THE EFFECT OF ZINC IN THE DIET FOR WEANED PIGLETS AND THE POSSIBILITIES OF SUBSTITUTION - REVIEW

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Abstract

Zinc in the body affects growth, development, reproductive ability, blood formation and metabolism of nucleic acids, proteins and carbohydrates. It plays a significant role in the development of cartilage and bone and has a positive effect on the development of skin derivatives. It is an essential ingredient of more than 200 enzymes; it influences the activity and stability of many of them and can be considered a significant antioxidant factor. Zinc acts on the function of the glands and activates the hormonal activity of the pituitary gland. It is essential for cellular immunity and cell proliferation, wound healing, leukocyte formation and function. It affects phagocytosis and antibody production. The zinc concentration in blood and blood plasma responds to changes in diet. Resorption occurs in the small intestine and is significantly affected by chemical form and solubility. The usability of zinc negatively affects the excess of calcium, phosphorus, iron, copper, cadmium, lead and coarse fiber in the feed. Excretion of endogenous zinc takes place via saliva, pancreatic and intestinal juices and bile, with a large amount of excretion by colostrum and milk. Zinc not resorbed and zinc excreted into the digestive tract leaving in the feces. The need for zinc is relatively high in juveniles with high growth rates. The underlying symptoms of the deficiency are reduced feed intake, decrease of growth, changes in skin, mucous membranes, impaired healing of wounds, weakening of immune functions and reproductive disorders.

Zinc and its compounds have a number of positive effects that make piglets better offset by changing the feed, environment, and weaning stress. The use of high therapeutic doses of zinc oxide in feed for weaned piglets has hitherto been a common practice that has allowed pig farmers to stimulate growth while keeping diarrhea and disease under control in a critical period after weaning. However, zinc also has a number of negative effects to be taken into account when used in high doses.

Key Words: Zinc, zinc oxide, pig, piglet, weaning

An important factor influencing the quality of mineral nutrition is the bioavailability of nutrients in the animal's organism, which depends on the binding to an inorganic or organic component. While the usability of inorganic zinc compounds (e.g. sulphates, oxides) is very low (10-12%), the unused residue excreted from the animal's body adversely affect the environment mainly by soil accumulation. In connection with the effort to maximize the digestibility of the nutrients used in animal nutrition and at the same time as the lowest environmental burden, minerals in organic form (chelates), which are used up to 90% in the body of the animal, are increasingly used, and excretion of the remainder environmental contamination is reduced (Wang, 2010). The accumulation of chelated microelements in the soil due to their very high digestibility is negligible and therefore does not threaten the natural biological processes in the soil. When using these forms of microelements it is possible to achieve better vitality of weaned piglets, reduce weaning stress, improve immunity and reduce losses.

Zinc is therefore an indispensable element in the nutrition of pigs, and its need must always be taken into account when setting of feed mixtures. The recommended content of Zn in piglets is between 100-130 mg / kg of the mixture, with conventional feeds containing approximately 30-40 mg of Zn and the remainder being supplemented on the required level. In order to minimize the burden on the environment, the maximum concentration of Zn in feed for pigs at 150 mg / kg (EU Regulation 1334/2003) was set. This concerns the normal nutritional use of Zn and its compounds as essential components of mineral nutrition in feed for pigs, however much attention should be paid to the use of high pharmacological doses of zinc oxide (ZnO) at the level of 1500 to 4000 mg / kg (ppm) in feed for piglets at the time of weaning where zinc is used as an antimicrobial agent and growth stimulator. Already in the 1980s, high levels of ZnO have been found to reduce the incidence of diarrhea and improve growth in weaned piglets (Poulsen, 1989). This use was made more prominent at the time of the ban on the use of antibiotics as growth stimulants (2006), which allowed the use of high doses of ZnO for veterinary prescription even in some countries with a previous ban. The mechanism of growth stimulation through ZnO is not yet fully elucidated and probably occurs through multiple regulatory pathways. For example, it has been shown that ZnO regulates secretion of brain-gut peptides that stimulate feed intake (Li et al., 2010). ZnO reduces secretion of ions to the intestinal lumen, thereby enhancing water resorption and preventing diarrhoea. ZnO reduces the release of pro-inflammatory histamine, by inhibiting proliferation and activation of intestinal mast cells (Kim et al., 2012). Supplementation of weaning diets of piglets with ZnO during a short period of time at relatively high doses (2,500ppm) stabilizes intestinal microbiota and prevents attachment of pathogenic bacteria (Starke et al.,2012). In in vivo studies with weaned piglets, a diet with pharmacological concentrations of ZnO has been shown to reduce paracellular permeability and prevent the translocation of pathogenic bacteria such as E. coli and Enterococcus spp. in mesenteric lymph nodes of the small intestine (Huang et al., 1999). However, ZnO has also been found to have no effect on killing or the number of E. coli in vivo or in vitro, and the effect of zinc is rather systemic via blood than direct gastrointestinal effects (Jensen-Waern et al., 1998; Roselli et al., 2003).

