THE EFFECTS OF INCREASING SID LYSINE:ME RATIO IN GROWING AND FINISHING PIGS AND THE EFFECT OF COPPER AND ZINC SUPPLEMENTATION IN WEANLING PIGS

by

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Abstract

Seven experiments were conducted to estimate the optimal standardized ileal digestible (SID) lysine:ME ratio for growing and finishing pigs. Experiment 1 determined an optimal SID lysine:ME ratio of 3.16 g/Mcal for 38 to 65 kg gilts. Experiment 2 reported an optimal level of 2.58 g SID lysine/Mcal ME for 55 to 80 kg gilts. Experiment 3 determined an optimal SID lysine:ME ratio of 2.55 g/Mcal for 85 to 110 kg gilts. In Exp. 4 and 5, growth rates were improved with porcine circovirus type 2 vaccine, with the optimal SID lysine:ME ratio for 38 to 65 kg gilts and barrows being 2.99 and 3.36 g SID lysine/Mcal ME, respectively. In Exp. 6 and 7, the optimal SID lysine:ME ratio was 1.86 and 2.61 g/Mcal for 102 to 125 kg gilts and 98 to 118 kg barrows, respectively. These trials indicate the optimal SID lysine:ME ratio for commercial growing and finishing pigs has increased compared with earlier estimates.

Four experiments were also performed to determine the effect of copper (Cu) and zinc (Zn) supplementation on growth performance of weanling pigs. In Exp. 1, both 3,000 ppm Zn from zinc oxide (ZnO) and 150 ppm Cu from tri-basic copper chloride (TBCC) independently improved growth performance in weanling pigs due to increased feed intake. Similar results were observed in Exp. 2, where 3,000 ppm Zn from ZnO increased ADG and ADFI. Also, 125 ppm Cu from copper sulfate ($CuSO_4$) increased growth rate due to enhanced feed intake, with Cu supplementation from TBCC offering intermediate results to $CuSO_4$ and no Cu supplementation. For the first 28-d of Exp. 3, similar additive responses were observed to adding Cu and Zn to the diets of weanling pigs. However, from d 28 to 42 the combined use of Cu and Zn produced decreased performance compared each used singularly. Similarly in Exp.4, $CuSO_4$ and ZnO improved growth performance, however the benefit was not additive. These trials showed growth promoting advantages to adding Cu and Zn to weanling diets, but additive responses were inconsistent.

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CHAPTER 1 - Effects of increasing dietary standardized ileal digestible lysine:ME ratio for gilts grown in a commercial finishing environment

Abstract

Three experiments were conducted to observe the effects of increasing dietary standardized ileal digestible (SID) lysine:ME ratio for growing and finishing gilts. Diets in all 3 experiments were corn-soybean meal based and contained 0.15% L–Lysine HCl and 3% added fat from choice white grease. Desired SID lysine:ME levels were achieved by altering levels of corn and soybean meal in the diet. Each experiment consisted of 6 treatments with 7 pens per treatment and approximately 27 gilts (PIC 337 × 1050) per pen. In Exp. 1, 1,085 gilts (initially 38.2 kg) were fed SID lysine:ME ratios of 2.01, 2.30, 2.58, 2.87, 3.16, or 3.45 g/Mcal for 28 d. As the SID lysine:ME ratio increased, ADG, G:F, feed cost per kilogram of gain, and income over feed cost (IOFC) improved (quadratic, $P < 0.003$) with optimal performance and economic responses reached at the SID lysine:ME ratio of 3.16 g/Mcal. Gilts in this trial required approximately 21.8 g of SID lysine intake per kilogram of BW gain from 38 to 65 kg. In Exp. 2, 1,092 (initially 55.2 kg) gilts were fed SID lysine:ME ratios of 1.89, 2.12, 2.35, 2.58, 2.81, or 3.04 g/Mcal for 28 d. Average daily gain, G:F, and IOFC improved (linear, $P < 0.02$) as SID lysine:ME ratio increased, with minor differences at levels above 2.58 g/Mcal. Gilts in this trial required approximately 19.6 g SID lysine per kilogram of BW gain from 55 to 80 kg to maximize growth and economic criteria. In Exp. 3, 1,080 gilts (initially 84.1 kg) were fed SID lysine:ME ratios of 1.55, 1.75, 1.95, 2.05, 2.35, or 2.55 g/Mcal for 29 d. As the SID lysine:ME ratio increased, ADG, G:F, feed cost per kilogram of gain, and IOFC improved (linear, $P < 0.001$); performance and economic responses were maximized at the highest SID lysine:ME ratio of 2.55 g/Mcal ME. Gilts in this trial required 23.0 g SID lysine per kilogram of BW gain from 85 to 110 kg. The equation SID lysine:ME ratio = -0.011 × BW, kg + 3.617 estimates the optimal SID lysine:ME ratios for growth and economic performance for gilts (PIC 337 × 1050) in this commercial finishing environment. These studies showed both economic and performance advantages to increasing the SID lysine:ME ratio for growing and finishing gilts over previously reported optimal levels.

Key words: finishing, gilt, lysine, swine

Introduction

Evaluating lysine requirements of the current high-lean pig genotypes is essential for generating cost-effective diets for growing and finishing pigs. Lysine requirements have been reported for lean genotypes (Cline et al., 2000; De La Llata et al., 2007; Main et al., 2008), and prediction models have been generated to estimate the lysine requirement from growth and changes in body composition (Schinckel and de Lange, 1996; NRC, 1998; Smith et al., 1999). These models use protein and lipid accretion and then calculate the energy requirement to meet the animal's maintenance needs and compositional changes. An ideal standardized ileal digestible (SID) lysine:ME ratio can be estimated on the basis of the requirement for lysine as well as energy. In addition, the optimal SID lysine:ME ratio of a diet can be used over a range of dietary energy levels (Chiba et al., 1991; Bikker et al., 1994; De La Llata et al., 2001).

Several non-dietary factors, including gender, genotype, health status, and environmental conditions, affect the lysine requirement for growing and finishing pigs (Baker, 1986; Campbell and Taverner, 1988; Friesen et al., 1994a; Williams et al., 1997). Therefore, empirical estimates under actual commercial production conditions are essential for confirming modeled estimates. Reevaluation of the requirements is also needed as progress is made in genetic lines. Thus, our objective was to reevaluate the optimal SID lysine:ME ratio for gilts in a commercial environment previously reported by Main et al. (2008).

Materials and Methods

General

All practices and procedures used in these experiments were approved by the Kansas State University Institutional Animal Care and Use Committee.

Three experiments were conducted to evaluate the effects of increasing the SID lysine:ME ratio over a variety of weight ranges of growing and finishing gilts (337 × 1050; PIC, Hendersonville, TN) in a commercial finishing environment. All pigs received 2 full doses of commercially available porcine circovirus type 2 (PCV2) vaccine (Circumvent PCV, Intervet Inc., Millsboro, DE) while in the nursery. Upon placement into the finisher and before the

beginning of each experiment, pigs were placed on diets that met or exceeded the NRC (1998) nutrient requirements. These studies were conducted at a commercial finishing site in southwestern Minnesota. The barns were double curtain sided with completely slatted flooring and a deep pit for manure storage. The research barns contain 48 pens (3.05 × 5.49 m); each pen contained a 5-hole conventional dry feeder (STACO, Inc., Schaefferstown, PA) and a cup waterer to allow ad libitum consumption of feed and water. An automated feeding system (FeedPro; Feedlogic Corp., Willmar, MN) was used to deliver and record feed amounts on an individual pen basis. These studies were conducted in the same facilities with the same genetic lines as previous studies by De La Llata et al. (2007) and Main et al. (2008).

All dietary treatments were corn-soybean meal based with 0.15% L-lysine HCl and 3% added fat in the form of choice white grease. Treatment SID lysine:ME ratios were achieved by replacing corn with soybean meal. Dietary nutrient values for treatments were determined by using ingredient values from the NRC (1998). All other nutrients were formulated to meet or exceed the animals' requirements (NRC, 1998). Test diets were sampled in each experiment, and a subsample of each diet was analyzed for amino acid concentrations. Amino acid analysis was performed by Ajinimoto Heartland LLC (Chicago, IL) by HPLC (AOAC, 2000).

In each experiment, pens of pigs were allotted to 1 of 6 dietary treatments in a completely randomized design with 7 pens per treatment. Each pen contained 24 to 27 pigs, and treatments were allotted to maintain equal average initial pen counts across dietary treatments. During each experiment, pig weights (by pen) and feed disappearance were determined at approximately 14-d intervals to determine ADG, ADFI, G:F, daily SID lysine intake, SID lysine intake per kilogram of gain, feed cost per kilogram of gain, and income over feed cost (IOFC). Feed costs were determined by valuing corn and 46.5% soybean meal at $204.97 and $385.80 per 1000 kg, respectively. Income over feed cost (IOFC) was calculated by assessing a value to the weight gain per pig ($132 per 100 kg) during the trial and subtracting the feed costs incurred during the trial on a per-pig basis.

Experiment 1

A total of 1,085 (38 to 65 kg) gilts were used in this 28-d study. Dietary treatments were formulated to SID lysine:ME ratios of 2.01, 2.30, 2.58, 2.87, 3.16, and 3.45 g/Mcal, which correspond to dietary SID lysine levels of 0.70, 0.80, 0.90, 1.00, 1.10, and 1.20% (Table 1). Pigs

in this trial were negative for porcine reproductive and respiratory syndrome virus (PRRSv) at weaning.

Experiment 2

A total of 1,092 (55 to 80 kg) gilts were used in this 28-d growth trial. Dietary treatments were formulated to SID lysine:ME ratios of 1.89, 2.12, 2.35, 2.58, 2.81, and 3.04 g/Mcal, which correspond to dietary SID lysine levels of 0.66, 0.74, 0.82, 0.90, 0.98, and 1.06% (Table 2). To maintain a minimum SID threonine:lysine ratio of 62% and a SID methionine and cysteine:lysine ratio of 58%, L-threonine and DL-methionine were added as needed. Pigs in this trial were PRRSv positive at weaning.

Experiment 3

A total of 1,080 (84 to 110 kg) gilts were used in this 29-d experiment. Dietary treatments were formulated to SID lysine:ME ratios of 1.55, 1.75, 1.95, 2.15, 2.35, and 2.55 g/Mcal, which correspond to dietary SID lysine levels of 0.54, 0.61, 0.68, 0.75, 0.82, and 0.89% (Table 3). To maintain a minimal SID threonine:lysine ratio of 62%, L-threonine was added as needed. Pigs in this trial were PRRSv negative at weaning.

Statistical Analysis

In each experiment, treatments were arranged in a completely randomized design. Analysis of variance was performed on the data from each experiment by using the MIXED procedure of SAS version 9.1 (SAS Inst. Inc., Cary, NC) with pen as the experimental unit in each experiment. Dietary lysine treatments were treated as fixed factors in the model, and contrast statements were then used to evaluate linear and quadratic polynomial effects associated with increasing the dietary SID lysine:ME ratio. Responses having a significant quadratic response were analyzed for a breakpoint according to procedures described by Robbins et al. (2006). Breakpoint estimates were determined using a one-slope or two-slope broken-line regression model using the NLIN procedure of SAS (Robbins et al., 2006).

Results and Discussion

Analyzed amino acid levels for diets from Exp. 1, 2, and 3 are shown in Tables 4, 5, and 6, respectively. Formulated diet values are included in parentheses. For each experiment,

analyzed concentrations of amino acids for the feed samples collected were similar to calculated total values (within the acceptable limits for analytical variation).

