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Feed ingredients that improve health

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There is now a growing body of evidence that physiologically active dietary ingredients besides antibiotics may improve health and performance of pigs. Others in this session have discussed the evaluation of such ingredients in practice; this paper will focus on what the scientific literature says about them.

The group of technologies considered herein is restricted to dietary ingredients that have physiological activity beyond provision of bioavailable nutrients and to formulation practices and feeding methods that similarly alter physiological conditions. Many of them are suggested to provide benefits through impacts on microbial populations in the digestive tract and/or influence on immunity, although other modes of action also fall within the scope of this discussion. Consideration of microbial populations in the digestive tract draws attention to growth and survival of pathogens, but includes the potential importance of commensal bacteria also.

The industry now has a rich supply of potential dietary technologies available for evaluation and use (Table 1).

A thorough discussion of all of these potential dietary tools is beyond the scope of this paper, but three of them are discussed to some extent herein. The products chosen for focus in this paper (acids, mannan oligosaccharides and immune egg products) are not universally used by the industry. Spray-dried plasma has already been adopted

by the industry, and its power is shown in an overview of average responses in growth rate to products that have been heavily studied (Table 2).

This review relies heavily on the powerful but imperfect statistical approach of meta-analysis. A meta-analysis is a combination of a large number of experiments into a single statistical analysis, often using the treatment mean values from an experiment as the experimental unit values in the meta-analysis. Meta-analysis is useful because it achieves substantial experimental power through the amalgamation of several experiments, overcoming the unfortunate fact that most single experiments have too little experimental power to detect treatment effects large enough to be economically important. It also provides an unusually broad inference space because of the range of conditions under which the several experiments are conducted.

The results of a meta-analysis reflect the experiments included, so it is important that those experiments are a representative sample of the population of conducted or potential experiments. A biased sample leads to biased results. That is a special problem when dealing with the published literature because of the tendency of scientists or journals to choose not to publish data that fail to show statistically significant differences among experimental treatments. That regrettable tendency results in a bias in the refereed literature, which results in an unavoidable bias in the results of a meta-analysis based on the scientific

Table 1: An incomplete list of potential dietary technologies to improve pig health and productive performance

Energy & protein sources	Additives	Feeding management
Spray-dried plasma	Immune egg products	Low-protein diets
Milk protein products	Mannan oligosaccharides	Restricted feeding
Egg products, conventional	Fructo-oligosaccharides	Fermented liquid feed
Alternate cereals	Other oligosaccharides	
Lactose	Direct-fed microbials (bacteria)	
	Essential oils	
	Acids	
	Zinc oxide	
	Copper sources	
	Yeasts/yeast products	
	Bacteriocins	
	Bacteriophage	
	Enzymes	
	Nucleosides	

Table 2: Estimates from multiple studies of mean increases in growth rate of weanling pigs produced by selected feed ingredients^A

Ingredient	% Increase
Spray-dried plasma	23-27
Acids	12
Milk whey proteins	4
Mannan oligosaccharides	4

^AData restricted to summaries of more than 10 comparisons.

literature. Note that this bias affects any review of the literature, but is most obvious when the review is formalized and quantitative as in the case of a meta-analysis. As noted later, we suggest that this bias is likely less prominent in some situations than in others.

Acids

Addition of acids to pig diets has been suggested to improve growth performance. The perceived mechanisms include reducing the pH of the stomach contents, which in turn may improve nutrient digestion and change the microbial populations in stomach digesta, a change that may alter populations throughout the digestive tract. It is also thought that acids in undissociated form can enter bacterial cells, where they dissociate and damage or kill the cell. Different acids may have different effects.

It is common to feed combinations of acids rather than individual ones, and often the combinations include inorganic as well as organic acids. Unfortunately, most of the published data address single acids.

A review of a substantial body of pertinent data (M.T. Che and J.E. Pettigrew, unpublished) shows impressive increases in growth rate of 12% ($P < 0.001$; **Table 2**) during the first 2 weeks after weaning, 6% ($P < 0.001$) during the first 4 weeks, 4% ($P = 0.01$) during the growing phase and 3% ($P = 0.02$) during finishing when acids are added to the diet. These numbers are almost certainly too high to an unknown extent due to bias in the literature as discussed above. The response to acids is remarkably robust, with no detectable influence in starting pigs of weaning age, presence of animal proteins in the diet, growth rate, acid inclusion level or acid type (of those tested) on the size of response. There also appear to be increases of about 1 percentage unit in dry matter digestibility ($P = 0.01$) and in protein digestibility ($P = 0.001$).

Mannan oligosaccharides

Products described as mannan oligosaccharides contain mannose, but are more complex than suggested by the term, being preparations of the outer layer of the cell wall

of yeast. The mannose is key to one perceived mechanism of action of this product.

Most enteric pathogens must attach to the intestinal wall in order to proliferate and cause disease; more specifically they attach to carbohydrates as the binding sites. Several pathogens, including some *E. coli*, attach to mannose units on the mucosal surface. It is perceived that the yeast cell wall fragment containing a mannose unit in the lumen of the intestine may bind to the pathogens, preventing the pathogens from binding to the intestinal wall. The product must survive the digestive processes and reach the lower intestine in order to function in this manner.

Recent unpublished results from our laboratory (Miguel et al., 2006) confirm that a mannan oligosaccharide product changes the microbial populations in the digestive tract of young pigs. It is also clear from a meta-analysis that a mannan oligosaccharide increases growth rate of young weaned pigs by about 4% ($P < 0.01$; **Table 2**; Miguel et al., 2004). The response is larger where pigs grow more slowly.

The product also affects the immune system (Pettigrew et al., 2005). It is not clear whether that effect is primary, or whether it is secondary to the change in microbial populations. We are now engaged in studies to help us understand more clearly the protective effects of this product.

Immune egg products

Hens immunized against pig pathogens produce antibodies against those pathogens and deposit them in eggs. Those eggs or their components can then be fed to pigs to provide passive immunity to the diseases in question. Selection of the most appropriate antigen and hen immunization schedule appears critical to success. In most experiments to date, antibodies have been raised to surface antigens of *E. coli*, including the K88 and F18 antigens.

It is now clear that this technology can be enormously effective in reducing the percentage of pigs that die or show clinical signs, or subjective diarrhea scores (e.g. Yokoyama et al., 1997; Marquardt et al., 1999; Owusu-Asiedu et al., 2002; Chernysheva et al., 2003), although failures to provide benefits (e.g. Chernysheva et al., 2003; 2004) also occurred. In some cases, disease was largely controlled by spray-dried plasma and there was no further benefit from immune egg products (e.g. Owusu-Asiedu, 2002).

In all of the disease challenge experiments reviewed, the immune egg products were introduced either before or at the same time as the challenge organism. Evidence was not found that immune egg products can cure an existing enteric infection. In fact, there is evidence that pretreating pathogenic *E. coli* with an immune egg product prevents binding of the organism to intestinal mucosal cells, but that the product does not dislodge organisms already bound to intestinal cells (Jin et al., 1998), casting doubt on the therapeutic value of these products.

Summary

The industry now has a rich supply of dietary technologies available for potentially improving pig health. Among the products for which the available data are encouraging are acids, mannan oligosaccharides and immune egg products. Salient issues on these products are briefly reviewed.

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