Weaning often results in small-intestinal atrophy and dysfunction in piglets, which is a major factor responsible for growth retardation and diarrhea. The use of high levels of ZnO in feed helps maintaining the normal morphology of the gastrointestinal tract in weaned pigs (Li et al., 2001; Carlson et al., 1998), suggesting that ZnO protects the small intestine from damage associated with weaning. This is probably due to the effect of ZnO on increasing expression of genes for Insulin-like growth factor-I (IGF1) and its receptors, which is an important regulator of growth and differentiation of intestinal cells (Li et al., 2006). Thus, the beneficial effect of ZnO during weaning can be the consequence of preventing the damage of the intestines.

The antibacterial activity of ZnO is considered to be due to the generation of hydrogen peroxide from its surface (Sawai et al., 1998). It is assumed that increasing the surface area of ZnO particles (decreasing particle size) may increase the efficiency of hydrogen peroxide production and hence antibacterial activity. Osamu Yamamoto (2001) confirmed the suspect and found that the antibacterial activity of ZnO increased with decreasing particle size and increasing powder concentration. Therefore, ZnO particle forms have been recently investigated and utilized to achieve surface magnification either by size reduction (nanoparticles) or by forming a porous surface (porous particle). Wang et al. (2017) suggested that zinc oxide nanoparticles (1200 mg/kg) might be used as a substitute for colistin sulfate and high dietary ZnO in weaned piglets. Long et al. (2017) used low levels of porous particles and ZnO nanoparticles to find out their potential to replace high doses of ZnO in weaning piglets. They concluded that dietary supplementation with low dose of porous and nano ZnO has similar (even better) effect on improving growth performance and intestinal morphology, reducing diarrhea and intestinal inflammatory as high dose of regular ZnO. In addition, porous ZnO particles had a more pronounced effect on diarrhea reduction than ZnO nanoparticles; on the contrary, nanoparticles had a better anti-inflammatory effect. It has also been found that the usage of porous and nanoparticles in low concentrations promotes adaptation to oxidative stress as well as high concentrations of regular ZnO. These particles can fully replace high doses of ZnO even at low feed concentration and thus reduce the negative impact of the use of zinc compounds on the environment.

ZnO originally appeared to be the ideal way to reduce the incidence of diarrhea and to promote the growth performance of piglets at the time of weaning, unfortunately, its use also brings a number of negative impacts. These include frequently discussed microbial resistance. Resistance to zinc itself appears, but above all, the context appears between intensive Zn use and bacterial resistance to antibiotics (Bednorz et al., 2013). This is apparently a consequence of the genetic coupling, as genes of heavy metal resistance and those of antibiotic resistance are sometimes associated. Consequently, the selection of bacteria resistant to Zn leads to the co -selection of bacteria resistant to some antibiotics. Another negative effect of zinc is its possible toxicity. It is a heavy metal that is toxic to most living organisms including pigs. It may affect piglet health and performance (marked depression in feed intake) if used for longer periods (3-4 weeks). High doses of ZnO are therefore only applied for a short time (maximum 14 days) when no adverse effects on animal health have been identified. Another negative is the nutritional interactions detected due to the overproduction of transport proteins that bind to metals such as copper, iron or selenium. Decreased absorption of iron and copper can lead to anemia in piglets (Sandström, 2001). Additional interactions exist between Zn and phytase where high concentrations of Zn prevent phosphorus releasing by phytase and it leads to phosphorus deficiency (Lizardo, 2004). In addition, impurities in commercial ZnO may cause contamination with heavy metals such as cadmium which are subsequently deposited in the body and its high concentrations may persist from the time of weaning to the time of slaughter at values that are unsuitable for human consumption.