In Exp. 1 (38 to 65 kg gilts), ADG and G:F improved (quadratic, $P < 0.003$, Table 7) with increasing SID lysine:ME ratios, with the greatest improvement through 3.16 g/Mcal. Broken-line analysis showed breakpoints of 2.97 and 3.01 g SID lysine/Mcal ME for ADG and G:F, respectively. Although the magnitude of response was relatively small, ADFI decreased (linear, $P = 0.04$) with increasing SID lysine:ME ratio. This decrease in feed intake may be related to the increases in dietary protein level or the proportion of soybean meal incorporated in the diet. Main et al. (2008) observed similar decreases in feed intake as lysine increased in the diet of 35 to 60 kg gilts when soybean meal was used as the amino acid source. Daily SID lysine intake increased (linear, $P < 0.004$) with increasing dietary lysine. Lysine intake per kilogram of gain increased (quadratic, $P = 0.001$) with increasing dietary lysine. Optimal performance was achieved at 3.16 g SID lysine/Mcal ME when pigs consumed 21.8 g SID lysine per kilogram of BW gain. Feed cost per kilogram of gain decreased (quadratic, $P = 0.001$) with increasing SID lysine:ME ratios, and IOFC increased (quadratic, $P = 0.001$) with increasing SID lysine:ME ratio; the greatest return was achieved at 3.16 g lysine/Mcal. In this experiment, optimal economic and performance response criteria occurred at similar SID lysine:ME ratios. Main et al. (2008) observed a slightly lower optimal total lysine:ME ratio of 3.23 g/Mcal (2.84 g SID lysine/Mcal ME) when gilts consumed 21.3 g SID lysine per kilogram of BW gain. Friesen et al. (1994b) also evaluated the lysine requirement for 34 to 55 kg gilts and reported that performance was maximized at 2.75 g apparent ileal digestible (AID) lysine/Mcal ME, or approximately 2.95 g SID lysine/Mcal ME by utilizing the NRC (1998) digestibility coefficients for corn-soybean meal diets. Results of Exp. 1 revealed advantages to increasing the SID lysine:ME ratio above levels reported as optimal in previous experiments.

In Exp. 2 (55 to 80 kg gilts), ADG, G:F, and final weight improved (linear, $P < 0.05$, Table 8) as SID lysine:ME ratio increased in the diet. The greatest improvement in ADG and G:F was observed as SID lysine:ME ratio increased to 2.58 g SID lysine/Mcal ME, and there was a small numeric increase in ADG at 2.81g SID lysine/Mcal ME. No differences were detected ($P > 0.10$) for ADFI. Therefore, daily SID lysine intake increased (linear, $P = 0.001$) as dietary SID lysine levels increased. Standardized ileal digestible lysine intake per kilogram of gain also increased (linear, $P = 0.001$) as lysine density of the diets increased. Because optimal

growth performance occurred at 2.58 g SID lysine/Mcal ME, approximately 19.6 g SID lysine were required for each kilogram of gain. No differences were observed ($P > 0.10$) for feed cost per kilogram of gain; however, IOFC increased (linear, $P = 0.02$) as SID lysine:ME ratio increased. Similar to the growth response, the highest IOFC was for pigs fed the diet containing 2.58 g SID lysine/Mcal ME. These data illustrate that 2.58 g SID lysine/Mcal ME provides the optimal growth and economic return for 55 to 80 kg gilts. Main et al. (2008) determined a slightly lower optimal requirement of 2.44 g SID lysine/Mcal ME for 60 to 85 kg gilts, which translated to 21.0 g SID lysine per kilogram of gain. Friesen et al. (1994b), however, observed a slightly higher optimal requirement of 2.46 g AID lysine/Mcal ME (2.72 g SID lysine/Mcal ME) in 55 to 72.5 kg gilts. Therefore, the optimal SID lysine:ME ratio from Exp. 2 was only slightly numerically greater than that reported in previous trials.

In Exp. 3 (84 to 110 kg gilts), ADG and G:F improved (linear, $P < 0.001$, Table 9) with increasing SID lysine:ME ratio. Feed intake was not ($P > 0.10$) affected by increasing dietary lysine. Final weight, daily SID lysine intake, and SID lysine intake per kilogram of gain increased (linear, $P < 0.001$) with increasing SID lysine. Feed cost per kilogram of gain decreased (linear, $P = 0.001$) with increasing SID lysine:ME ratio. The decreased costs were driven by the improvements in G:F. Income over feed cost increased (linear, $P = 0.001$) from \$13.84/pig at 1.55 g SID lysine/Mcal ME to \$17.94/pig at 2.55 g SID lysine/Mcal ME. The improvements in ADG and G:F with increasing SID dietary lysine both helped drive improvements in IOFC. In Exp. 3, optimal economic and growth responses occurred at the highest lysine level evaluated (2.55 g SID lysine/Mcal ME). Main et al. (2008) determined an optimal SID lysine:ME ratio of 1.90 g/Mcal for 100 to 120 kg gilts that were consuming 19.4 g of SID lysine per kilogram of BW gain. By estimating the amount of fat-free lean gain within the feeding period, Main et al. (2008) also predicted a similar requirement of 1.96 g SID lysine/Mcal ME. Friesen et al. (1995) observed optimal performance in 104 to 136 kg gilts when 2.16 g of AID lysine/Mcal ME was provided. On the basis of NRC digestibility coefficients, the optimal SID lysine:ME ratio observed by Friesen et al. (1995) would be 2.29g/Mcal. However, both starting and ending pig weights were heavier in both Main et al. (2008) and Friesen et al. (1995) than pigs in our study, which may explain the lower requirement.

Advantages to increasing the SID lysine:ME ratio above that reported as optimal by Main et al. (2008) were observed in Exp. 1 and 3; however, the optimal SID lysine:ME ratio observed

in Exp. 2 was similar to current recommendations. One of the distinct differences between pigs in Exp. 1 and 3 and those in Exp. 2 was PRRSv status. Pigs in Exp. 1 and 3 were weaned without any evidence of PRRS infection, whereas those in Exp. 2 were PRRSv positive. Williams et al. (1997) showed that healthier pigs require increased dietary lysine because of increased potential for protein deposition compared with pigs with chronic immune stimulation. Klasing and Austic (1984) also showed an increase in skeletal muscle catabolism in broiler chicks that were injected with either sheep red blood cells or *E. coli* compared with chicks injected with saline. Immune responses alter the composition of growth because skeletal muscle accretion is reduced to a greater degree than visceral growth, resulting in lower yields of lean tissue (Klasing and Korver, 1997). Therefore, pigs in Exp. 2 may have not responded to high dietary lysine levels because of decreased potential for protein deposition from the PRRSv infection.

One possible explanation for the increase in response to higher levels of dietary lysine is vaccination against PCV2. Porcine circovirus type 2 vaccine has been shown to reduce mortality and improve overall performance of finishing pigs (Horlen et al., 2008, Jacela et al., 2008; Potter et al., 2008). As mentioned earlier, healthy pigs have increased daily dietary lysine needs because of increased lean tissue deposition; however, healthy pigs also have increased daily feed intake (Williams et al., 1997). The increased feed intake may or may not satisfy the pigs' need for additional dietary lysine. The effect of PCV2 vaccination on the SID lysine:ME requirement should be evaluated to determine whether vaccinated pigs require more SID lysine/Mcal ME than non-vaccinates to meet their enhanced needs for protein deposition.

Another explanation for the response to higher SID lysine:ME ratios may be that increased BW gain was not reflective of increased lean mass growth. Johnston et al. (2009) observed increases in growth and efficiency when feeding lysine levels greater than previously defined optimal levels; however, carcass yield was reduced with increasing lysine with no differences in primal cut weights. Johnston et al. (2009) concluded that whole-body growth from increasing dietary lysine did not translate into increased lean growth.

Figure 1 depicts prediction equations for the ideal SID lysine:ME ratio obtained by plotting the optimal level in each of our 3 studies against the midpoint of BW. The ideal SID lysine:ME ratio was based on the ratio that generated the greatest level of IOFC. This equation, SID lysine:ME ratio = -0.011 × BW, kg + 3.617, estimates the optimal SID lysine:ME ratios for growth and economic performance for gilts (PIC 337 × 1050) in this commercial finishing

environment. Prediction equations for the optimum SID lysine:ME ratios from Main et al. (2008) and De La Llata et al. (2007) also were plotted to show any difference over time as each of these studies were conducted in the same facilities with similar genetic lines. The rate of change in the SID lysine:ME ratio as BW increases was reduced in our experiment compared with the two aforementioned studies.

These trials indicated that optimal SID lysine:ME ratios for 38 to 65 kg gilts and 55 to 80 kg gilts are 3.16 and 2.58g/Mcal, respectively, and that 84 to 100 kg gilts responded linearly through the highest level of 2.55 g/Mcal. Additional research is warranted to evaluate factors influencing the response to increased levels of dietary lysine fed to PRRSv-negative pigs that have also been vaccinated for PCV2.

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Figures and Tables

Table 1-1. Composition of diets, Exp. 1 (as-fed basis)[1]

	SID[2] lysine:ME, g/Mcal					
	2.01	2.30	2.58	2.87	3.16	3.45
	SID lysine, %					
Item	0.70	0.80	0.90	1.00	1.10	1.20
Ingredient, %						
Corn	79.40	75.42	71.45	67.47	63.50	59.52
Soybean meal (46.5% CP)	15.49	19.47	23.44	27.42	31.39	35.37
Choice white grease	3.00	3.00	3.00	3.00	3.00	3.00
Monocalcium P (21% P)	0.50	0.50	0.50	0.50	0.50	0.50
Limestone	0.90	0.90	0.90	0.90	0.90	0.90
Salt	0.35	0.35	0.35	0.35	0.35	0.35
Copper sulfate	0.03	0.03	0.03	0.03	0.03	0.03
Vitamin premix[3]	0.08	0.08	0.08	0.08	0.08	0.08
Trace mineral premix[4]	0.08	0.08	0.08	0.08	0.08	0.08
L-Lys HCl	0.15	0.15	0.15	0.15	0.15	0.15
Phytase[5]	0.02	0.02	0.02	0.02	0.02	0.02
Total	100.00	100.00	100.00	100.00	100.00	100.00
Calculated analysis						
SID amino acids, %						
Lys	0.7	0.8	0.9	1.0	1.1	1.2
Ile:Lys	70	70	69	69	69	69
Leu:Lys	175	165	157	151	146	141
Met:Lys	31	29	28	27	26	26
Met & Cys:Lys	64	60	58	56	54	53
Thr:Lys	63	62	61	60	60	59
Trp:Lys	19	19	19	19	20	20
Val:Lys	83	81	79	78	77	76
ME, kcal/kg	3,484	3,483	3,481	3,480	3,478	3,477
Total lysine, %	0.79	0.90	1.01	1.12	1.23	1.34
CP, %	14.1	15.6	17.1	18.6	20.1	21.7
Ca, %	0.51	0.52	0.54	0.55	0.56	0.57
P, %	0.43	0.45	0.47	0.48	0.50	0.52
Available P, %[6]	0.24	0.24	0.25	0.25	0.26	0.26
Diet cost, $/1000 kg[7]	256.28	263.80	271.31	278.82	286.33	293.85

[1]A total of 1,085 gilts (PIC 337 × 1050) were housed at approximately 27 pigs per pen and 7 replications per treatment in a 28-d trial.

[2]Standardized ileal digestible.

[3]Vitamin premix provided per kg of diet: 6,614 IU of vitamin A, 826.7 IU of vitamin D_3, 26.46 IU of vitamin E, 2.65 mg of vitamin k, 0.02 mg of vitamin B_{12}, 29.76 mg of niacin, 16.53 mg of pantothenic acid, and 4.96 mg of riboflavin.

[4]Trace mineral premix provided per kg of diet: 13.23 mg Cu from Cu sulfate, 0.24 mg I from Ca iodate, 132.28 mg Fe from Fe sulfate, 31.75 mg Mn from Mn sulfate, 0.24 mg Se from Na selenite, and 132.28 mg Zn from Zn sulfate.

[5]Natuphos classic (BASF Corp.) provided (per kg of complete diet): 300 FTU of phytase.

[6]Phytase provided 0.08% available P to the diet.

