

## Effects of Porous Zinc Oxide on Fecal Trace Element Content, Cecal Content, Fecal Short-Chain Fatty Acid Content, and Gut Microbiota Diversity in Weaned Piglets: Postprint

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**Date:** 2018-12-25T00:00:00+00:00

### Abstract

This study aimed to investigate the effects of dietary porous zinc oxide supplementation on trace element content in feces, short-chain fatty acid content in cecal content and feces, and intestinal microbiota diversity in weaned piglets. A total of 192 21-day-old weaned piglets with a body weight of  $(6.32 \pm 0.24)$  kg were randomly allocated into 4 groups, with 6 replicates per group and 8 piglets per replicate (half male and half female). Group A (positive control) was fed a basal diet supplemented with 3,000 mg/kg conventional zinc oxide, group B (negative control) was fed the basal diet, group C was fed a basal diet supplemented with 750 mg/kg porous zinc oxide, and group D was fed a basal diet supplemented with 1,500 mg/kg porous zinc oxide. The experimental period lasted 14 days. The results showed: 1) Compared with group A, fecal zinc content in piglets of groups B, C, and D was significantly decreased ( $P < 0.05$ ); fecal manganese content in group C was significantly higher than that in groups A and D ( $P < 0.05$ ), with no significant difference from group B ( $P > 0.05$ ). 2) Compared with group B, cecal acetic acid content in groups A, C, and D increased by 33.58%, 44.74%, and 39.79%, respectively ( $P < 0.05$ ), and cecal propionic acid content in groups C and D was significantly increased ( $P < 0.05$ ); compared with group A, there were no significant changes in various short-chain fatty acid contents in cecal content of groups C and D ( $P > 0.05$ ); there were no significant differences in various short-chain fatty acid contents in feces among all groups ( $P > 0.05$ ). 3) Compared with group A, the number of unique operational taxonomic units (OTUs) in jejunal content of groups B, C, and D was substantially increased, and the Chao1 and ACE indices were gradually increased in groups B, C, and D, with a trend toward increased Simpson index ( $P = 0.0959$ ). At the phylum level of microbiota, with increasing porous zinc oxide supplementation,

the relative abundance of Firmicutes increased, while the relative abundance of Proteobacteria and Actinobacteria decreased; at the genus level of microbiota, compared with group B, the relative abundance of Streptococcus in groups A and D increased, the relative abundance of Lactobacillus decreased, and the relative abundance of Rothia in groups A and C increased. These results indicate that dietary supplementation of porous zinc oxide in weaned piglets can increase short-chain fatty acid content in cecal content, which is beneficial for improving intestinal microbiota diversity and the intestinal microecological environment; compared with conventional zinc oxide, porous zinc oxide can also reduce zinc emission in feces of weaned piglets, conserve zinc resources, and reduce environmental pollution.

## Full Text

### Effects of Porous Zinc Oxide on Fecal Microelement Contents, Short-Chain Fatty Acid Levels in Cecal Content and Feces, and Intestinal Microbial Diversity of Weaned Piglets

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## Abstract

This experiment investigated the effects of dietary porous zinc oxide (P-ZnO) supplementation on fecal microelement contents, short-chain fatty acid (SCFA) levels in cecal content and feces, and intestinal microbial diversity in weaned piglets. A total of 192 piglets weaned at 21 days with an average body weight of  $(6.32 \pm 0.24)$  kg were randomly allocated into four groups, each consisting of six replicates with eight piglets per replicate (half male and half female). Group A (positive control) received a basal diet supplemented with 3,000 mg/kg common ZnO, Group B (negative control) received the basal diet only, Group C received the basal diet with 750 mg/kg P-ZnO, and Group D received the basal diet with 1,500 mg/kg P-ZnO. The experiment lasted 14 days. The results showed: (1) Compared with Group A, fecal zinc content was significantly reduced in Groups B, C, and D ( $P < 0.05$ ). Fecal manganese content in Group C was significantly higher than in Groups A and D ( $P < 0.05$ ) but did not differ significantly from Group B ( $P > 0.05$ ). (2) Compared with Group B, cecal acetic

