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Ban of pharma ZnO in piglets: TIPS ON ITS MODE OF ACTIONS TO SELECT PROPER ALTERNATIVES

"The multifunctional effects of pharmacological zinc oxide are not anymore available for European piglets' producers. Nevertheless, many universities and research program keep on studying its mode of action to better understand which alternatives are the best. Among the key mechanisms to focus on zinc bioavailability, its ability to manage gut integrity and indirectly to modulate inflammation or microbiota are probably the most important to keep in mind."

It has been already more than half a year since the ban of the use of ZnO at pharmacological levels happened in piglets in the European commission. Nevertheless, several countries like France or Germany were exposed to this challenge even before due to the earlier expiration of authorisation of the sources available. Have piglets producers found the proper alternatives since?

Market feedbacks estimate that half of the market may have already selected their alternative when the other half is still exploring the possibilities.

TIPS 1: THERE WAS ZINC IN PHARMACOLOGICAL ZINC OXIDE!

A certain market confusion occurred in 2021 with the emergence of numerous additive suppliers suddenly interested by this pharmacological zinc oxide removal. Ranging from probiotics to MCFA and including botanicals, nutritionists may have forgotten for a while that there is essential zinc in zinc oxide. A transitory zinc deficiency can happen at weaning so why not choosing a nutritional zinc oxide that can both achieve zinc bioavailability and gut microbiota management?

A recent study done by SEGES (leading innovation center in Denmark) and published by Nielsen et al, in 2022, revealed the apparent total tract digestibility (ATTD) of 6 different zinc sources supplemented during the first 14 days after weaning at 100ppm Zn (figure 1). Potentiated zinc (HiZox®) displayed a numerically improved bioavailability among sources compared to other inorganic sources and even an organic source such as Zinc Glycinate. This may be due to its unique physico-chemical properties that makes its dissolution optimal, steady rate to provide a continuous diffusion of ionic zinc without binding to antagonists.

TIPS 2: CHOOSE CAREFULLY YOUR NEW ZINC SOURCE

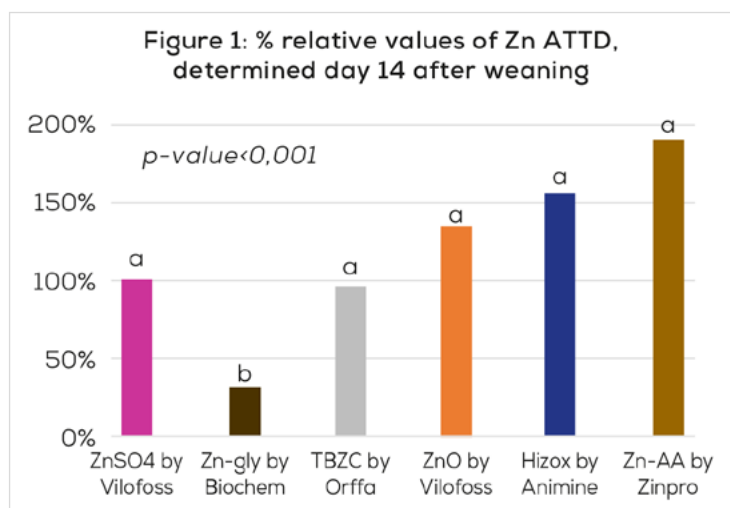
Recent publications highlighted why considering physical & chemical characteristics of zinc sources is crucial to predict their bioavailability. During a 3-year PhD thesis, more than 30 well-defined grades of zinc oxide (ZnO) were collected from around the world and analyzed. The results showed that their micro characteristics strongly influence their dissolution kinetics and thus final bioavailability.

The different analyzed sources can be sorted into three main categories:

- ‘Large Dense Particles’ (LDP) are found in coarse ZnO powders. These are large non-porous particles which dissolve too slowly to become bio-accessible to the intestinal zinc transporters and thus have poor bioavailability.
- ‘Small Aggregate Particles’ (SAP) are powders with a smaller particle size, high Specific Surface Area (SSA) and lower density than LDP. These powders dissolve too quickly, rapidly bind to antagonists and have limited final bioavailability.
- ‘Small Aggregated and Agglomerated Particles’ (SAAP). Potentiated zinc (HiZox®) is alone in this category, it is a source with a larger particle size than SAP but with a high Specific Surface Area. It dissolves at an optimal, steady rate to provide a continuous diffusion of ionic zinc.