[7]Diet costs were based on corn at $204.97/1000 kg and 46.5% soybean meal at $385.80/1000 kg.

Table 1-2. Composition of diets, Exp. 2 (as-fed basis)[1]

	SID[2] lysine:ME, g/Mcal					
	1.89	2.12	2.35	2.58	2.81	3.04
	SID lysine, %					
Item	0.66	0.74	0.82	0.90	0.98	1.06
Ingredient, %						
Corn	80.99	77.81	74.68	71.48	68.33	65.12
Soybean meal (46.5% CP)	13.90	17.10	20.25	23.45	26.60	29.80
Choice white grease	3.00	3.00	3.00	3.00	3.00	3.00
Monocalcium P (21% P)	0.63	0.61	0.59	0.58	0.56	0.54
Limestone	0.85	0.85	0.85	0.85	0.85	0.85
Salt	0.35	0.35	0.35	0.35	0.35	0.35
Vitamin premix[3]	0.05	0.05	0.05	0.05	0.05	0.05
Trace mineral premix[4]	0.05	0.05	0.05	0.05	0.05	0.05
L-Lys HCl	0.15	0.15	0.15	0.15	0.15	0.15
DL-Met	---	---	---	0.005	0.015	0.035
L-Thr	----	---	0.005	0.010	0.015	0.025
Phytase[5]	0.025	0.025	0.025	0.025	0.025	0.025
Total	100.0	100.0	100.0	100.0	100.0	100.0
Calculated analysis						
SID amino acids, %						
Lys	0.66	0.74	0.82	0.90	0.98	1.06
Ile:Lys	70	70	70	69	69	69
Leu:Lys	180	171	163	157	152	148
Met:Lys	32	30	29	29	29	30
Met & Cys:Lys	65	62	60	58	58	58
Thr:Lys	63	62	62	62	62	62
Trp:Lys	19	19	19	19	19	20
Val:Lys	84	82	80	79	78	77
ME, kcal/kg	3,485	3,484	3,484	3,483	3,483	3,483
Total lysine, %	0.75	0.84	0.92	1.01	1.10	1.19
CP, %	13.5	14.7	15.9	17.1	18.3	19.6
Ca, %	0.51	0.52	0.52	0.53	0.54	0.54
P, %	0.46	0.46	0.47	0.48	0.49	0.50
Available P, %[6]	0.29	0.29	0.29	0.29	0.29	0.29
Diet cost, $/1000 kg[7]	256.42	262.28	268.28	274.43	280.67	287.28

[1]A total of 1,092 gilts (PIC 337 × 1050) were housed at 26 pigs per pen and 7 replications per treatment in a 28-d trial.

[2]SID = standard ileal digestible.

[3]Vitamin premix provided per kg of diet: 4,409 IU of vitamin A, 551.2 IU of vitamin D_3, 17.64 IU of vitamin E, 1.76 mg of vitamin k, 0.02 mg of vitamin B_{12}, 19.84 mg of niacin, 11.02 mg of pantothenic acid, and 3.31 mg of riboflavin.

[4]Trace mineral premix provided per kg of diet: 8.27 mg Cu from Cu sulfate, 0.15 mg I from Ca iodate, 82.67 mg Fe from Fe sulfate, 19.84 mg Mn from Mn sulfate, 0.15 mg Se from Na selenite, and 82.67 mg Zn from Zn sulfate.

[5]Optiphos 2000 (Enzyvia, Sheridan, IN) provided (per kg of complete diet): 500 FTU of phytase.

[6]Phytase provided 0.10% available P to the diet.

[7]Diet costs were based on corn at $204.97/1000 kg and 46.5% soybean meal at $385.80/1000 kg.

Table 1-3. Composition of diets, Exp. 3 (as-fed basis)[1]

	SID[2] lysine:ME, g/Mcal					
	1.55	1.75	1.95	2.15	2.35	2.55
	SID lysine, %					
Item	0.54	0.61	0.68	0.75	0.82	0.89
Ingredient, %						
Corn	85.84	83.07	80.30	77.54	74.76	72.00
Soybean meal (46.5% CP)	9.12	11.91	14.69	17.47	20.25	23.03
Choice white grease	3.00	3.00	3.00	3.00	3.00	3.00
Monocalcium P (21% P)	0.58	0.56	0.55	0.53	0.52	0.50
Limestone	0.85	0.85	0.85	0.85	0.85	0.85
Salt	0.35	0.35	0.35	0.35	0.35	0.35
Vitamin premix[3]	0.05	0.05	0.05	0.05	0.05	0.05
Trace mineral premix[4]	0.05	0.05	0.05	0.05	0.05	0.05
Lysine HCl	0.15	0.15	0.15	0.15	0.15	0.15
L-Threonine	-	-	-	-	0.005	0.01
Phytase[5]	0.01	0.01	0.01	0.01	0.01	0.01
Total	100.00	100.00	100.00	100.00	100.00	100.00
Calculated analysis						
SID amino acids, %						
Lys	0.54	0.61	0.68	0.75	0.82	0.89
Ile:Lys	71	71	70	70	70	69
Leu:Lys	200	188	178	170	164	158
Met:Lys	35	33	31	30	29	28
Met & Cys:Lys	71	68	64	62	60	58
Thr:Lys	65	64	63	62	62	62
Trp:Lys	18	18	19	19	19	19
Val:Lys	88	85	83	82	80	79
ME, kcal/kg	3,490	3,489	3,488	3,488	3,487	3,487
Total lysine, %	0.62	0.69	0.77	0.85	0.92	1.00
CP, %	11.70	12.70	13.80	14.90	15.90	17.00
Ca, %	0.49	0.49	0.50	0.50	0.51	0.52
P, %	0.42	0.43	0.44	0.45	0.46	0.47
Available P, %[6]	0.22	0.22	0.22	0.22	0.22	0.22
Diet cost, $/1000 kg[7]	243.07	248.21	253.37	258.52	263.80	269.08

[1]A total of 1,080 gilts (PIC 337 × 1050) were housed at approximately 27 pigs per pen and 7 replications per treatment in a 29-d trial.

[2]Standardized ileal digestible.

[3]Vitamin premix provided per kg of diet: 4,409 IU of vitamin A, 551.2 IU of vitamin D_3, 17.64 IU of vitamin E, 1.76 mg of vitamin k, 0.02 mg of vitamin B_{12}, 19.84 mg of niacin, 11.02 mg of pantothenic acid, and 3.31 mg of riboflavin.

[4]Trace mineral premix provided per kg of diet: 8.27 mg Cu from Cu sulfate, 0.15 mg I from Ca iodate, 82.67 mg Fe from Fe sulfate, 19.84 mg Mn from Mn sulfate, 0.15 mg Se from Na selenite, and 82.67 mg Zn from Zn sulfate.

[5]Optiphos 2000 (Enzyvia, Sheridan, IN) provided (per kg of complete diet): 200 FTU of phytase

[6]Phytase provided 0.05% available P to the diet.

[7]Diet costs were based on corn at $204.97/1000 kg and 46.5% soybean meal at $385.80/1000 kg.

Table 1-4. Chemical composition of diets (Exp. 1)[1]

	SID[2] lysine:ME, g/Mcal					
	2.01	2.30	2.58	2.87	3.16	3.45
	SID lysine, %					
Item, %[3]	0.70	0.80	0.90	1.00	1.10	1.20
CP	13.6 (14.1)	14.6 (15.6)	16.1 (17.1)	16.8 (18.6)	19.1 (20.1)	19.4 (21.7)
Lys	0.78 (0.79)	0.86 (0.90)	0.99 (1.01)	1.06 (1.12)	1.14 (1.23)	1.24 (1.34)
Cys	0.22 (0.27)	0.24 (0.29)	0.27 (0.31)	0.27 (0.33)	0.30 (0.35)	0.31 (0.37)
Ile	0.54 (0.56)	0.59 (0.63)	0.67 (0.71)	0.71 (0.78)	0.81 (0.86)	0.84 (0.93)
Leu	1.31 (1.35)	1.36 (1.46)	1.48 (1.57)	1.54 (1.67)	1.68 (1.78)	1.74 (1.88)
Met	0.22 (0.24)	0.23 (0.26)	0.25 (0.28)	0.28 (0.30)	0.27 (0.32)	0.29 (0.34)
Met+Cys	0.45 (0.50)	0.47 (0.55)	0.52 (0.59)	0.55 (0.63)	0.57 (0.67)	0.60 (0.71)
Thr	0.50 (0.52)	0.54 (0.58)	0.60 (0.64)	0.62 (0.70)	0.71 (0.76)	0.77 (0.83)
Trp	0.14 (0.15)	0.15 (0.17)	0.18 (0.20)	0.20 (0.22)	0.22 (0.24)	0.23 (0.27)
Val	0.63 (0.66)	0.68 (0.74)	0.76 (0.81)	0.80 (0.89)	0.87 (0.96)	0.91 (1.03)

[1]A total of 1,085 gilts (PIC 337 × 1050) were housed with approximately 27 pigs per pen and 7 replications per treatment in a 28-d trial.

[2]Standardized ileal digestible.

[3]Analyzed values for protein and amino acids are shown and are based on a composite sample from 3 different collection times. Calculated values are shown in parentheses.

Table 1-5. Chemical composition of diets (Exp. 2)[1]

	SID[2] lysine:ME, g/Mcal					
	1.89	2.12	2.35	2.58	2.81	3.04
	SID lysine, %					
Item, %[3]	0.66	0.74	0.82	0.90	0.98	1.06
CP	14.4 (13.5)	14.3 (14.7)	15.9 (15.9)	16.6 (17.1)	17.68 (18.3)	18.3 (19.6)
Lys	0.75 (0.75)	0.73 (0.84)	0.84 (0.92)	0.90 (1.01)	0.95 (1.10)	0.97 (1.19)
Cys	0.20 (0.25)	0.20 (0.26)	0.22 (0.28)	0.24 (0.29)	0.25 (0.31)	0.25 (0.31)
Ile	0.50 (0.53)	0.51 (0.59)	0.56 (0.65)	0.63 (0.71)	0.68 (0.77)	0.68 (0.83)
Leu	1.22 (1.31)	1.21 (1.40)	1.28 (1.48)	1.40 (1.57)	1.46 (1.65)	1.44 (1.74)
Met	0.26 (0.24)	0.25 (0.26)	0.27 (0.27)	0.29 (0.29)	0.30 (0.32)	0.32 (0.36)
Met+Cys	0.47 (0.49)	0.46 (0.52)	0.49 (0.55)	0.53 (0.59)	0.55 (0.64)	0.56 (0.69)
Thr	0.52 (0.49)	0.52 (0.54)	0.56 (0.60)	0.63 (0.65)	0.66 (0.71)	0.64 (0.77)
Trp	0.14 (0.14)	0.14 (0.16)	0.15 (0.18)	0.17 (0.20)	0.18 (0.21)	0.19 (0.23)
Val	0.59 (0.63)	0.59 (0.69)	0.65 (0.75)	0.72 (0.81)	0.76 (0.87)	0.75 (0.93)

[1]A total of 1,092 gilts (PIC 337 × 1050) were housed with approximately 26 pigs per pen and 7 replications per treatment in a 28-d trial.

[2]Standardized ileal digestible.

[3]Analyzed values for protein and amino acids are shown and are based on a composite sample from 3 different collection times. Calculated values are shown in parentheses.

