacological levels (up to 3000 ppm) of Zn offer an effective dietary tool to ameliorate and (or) prevent post-weaning diarrhea thereby acting as a growth promoter in weaned pigs (Hill et al., 2000). Although not fully understood, these effects have been attributed to the ability of Zn to modulate the animal’s defense mechanisms (e.g. increased gene expression of antimicrobial peptides in the small intestine) (Wang et al., 2004), and the intestinal microbial population (e.g. maintaining the stability and diversity of intestinal microbiota). Clearly, ZnO fed at pharmacological levels can be a cost-effective strategy for controlling post-weaning diarrhea, although at such high levels concerns about environmental contamination must be considered.

**Organic Acids**

Supplementing nursery pig diets with organic acids has been proposed as a feasible strategy to maintain gut health and improve growth performance (Heo et al., 2012). During the weaning transition piglets are unable to maintain proper gastric pH due to such factors as dietary changes and inability to produce sufficient acid in the stomach. Thus, piglets often have high gastric pH (up to 5.0), during the weaning transition compared with a mature pig whose pH ranges from 2.0 to 3.0. To optimize nutrient digestion and prevent pathogen overgrowth, maintaining a low gastric pH is critical. Dietary addition of organic acids such as citric, fumaric, lactic and formic acids to weaned pig diets is used as a strategy to maintain low gastric pH and control proliferation of pathogenic bacteria and thereby improve growth performance and health of piglets (Heo et al., 2012). Available organic acid products contain either a single acid or combination of acids. Generally, inconsistencies are reported as to the effectiveness of these products regardless of the formulation.
Pre- and Probiotics

Probiotics and prebiotics are other feed additives that are used to promote gut health and maintain piglet performance of weaned pigs. Probiotics are live microorganisms which when administered in adequate amounts confers a health benefit on the host. The beneficial effects of these additives are mediated through one or more of the following mechanisms in the gut: (1) stimulation of a healthy microbiota, (2) prevention of enteric colonization by pathogens, (3) improving digestive capacity and lowering the pH, (4) improving mucosal immunity, or (5) enhancing gut tissue maturation and integrity (de Lange et al., 2010). Microorganisms to be used as probiotics should be able to survive in the gastric acid and bile salts. The three categories of organisms that are commonly used as probiotics are bacillus, yeast and lactic acid-producing bacteria such as Lactobacillus, Bifidobacterium, and Enterococcus (de Lange et al., 2010). As recently reviewed by de Lange et al. (2010) and Heo et al. (2012), there are many studies that have demonstrated positive effects of probiotic supplementation on performance and controlling post-weaning diarrhea in newly-weaned piglets. However, it is important to note that there are other studies that have failed to demonstrate such positive effects (see review by Heo et al., 2012). In general, such inconsistencies can be explained by differences in dosage, and type of strain of probiotic, sanitation conditions, and diet type.

A prebiotic is "a selectively fermented ingredient that allows specific changes, both in the composition and (or) activity of microbiota, that confer benefits upon host well-being and health" (Gibson et al., 2004). In general, the addition of prebiotics is targeted at stimulating the proliferation and activities of bacteria associated with a healthy gut, such as bifidobacteria and lactobacilli. Supplementing nursery pig diets with fermentable carbohydrates (including resistant starch) has been shown to alter the composition and activity of intestinal microbiota (Molist et al., 2012). For instance, the addition of inulin and sugar beet pulp to nursery pig diets was shown to alter the composition of bacterial microbiota in weaned piglets. In recent studies, we demonstrated that addition of low levels of coarsely ground wheat bran to weaned pig diets prevented intestinal colonization with pathogenic E. coli and altered the microbial diversity (Molist et al., 2012). Supplementing a starter diet with non-starch polysaccharides hydrolysis products resulting from feed enzyme treatment reduced the severity of infection in piglets challenged with pathogenic E. coli (Kiarie et al., 2008). Thus, intake of prebiotics can contribute to maintenance of gut health in piglets and there is evidence to suggest that combining prebiotics with probiotics may have enhanced benefits on gut health and development in newly-weaned piglets.