acid content increased by 33.58%, 44.74%, and 39.79% in Groups A, C, and D, respectively ( $P < 0.05$ ), while cecal propionic acid content was significantly elevated in Groups C and D ( $P < 0.05$ ). No significant differences were observed in any SCFA levels among Groups A, C, and D ( $P > 0.05$ ), and fecal SCFA contents did not differ significantly across all groups ( $P > 0.05$ ). (3) Compared with Group A, the number of unique operational taxonomic units (OTUs) in jejunal content substantially increased in Groups B, C, and D, with Chao1 and ACE indices showing a gradual upward trend, and Simpson index demonstrating an increasing tendency ( $P = 0.0959$ ). At the phylum level, increasing P-ZnO supplementation elevated the relative abundance of Firmicutes while reducing Proteobacteria and Actinobacteria. At the genus level, compared with Group B, the relative abundance of Streptococcus increased in Groups A and D, Lactobacillus decreased in Groups A and D, and Rothia increased in Groups A and C. In conclusion, dietary P-ZnO supplementation enhanced cecal SCFA content and intestinal microbial diversity while improving the intestinal microenvironment. Compared with common ZnO, P-ZnO reduced fecal zinc excretion, conserved zinc resources, and mitigated environmental pollution.

**Keywords:** porous zinc oxide; microelement; short-chain fatty acids; intestinal flora; weaned piglets

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## Introduction

Modern swine production typically weans piglets at 18–28 days of age, a transition that introduces significant environmental and physiological stress, often causing diarrhea, growth retardation, and even mortality, thereby imposing substantial economic losses. Pharmacological levels of zinc oxide (approximately 3,000 mg/kg) in feed have been shown to significantly reduce diarrhea rates and improve feed intake and daily weight gain in weaned piglets. However, prolonged supplementation of high-dose ZnO adversely affects growth performance, with benefits lasting only about three weeks post-weaning before toxic effects emerge. Moreover, ZnO utilization is poor, with approximately 80% excreted in feces, causing zinc waste and environmental pollution. Growing environmental concerns have spurred research into novel ZnO forms with higher efficiency and lower emissions. Porous zinc oxide, produced through new processes, exhibits better flowability, larger specific surface area, and lower acid-binding capacity than conventional ZnO, effectively reducing post-weaning diarrhea while promoting growth. Short-chain fatty acids and gut microbiota are closely associated with post-weaning diarrhea and intestinal health, yet few studies have examined P-ZnO's effects on these parameters. Therefore, this trial explored the impacts of varying P-ZnO supplementation levels on fecal microelement excretion, intestinal SCFA levels, and microbial diversity to provide theoretical and scientific basis for P-ZnO application in piglet diets.

## 1.1 Experimental Materials

Porous zinc oxide (75% Zn content) was provided by Animine, France, while common zinc oxide (79% Zn content) was supplied by Hubei Bohua Agriculture and Animal Husbandry Technology Co., Ltd.

## 1.2 Experimental Design and Diets

A total of 192 healthy 21-day-old “Duroc × Landrace × Yorkshire” weaned piglets with an average body weight of  $(6.32 \pm 0.24)$  kg were randomly allocated into four groups based on similar body weight: Group A (positive control, basal diet + 3,000 mg/kg common ZnO), Group B (negative control, basal diet only), Group C (basal diet + 750 mg/kg P-ZnO), and Group D (basal diet + 1,500 mg/kg P-ZnO). Each group comprised six replicates with eight piglets per replicate (half male and half female). The experiment lasted 14 days. The basal diet was formulated according to NRC (2012) nutrient requirements for piglets. Composition and nutrient levels are presented in Table 1 .

**Table 1** Composition and nutrient levels of the basal diet (air-dry basis)

Items	Content
<b>Ingredients</b>	
Expanded corn	
Dehulled soybean meal	
Speed detonation soybean	
Soybean protein concentrate	
Fermented soybean meal	
Imported fish meal	
Plasma protein powder	
Whey powder (low protein)	
Acidifier	
Soybean oil	
Sugar	
Choline chloride	
L-Lys • HCl (98%)	
Met	
Thr	
CaHPO	
Sodium glutamate	
Premix <sup>1</sup>	
<b>Total</b>	
<b>Nutrient levels<sup>2</sup></b>	
DE (MJ/kg)	
CP	
Lys	
AP	

<sup>1</sup>Premix provided per kilogram of diet: VA 550.00 IU, VD 400.00 IU, VE 50.00 IU, VK 1.00 mg, VB 2.50 mg, VB 4.50 mg, VB 3.50 mg, VB 0.04 mg, pantothenic acid 20.00 mg, niacin 35.00 mg, biotin 0.10 mg, folic acid 0.40 mg, choline 500.00 mg, Cu (CuSO · 5H O) 12.00 mg, Fe (FeSO ) 110.00 mg, Zn (ZnSO ) 100.00 mg, Mn (MnSO · H O) 10.00 mg, I (KI) 0.40 mg, Se (Na Se O) 0.30 mg.