Table 1-6. Chemical composition of diets (Exp. 3)[1]

	SID[2] lysine:ME, g/Mcal					
	1.55	1.75	1.95	2.15	2.35	2.55
	SID lysine, %					
Item, %[3]	0.54	0.61	0.68	0.75	0.82	0.89
CP	10.9 (11.7)	15.0 (12.7)	13.2 (13.8)	15.9 (14.9)	15.2 (15.9)	15.9 (17.0)
Lys	0.62 (0.62)	0.92 (0.69)	0.79 (0.77)	0.99 (0.85)	0.93 (0.92)	1.07 (1.00)
Cys	0.20 (0.23)	0.24 (0.25)	0.22 (0.26)	0.27 (0.28)	0.25 (0.29)	0.28 (0.31)
Ile	0.42 (0.44)	0.59 (0.49)	0.54 (0.54)	0.65 (0.59)	0.63 (0.65)	0.71 (0.70)
Leu	1.11 (1.18)	1.42 (1.26)	1.29 (1.33)	1.49 (1.41)	1.41 (1.48)	1.58 (1.56)
Met	0.19 (0.21)	0.27 (0.22)	0.22 (0.23)	0.28 (0.25)	0.24 (0.26)	0.27 (0.28)
Met+Cys	0.40 (0.44)	0.51 (0.47)	0.45 (0.50)	0.55 (0.53)	0.50 (0.55)	0.54 (0.58)
Thr	0.42 (0.42)	0.60 (0.46)	0.51 (0.50)	0.64 (0.55)	0.58 (0.60)	0.64 (0.64)
Trp	0.12 (0.11)	0.17 (0.13)	0.16 (0.14)	0.17 (0.16)	0.17 (0.18)	0.17 (0.19)
Val	0.48 (0.54)	0.67 (0.59)	0.60 (0.65)	0.78 (0.70)	0.71 (0.75)	0.80 (0.80)

[1]A total of 1,080 gilts (PIC 337 × 1050) were housed with approximately 27 pigs per pen and 7 replications per treatment in a 29-d trial.

[2]Standardized ileal digestible.

[3]Analyzed values for protein and amino acids are shown and are based on a composite sample from 3 different collection times. Calculated values are shown in parentheses.

Table 1-7. Effects of standardized ileal digestible (SID) lysine:ME ratio on growth and economic performance of 38 to 65 kg gilts (Exp. 1)[1]

	SID lysine:ME, g/Mcal								
	2.01	2.30	2.58	2.87	3.16	3.45			
	SID lysine, %							Probability, *P* <	
Item	0.7	0.8	0.9	1.0	1.1	1.2	SEM	Linear	Quadratic
Initial weight, kg	38.2	38.1	38.2	38.3	38.3	38.2	0.99	0.94	0.98
ADG, kg	0.82	0.87	0.93	0.95	0.97	0.97	0.011	0.001	0.003
ADFI, kg	1.97	1.95	1.95	1.92	1.91	1.91	0.026	0.04	0.93
G:F	0.42	0.45	0.48	0.49	0.51	0.51	0.003	0.001	0.001
Final weight, kg	61.3	62.4	64.2	64.8	65.3	65.5	1.17	0.004	0.38
Daily SID lysine intake, g	13.8	15.6	17.5	19.2	21.0	22.9	0.25	0.001	0.85
SID lysine intake/kg gain, g	16.8	18.0	18.9	20.3	21. 8	23.5	0.13	0.001	0.001
Feed cost/kg gain, $[2]	0.61	0.59	0.57	0.57	0.57	0.57	0.004	0.001	0.001
IOFC, $/head[2,3]	16.35	17.72	19.50	20.02	20.39	20.39	0.257	0.001	0.001

[1]A total of 1,085 gilts (PIC 337 × 1050) were housed with approximately 27 pigs per pen and 7 replications per treatment in a 28-d trial.

[2]Feed costs were based on corn at $204.97/1000 kg and 46.5% soybean meal at $385.80/1000 kg.

[3]Income over feed cost = value of gain at $132.28/100 kg live weight - feed costs during trial period.

Table 1-8. Effects of standardized ileal digestible (SID) lysine:ME ratio on growth and economic performance of 55 to 80 kg gilts (Exp. 2)[1]

	SID lysine:ME, g/Mcal								
	1.89	2.12	2.35	2.58	2.81	3.04			
	SID lysine, %							Probability, *P* <	
Item	0.66	0.74	0.82	0.90	0.98	1.06	SEM	Linear	Quadratic
Initial weight, kg	55.2	55.2	55.2	55.2	55.2	55.2	1.07	0.99	0.98
ADG, kg	0.90	0.89	0.95	0.97	0.98	0.96	0.015	0.001	0.12
ADFI, kg	2.14	2.10	2.16	2.11	2.19	2.11	0.043	0.95	0.71
G:F	0.42	0.42	0.44	0.46	0.45	0.46	0.008	0.001	0.32
Final weight, kg	80.5	80.2	81.8	82.5	82.8	82.6	1.09	0.05	0.68
Daily SID lysine intake, g	14.1	15.6	17.8	19.0	21.5	22.3	0.37	0.001	0.63
SID lysine intake/kg gain, g	15.7	17.5	18.7	19.6	22.0	23.2	0.35	0.001	0.61
Feed cost/kg gain, $[2]	0.61	0.62	0.61	0.59	0.62	0.62	0.011	0.67	0.34
IOFC, $/head[2,3]	18.09	17.54	19.09	19.95	19.18	19.00	0.498	0.02	0.12

[1]A total of 1,092 gilts (PIC 337 × 1050) were housed with approximately 26 pigs per pen and 7 replications per treatment in a 28-d trial.

[2]Feed costs were based on corn at $204.97/1000 kg and 46.5% soybean meal at $385.80/1000 kg.

[3]Income over feed cost = value of gain at $132.28/100 kg live weight - feed costs during trial period.

Table 1-9. Effects of standardized ileal digestible (SID) lysine:ME ratio on growth and economic performance of 84 to 110 kg gilts (Exp. 3)[1]

	SID lysine:ME, g/Mcal								
	1.55	1.75	1.95	2.15	2.35	2.55			
	SID lysine, %							Probability, *P* <	
Item	0.54	0.61	0.68	0.75	0.82	0.89	SEM	Linear	Quadratic
Initial weight, kg	84.2	84.1	84.2	84.1	84.1	84.1	1.27	0.98	0.98
ADG, kg	0.83	0.87	0.87	0.93	0.95	0.98	0.014	0.001	0.90
ADFI, kg	2.54	2.58	2.52	2.54	2.54	2.54	0.030	0.76	0.93
G:F	0.33	0.34	0.35	0.37	0.37	0.39	0.004	0.001	0.95
Final weight, kg	108.2	109.5	109.8	111.1	111.7	112.7	1.40	0.02	0.99
Daily SID lysine intake, g	13.7	15.8	17.2	19.0	20.9	22.6	0.23	0.001	0.91
SID lysine intake/kg gain, g	16.6	18.1	19.7	20.4	22.1	23.0	0.25	0.001	0.26
Feed cost/kg gain, $[2]	0.75	0.74	0.73	0.71	0.71	0.70	0.009	0.001	0.87
IOFC, $/head[2,3]	13.84	14.91	15.11	16.70	16.93	17.94	0.463	0.001	0.97

[1]A total of 1,080 gilts (PIC 337 × 1050) that were housed at approximately 27 pigs per pen and 7 replications per treatment in a 29-d trial.

[2]Feed costs were based on corn at $204.97/1000 kg and 46.5% soybean meal at $385.80/1000 kg.

[3]Income over feed cost = value of gain at $132.28/100 kg live weight - feed costs during trial period.

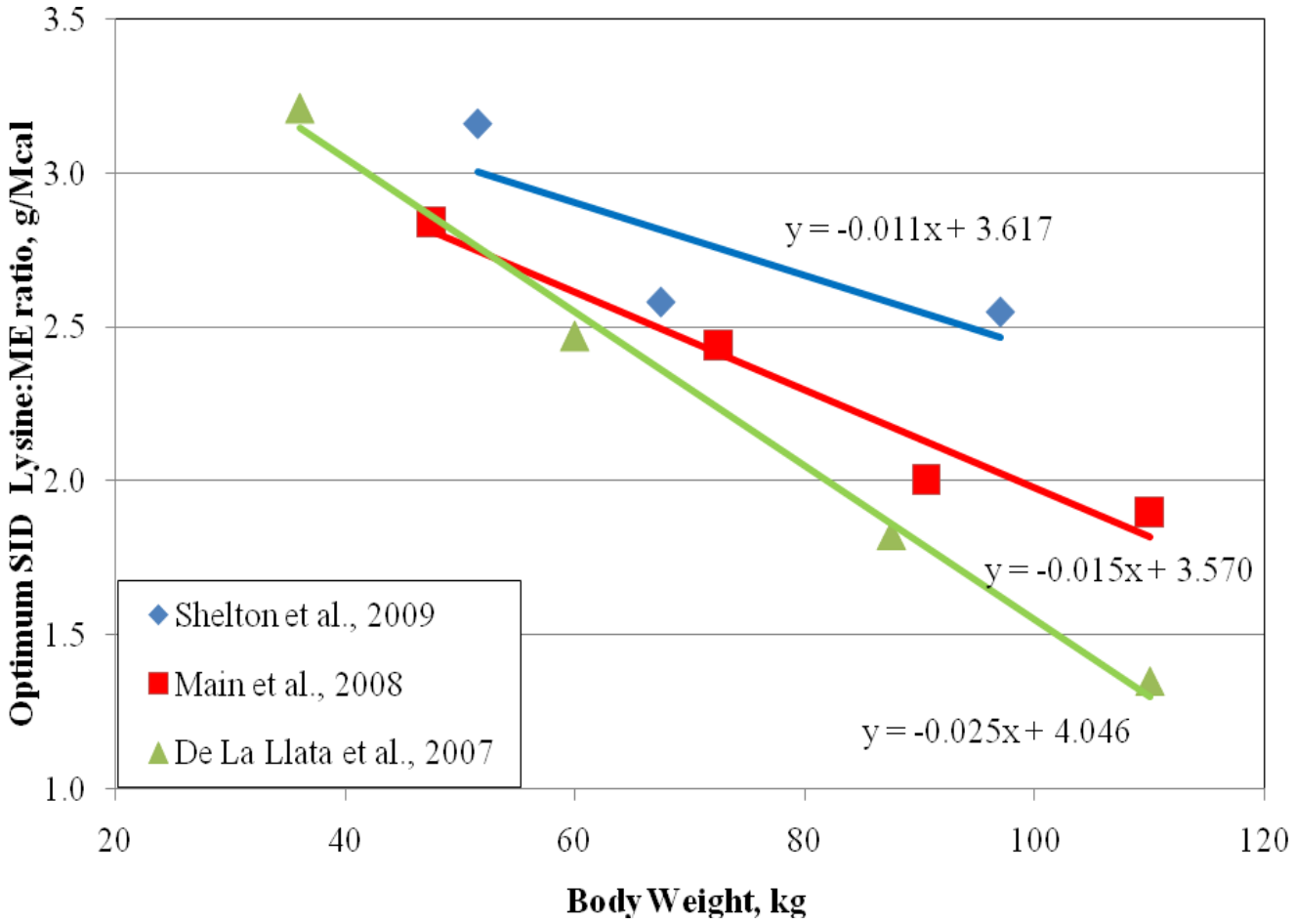

Figure 1. Optimal SID lysine:ME ratio prediction equations were developed for PIC Line 337 gilts based on optimal growth performance.

