

Understanding the multiple facets of zinc in pig production

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The success of zinc oxide in piglet diets is challenged by concerns about some detrimental consequences for animal and human health, and the environment. Recent studies have shown that the use of zinc in pig production can show two facets in opposite directions.

Its usage is versatile: generally as a nutritional source in all diets, but more specifically also as a gut flora regulator after weaning. This makes a clear difference between the nutritional and the pharmacological dosage. Zinc interacts with other dietary factors, for example with phytate, but the strongest antagonist may not be the expected one. Zinc oxide at high dose exerts an effect on piglet gut microbiota, but not always the expected one. What is sure is that the excess of zinc in pig feeds increases the risk of counter performance, of environmental accumulation, and of bacterial resistance.

A potentiated form of zinc oxide, HiZox, is a cost effective, safe and sustainable solution for piglet gut health.

Dosage levels

When supplied in order to fulfil animal requirements, zinc must be ingested, absorbed, and metabolised. The primary objective is to prevent clinical and sub-clinical deficiencies in all animal species and categories. Any supra-nutritional dosage must be justified as homeostasis regulates and limits the capacity for intestinal absorption. In premixes, cost effective sources are either zinc oxide or zinc sulphate. The choice between the two forms is today more a question of price, safety levels, technological properties, and formulation habits.

Bioavailability studies are poor, outdated and difficult to interpret as the quality of zinc oxide products in the market is highly heterogeneous. This explains a high variability in the bioavailability of zinc oxide sources: relative biological values in pigs have been measured from 50% up to 110% in comparison to zinc sulphate.

When supplied at pharmacological level in



Parakeratosis – a symptom of clinical zinc deficiency.

piglet diets, the expectation to improve growth performance and/or reduce post-weaning diarrhoea mostly comes from direct effects at intestinal level.

Modes of action are still debated, but it seems that a modification of intestinal microbiota will induce indirect effects on the host.

Recent *in vitro* susceptibility studies on 75 reference strains of intestinal origin did not show any higher antibacterial activity on specific bacterial groups, but differences were measured at the species level.

Post-weaning diarrhoea is mostly induced by the adhesion of fimbriated enterotoxigenic *E. coli* strains (ETEC) on specific receptors on the enterocytes.

Zinc oxide dose and source can affect the adhesion of *E. coli* under *in vitro* conditions, both with ileal loop model and pig jejunal epithelial cells (IPEC). Numerous studies have shown that high dosed ZnO improves growth of *E. coli* challenged piglets.

Interaction with phytase

It is well known that dietary phytate reduces the bioavailability of some macrominerals and trace elements like zinc. However, recent findings have proven that phytic acid does not exert the same antagonism if native zinc is distinguished from supplemented zinc.

Plant phytate only interacts with endogenous zinc. Bioavailability of zinc from supplemented sources supplied at nutritional levels seems independent of dietary phytate content.

The chelation of phytate to divalent mineral like zinc can reduce the accessibility of phytase to phytate-P. Thus, excessive levels of zinc may interfere with the release of phytate bound phosphorous.

There is a risk of short term P deficiency, reduced growth performance and longer term impaired bone mineralisation in piglet diets which combine low inorganic P supplementation and pharmacological dosage of zinc oxide.

Linked to the development of microbial resistance or not, zinc oxide at pharmacological dosage is excessively used, especially in countries without strict regulation applied to maximum zinc dietary levels. It is not uncommon that high dosed ZnO is incorporated in the whole nursery phase, and even in early grower period.

However, detrimental effects rapidly overcome the expected benefits on piglet growth and health: at four weeks of supplementation, body weight gain and general health status of piglets, measured by acute phase protein PigMAP, can be degraded.

2500mg Zn/kg incorporated in the diet immediately after weaning may positively affect the immune responses of piglets infected with salmonella, but for a short period of two weeks: after, they show degraded body weight gain and lower T cell populations in the ileal lymph nodes.

E. coli populations

It is common in the industry to expect that gut health should be improved with increased abundance of lactobacilli ('the good bacteria') and decreased enterobacteria ('the bad microbes').