<sup>2</sup>DE and AP were calculated values; other nutrient levels were measured values.

### 1.3 Experimental Animals and Management

The feeding trial was conducted at the research farm of Tangrenshen Group Co., Ltd. Piglets were housed in nursery pens with slatted floors, fed pelleted diets ad libitum, and provided free access to water. Sanitation and disinfection were performed regularly according to standard procedures, and routine immunization protocols were followed.

### 1.4 Sample Collection

On day 13 at 16:00, one piglet per replicate was selected for sterile collection of rectal content (feces), which was divided into two portions placed in 10 mL cryovials and immediately stored in liquid nitrogen—one for microelement analysis and the other for SCFA analysis. On day 14, one piglet per replicate was slaughtered for sterile collection of mid-jejunum and cecal contents, which were placed in 5 mL cryovials and immediately stored in liquid nitrogen. All samples were subsequently transferred to a -80°C freezer for storage.

### 1.5 Analytical Methods

**1.5.1 Dietary Nutrient Content Determination** Dietary crude protein was determined according to national standard GB/T 6432-1994, lysine according to GB/T 18246-2000, calcium according to GB/T 6436-2002, and total phosphorus according to GB/T 6437-2002.

**1.5.2 Fecal Microelement Content Determination** Fecal microelements were analyzed using an atomic absorption spectrometer (Thermo Fisher ICE3500, USA). Fresh fecal samples were dried at 65°C, ground, passed through a 40-mesh sieve, and stored in sealed bags. Approximately 1-2 g of sample was weighed into a crucible, carbonized on an electric furnace, and ashed in a muffle furnace at 550°C for 4 hours until carbon-free and gray-white. After cooling, 10 mL concentrated nitric acid was added, heated to slight boiling for 5 minutes, filtered hot into a 100 mL volumetric flask, cooled, and diluted to volume for analysis.

**1.5.3 SCFA Content Determination in Cecal Content and Feces** SCFA levels were determined by gas chromatography (Shimadzu GC-2014ATF/SPL, Japan). One gram of sample was mixed with 4 mL ultrapure

water, vortexed for 30 minutes, and centrifuged at 15,000 r/min for 15 minutes. The supernatant was transferred, and the process was repeated once. Combined supernatants were diluted to 10 mL, and 4.5 mL aliquots were mixed with 25% metaphosphoric acid at a 9:1 volume ratio and fixed for over 3 hours. Samples were then centrifuged at 15,000 r/min for 10 minutes, filtered through a 45 μm membrane, and transferred to vials.

Chromatographic conditions: DB-FFAP column (30 mm × 250 μm × 0.25 μm); carrier gas: high-purity nitrogen at 0.8 mL/min; auxiliary gas: high-purity hydrogen; FID temperature: 280°C; injector temperature: 250°C; split ratio: 50:1; injection volume: 1 μL. Temperature program: initial 60°C, increased at 20°C/min to 220°C, held for 1 minute.

**1.5.4 Intestinal Microbial Diversity Analysis** Samples were sent to Shanghai Personal Biotechnology Co., Ltd. for high-throughput sequencing of the 16S rRNA gene in jejunal content.

## 1.6 Data Processing and Statistical Analysis

Data were processed using Excel 2007 and analyzed by one-way ANOVA using SAS 8.0 software. Tukey's test was used for multiple comparisons among groups. Results are expressed as means with SEM indicating dispersion. Statistical significance was declared at  $P < 0.05$ .

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## 2.1 Effects of Porous Zinc Oxide on Fecal Microelement Contents in Weaned Piglets

As shown in Table 2, compared with Group A (3,000 mg/kg common ZnO), fecal zinc content was significantly reduced in Groups B, C, and D ( $P < 0.01$ ). Fecal manganese content in Group C was significantly higher than in Groups A and D ( $P < 0.01$ ) but did not differ significantly from Group B ( $P > 0.05$ ). No significant differences were observed in fecal copper or iron contents among groups ( $P > 0.05$ ).