Antibodies

Products containing high contents of antibodies against specific pathogens have been shown to effectively control incidences of disease caused by such
pathogens. Several studies have shown that supplementing nursery pig diets with products that contain antibodies against E. coli K88, the pathogen responsible for post-weaning diarrhea in piglets, maintains growth performance and minimizes incidences of post-weaning diarrhea (King et al., 2008). Because antibodies are very specific, such products will work best if used in situations where the target pathogen is responsible for piglet diarrhea.

**Nucleotides and Nucleotide-Rich Products**

Nucleotides are low-molecular-weight intracellular compounds which are naturally present in all living cells and are involved in structural, metabolic, energetic and regulatory functions and are present in greater amounts in sow milk than in a high quality creep feed. The need for nucleotides during periods of stress such as weaning may exceed endogenous supply. Thus, it has been proposed that feeding a diet with supplemented exogenous nucleotides might help piglets to develop the gastrointestinal tract and immune functions with the transition at weaning (Lee et al., 2007). Although not fully elucidated, there is enough evidence to suggest that dietary nucleotides supplementation may positively impact piglet growth and intestinal integrity (Domeneghini et al., 2004). For example, feeding piglets a diet supplemented with nucleotides-rich yeast extracts at 1 g/kg for 28 days showed comparable growth performance compared with piglets received a diet with antibiotics after weaning (Patterson et al., unpublished data); however others failed to show such an effect (Domeneghini et al., 2004). The fact that most nucleotides-rich products are yeast fermentation extracts, they may contain other active compounds (e.g. β-glucans and peptides) that may influence the responses.

**Diet Manipulation Strategies - Dietary Protein Content**

Nursery pig diets are often formulated to contain high levels of crude protein, much of which the piglet is not able to retain. Also, it has been known for a long time now that high dietary crude protein content in piglet diets might be a predisposing factor to intestinal proliferation of pathogenic bacteria (Ball and Ahern, 1987). Fermentation of protein in the gut leads to the production of potentially toxic substances such as ammonia and amines which enhances the conditions for the development of post-weaning diarrhea in piglets. Based on this, there has been a great interest to determine whether low protein-amino acid supplemented diets may be useful as part of an overall nutritional strategy for managing piglets in antibiotic-free feeding programs. Indeed, results of several studies (see review by Heo et al., 2012), have shown that feeding weaned pigs diets with lower crude content reduces intestinal concentration of protein fermentation products (e.g. ammonia), reduces inflammatory responses and minimizes the number of pathogenic bacteria attached to intestinal mucosa during a disease challenge.

A major concern with this strategy is feeding a low protein diet will compromise piglet growth performance (Heo et al., 2012) mainly because of
reduced supply of essential amino acids, such as isoleucine and valine. However, other studies have demonstrated that if low protein diets are formulated to supply sufficient amounts of essential amino acids (i.e., lysine, methionine, tryptophan, threonine, valine, and isoleucine), acceptable piglet performance and health can be maintained (Heo et al., 2012). There is also evidence that piglets may be able to compensate later in life for reductions in growth performance during the post-weaning period, which may explain why long-term performance of piglets was not influenced by low protein even though performance immediately after weaning was reduced (Kim et al., 2011). Nevertheless, extensive studies are warranted to better understand how low protein diets may be utilized as a strategy to manage piglet gut health in the absence of in-feed antibiotics.

**Conclusions**

Reduced growth performance and the associated enteric diseases, including post-weaning diarrhea, are major concerns in the immediate post-weaning period that lead to considerable economic losses to the swine industry. The practice of using antibiotic-containing nursery diets to mitigate these challenges has come under increasing pressure for fear of contribution to emergence of antibiotic-resistant bacteria, which in turn jeopardizes human health. To minimize production and economic losses associated with the removal of in-feed antibiotics, a large number of alternative feed additives and feeding strategies have been proposed. Whereas there is more work required to better understand how majority of the available additives can be effectively utilized, there is ample evidence to support the use of some of the additives in this regard. Diet formulation strategies to support intestinal health will become an important component of the overall approaches to manage piglets in antibiotic-free feeding regimens. It clearly evident from the several studies that for many of the additives and feeding strategies available, the most effective application will be achieved when used in combinations.

**References**


