# How betaine affects the gut of weaning piglets

Betaine positively influences gut health of weaning piglets. Betaine can support nutrient digestion and absorption, improve the physical barrier of protection, impact microbiota and enhance piglets' defence.

BY LIEN VANDE MAELE, CENTRAL TECHNICAL MANAGER, ORFFA

Betaine is a naturally occurring compound, widely distributed in animals and plants. As a feed additive, available in anhydrous or hydrochloride form, it can be supplemented to animal diets for a variety of purposes.

One of these purposes can be the very efficient methyl donor capacity of betaine, which mostly takes place in the liver. Thanks to the transfer of a labile methyl group, synthesis of various compounds like methionine, carnitine and creatine is promoted.

This way, betaine influences protein, lipid and energy metabolism and, consequently, beneficially modifies carcass composition.

Another reason to add betaine in a feed is related to its function as a protective organic osmolyte. In that function, betaine helps cells all over the body maintain water balance and cellular activity, especially during stress. A well-known example is the positive impact of betaine on animals under heat stress. In pigs, different beneficial effects of supplementing with betaine are described. This article will focus on the role of betaine as a feed additive to support gut health in weaning piglets.

## Increased digestibility

Several studies with betaine reported influences on ileal or total tract digestibility of nutrients in pigs. The repeated observation of increased ileal digestibility of fibre (either crude fibre or neutral and acid detergent fibre) suggests betaine stimulates bacterial fermentation in the small intestine, since intestinal cells do not produce fibre-degrading enzymes. The fibre fraction of plants holds nutrients, which can be released during this microbial fibre degradation.

Consequently, improved dry matter and crude ash digestibility was also observed. On total tract level, an improvement of crude protein (+6.4%) and dry matter (+4.2%) digestibility

Figure 1 - Activities of intestinal digesta enzymes in piglets supplemented with betaine at 0 mg/kg, 1,250 mg/kg or 2,500 mg/kg diet.

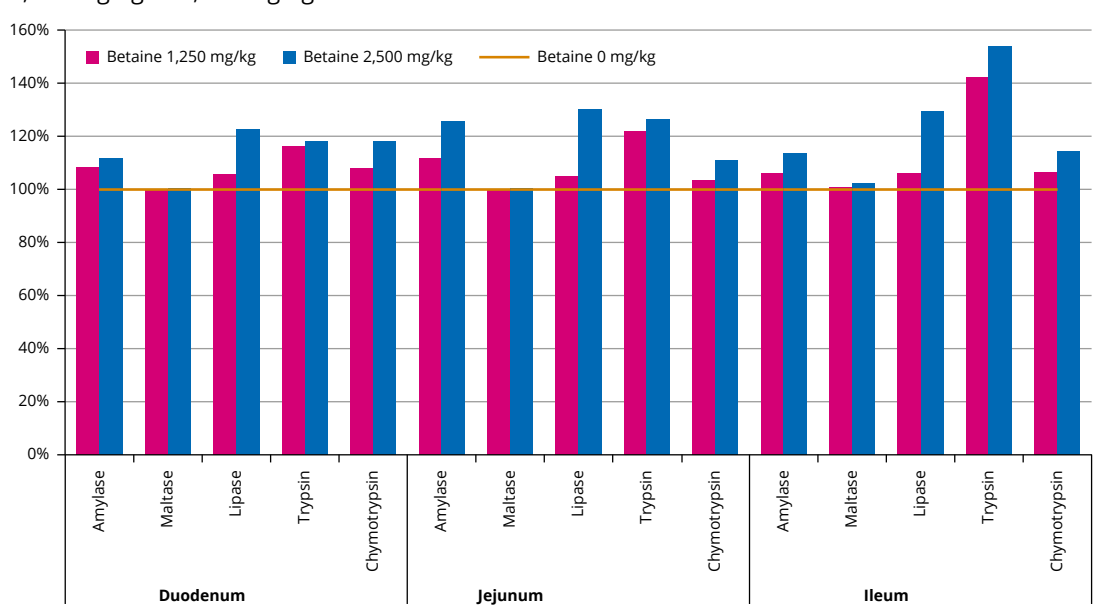



PHOTO: SHUTTERSTOCK

**Incorporation of betaine in pig diets also leads to a reduction in the maintenance energy requirement of the animal.**

was reported in piglets supplemented with 800 mg betaine/kg in their diet. In addition, a different study showed improved apparent total tract digestibility of crude protein (+3.7%) and ether extract (+6.7%) by supplementing 1,250 mg/kg betaine.

