The value of direct immune support as an alternative to AGPs

The topic of antibiotic growth promoters (AGPs) and their potential replacement continues to be of great interest to swine producers, with a wide range of options now available for those who are either prevented from using AGPs by local regulations, or prefer to use an alternative.

by Liz Mee,
Technical Manager,
Micron Bio-Systems.
www.micronbio-systems.co.uk

Understandably, growing concerns around the increased resistance of some pathogenic bacteria to existing antibiotics continue to put AGP use under the spotlight.

The use of AGPs was banned in the European Union in 2006 and a number of countries have since followed suit, with many others currently considering taking similar positions. However, one of the challenges facing those looking to develop alternatives is that the mechanisms by which AGPs deliver improvements in feed efficiency and weight gain have never been completely understood. Replicating the response in the pig is therefore far from straightforward.

Understanding AGP response

One theory is that AGPs appear to reduce the production of harmful metabolites by non-beneficial intestinal microflora – including ammonia and bile salt degradation products – whilst also lowering the level of competition for feed nutrients by reducing numbers of pathogenic bacteria in the intestinal tract. In addition, by inhibiting sub-clinical infections, AGPs potentially reduce the metabolic costs of an ongoing immune response.

An alternative mode of action that has also been proposed is the potential for AGPs to accumulate in inflammatory cells (phagocytes) and thereby inhibit the inflammatory response of the intestines.

The result is a thinner mucosal layer within the intestinal wall of AGP-fed pigs, which both increases uptake and utilisation of nutrients and reduces the energy cost of the inflammation.

Both mechanisms highlight the importance of the digestive tract, and the vast majority of the AGP alternatives currently on the market therefore aim to exert an effect by positively influencing gut microflora, feed digestion and intestinal health. Since intestinal microflora can also influence the development of the mucosal immune system, it is possible that such additives may also indirectly enhance immune response.

Differing modes of action

Yet the modes of action by which this is achieved vary considerably, even if most act to achieve broadly similar results, such as the reduction in potential bacterial pathogens within the digestive tract (Table 1).

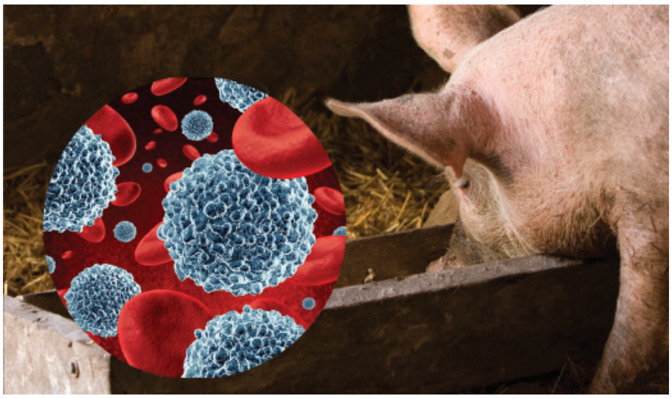
For example, acidifiers – typically organic acids – reduce the pH of the intestinal tract and possess antimicrobial activity against Gram-negative bacteria.

Certain plant extracts have also been used, such as carvacrol, thymol and anethole, which can exert antimicrobial and antioxidant activity, whilst also stimulating the secretion of digestive enzymes and saliva to improve overall nutrient digestibility.

In contrast, the application of feed enzymes, including xylanases, beta-glucanases and phytases, delivers improved pig performance as a result of the breakdown of dietary components that cannot be digested by endogenous enzymes.

Not only does this directly improve digestive efficiency and reduce potential anti-nutritional effects, but in some cases it can also alter the substrates available to gut microbes, leading to a beneficial shift in the microbiome.

Probiotics and prebiotics have also been used to help mitigate the impact when AGPs are removed from the diet. The former includes various species of lactobacilli, as well as some yeast cultures, and these additives generally act



through competitive exclusion of potential pathogenic microbes within the intestinal tract.

Additional activities include secretion of antimicrobial substances and strengthening of the gut epithelial barrier, thereby making it less prone to pathogens.

Prebiotics typically alter the microbiome by providing a nutrient source for beneficial species of gut microbes, such as bifidobacterium and lactobacilli, resulting in a similar effect to that described for probiotics above.