TIPS 3: FOCUS ON ZINC SOURCE ABLE TO IMPROVE GUT INTEGRITY

A review of 20 published papers explains the



impact of zinc oxide on gut integrity. This parameter is key around weaning to avoid mucosa depletion and secure tight junctions in a period when feed intake is compromised. In this review, supplemented doses of zinc oxide were sorted in 2 categories: medium zinc levels (from 200 to 2000 mg Zn) or high zinc levels (from 2000 to 3000 mg Zn). The summary revealed as

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HiZox®
POTENTIATED ZINC

CoRouge®
MONOVALENT COPPER

ManGrin®
HIGHLY PURIFIED MANGANESE

HiZox®
POTENTIATED ZINC

High

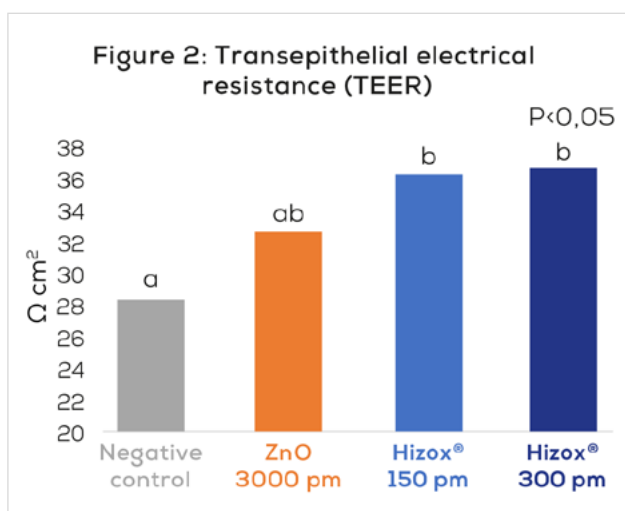
- ✓ Concentration
- ✓ Flowability
- ✓ Safety standards
- ✓ Stability
- ✓ Bioavailability
- ✓ Animal performance



example that expression of proteins involved in tight junction (ZO-1) was positively affected in 92% of trials with high ZnO and in 78% of the studies with medium ZnO.

Improving gut integrity is a key mode of action of ZnO and reduces passive transcellular absorption while preventing uncontrolled transport of potentially harmful agents (ex: endotoxins).

A study published with Ghent university revealed that nutritional dose of potentiated zinc (HiZox®) performs at least as good as pharmacological ZnO on gut integrity (see figure 2). TEER is a marker of gut integrity: the permeability of the mucosa decreases when TEER increases.



TIPS 4: TARGET ZINC SOURCE DESIGNED TO MITIGATE GUT INFLAMMATION

A second literature review gathered 26 published

papers focusing on inflammatory markers. It revealed the beneficial effects of medium Zn level (200-1000 ppm Zn including potentiated zinc HiZox®) or high zinc levels (> 2000 ppm) from ZnO. These papers studied gene expression in intestinal mucosa or quantification in blood of the following inflammatory biomarkers: interleukin 1 family (IL-1), interleukin 6 (IL-6), tumor necrosis factor alpha (TNF- α), and interferon gamma (IFN- γ). All of these biomarkers produced by the cells of the immune system have ability to initiate inflammatory response.

According to this literature review, high or medium levels of ZnO supplementation can reduce the overproduction of pro-inflammatory cytokines. It was found that pharmacological levels of ZnO can significantly decrease the gene expression and/or the concentration of IL-1, IL-6, TNF- α , and IFN- γ .

SUMMARY

The multifunctional effects of pharmacological zinc oxide are not anymore available for European piglets' producers. Nevertheless, many universities and research program keep on studying its mode of action to better understand which alternatives are the best. Among the key mechanisms to focus on zinc bioavailability, its ability to manage gut integrity and indirectly to modulate inflammation or microbiota are probably the most important to keep in mind. There is a source of potentiated zinc available on the market that can address all of these mechanisms.