3. Does dietary Zn have an impact on inflammatory status?

BY THE ANIMINE TECHNICAL TEAM. WWW.ANIMINE.EU

W elcome to the third in Animine's series of articles, which reviews scientific literature on the effects of the pharmacological dosage of zinc oxide (ZnO) in weaned piglet diets. In the European Union, medicated ZnO will be totally banned from June 2022. It is interesting to note that abroad there is also a growing number of countries following this tendency, such as China, where the supplementation of pharmacological levels of ZnO is already restricted.

The pharmacological dosage of ZnO is well known for its effect on diarrhoea reduction and improved weight gain of weaned piglets. However, even after decades of use, there is still no consensus on its modes of action. This series of articles will review existing scientific literature with a particular focus on its key effects and mechanisms.
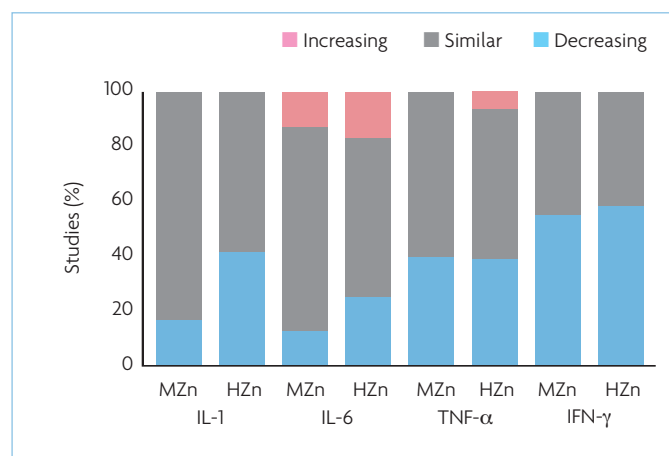
It will also be inspired from the latest outcomes of the ZincOSupp research network supervised by Animine. This ambitious scientific programme, involving several renowned universities, addresses the suppression of pharmacological ZnO, while studying the proper supplementation of the potentiated zinc source, HiZox.

Relationship between dietary Zn and inflammation

A literature review was performed from AniLib database (Animine internal library). From a total of 152 publications on pharmacological use of ZnO in weaned piglets, 26 papers were selected for the purpose of this review. Filtering criteria were:
• ZnO supplementation at 2,000-3,000mg Zn/kg of complete diet compared to a negative control (supplementation <200ppm Zn).
• Analyses of 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).

Fig. 1. Effect of dietary Zn on inflammatory markers (significant effect or trend). MZn = medium Zn level (200-1000ppm Zn); HZn = high Zn level (>2,000ppm).

References of selected papers:

Animal Feed Science and Technology	2013, 2020
Animals	2015, 2021
Animal Nutrition	2017
Asian-Australasian JAS	2018
Animal Production Science Journal	2018
Animal Science Journal	2014
British Journal of Nutrition	2013, 2014, 2018
Biological Trace Element Research	2017, 2018
Canadian Journal of Animal Science	2006, 2014
Frontiers in Veterinary Science	2021
Innate Immunity	2014
Journal of Animal Science	2016
Journal of Nutritional Science and Vitaminology	2020
Journal of Trace Elements in Medicine and Biology	2018
Oncotarget	2017
PLOS One	2014, 2017
Scientific Reports	2019
WUR report	2016

These biomarkers are produced by cells of the immune system, including macrophages, and initiate inflammatory response.

Weaning is a stressful event which is associated with increased inflammation status. The gene expression of inflammatory cytokines in the gut is upregulated during this period. Some pro-inflammatory cytokines, like TNF-α and IFN-γ, increase the intestinal permeability through the disruption of tight junctions. Fig. 1 summarises what literature says about the effect of Zn on inflammatory cytokines. It represents the percentage of studies which demonstrated an increasing (in pink), decreasing (in blue), or no effect (grey) of medium (MZn) or high (HZn) zinc levels in comparison to a negative control. Only statistically significant differences were selected for increasing or decreasing effects.

High or medium levels of ZnO supplementation can reduce the overproduction of proinflammatory cytokines, according to this literature review (Fig. 1; blue colour). 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, in 42%, 25%, 39%, and 60% of the selected studies, respectively, when compared to the control group. Medium zinc levels were often associated with alternative zinc oxide sources (ex: potentiated ZnO). ∎