CHAPTER 2 - Effects of porcine circovirus type 2 vaccine and increasing standardized ileal digestible lysine:ME ratio on growth performance and carcass composition of growing and finishing pigs housed in commercial facilities

Abstract

A series of 4 experiments were conducted to examine the effects of porcine circovirus type 2 (PCV2) vaccination on the response to increasing dietary lysine in growing and finishing pigs (PIC 337 × 1050). Vaccination treatments included PCV2 vaccinates (Circumvent PCV, Intervet Inc., Millsboro, DE) and non-vaccinates that were allotted at weaning. One half of the pigs were vaccinated on d 1 and 22 after weaning and all pigs were inoculated with serum containing porcine reproductive and respiratory virus (PRRSv) 30-d after weaning as part of this production system's protocol. Experiments 1 and 2 evaluated 38 to 65 kg gilts and barrows, respectively, and Exp. 3 and 4 evaluated 100 to 120 kg gilts and barrows, respectively. Treatments were allotted in a completely randomized design into 2 × 4 factorials with 2 PCV2 treatments (vaccinates and non-vaccinates) and 4 standardized ileal digestible (SID) lysine:ME ratios (2.24, 2.61, 2.99, and 3.36 g/Mcal in Exp. 1 and 2 and 1.49, 1.86, 2.23, and 2.61 g/Mcal in Exp. 3 and 4). There were 5 pens per treatment with 18 to 27 pigs per pen depending on the experiment. During the nursery period before Exp. 1 and 2, the second PCV2 vaccination reduced ($P < 0.04$) ADG and ADFI in vaccinates compared with non-vaccinates. However, after pigs were inoculated with PRRSv, PCV2 vaccinates had improved ($P < 0.001$) G:F and a trend ($P = 0.08$) for improved ADG compared with non-vaccinates. At the start of Exp. 1 and 2, the number pigs per pen were greater ($P < 0.001$) in vaccinate pens due to greater survival than non-vaccinates, and this increase was maintained throughout the experiments. No PCV2 vaccination × SID lysine:ME ratio interactions were observed ($P > 0.10$) in any of the 4 studies. In Exp. 1 and 2, PCV2 vaccinates had increased ($P < 0.001$) ADG compared with non-vaccinates. The growth response was primarily due to increases in ADFI, suggesting a greater g/d lysine requirement for PCV2 vaccinates than non-vaccinates. In Exp. 1, increasing SID lysine:ME ratio increased (quadratic; $P < 0.04$) ADG and G:F up through 2.99 g/Mcal. In Exp. 2, increasing the SID lysine:ME ratio improved (linear; $P < 0.001$) G:F. In Exp. 3, increasing the

SID lysine:ME ratio increased (quadratic; $P < 0.05$) ADG and G:F with improvements through 1.86 g /Mcal. In Exp. 4, increasing the SID lysine:ME ratio increased ADG (linear; $P < 0.001$) and G:F (quadratic; $P = 0.03$) . Although PCV2 vaccination improved growth, the corresponding increase in ADFI did not increase the SID lysine:ME ratio for growing and finishing barrows and gilts.
Key words: growth, finishing pigs, lysine, porcine circovirus type 2 vaccine

Introduction

Porcine circovirus type 2 (PCV2) greatly increased in the U.S. pig population in the mid 2000's and is characterized by increased mortality and decreased growth rate (Segalés et al., 2006). As a result of porcine circovirus disease (PCVD), in some cases it was not uncommon to see growing-finishing pig mortality approach 20% (Horlen et al., 2007). Clinical signs of PCVD include but are not limited to enlarged lymph nodes, labored breathing, as well as poor body condition and muscle wasting (Harding et al., 1998; Sorden, 2000). Vaccination for PCV2 has been shown to increase growth rates and reduce mortality in growing and finishing pigs (Horlen et al., 2008, Jacela et al., 2008; Potter et al., 2008). With increased ADG and G:F of pigs vaccinated for PCV2 compared with those not vaccinated, it might be speculated that dietary amino acid needs may be increased as well. Williams et al. (1997a; b) observed increased lysine requirement estimates in pigs with low immune system activity. This was speculated to be a result of increased lean tissue deposition in pigs with low immune system activity compared with pigs under a greater health challenge.

Lysine requirement estimates have been modeled and calculated (Cromwell et al., 1993; NRC 1998; Cline et al. 2000; Main et al. 2008); however, recent studies by Shelton et al. (2008; 2009) have found improvements in growth and efficiency to feeding higher dietary lysine levels than these earlier estimates published by Main et al. (2008). Therefore, along with the advancement in genetic lines, the increase in health status and growth rate due to the PCV2 vaccination may be one of the main factors driving an increase in lysine requirements observed by Shelton et al. (2008; 2009). Therefore, the objective of these experiments was to evaluate the effects of PCV2 vaccination on pig performance and determine whether it influences the dietary lysine requirement.

Materials and Methods

General

Procedures in this experiment were approved by the Kansas State University Institutional Animal Care and Use Committee. The experiment was conducted at commercial research finishing facilities in southwestern Minnesota. These facilities were double curtain sided with completely slatted flooring. Each of the 4 research barns contain 48 pens (3.05 × 5.49 m) with each pen containing a 5-hole conventional dry feeder (STACO, Inc., Schaefferstown, PA) and a cup waterer to allow ad libitum consumption of feed and water. An automated feeding system (FeedPro^{TM}; Feedlogic Corp., Willmar, MN) was used to deliver and recording feed amounts on an individual pen basis.

Allotment and Application of Porcine Circovirus Type 2 Vaccine

For all experiments, a total of 2,571 barrows and gilts (PIC 337 × 1050; Hendersonville, TN: initially 5.7 kg) were weaned into 1 of the research finisher barns. Pens were double stocked with 56 pigs per pen, and gilts and barrows were penned separately. A total of 46 pens were used; 24 pens contained barrows, and 22 pens contained gilts. Industry standard nursery diets were budgeted and fed to all pigs during this phase that met or exceeded all nutrient requirements as outlined by the NRC (1998). All pigs were vaccinated for *M. hyopneumoniae* while in the farrowing facility. The PCV2 vaccination treatments were allotted by pen at placement to both barrow and gilt pens in a completely randomized design within gender. The number of vaccinated and unvaccinated pigs was equal within gender. Vaccine treatments included either no PCV2 vaccine or vaccination with 2 doses of commercial PCV2 vaccine (Circumvent PCV, Intervet Inc., Millsboro, DE) given according to label directions on d 1 and 22 after weaning. As part of this farm's standard production protocol, all pigs were then injected with serum containing porcine reproductive and respiratory virus (PRRSv) on d 30 after weaning. Briefly, serum which had been derived from a PRRSv infected pig and PRRSv viral particle quantity estimated using PCR was diluted 1:1,000 with sterile water and administered to pigs IM. Further analysis with real time PCR found the serum contained 1.7×10^3 viral copies per reaction.

Pig weights (by pen) and feed disappearance were measured in approximately 14-d intervals throughout the nursery period. On the basis of these measurements, ADG, ADFI, and

G:F were calculated for each pen. On d 51, the original pens of barrows or gilts, which were double stocked at 56 pigs per pen, were split to form 2 new pens of pigs of 22 to 27 pigs per pen, depending on the number of pigs remaining. All gilts were moved to an adjacent barn of similar design, with barrows remaining in the original site. The proportion of pigs throughout the pre-test and experimental periods was also determined to observe any differences in removal and mortality between vaccine treatments.

Finishing Period

For Exp. 1 and 2, a total of 1,008 gilts (initially 38.3 kg) and 1,002 barrows (initially 38.9) were selected and used in 28-d trials. Four experimental diets were used in Exp. 1 and 2 with standardized ileal digestible (SID) lysine:ME ratios of 2.24, 2.61, 2.99, and 3.36 g/Mcal, which correspond to SID concentrations of 0.78, 0.91, 1.04, and 1.17 % or total lysine concentrations of 0.88, 1.02, 1.17, and 1.31 % (Table 1). Standard ileal digestible amino acid values from the NRC (1998) were used in diet formulation. Diets were corn-soybean meal-based with 0.15% added L-lysine HCl. Corn and soybean meal concentrations were changed to achieve the desired SID lysine:ME ratio in the diet. In addition, all diets contained 3% added fat from choice white grease. Diets were formulated to meet all other requirements recommended by NRC (1998). Test diets were sampled in each experiment, and a subsample of each diet was analyzed for amino acid concentrations (Table 2 and 3, for Exp. 1 and 2, respectively). Amino acid analysis was performed by Ajinimoto Heartland LLC (Chicago, IL) by HPLC (AOAC, 2000). After the conclusion of Exp. 1 and 2, all pigs were placed on diets that contained at least 2.58 g SID lysine/Mcal ME. Before beginning Exp. 3 and 4, some pigs were removed from each pen, with more pigs removed from vaccinated pens to attempt to minimize the difference in pig density and initial weight between the PCV2 vaccinates and non-vaccinates.

A total of 930 gilts (initially 101.8 kg) and 825 barrows (initially 97.7 kg) were then used in Exp. 3 and 4 for 28 and 21 d, respectively. Four experimental diets were again used with SID lysine:ME ratios of 1.49, 1.86, 2.23, and 2.61 g/Mcal, which correspond to dietary SID lysine concentrations of 0.52, 0.65, 0.78, and 0.91 % or total lysine concentrations of 0.59, 0.74, 0.88, and 1.02 % (Table 4). Similar to Exp. 1 and 2, diets were corn-soybean meal-based with 0.15% added L-lysine HCl and 3% added fat from choice white grease. Diet samples were collected

from each diet in each experiment and analyzed for amino acid concentrations (Table 5 and 6 for Exp. 3 and 4, respectively).

For each experiment, dietary treatments were allotted within PCV2-vaccinated and non-vaccinated pens in a completely randomized design. Each experiment had 5 replications for each diet and vaccine treatment combination. Pen densities varied from 18 to 27 pigs per pen depending on the experiment.

Pig weights (by pen) and feed disappearance were measured throughout the experiments. On the basis of these measurements, ADG, ADFI, G:F, daily SID lysine intake, and SID lysine intake per kg BW gain were calculated for each pen. At the conclusion of the growth portion of Exp. 3 and 4, the pigs were marketed to a USDA-inspected packing plant (JBS Swift & Company processing plant, Worthington, MN) and carcass data was collected. Pen data for yield, backfat depth, loin depth, percentage lean, fat-free lean index, and live value were determined by the packing plant. Yield reflects the percentage of HCW relative to live weight (obtained at the packing plant).

Statistical Analysis

Data from the nursery pre-test period was analyzed as a 2 × 2 factorial (gender and PCV2 vaccination status). Both vaccine treatment and gender were treated as fixed effects in the model. The nursery growth and finishing weight responses were analyzed using the PROC MIXED procedure in SAS (SAS Institute Inc., Cary, NC). The percentage of remaining pigs was analyzed using the PROC GENMOD procedure in SAS utilizing a Poisson distribution. The original pen was used as the experimental unit in all these analyses.

Data from Exp. 1, 2, 3, and 4 were analyzed as a completely randomized design with treatments arranged as a 2 × 4 factorial in a split plot for each experiment. The 2 PCV2 vaccine treatments were applied on the whole plot and the 4 dietary lysine concentrations served as the split plot treatment factor. The denominator degrees of freedom were calculated using the Kenward-Roger correction. Vaccine treatments and dietary lysine concentrations were treated as fixed effects for analysis. Growth and carcass data were analyzed using the MIXED procedure in SAS, and pen counts were analyzed using the GENMOD procedure in SAS. Dietary lysine values were used as dose levels to test for linear and quadratic responses to dietary treatments.

Pen was used as the experimental unit in all analyses. Effects were considered significant if their *P*-values were < 0.05 and trends if their *P*-values were < 0.10.

Results

For each experiment, the analyzed concentrations of amino acids for the feed samples collected were similar to the calculated total values (within the acceptable limits for analytical variation).

The nursery pre-trial performance is shown in Table 7. From d 0 to 15, no difference in ADG, ADFI, or G:F was observed ($P > 0.10$) between vaccinates and non-vaccinates, indicating that the first injection of PCV2 vaccine did not affect performance. However, in the period after the second injection (d 15 to 29), PCV2-vaccinated pigs had decreased ($P = 0.02$) ADG compared with non-vaccinates; which appears to be a result of decreased ($P = 0.04$) ADFI. Gilts had greater ($P < 0.04$) ADG and ADFI than barrows. A trend was also observed ($P = 0.07$) for a gender × vaccine interaction for G:F from d 15 to 29. This interaction was due to a slight improvement in G:F in vaccinated barrows and a slight decrease in G:F in vaccinated gilts compared to unvaccinated gilts. In the period after inoculation with PRRSv (d 29 to 50), PCV2 vaccinates had improved ($P = 0.001$) G:F and a trend for increased ($P = 0.08$) ADG compared with non-vaccinates. Gilts also had poorer ($P < 0.005$) G:F compared with barrows from d 29 to 50. Over the entire 50-d nursery period, no differences were observed ($P > 0.10$) for ADG, ADFI, or final weight between gender or between PCV2 vaccinates and non-vaccinates. However, G:F was improved ($P = 0.001$) with PCV2 vaccination and improved ($P < 0.03$) for barrows compared with gilts. Also, no differences were observed ($P > 0.10$) in the percentage of pigs remaining in pens throughout the nursery portion of the study (d 15, 29, or 50; Table 8).