## Enzyme production

A possible reason for observing improved digestibility of nutrients is an influence of betaine on enzyme production. In a recent *in vivo* study regarding the effect of betaine supplementation in weaned piglets, the activities of digestive enzymes (amylase, maltase, lipase, trypsin and chymotrypsin) in digesta were evaluated (*Figure 1*). All enzymes except maltase showed increased activity, and the effect of betaine was more pronounced at 2,500 mg betaine/kg feed than at 1,250 mg/kg. Increased activity could result from higher enzyme production, but also from improved catalytic efficiency of the enzymes.

In an *in vitro* trial, it was demonstrated that by adding NaCl to create hyperosmolarity, trypsin and amylase activity are inhibited. The inclusion of different levels of betaine in this test restored the inhibitory effect of NaCl and increased enzyme activity. However, when no NaCl was added to the buffer solution, betaine inclusion did not influence enzyme activity at lower concentration but did show an inhibitory effect at relatively high concentration.

## Reduced maintenance energy

Increased digestibility does not solely explain the reported improved growth performance and feed conversion in pigs supplemented with dietary betaine. Incorporation of betaine in pig diets also leads to reduced maintenance energy requirement of the animal. A hypothesis for this observed effect is the reduced need for ion pumping, an energy-requiring process, when betaine is available for maintaining the intracellular osmolarity. Under conditions where energy intake is limiting, effects of betaine supplementation are therefore expected to be more pronounced by increasing the availability of energy for growth instead of maintenance.

## Intestinal structure

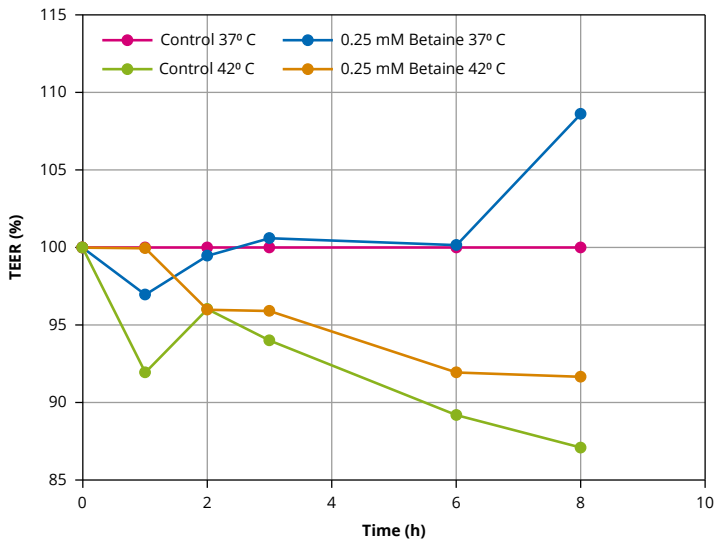
The epithelial cells lining the intestinal wall need to cope with highly variable osmotic conditions generated by the luminal content during nutrient digestion. Meanwhile, these enterocytes need to control the exchange of water and different nutrients between the intestinal lumen and the plasma. To protect the cells against these challenging conditions, betaine is an important organic osmolyte. Examining betaine concentrations in different tissues shows that intestinal tissue contains considerably high betaine levels. Moreover, it has been observed that these levels can be influenced by dietary betaine concentration. Well-balanced cells will have better proliferation and good resilience. Accordingly, researchers found that increasing betaine levels in piglets increased duodenal villus height and ileal crypt depth, and that the villi were more uniform.

In another study, increased villus height were observed in the duodenum, jejunum and ileum without influence on the crypt depth. The protective effects of betaine on intestinal structure might be even more important under specific (osmotic) challenges, as observed in broilers infected with coccidia.