Common examples include the mannan oligosaccharides (MOS) found in yeast cell walls and the fructo-oligosaccharides (FOS) present in many plant materials, such as chicory and artichokes.

Direct immune stimulation

However, there is now a strong case for an alternative approach that more directly stimulates and supports the immune system.

Firstly, pigs can be exposed to a wide variety of stressful situations during their lifetime, and it is known that stress hormones like the glucocorticords and catecholamines can negatively impact the immune system and increase susceptibility to infectious micro-organisms.

Many of these stressful situations occur early in the production cycle when the young pig's immune system is still developing, with the result that any reduction in immune response has an even greater impact on performance. For example, research has shown that even mild handling stress, such as once-a-day weighing, can negatively affect the composition of microbial populations in the gut, whilst social stress can increase the virulence of certain detrimental gut microflora.

In addition, although pathogens within the digestive tract can pose a considerable threat to pigs throughout their productive life, other routes of infection are also important. For example, pneumonia caused by inhalation of Streptococcus spp. bacteria via the respiratory tract is responsible for considerable losses within the swine industry, whilst skin damage can expose the pig to environmental pathogens.

Costs of poor immunity

In addition, the effectiveness of vaccinations – which play a critical role in modern production systems – is dependent upon a strong response from a healthy immune system. If the immune system is compromised in any way, whether due to pig genetics, stress, poor environmental conditions or mycotoxins, vaccine efficacy is reduced with potentially serious economic consequences.

A more robust immune response is also clearly of benefit in fighting any infection, and can have a considerable impact through reduced costs of treatment as well as avoiding subsequent reductions in perfor-

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mance. The opportunity to use nutritional supplements to directly support immune function is therefore of great interest, and has considerable potential when looking to replace the positive benefits of AGPs. To date, the most promising of these supplements are derived from the yeast Saccharomyces cerevisiae, and in particular those containing purified beta-glucans extracted from the yeast cell walls.

Increased immune activity

These beta-glucans provide a direct effect by reacting with elements of the immune system such as macrophages following absorption into the epithelium of the gut.

This triggers a cascade of activation events, leading to an overall increase in immune activity that is then available to more effectively tackle pathogens, including those introduced as vaccines.

Concerns regarding the potential energy cost of such an enhanced immune response, and the possible impact on pig performance, have proven unfounded. It has also become clear that the structure and particle size of the beta-glucans is critical, with the beta-glucans within S. cerevisiae far more effective than those derived from other sources, such as plant cell walls.

These benefits are in addition to the current use of other extracts from S. cerevisiae to improve pig performance, such as the prebiotic MOS, as well as use of the intact yeast as a probiotic able to competitively reduce populations of pathogenic microbes in the gut.

The use of S. cerevisiae-derived beta-glucans to directly stimulate immune response therefore represents a valuable additional mode of action, further expanding the options available to those looking to use AGP alternatives. When combined with the already well recognised pre- and probiotic activities associated with S. cerevisiae in a supplement such as ImmuGuard, the result is greater resilience to infection regardless of the source and particularly during early life. ■

Type	Examples	Mode of action
Acidifiers	Organic acids (formic, propionic, butyric)	• Reduces the pH of the intestinal tract • Antimicrobial activity against Gram-negative bacteria
Enzymes	Xylanase, beta-glucanase, phytase	• Breakdown of hard-to-digest dietary components • Improves feed conversion efficiency •Substrates produced can support beneficial gut microbes
Probiotics	Bacterial (eg. Lactobacilli spp,) or yeast (eg. Saccharomyces cerevisiae)	• Competitive exclusion of potential pathogens • Secretion of antimicrobial substances • Strengthening of the gut epithelial barrier • Positive influence on digestive tract immune system
Prebiotics	Mannan and fructo-oligosaccharides (MOS, FOS)	• Nutrient source for beneficial gut microbes • These microbes then produce similar effects to probiotics
Plant extracts	Carvacrol, thymol, anethole	• Antimicrobial activity • Antioxidant activity • Stimulates secretion of digestive enzymes and saliva • Improves feed digestibility
Immunity stimulants	Beta-glucans (eg. from Saccharomyces cerevisiae)	• Directly supports innate immune system • Improves immune response to all infections • Increases efficacy of vaccines

Table 1. Mode of action of a range of feed additives used as alternatives to AGPs.