For each of the 4 experiments, no PCV2 vaccine × lysine interactions were observed ($P > 0.10$) for any of the growth or carcass criteria (Tables 9, 10, 11, and 12). In Exp. 1 (38 to 60 kg gilts), PCV2-vaccinated pigs tended ($P = 0.08$) to be heavier (1.6 kg) at initiation of the trial (d 0) and had an increased ($P = 0.001$) number of pigs per pen (3.6 pigs more per pen) compared with non-vaccinates (Table 9). This initial difference was due to the increase in removals and decrease in pre-trial performance of pigs in non-vaccinated pens. Vaccinated pigs had increased ($P < 0.001$) ADG, final weight, and daily SID lysine intake, and tended to have increased ($P = 0.10$) G:F compared with non-vaccinates. The increased growth for PCV2 vaccinates was

primarily driven by increased (P = 0.001) ADFI compared with non-vaccinates. In addition, at the conclusion of the experiment, pens of pigs vaccinated with PCV2 vaccine maintained a greater (P = 0.001) pen head count (5.0 more pigs per pen) than non-vaccinates. Average daily gain and G:F improved (quadratic; P < 0.04) as the SID lysine:ME ratio increased through 2.99 g/Mcal. Feed intake tended to decrease (linear; P = 0.06) as the SID lysine:ME increased. Increasing dietary lysine also increased (linear; P < 0.001) daily lysine intake and SID lysine/kg gain. The optimal SID lysine:ME ratio for 38 to 60 kg gilts was 2.99 g/Mcal where both PCV2 vaccinated and non-vaccinated gilts consumed 21.5 g SID lysine/kg gain.

In Exp. 2 (39 to 65 kg barrows), similar to the gilts in Exp. 1, PCV2 vaccinates tended to be heavier (P = 0.06) at the start of the experiment and had increased (P = 0.001) initial pen head count (4.4 more pigs per pen) compared with non-vaccinates (Table 10). Vaccination for PCV2 also increased (P < 0.04) ADG, final weight, and daily lysine intake and tended to improve (P = 0.10) G:F. Similar to Exp.1 the increased growth in PCV2 vaccinated pigs compared with non-vaccinates was driven primarily by increased (P = 0.001) ADFI. At the conclusion of Exp. 2, pen head counts were greater (P = 0.001) for PCV2-vaccinated pens than for non-vaccinated pens by 7 pigs. Increasing SID lysine:ME ratio had no effect (P > 0.10) on ADG, but increased (linear; P < 0.001) G:F, daily SID lysine intake, and SID lysine intake/kg gain. However similar to Exp. 1, ADFI tended to decrease (linear; P = 0.07) as dietary lysine increased. Optimal performance for 39 to 65 kg barrows was observed at the highest level of 3.36 g SID lysine/Mcal ME where barrows consumed 25.0 g SID lysine/kg gain.

In Exp. 3 (102 to 125 kg gilts), PCV2-vaccinated pigs had increased (P < 0.002) starting weight and 2 more pigs per pen than non-vaccinates. The smaller difference in pigs per pen was a result of removing more pigs from PCV2 vaccinated than non-vaccinated pens at initial barn marketing, which began just before the start of Exp. 3 and 4 (Table 11). No differences in ADG or ADFI were detected (P > 0.10) between PCV2 vaccinates and non-vaccinates. However, PCV2 vaccinates had increased (P < 0.03) G:F, final weight, final head count, SID lysine intake/kg gain, and backfat thickness. Both ADG and G:F improved (quadratic; P < 0.05) as the SID lysine:ME ratio increased, with ADG improving through 1.86 g/Mcal and G:F improving through 2.23 g/Mcal. Feed intake tended to decrease (linear; P = 0.09) as dietary lysine increased. But despite the decreases in feed intake, daily SID lysine intake and SID lysine intake/kg gain increased (linear; P < 0.001) with increasing dietary lysine. No dietary lysine

effects were observed ($P > 0.10$) for any of the carcass criteria. Based on improvement in G:F, the optimal SID lysine:ME ratio for 102 to 125 kg gilts appeared to be 2.23 g/Mcal, with gilts consuming 24.1 g SID lysine/kg gain.

In Exp. 4 (98 to 118kg barrows), there was a difference ($P = 0.001$) in the initial average pen head count, with vaccinate pens having almost 3 more pigs per pen than non-vaccinated pens (Table 12). However, there was no difference ($P = 0.10$) in starting weight between vaccination treatments. Both ADG and ADFI were decreased ($P < 0.04$) in vaccinated pens compared with non-vaccinated pens, and the average pen head count was greater ($P = 0.001$) at the conclusion of the trial for vaccinated pens. In this study, ADG, G:F, daily SID lysine intake, and SID lysine intake/kg gain increased (linear; $P < 0.001$) through the greatest SID lysine:ME ratio of 2.61 g/Mcal, with the greatest change occurring when the ratio increased from 2.23 to 2.61 g/Mcal. Increasing dietary lysine tended to first increase and then decrease (quadratic; $P = 0.06$) ADFI. Similar to Exp. 3, no differences in any carcass characteristics were observed ($P > 0.10$) as the SID lysine:ME ratio increased. Therefore, the optimal SID lysine:ME ratio in this study was 2.61 g/Mcal for 97 to 118 kg barrows consuming 27.3 g SID lysine/kg gain.

Discussion

Porcine circovirus type 2 is one of the main causative agents for PCVD, which can be characterized by chronic muscle wasting and lymph node enlargement as a result of postweaning multisystemic wasting syndrome (Horlen et al., 2007). It greatly increased in the U.S. pig population in the mid 2000's and is characterized by increased mortality and decreased growth rate (Horlen et al., 2008). One theory is that PCV2 weakens the pig's immune system and predisposes the pigs to additional infections. This is supported by Kixmoller et al. (2008) who observed lower quantities of coinfecting agents in pigs vaccinated against PCV2 compared with non-vaccinated counterparts. Vaccination for PCV2 has been shown to reduce mortality and increase growth performance (Horlen et al., 2008, Jacela et al., 2008; Potter et al., 2008). Results of our trials demonstrate the same benefit of reduced mortality and increased growth rate with the greatest impact in the early finisher phase and after the challenge of PRRS inoculation. These results are consistent with Oppriessnig et al. (2004) who demonstrated that cofactors, such as PRRS, increase the severity of PCVD.

Our data also agrees with Kane et al. (2009) and Potter et al. (2009) that demonstrated that the PCV2 vaccine used in these experiments reduces nursery performance, but increases finisher performance. The reduced nursery growth performance appears to be due from decreased feed intake after vaccination. The second injection in a 2-dose program seems to decrease feed intake to a greater degree, compared to the initial injection (Potter et al., 2009).

The use of PCV2 vaccine created an excellent model to demonstrate differences in pig performance due to an immune challenge in Exp. 1 and 2. Results from Exp. 1 indicate that 38 to 60 kg gilts required 2.99 g SID lysine/Mcal ME for maximal performance, while in Exp. 2, 39 to 65 kg barrows showed a linear response to increasing SID lysine:ME ratio on G:F through 3.36 g SID lysine/Mcal ME. Shelton et al. (2008) observed similar improvements in growth and feed efficiency for 38 to 65 kg gilts up to 3.16 g SID lysine/Mcal ME. Main et al. (2008) observed increases in gain and efficiency through only 2.84 g SID lysine/Mcal ME for 35 to 60 kg gilts and 43 to 70 kg barrows. Our study was conducted in the same facilities with the same genetic lines as those in Main et al. (2008) and Shelton et al. (2008). Our studies showed similar responses to higher SID lysine:ME ratios as those observed by Shelton et al. (2008) and slightly higher responses than Main et al. (2008). Results indicated that the lower growth performance from the immune challenge decreased the lysine requirement when expressed on a g/d basis; but not when expressed relative to the energy level of the diet (g/Mcal ME), relative to the weight gain of the pigs (g/kg of gain), or as a percentage of the diet.

Health status has been shown to affect the lysine requirement estimate of weanling and finishing pigs (Williams et al., 1997a, b). Williams et al. (1997a, b) observed increased lysine requirements in pigs with low immune system stimulation and attributed the cause to increased lysine needs to accommodate increased protein deposition. This suggests that healthy pigs may require a greater concentration of dietary lysine than health challenged pigs. Williams' et al. (1997a, b) data confirmed the findings of Klasing and Austic (1984). They observed increased skeletal muscle break down in broiler chicks with high the immune system stimulation by injection of either E. coli or sheep red blood cells, suggesting the animals with less immune system activity will have greater rate of protein deposition. This suggests that healthy animals may require a greater dietary lysine concentration due to decreased protein accretion compared with animals with high immune activation. Our study showed no difference in response to increasing the SID lysine:ME ratio in PCV2 vaccinates compared with non-vaccinates. Despite

this, PCV2 vaccinates had increased ADFI in Exp. 1 and 2 compared with non-vaccinates, suggesting that within that stage of growth, PCV2 vaccinates would have an increased daily lysine requirement to accommodate for greater protein deposition rates.

Experiments 1 and 2 showed increased performance in PCV2 vaccinates as compared to non-vaccinates, however that growth advantage was not observed in Exp. 3 or 4. Pens vaccinated for PCV2 had higher pen counts (up to 5 pigs per pen) in each of the 4 experiments than non-vaccinated pens. The difference in pig density may have limited the improvements in growth for PCV2 vaccinates due to pig spatial and feeder space limitations. Limited research has been done to estimate feeder trough space requirements for growing and finishing pigs. Throughout these 4 experiments, feeder trough space ranged from 5.4 to 8.4 cm per pig. Feeder space recommendations range from 2.5 (Farrin, 1990) to 7.4 cm feeder trough space for a 100 kg pig (English et al., 1988). In addition, studies have also shown that pigs will alter their behavior when feeder space is decreased to compensate and render growth performance unaffected (Hyun and Ellis, 2002). Therefore, feeder space was likely not a limiting factor. Based on equations from Gonyou et al. (2006), pig space would not have been limiting in Exp. 1 and 2 between vaccinated and non-vaccinated pens as pens had not reached the critical k-value of 0.0336 ($k = (BW^{0.667})/(\text{floor space per pig})$) at which space becomes a liming factor for growth rate despite the differences in number of pigs per pen. In Exp. 3 and 4, pig space may have been a confounding factor as PCV2 vaccinated pens would have reached the k-value during the early portion of the Exp. 3 and 4, while non-vaccinated pens would reach the critical limit at a later time in trial. This in mind, Jacela (2009) showed that the improved growth from PCV2 vaccination is primarily observed early in the finishing stage, and therefore we would not anticipate any performance differences between vaccine treatments in Exp. 3 and 4.

In Exp. 3, performance was maximized in 102 to 125 kg gilts when 2.23 g SID lysine/ Mcal ME was fed. Main et al. (2008) determined an optimal SID lysine:ME ratio 1.90 g/Mcal. Friesen et al. (1995) observed optimal performance in 104 to 136 kg gilts when 2.16 g of AID lysine/Mcal ME was provided. By utilizing the NRC conversion factors, the optimal SID lysine:ME ratio observed by Friesen et al. (1995) would be similar at 2.29 g/Mcal. Shelton et al. (2008) observed linear improvements in ADG and G:F through 2.55 g SID lysine/Mcal ME for 85 to 110 kg gilts. The greater requirement estimate observed by Shelton et al (2008) may be due to the lower BW, but is still greater than the requirement estimate from previous trials.