## Gut barrier effect

The intestinal barrier mainly consists of epithelial cells, attached to each other by tight junction proteins. The integrity of this barrier is fundamental to prevent the entry of harmful

Figure 2 - *In vitro* effect of high temperature and betaine on the trans-epithelial electrical resistance (TEER) of cells.




substances and pathogenic bacteria that otherwise would cause inflammation. In pigs, a negative effect on the gut barrier can occur as a result of mycotoxin contamination of feed or as one of the negative impacts of heat stress.

To measure the influence on the barrier effect, *in vitro* tests on cell lines, measuring trans-epithelial electrical resistance (TEER), are often used. With the application of betaine, improved TEER was observed in multiple *in vitro* experiments. When cells are exposed to high temperatures (42°C), there is a decrease in TEER (*Figure 2*). The addition of betaine in the growth medium of these heat-exposed cells counteracted the decreased TEER, indicating improved heat resistance.

Additionally, *in vivo* research in piglets measured increased expression of tight junction proteins (occludin, claudin-1 and zonula occludens-1), in the jejunal tissue of animals on a diet with 1,250mg/kg betaine compared to control. Also, the marker for intestinal mucosal injury – diamine oxidase activity in the plasma of these pigs – was significantly lower, indicating a stronger gut barrier. When betaine was supplemented to the diet of growing finishing pigs, increased gut tensile strength was measured at slaughter.

## Antioxidative effects

Some recent studies link betaine to the antioxidative system and describe reduced free radicals, lower malondialdehyde (MDA) levels and improved glutathione peroxidase (GSH-Px) activity. A recent study in piglets showed an increase in GSH-Px activity in the jejunum, while MDA was not influenced by dietary betaine.

## Microbiota

Betaine acts not only as an osmoprotectant in animals. Multiple bacteria can also accumulate betaine by de novo synthesis or by transport from the environment. There are indications that betaine can have a positive effect on the bacterial population of the gastrointestinal tract of weaned piglets. Total ileal bacterial numbers, and specifically the number of bifidobacteria and lactobacilli, were increased. Also, lower numbers of enterobacteria were found in the faeces.

## Decreased diarrhoea rate

A last observed effect of betaine on gut health in weaning piglets is a decrease in diarrhoea rate. This effect could be dosage-dependent – dietary supplementation of 2,500 mg/kg betaine was more effective than 1,250 mg/kg in decreasing the diarrhoea rate. However, performance of weaned piglets was similar at both supplementation levels. Other research has shown lower diarrhoea rates and morbidity in weaned piglets when betaine was supplemented at 800 mg/kg.

## Betaine hydrochloride (HCl) as acidifier

Another interesting concept is the potential acidifying effect of betaine HCl as a source of betaine. In human medicine, betaine HCl supplements are available, often in combination with pepsin, to support people with stomach problems and digestive troubles. Betaine HCl serves in this case as a safe source of hydrochloric acid. Although no information is available about this property when betaine HCl is included in piglet feed, it could be of great importance. For the young weaning piglet, it is known that gastric pH can be relatively high (pH>4), impairing the activation of the protein-degrading enzyme pepsin from its precursor pepsinogen. Optimal protein digestion is not only important for good availability of this nutrient for the animal. Undigested protein leads to unwanted proliferation of opportunistic pathogenic bacteria and increases problems with post-weaning diarrhoea. The low pKa value of approximately 1.8 for betaine leads to the dissociation of betaine HCl after ingestion, resulting in acidification of the stomach.

That transient reacidification has been observed in a pilot study in humans and in a study in dogs. After a single dose of either 750 mg or 1,500 mg betaine HCl, gastric pH of dogs previously medicated with a stomach acid reducing agent severely dropped from an approximate pH 7 to pH 2. In the unmedicated control dogs, however, the stomach pH level was approximately 2, independent of the supplementation with betaine HCl.

## Betaine benefits gut health

Betaine positively influences gut health of weaning piglets. This review of literature highlights how betaine can support nutrient digestion and absorption, improve the physical barrier of protection, impact microbiota and enhance piglets' defence.

*References available on request (maele@orffa.com).*