Traditionally, it is expected that the supplementation of gut flora regulators will reduce faecal shedding of *E. coli*. However, some early studies with cultured bacteria or more recent experiments with molecular analysis did not confirm this assumption.

The supplementation of 2500mg/kg Zn for two weeks after weaning modifies the profile of lactic acid bacteria, with reduced lactobacilli, and significant changes in concentrations of weissella, leuconostoc and

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streptococcus. An increase in the total number of Gram negative enterobacterial species may lead to a reduction of the occurrence of pathogenic E. coli strains.

The effects of high dosed ZnO on digestive tract micro-organisms can be compared with other gut health promoters. What may seem surprising is that some acids appear to increase numbers of coliforms and E. coli in the stomach, and have equivocal influences on them in the small intestine.

In parallel, lactobacilli are not clearly affected when measured in the stomach, but are usually reduced in the small intestine.

How dietary acids affect bacterial populations in the digestive tract also needs further evaluation. Recent experiments with antibiotics raised similar questions: pigs which were fed an antibiotic combination showed with traditional culture methods an increase in E. coli enumerations in the small intestine. Molecular analysis confirmed that the higher proportion of proteobacteria was mostly driven by an increase in E. coli populations. Further studies with culture independent techniques utilising analysis of rRNA genes are needed to measure the effects of dietary changes on intestinal and faecal microbial communities in research facilities and in typical commercial settings.

Trace mineral as a nutrient

Pig wastes are generally considered as valuable sources of minerals when used as fertilisers. However, in areas of intensive pig production, continuous spraying of Zn rich manure induces a risk of accumulation in the different environmental compartments (sediment, water and soil).

Even if they are supplemented for a short period of time, high doses of zinc oxide in

piglet diets have a significant impact on the quantity of zinc excreted. A new software, siMMin, developed with the support of INRA (French National Institute for Agricultural Research), enables the zinc concentration of pig wastes from dietary changes to be predicted. When zinc oxide is supplemented at 3kg/T for a period of two weeks after weaning, siMMin shows that it increases the total quantity of zinc excreted in the pig's growing life by almost 30%.

Microbial resistance

Antibacterial compounds are commonly used in piglet diets, whatever they are, either antibiotics at therapeutic or growth-promoting levels, or other feed additives, like minerals zinc and copper, acidifiers, essential oils, etc. An intensive usage of products with antimicrobial activity naturally leads to the development of bacterial resistance.

This is well known for antibiotics, which are more and more banned for in-feed routine usage. Such pressure from regulatory bodies and public health organisations will be more strongly applied to feed additives like used or misused minerals. When an intensive usage of zinc is

Early advertising for the beneficial properties of zinc.



practiced in areas of intensive animal production, it may play a role in the spread of antibiotic resistant bacteria by co-resistance, i.e. presence of different resistance determinants on the same genetic element.

Multi-resistance of E. coli has been significantly associated with zinc concentration in pig manure. Zinc resistance of Staphylococcus aureus of animal origin is strongly associated with methicillin resistance, suggesting that it may be partly implicated in the emergence of some MRSA (Methicillin Resistant Staphylococcus aureus).

Regular zinc oxide

'The dose makes the poison': this is particularly true for zinc oxide in piglet diets, which is often supplemented in excess. The success of this cheap feed ingredient can however lead to inappropriate usages. It is also difficult to rely on a constant quality as regular zinc oxide products show very different chemical and physical properties.

HiZox is a potentiated form of zinc oxide which has proven increased performance compared to regular zinc oxide:

- In vitro, with significant superior inhibitory effect on the growth of pathogenic E. coli strains.
- Ex vivo, with significantly stronger and more rapid capacity to repress the growth of intestinal bacteria in the stomach and the jejunum of weaned piglets.
- In E. coli challenged piglets, with similar responses than high dosed zinc oxide.
- In vivo, either by replacing the pharmacological dosage of conventional ZnO by a dramatically reduced level of HiZox, or supplied in any piglet diets as a gut health promoter, both in research stations and in field trials.



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