Performance in Exp. 4 was maximized at the highest SID lysine:ME ratio of 2.61 g/Mcal for 97 to 118 kg barrow consuming 27.3 g SID lysine/kg BW gain. This response was similar to that of Shelton et al. (2008) for 85 to 110 kg gilts where performance increased linearly through the highest level of 2.55 g SID lysine/Mcal ME with gilts consuming 23.0 g of SID lysine/kg BW gain. However, Main et al. (2008) observed a much lower optimal SID lysine:ME ratio of 1.90 g SID lysine/Mcal ME for 102 to 120 kg barrows.

No significant responses were detected to increasing SID lysine:ME ratio on carcass measurements in either Exp. 3 or 4. We would anticipate an increase in lean composition of the carcass as the SID lysine:ME ratio was increased to the requirement due to increased protein accretion (Cromwell et al., 1993; Hahn et al., 1995; De La Llata et al., 2007). Johnston et al. (2009) concluded that increases in whole body growth from increasing the lysine curve above the genetic supplier's recommendations (PIC. 2008) may not be reflective of carcass growth, and increases in dietary lysine may be negatively correlated with carcass yield. Our two studies did not observe any difference in yield with increasing dietary lysine, and observed no advantage in backfat reduction or loin depth with increasing the SID lysine:ME ratio.

In conclusion, this study has shown similar advantages to increasing the SID lysine:ME ratio as Shelton et al. (2008; 2009), which are greater in magnitude than those previously reported in the same facility by Main et al. (2008). No differences in the optimal SID lysine:ME ratio were observed between PCV2 vaccinates and non-vaccinates; however, the increased growth from increased ADFI in Exp. 1 and 2 would suggest that PCV2 vaccinates have increased daily lysine requirements on a g/d basis compared with non-vaccinates from 40 to 60 kg.

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Figures and Tables

Table 2-1. Composition of diets, Exp. 1[1] and 2[2] (as-fed basis)

	SID[3] lysine:ME, g/Mcal			
	2.24	2.61	2.99	3.36
	SID lysine, %			
Item	0.78	0.91	1.04	1.17
Ingredient, %				
Corn	75.52	70.16	64.81	59.44
Soybean meal (45% CP)	19.38	24.74	30.09	35.45
Choice white grease	3.00	3.00	3.00	3.00
Monocalcium P (21% P)	0.54	0.51	0.48	0.45
Limestone	0.90	0.90	0.90	0.90
Salt	0.35	0.35	0.35	0.35
L-Thr	0.005	0.015	0.020	0.030
Met hydroxy analog	---	0.015	0.045	0.070
Vitamin and trace mineral premix[4]	0.10	0.10	0.10	0.10
Phytase[5]	0.013	0.013	0.013	0.013
Liquid Lys (60% Lys)	0.195	0.195	0.195	0.195
Total	100.00	100.00	100.00	100.00
Calculated analysis				
SID amino acids, %				
Lys	0.78	0.91	1.04	1.17
Ile:Lys	70	69	69	69
Leu:Lys	167	156	148	142
Met:Lys	29	29	30	31
Met & Cys:Lys	61	59	58	58
Thr:Lys	62	62	62	62
Trp:Lys	19	19	20	20
Val:Lys	81	79	77	76
ME, kcal/kg	3,483	3,483	3,481	3,481
Total Lys, %	0.88	1.02	1.17	1.31
CP, %	15.4	17.5	19.5	21.6
Ca, %	0.53	0.54	0.56	0.57
P, %	0.46	0.47	0.49	0.51
Available P, %[6]	0.27	0.27	0.27	0.27

[1]A total of 1,008 gilts (PIC 337 × 1050) were used in this 28-d trial with 5 replications per PCV2 vaccination and diet combination.
[2]A total of 1,002 barrows (PIC 337 × 1050) were used in this 28-d trial with 5 replications per PCV2 vaccination and diet combination.
[3]Standardized ileal digestible.
[4]Vitamin and trace mineral premix provided per kg of diet: 4,509 IU of vitamin A, 701.5 IU of vitamin D_3, 24.05 IU of vitamin E, 1.40 mg of vitamin K, 3.01 mg of Riboflavin, 15.03 mg of vitamin B_{12}, 18.04 mg of Niacin, 12.03 mg of pantothenic acid, 40.08 mg of Mn from Mn oxide, 100.21 mg Zn from Zn sulfate, 90.19 mg Fe from Fe sulfate, 10.02 mg Cu from Cu sulfate, 0.30 mg of Se from Na selenite, and 0.50 mg of I from EDDI.
[5]OptiPhos 2000 (Enzyvia; Sheridan, IN) provided (per kg of complete diet) 500 FTU of phytase.
[6]Phytase provided 0.10% available P to the diet.

Table 2-2. Chemical composition of diets (Exp. 1)[1]

	SID[2] lysine:ME, g/Mcal			
	2.24	2.61	2.99	3.36
	SID lysine, %			
Item, %	0.78	0.91	1.04	1.17
CP	13.8 (15.4)[3]	15.4 (17.5)	17.4 (19.5)	19.3 (21.6)
Essential amino acids				
Arg	0.88	1.03	1.17	1.34
His	0.38	0.42	0.47	0.53
Ile	0.60 (0.62)	0.69 (0.71)	0.78 (0.81)	0.88 (0.91)
Leu	1.28 (1.43)	1.43 (1.57)	1.58 (1.71)	1.72 (1.84)
Lys	0.86 (0.88)	0.99 (1.02)	1.11 (1.17)	1.27 (1.31)
Met	0.25 (0.25)	0.28 (0.29)	0.30 (0.34)	0.33 (0.39)
Met + Cys	0.48 (0.54)	0.53 (0.60)	0.58 (0.68)	0.64 (0.76)
Phe	0.75	0.85	0.95	1.06
Thr	0.57 (0.57)	0.63 (0.66)	0.71 (0.75)	0.81 (0.84)
Trp	0.16 (0.17)	0.18 (0.20)	0.22 (0.23)	0.24 (0.26)
Val	0.65 (0.72)	0.74 (0.82)	0.83 (0.91)	0.94 (1.01)
Nonessential amino acids				
Ala	0.76	0.83	0.91	0.99
Asp	1.39	1.63	1.85	2.14
Cys	0.23	0.25	0.28	0.31
Glu	2.47	2.81	3.15	3.54
Gly	0.57	0.65	0.73	0.84
Pro	0.83	0.88	0.93	1.00
Ser	0.70	0.79	0.89	1.00
Tyr	0.41	0.48	0.52	0.61

[1]A total of 1,008 gilts (PIC 337 × 1050) were used in this 28-d trial with 5 replications per PCV2 vaccination and diet combination.
[2]Standardized ileal digestible.
[3]Values in parentheses indicate formulated values.

Table 2-3. Chemical composition of diets (Exp. 2)[1]

	SID[2] lysine:ME, g/Mcal			
	2.24	2.61	2.99	3.36
	SID lysine, %			
Item, %	0.78	0.91	1.04	1.17
CP	13.6 (15.4)[3]	15.1 (17.5)	17.3 (19.5)	19.1 (21.6)
Essential amino acids				
Arg	0.86	0.99	1.17	1.29
His	0.38	0.42	0.48	0.52
Ile	0.57 (0.62)	0.66 (0.71)	0.75 (0.81)	0.81 (0.91)
Leu	1.28 (1.43)	1.38 (1.57)	1.54 (1.71)	1.65 (1.84)
Lys	0.85 (0.88)	0.96 (1.02)	1.12 (1.17)	1.23 (1.31)
Met	0.25 (0.25)	0.27 0.29)	0.30 (0.34)	0.33 (0.39)
Met + Cys	0.48 (0.54)	0.52 (0.60)	0.58 (0.68)	0.63 (0.76)
Phe	0.76	0.83	0.94	1.04
Thr	0.56 (0.57)	0.62 (0.66)	0.71 (0.75)	0.78 (0.84)
Trp	0.15 (0.17)	0.17 (0.20)	0.21 (0.23)	0.20 (0.26)
Val	0.65 (0.72)	0.72 (0.82)	0.83 (0.91)	0.91 (1.01)
Nonessential amino acids				
Ala	0.78	0.82	0.90	0.99
Asp	1.39	1.58	1.85	2.04
Cys	0.23	0.25	0.28	0.30
Glu	2.48	2.74	3.13	3.43
Gly	0.58	0.64	0.73	0.82
Pro	0.97	1.01	1.04	1.19
Ser	0.70	0.77	0.89	0.97
Tyr	0.42	0.47	0.51	0.56

[1]A total of 1,002 barrows (PIC 337 × 1050) were used in this 28-d trial with 5 replications per PCV2 vaccination and diet combination.
[2]Standardized ileal digestible.
[3]Values in parentheses indicate formulated values.

Table 2-4. Composition of diets, Exp. 3[1] and 4[2] (as-fed basis)

	SID[3] lysine:ME, g/Mcal			
	1.49	1.86	2.23	2.61
	SID lysine, %			
Item	0.52	0.65	0.78	0.91
Ingredient, %				
Corn	86.46	81.12	75.77	70.41
Soybean meal (45% CP)	8.66	14.01	19.36	24.72
Choice white grease	3.00	3.00	3.00	3.00
Monocalcium P (21% P)	0.40	0.38	0.35	0.32
Limestone	0.85	0.85	0.85	0.85
Salt	0.35	0.35	0.35	0.35
L-Thr	---	0.01	0.02	0.035
Met hydroxy analog	---	---	0.005	0.025
Vitamin and trace mineral premix[4]	0.08	0.08	0.08	0.08
Phytase[5]	0.013	0.013	0.013	0.013
Liquid Lys (60% Lys)	0.195	0.195	0.195	0.195
Total	100.00	100.00	100.00	100.00
Calculated analysis				
SID amino acids, %				
Lys	0.52	0.65	0.78	0.91
Ile:Lys	71	70	70	69
Leu:Lys	204	182	167	156
Met:Lys	35	32	30	30
Met & Cys:Lys	73	66	61	60
Thr:Lys	65	65	64	65
Trp:Lys	18	18	19	19
Val:Lys	89	84	81	79
ME, kcal/kg	3,494	3,494	3,492	3,492
Total Lys, %	0.59	0.74	0.88	1.02
CP, %	11.4	13.4	15.5	17.5
Ca, %	0.45	0.46	0.48	0.49
P, %	0.39	0.40	0.42	0.43
Available P, %[6]	0.23	0.23	0.23	0.23

[1]A total of 930 gilts (PIC 337 × 1050) were used in this 28-d trial with 5 replications per PCV2 vaccination and diet combination.
[2]A total of 825 barrows (PIC 337 × 1050) were used in this 21-d trial with 5 replications per PCV2 vaccination and diet combination.
[3]Standardized ileal digestible.
[4]Vitamin and trace mineral premix provided per kg of diet: 3,608 IU of vitamin A, 561.2 IU of vitamin D_3, 19.24 IU of vitamin E, 1.12 mg of vitamin K, 2.41 mg of Riboflavin, 12.03 mg of vitamin B_{12}, 14.43 mg of Niacin, 9.62 mg of pantothenic acid, 32.07 mg of Mn from Mn oxide, 80.17 mg Zn from Zn sulfate, 72.15 mg Fe from Fe sulfate, 8.02 mg Cu from Cu sulfate, 0.24 mg of Se from Na selenite, and 0.40 mg of I from EDDI.
[5]OptiPhos 2000 (Enzyvia; Sheridan, IN) provided (per kg of complete diet) 500 FTU of phytase.
[6]Phytase provided 0.10% available P to the diet.