**Table 2** Effects of porous zinc oxide on microelement contents in feces of weaned piglets (air-dry basis)

Items	Group A	Group B	Group C	Group D	P-value
Zinc (mg/kg)	21,179.00	4,740.00	7,312.00	8,984.00	<0.0001
Manganese (mg/kg)	580.74	641.71	661.03	542.72	

Values in the same row with different superscripts differ significantly ( $P < 0.05$ ). The same applies below.

## 2.2 Effects of Porous Zinc Oxide on SCFA Contents in Cecal Content and Feces of Weaned Piglets

As shown in Table 3, compared with Group B, cecal acetic acid content increased by 33.58%, 44.74%, and 39.79% in Groups A, C, and D, respectively ( $P < 0.05$ ). Cecal propionic acid content was significantly elevated in Groups C and D ( $P < 0.05$ ), while Group A showed no significant change ( $P > 0.05$ ). No significant differences were observed in cecal isobutyric, isovaleric, or valeric acid contents among groups ( $P > 0.05$ ). SCFA levels in cecal content did not differ significantly among Groups A, C, and D ( $P > 0.05$ ). Additionally, fecal SCFA contents showed no significant differences across all groups ( $P > 0.05$ ).

**Table 3** Effects of porous zinc oxide on short-chain fatty acid contents in cecal content and feces of weaned piglets

Items	Group A	Group B	Group C	Group D	P-value
<b>Cecal content</b>					
Acetic acid	1,620.00	1,212.70	1,755.30	1,695.20	
Propionic acid	679.40	554.30	816.90	719.50	
Isobutyric acid					
Butyrate					
Isovaleric acid					
Valerate					
<b>Feces</b>					
Acetic acid					
Propionic acid					

### 2.3.1 Bacterial Clustering Analysis

Based on operational taxonomic units (OTUs) in jejunal content samples, Venn diagram analysis revealed 771 shared OTUs across Groups A, B, C, and D. Group A had 44 unique OTUs, Group B had 272, Group C had 146, and Group D had 169 [Figure 1: see original paper].

**Figure 1** OTUs clustering analysis results

### 2.3.2 -Diversity Analysis

Using QIIME software, sequences from each sample in the OTU abundance matrix were randomly resampled at various depths based on 90% similarity. Chao1 and ACE indices (reflecting community richness) and Shannon and Simpson indices (reflecting community evenness) were calculated. As shown in Table 4, compared with Group A, Chao1 and ACE indices gradually increased in Groups

B, C, and D, though differences were not significant ( $P>0.05$ ). Shannon index was highest in Group B (6.23), followed by Groups C (6.04) and D (5.84), and lowest in Group A (5.30). Simpson index followed a similar pattern, suggesting that high-dose common ZnO tended to reduce microbial richness and evenness, thereby decreasing diversity.

**Table 4** -diversity indices

Items	Group A	Group B	Group C	Group D	P-value
Chao1					
Shannon	5.30	6.23	6.04	5.84	
Simpson					

### 2.3.3 Intestinal Microbial Distribution at Phylum and Genus Levels

Based on taxonomic annotation, the top 20 most abundant species were analyzed at phylum and genus levels. At the phylum level [Figure 2: see original paper], dominant jejunal microbiota included Firmicutes, Proteobacteria, Actinobacteria, and Tenericutes. As P-ZnO supplementation increased, Firmicutes relative abundance increased while Proteobacteria and Actinobacteria decreased. Overall, ZnO supplementation substantially affected jejunal microbial structure and evenness. At the genus level [Figure 3: see original paper], dominant microbiota included Streptococcus, Lactobacillus, Rothia, and others. Compared with Group B, Groups A and D showed increased Streptococcus and decreased Lactobacillus, while Groups A and C exhibited increased Rothia. Additionally, Group C had the highest relative abundances of Acinetobacter and Ochrobactrum.