Significant environmental impact is last but not least negative aspect of high zinc doses in the mixture for weaning piglets (Meyer et al., 2002). Much of the Zn leaves the body in the form of excrement due to high doses and low bioavailability. Contamination of water resources and the accumulation of this element in the soil can occur, resulting in a change in the microbial processes in the soil and the overall change of the ecosystem. For example Denmark demonstrated that soil concentrations of zinc were increasing in their country and calculations showed, especially in acid and sandy soils, zinc levels had exceeded the predicted no-effect concentrations (PNECs) and might be on the point of becoming a 'toxic hazard' (Burch, 2017). However Denmark produces 32 million weaners per year in a relatively small country. If the production of weaners is compared with the number of human it works out at a ratio of 5.8: 1. In comparison in the EU it is a ratio of 0.5: 1 so Denmark produces over 11 times more weaners than the EU average. In addition, zinc soil levels were shown to be falling, especially where the land was grazed or crops were grown, so zinc concentrations in soil can be utilized too. Not all countries are therefore threatened by these dangers at the present time.

The Committee for Veterinary Medicinal Products (CVMP) of the European Medicines Agency (EMA) announced in December 2016 that in their opinion they found the risk/benefit balance was unfavourable for the therapeutic use of zinc oxide and that all products containing zinc oxide should have their marketing authorizations removed. Most European countries, however, do not feel affected by this problem, and rather than banning the use of ZnO, they would welcome the control and monitoring of Zn levels in soil and water in individual countries to gain new information and better understanding of the situation. These countries assumed that the CVMP would change its mind, or the European Commission would postpone the final decision that environmental contamination issues could be reviewed using the agreed assessment methodology and confirmed whether this was a real risk or not. However, in June 2017, the European Commission has decided to ban the use of veterinary drugs containing ZnO because of its negative environmental impact and the increase of the prevalence of antibiotic-resistant bacteria. According to the Commission Decision, existing marketing authorizations should be withdrawn and new marketing authorization applications rejected. The Commission has consulted the Member States on the possible adverse impact of an immediate ban in some countries and has decided to set a five-year period to withdraw the marketing authorisations of veterinary drugs containing zinc oxide. During the period marketing authorizations should be abolished, while allowing the development of appropriate and affordable alternatives and changing breeding practices without re-increasing use of antimicrobials.

It is necessary to focus intensively on the development of products and processes that would replace those existing with ZnO and create a completely new scenario that would address the situation in a comprehensive way. It is necessary to focus on improving the health by respecting all the principles of biosecurity, further exploiting the possibilities of vaccinations in piglets and sows. In terms of management, it is advisable to increase the weaning age of piglets to 28 days, while avoiding excessive loss of sow body condition in the last week of lactation. The clear tendency to use hyperprolific sows emphasizes the problem, since it results in more piglets weaned per sow per year, though these pigs are smaller and weaker, and therefore more sensitive to diseases. It is necessary to deal with the system of artificial lactation systems, to compensate the inability of the sow to maintain the potential growth of the piglets in big litters, as well as to support the intake of feed in piglets at the time of lactation and after weaning. In feed mixtures for piglets, it is advisable to use highly digestible sources of protein, reduce protein or energy, to increase the insoluble fiber content, to use additives that promote proper digestive physiology and intestinal microflora (Medel de la Torre, 2017).

It is very difficult to find a single substance that would replace the effect of antibiotics or ZnO, so it will probably be necessary to use a combination of several substances that can be fed together in feed or water. A suitable group of substances are organic acids and their salts, and medium chain fatty acids that are very effective against gram-negative and gram-positive bacteria and monoglycerides (Medel de la Torre, 2017). Another important group is essential oils and plant extracts, where the variability of the active substance content is disadvantageous and, on the contrary, the advantage is that it is mostly a whole group of substances with different effects. It is certainly advisable to use probiotics, prebiotics and enzymes as a further component of ZnO replacement additives. In recent years, a number of experiments have been made to test this issue, for example, the effectiveness of humic acids or brewer's yeasts for binding the E. coli toxin and clostridium. Silver nanoparticles or porcine immunoglobulins (Hedegaard, 2017) were also tested. The current task is to find a combination of substances that ensure optimum health and performance in weaning piglets without negative environmental impact.

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