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# **ZnO MODE OF ACTION IN PIGLETS:** FOCUS ON ZN BLOOD LEVELS, ITS HOMEOSTASIS AND ADG

Animine

"Zinc is an essential nutrient that play a crucial role in the body. Zinc deficiency can lead to a reduction on feed intake, increase of paracellular permeability, weakness of the immune system, etc. In other words, no feeding strategy should be entirely void of zinc, as the mineral absolutely needs to be supplied."

A fter the decision to ban the medicinal use of zinc oxide in piglet diets, industry is seeking for feed additives which can reduce the risk of digestive disorders in critical phases like the post-weaning period. Specific potentiated form of zinc oxide can be used in premixes at nutritional levels without prescription and can efficiently modulates intestinal bacterial populations and improve gut barrier function.

#### PHARMACOLOGICAL ZnO: HAVE WE EVER KNOWN HOW IT WORKS?

First it is needed to remind that only the pharmacological usage of zinc oxide in piglet diets is currently concerned by the ban. This means that the prohibition of ZnO in the European Union is restricted to medicated feeds which are prescribed by qualified veterinarians. This does not apply to the nutritional usage of zinc oxide which is routinely included in premixes and remains the dominant source of zinc utilised by the feed industry.

Zinc is an essential nutrient that play a crucial role in the body (modulation of the immune system, antioxidant pathways, cellular permeability...). Zinc deficiency can lead to a reduction on feed intake, increase of paracellular permeability, weakness of the immune system, etc. In other words, no feeding strategy should be entirely void of zinc, as the mineral absolutely needs to be supplied.

Pharmacological dosage of ZnO provides high quantity of zinc, in a period where feed intake is depleted, completed by interesting antimicrobial properties and is well known for its effect on diarrhoea reduction and weight gain of weaned piglets. However even after decades of use, there still no consensus on its modes of action.



Source: Bologna University

Animine research program ZINCOSUPP (including several theses with renowned European universities) is focusing its effort on understanding every potential hypothesis on the ZnO mode of action (see figure 1, adapted from University of Bologna, Italy). This article will focus on the first phase: correlations between zinc blood concentration, homeostasis and final performance.

#### EFFECTS OF ZnO FED LEVELS ON BLOOD ZINC LEVELS AND HOMEOSTASIS

An exhaustive literature review was performed from AniLib scientific database. Out of 151 publications on pharmacological use of ZnO in weaned piglets, 38 were selected as they contained data on blood Zinc concentration at the end of the studies.

References of selected papers:	
Acta Agriculturae Scandinavica	1995
Archives of Animal Nutrition	2011, 2013, 2014
Animal Feed Science and Technology	2017, 2018
Asian Australian JAS	2014, 2020
Asian Journal of Animal and Veterinary Advances	2012, 2013, 2018
British Journal of Nutrition	2014
Canadian JAS	2019
Journal of Animal Physiology and Animal Nutrition	2006
Journal of Animal Science	1970, 1993, 1996, 1999, 2001, 2002, 2009, 2013, 2019
Journal of Animal Science and Biotechnology	2020
Journal of Nutrition	1985, 2004
Journal of Trace Elements in Medicine and Biology	2018
Journal of Veterinary Diagnostic Investigation	2019
Journées de la Recherche Porcine	2003, 2005
KSU Swine Day	1998, 2008
PIOS one	2017
WUR report	2016



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**Figure 2:** Review of blood Zn concentration in piglets fed different dietary Zn content for 2 weeks post weaning.

As shown on Figure 2 (see yellow highlighted area), a zinc supplementation below requirements (estimated to be at 100 mg/kg, NRC 2012) lead to low blood zinc levels. Although the majority of the observations indicated a low zinc in the blood in this range, some trials observed a high concentration of zinc in the blood of piglets. This could be due to a high Zinc status at weaning due to intake of zinc rich creep feed before weaning.

An increase on blood Zinc levels (from 0 to 1.3 mg/L) linked with higher ZnO supplementation dosages, (from 200 to 500 mg/kg) is also observed in a dose-response manner. However, the supplementation of ZnO from 500 up to 1500-2000 mg/kg zinc in the complete feed, seems to reach a plateau on blood levels (see figure 2, green highlighted area). This illustrates how piglets are maintaining their homeostatic regulation and buffering the excess of dietary zinc.



When the zinc supplementation exceeds 2000 mg/ kg zinc (see figure 2, red highlighted part), the homeostatic regulation capacity of piglets is exceeded and blood zinc concentration rise again. At such high levels, higher variability of blood zinc concentrations is also observed. This might be related to weaning age and individual feed intakes of piglets involved in this set of literature review. The higher ZnO supplementation is, the higher will be the feed consumption, resulting in a higher risk of piglet toxicity due by-passed homeostatic regulation capacity.

### ANY CORRELATION BETWEEN BLOOD ZN CONCENTRATION & PIGLET PERFORMANCE?

A second exhaustive literature review was performed from AniLib scientific database. Out of 151 publications on pharmacological use of ZnO in weaned piglets, 19 papers were selected for the purpose of this new review. Filtering criteria were: daily weight gain, blood zinc concentration (at the end of 2-6 weeks studies) and ZnO supplementation levels (2-3000 mg Zn/kg complete diet).

References of selected papers:	
Animal Feed Science and Technology	2018
Animal	2015
Animals	2021
Asian Australian JAS	2020
Asian Journal of Animal and Veterinary Advances	2012, 2013
British Journal of Nutrition	2014
Journal of Animal Science	1993, 1996, 1999, 2001, 2002, 2009
Journal of Animal Science and Technology	2014
Journal of Trace Elements in Medicine and Biology	2018
Murdoch University report	2010
KSU Swine Day	2008
Veterinarni Medicina	2015
WUR report	2016

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The stress of weaning generally induces piglets anorexia in the first days right after the suckling period. As a direct consequence of this reduced feed intake, the supply of nutrients (incl. zinc) becomes limited in a very critical period of the young animals development. Thus, the risk of transitory sub-clinical zinc deficiency is a real issue that can be compensated by very high dietary Zn supplementations. Pharmacological dosage of ZnO can correct sub-optimal blood zinc levels below 1-2 mg/L. Growth improvement are generally observed following this repletion of the Zn circulating pool by ZnO.

Once minimum daily ingestion of zinc is naturally achieved by piglets, then blood Zn concentration is tightly regulated and is stabilised thanks to piglets homoeostatic balance. When blood Zn level is at the plateau, the effect of ZnO supplementation on body weight gain is less obvious but is still observed. Pharmacological dosage of zinc oxide has the potential to restore Zn status of the weaned piglet.

#### A POTENTIATED ZINC SOURCE AT PIGLETS RESCUE!

HiZox<sup>®</sup> is a potentiated zinc source for piglets manufactured in Europe that shares common points with pharmacological zinc oxide. Indeed, being a very bioavailable source of Zn, its supplementation can restore piglets Zn blood concentration and



**Figure 3**: Correlation between blood Zn levels and average daily gain of weaned piglets fed pharmacological levels of ZnO. First point of each line is a negative control (without ZnO or low dietary Zn concentration) and the last point is pharmacological dosage.

compensate the risk of transitory deficiency during the critical phase of weaning even when used at low and nutritional dosage.

Additionally, this additive presents a particular chemical and physical structure obtained with a unique patented process and that provides a powerful antibacterial effect, again at low dosage, to control pathogenic diarrhea.

This nutritional solution used for 10 years in Europe and Asia has demonstrated its efficacy in a large variety of situations, as long as it is well accompanied with proper management and biosecurity.