**Figure 2** Bacterial distribution in jejunum at phylum level

**Figure 3** Bacterial distribution in jejunum at genus level

## 3.1 Effects of Porous Zinc Oxide on Fecal Microelement Contents in Weaned Piglets

Zinc exhibits antagonistic interactions with copper and iron during absorption, where high dietary zinc reduces copper and iron utilization, potentially increasing their fecal excretion due to competition for shared transporters. In this study, compared with the negative control, supplementation with 3,000 mg/kg common ZnO or 750/1,500 mg/kg P-ZnO did not significantly affect fecal copper or iron contents, consistent with Carlson et al. and Wang Chao's findings. Typically, diets with high-dose ZnO are fortified with additional copper and iron to ensure adequate absorption despite antagonism, which may mitigate these

effects. The results also demonstrated that 750 and 1,500 mg/kg P-ZnO significantly reduced fecal zinc content compared with 3,000 mg/kg common ZnO. Wang et al. reported that 1,200 mg/kg nano-ZnO significantly decreased fecal zinc compared with ZnO plus colistin sulfate. Shen et al. demonstrated that coated ZnO could replace high-dose common ZnO to reduce fecal zinc, conserve zinc resources, and minimize environmental pollution, aligning with our findings. Additionally, Group C (750 mg/kg P-ZnO) showed significantly higher fecal manganese than Groups A and D, while Group B had significantly higher fecal manganese than Group D, suggesting no strong correlation between dietary zinc level and fecal manganese, consistent with Xu Shupeí's results.

### 3.2 Effects of Porous Zinc Oxide on SCFA Contents in Cecal Content and Feces of Weaned Piglets

Short-chain fatty acids—including acetic, propionic, butyric, isobutyric, valeric, and isovaleric acids—are produced by gut microbes through anaerobic fermentation of dietary fiber and resistant starch. Acetic acid is rapidly absorbed by intestinal epithelium and enters peripheral circulation to provide energy. Propionic acid is absorbed and transported to the liver for gluconeogenesis. Butyric acid serves as an energy source for colonic epithelial cells, promoting proliferation and development. SCFAs also lower intestinal pH, promote beneficial bacteria such as *Bifidobacterium*, and inhibit pathogen colonization. Thus, increased SCFA levels benefit intestinal health and animal growth. This study found that compared with the negative control, 3,000 mg/kg common ZnO and 750/1,500 mg/kg P-ZnO increased cecal acetic acid by 33.58%, 44.74%, and 39.79%, respectively, with P-ZnO also significantly elevating cecal propionic acid. No significant differences in cecal SCFAs were observed among ZnO-supplemented groups. The lack of difference between low- and high-dose ZnO groups resembles Starke et al.'s findings but contrasts with Janczyk et al., who reported decreased cecal propionic and isobutyric acids after four weeks of high-dose ZnO. This discrepancy may relate to supplementation duration, as negative effects may manifest after prolonged feeding.

### 3.3 Effects of Porous Zinc Oxide on Intestinal Microbial Diversity in Weaned Piglets

Beneficial and harmful bacteria in the piglet gut exist in dynamic equilibrium, which weaning stress disrupts, causing dysbiosis, diarrhea, and reduced feed conversion. This study revealed that compared with Groups B, C, and D, Group A (3,000 mg/kg common ZnO) had fewer total and unique OTUs, lower Chao1, ACE, and Shannon indices, and a declining trend in Simpson index, indicating that high-dose common ZnO reduced jejunal microbial diversity. Conversely, ZnO-free and low-dose ZnO diets enhanced diversity, possibly due to bacterial growth regulation under low-zinc conditions, consistent with Li Zhixue and Lü Hang's findings on ileal microbiota. Previous studies showed high-dose ZnO reduced *Lactobacillus* and increased *Streptococcus* in the ileum, decreased Lac-

tobacillus and *Escherichia coli* in jejunum and ileum of 35-day-old piglets, and tended to reduce cecal *Lactobacillus* and *Bifidobacterium*. These results suggest consistent effects of high-dose ZnO across intestinal segments, with jejunal and ileal microbiota substantially influencing hindgut communities. Our findings of decreased *Lactobacillus* and increased *Streptococcus* in Groups A and D compared with Group B align with previous research, though underlying mechanisms require further investigation.

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### Conclusion

Dietary supplementation with 750 and 1,500 mg/kg porous zinc oxide reduced fecal zinc excretion in weaned piglets, conserved zinc resources, and decreased environmental pollution. P-ZnO enhanced cecal SCFA content and improved intestinal microbial diversity and microenvironment. Compared with common zinc oxide, P-ZnO offers a more sustainable and environmentally friendly alternative for weaned piglet nutrition.

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