Table 2-5. Chemical composition of diets (Exp. 3)[1]

	SID[2] lysine:ME, g/Mcal			
	1.49	1.86	2.23	2.61
	SID lysine, %			
Item, %	0.52	0.65	0.78	0.91
CP	9.8 (11.4)[3]	10.8 (13.4)	13.7 (15.5)	15.2 (17.5)
Essential amino acids				
Arg	0.61	0.69	0.89	1.02
His	0.28	0.31	0.38	0.44
Ile	0.43 (0.42)	0.48 (0.52)	0.61 (0.62)	0.70 (0.71)
Leu	1.05 (1.16)	1.08 (1.30)	1.29 (1.44)	1.47 (1.57)
Lys	0.57 (0.59)	0.68 (0.74)	0.87 (0.88)	0.96 (1.02)
Met	0.17 (0.20)	0.21 (0.23)	0.25 (0.26)	0.28 (0.30)
Met + Cys	0.35 (0.43)	0.40 (0.48)	0.48 (0.54)	0.53 (0.61)
Phe	0.58	0.61	0.76	0.84
Thr	0.39 (0.41)	0.45 (0.50)	0.57 (0.59)	0.64 (0.68)
Trp	0.10 (0.11)	0.12 (0.14)	0.16 (0.17)	0.18 (0.20)
Val	0.49 (0.53)	0.52 (0.62)	0.66 (0.72)	0.74 (0.82)
Nonessential amino acids				
Ala	0.65	0.67	0.78	0.87
Asp	0.93	1.07	1.41	1.62
Cys	0.18	0.19	0.23	0.25
Glu	1.81	1.97	2.49	2.83
Gly	0.41	0.46	0.58	0.65
Pro	0.75	0.29	1.11	1.27
Ser	0.50	0.56	0.70	0.79
Tyr	0.33	0.34	0.42	0.47

[1]A total of 930 gilts (PIC 337 × 1050) were used in this 28-d trial with 5 replications per PCV2 vaccination and diet combination.
[2]Standardized ileal digestible.
[3]Values in parentheses indicate formulated values.

Table 2-6. Chemical composition of diets (Exp. 4)[1]

	SID[2] lysine:ME, g/Mcal			
	1.49	1.86	2.23	2.61
	SID lysine, %			
Item, %	0.52	0.65	0.78	0.91
CP	9.7 (11.4)[3]	10.9 (13.4)	13.6 (15.5)	15.1 (17.5)
Essential amino acids				
Arg	0.60	0.71	0.92	0.98
His	0.28	0.32	0.38	0.41
Ile	0.43 (0.42)	0.49 (0.52)	0.62 (0.62)	0.66 (0.71)
Leu	1.05 (1.16)	1.11 (1.30)	1.31 (1.44)	1.40 (1.57)
Lys	0.56 (0.59)	0.68 (0.74)	0.87 (0.88)	0.93 (1.02)
Met	0.20 (0.20)	0.19 (0.23)	0.25 (0.26)	0.26 (0.30)
Met + Cys	0.38 (0.43)	0.38 (0.48)	0.48 (0.54)	0.51 (0.61)
Phe	0.58	0.64	0.76	0.83
Thr	0.42 (0.41)	0.45 (0.50)	0.58 (0.59)	0.64 (0.68)
Trp	0.10 (0.11)	0.12 (0.14)	0.16 (0.17)	0.17 (0.20)
Val	0.48 (0.53)	0.53 (0.62)	0.67 (0.72)	0.72 (0.82)
Nonessential amino acids				
Ala	0.64	0.67	0.78	0.84
Asp	0.93	1.10	1.44	1.56
Cys	0.18	0.19	0.23	0.25
Glu	1.81	2.03	2.54	2.73
Gly	0.41	0.47	0.58	0.63
Pro	0.59	0.67	0.71	1.18
Ser	0.50	0.57	0.71	0.77
Tyr	0.32	0.36	0.43	0.45

[1]A total of 825 barrows (PIC 337 × 1050) were used in this 21-d trial with 5 replications per PCV2 vaccination and diet combination.
[2]Standardized ileal digestible.
[3]Values in parentheses indicate formulated values.

Table 2-7. Effects of porcine circovirus type 2 (PCV2) vaccination and gender on growth performance during the pre-trial period[1]

						Probability, $P <$		
	Barrow		Gilt			Gender ×		
PCV2 vaccination:	No	Yes	No	Yes	SEM	vaccine	Vaccine	Gender
Initial wt, kg	5.7	5.7	5.7	5.7	0.17	0.99	0.99	0.99
d 0 to 15[2]								
ADG, g	266	264	270	270	15.2	0.95	0.93	0.75
ADFI, g	394	372	396	392	18.4	0.62	0.46	0.55
G:F	0.67	0.71	0.68	0.69	0.017	0.30	0.15	0.48
d 15 to 29[3]								
ADG, g	420	403	445	417	9.2	0.56	0.02	0.04
ADFI, g	651	614	682	651	15.9	0.88	0.04	0.04
G:F	0.65	0.66	0.65	0.64	0.006	0.07	0.87	0.45
d 29 to 50[4]								
ADG, g	408	437	382	418	18.3	0.85	0.08	0.22
ADFI, g	731	725	706	726	29.6	0.66	0.81	0.69
G:F	0.56	0.60	0.54	0.58	0.007	0.54	0.001	0.005
d 0 to 50								
ADG, g	369	375	366	373	13.8	0.99	0.62	0.86
ADFI, g	607	588	606	604	21.4	0.69	0.63	0.71
G:F	0.61	0.64	0.60	0.62	0.006	0.09	0.001	0.03
Final wt, kg	24.4	24.5	24.2	24.5	0.80	0.94	0.82	0.88

[1]A total of 2,571 barrows and gilts (PIC 337 × 1050) were double stocked into a wean-to-finish barn and observed for 50 d to determine the effects of PCV2 vaccine on growth performance.
[2]The first PCV2 vaccine was given on d 1 of this study to the selected pens of pigs.
[3]The second PCV2 vaccine was given on d 22 of the study to the selected pens of pigs.
[4]All pigs were injected with live PRRS virus on d 30.

Table 2-8. Effects of porcine circovirus type 2 (PCV2) vaccination and gender on pigs remaining on test[1]

						Probability, $P <$		
	Barrow		Gilt			Gender ×		
PCV2 vaccination:	No	Yes	No	Yes	SEM	vaccine	Vaccine	Gender
d 0 pen count, no.	55.8	55.8	56.0	56.0				
Pigs remaining, %								
d 15[2]	99.7	99.5	99.3	99.6	0.31	0.39	0.41	0.76
d 29[3]	98.8	99.3	99.3	99.1	0.39	0.38	0.74	0.66
d 50[4]	95.1	98.7	96.2	97.5	1.01	0.25	0.38	0.39

[1]A total of 2,571 barrows and gilts were double stocked into a wean-to-finish barn and observed for 50 d to determine the effects of PCV2 vaccine on nursery growth performance.
[2]Time period after the first PCV2 vaccine (d 1).
[3]Time period after the second PCV2 vaccine (d 22).
[4]Time period after all pigs were injected with live PRRS virus (d 30).
[5]Day 71 corresponds to the beginning of Exp. 1 and 2.
[6]Day 99 corresponds to the conclusion of Exp. 1 and 2.

Table 2-9. Effects of SID lysine:ME ratio and PCV2 vaccination on 40- to 60- kg gilts (Exp. 1)[1]

	PCV2 vaccine[2]									Probability, $P <$				
	No				Yes					Vaccine ×			Lysine	
SID lysine:ME, g/Mcal:	2.24	2.61	2.99	3.36	2.24	2.61	2.99	3.36	SEM	Lysine	Vaccine	Lysine	Linear	Quadratic
Initial wt, kg	37.5	37.5	37.5	37.5	39.1	39.1	39.2	39.1	1.25	1.00	0.08	1.00	0.99	0.99
Initial pen head count	23.0	23.8	23.0	23.8	26.8	27.2	27.0	27.0	0.77	0.96	0.001	0.84	0.69	0.86
ADG, kg	0.69	0.73	0.78	0.74	0.81	0.87	0.86	0.84	0.017	0.33	0.001	0.002	0.02	0.002
ADFI, kg	1.63	1.64	1.61	1.59	1.84	1.84	1.79	1.75	0.038	0.88	0.001	0.22	0.06	0.45
G:F	0.42	0.44	0.48	0.47	0.44	0.47	0.49	0.48	0.012	0.67	0.10	0.001	0.001	0.04
Final wt, kg	58.0	59.4	60.4	59.1	61.7	63.5	63.4	62.5	1.35	0.99	0.001	0.48	0.46	0.18
Final pen head count	21.2	22.0	21.6	22.8	26.8	27.2	26.8	27.0	0.71	0.80	0.001	0.60	0.31	0.93
Daily SID lysine intake, g	12.68	14.92	16.78	18.58	14.33	16.77	18.56	20.43	0.390	0.99	0.001	0.001	0.001	0.37
SID lysine intake/kg gain, g	18.43	20.55	21.56	25.11	17.79	19.30	21.48	24.50	0.578	0.80	0.13	0.001	0.001	0.09

[1]A total of 1,008 gilts (PIC 337 × 1050) were used in this 28-d trial with 5 replications per PCV2 vaccination and diet combination.
[2]Vaccination for PCV2 was administered at placement into the wean-to-finish facility and again 3 wk later.

Table 2-10. Effects of SID lysine:ME ratio and PCV2 vaccination on 40 to 65 kg barrows (Exp. 2)[1]

	PCV2 vaccine[2]									Probability, $P <$				
	No				Yes								Lysine	
SID lysine:ME, g/Mcal:	2.24	2.61	2.99	3.36	2.24	2.61	2.99	3.36	SEM	Vaccine × Lysine	Vaccine	Lysine	Linear	Quadratic
Initial wt, kg	37.8	37.8	37.8	37.9	39.9	39.9	39.8	39.9	1.47	1.00	0.06	1.00	0.97	0.99
Initial pen head count	23.0	22.4	22.6	23.4	27.4	27.0	27.4	27.2	0.72	0.91	0.001	0.85	0.80	0.44
ADG, kg	0.80	0.78	0.87	0.87	0.93	0.94	0.93	0.96	0.032	0.44	0.001	0.39	0.13	0.66
ADFI, kg	1.98	1.87	1.90	1.84	2.15	2.15	2.05	2.05	0.067	0.77	0.001	0.31	0.07	0.86
G:F	0.40	0.42	0.46	0.47	0.43	0.44	0.45	0.47	0.009	0.18	0.10	0.001	0.001	0.63
Final wt, kg	61.8	63.1	64.3	64.9	66.1	66.5	65.8	66.9	1.79	0.87	0.04	0.77	0.30	0.99
Final pen head count	21.4	18.8	19.8	20.4	27.2	26.6	27.4	27.0	0.90	0.67	0.001	0.38	0.76	0.19
Daily SID lysine intake, g	15.45	17.03	19.80	21.47	16.77	19.58	21.32	23.95	0.653	0.71	0.001	0.001	0.001	0.96
SID lysine intake/kg gain, g	19.40	21.94	22.86	24.84	17.99	20.79	22.97	25.13	0.480	0.22	0.13	0.001	0.001	0.37

[1]A total of 1,002 barrows (PIC 337 × 1050) were used in this 28-d trial with 5 replications per PCV2 vaccination and diet combination.
[2]Vaccination for PCV2 was administered at placement into the wean-to-finish facility and again 3 wk later.

Table 2-11. Effects of SID lysine:ME ratio and PCV2 vaccination on 100 to 125 kg gilts (Exp. 3)[1]

	PCV2 vaccine[2]									Probability, *P* <				
	No				Yes								Lysine	
SID lysine:ME, g/Mcal:	1.49	1.86	2.23	2.61	1.49	1.86	2.23	2.61	SEM	Vaccine × Lysine	Vaccine	Lysine	Linear	Quadratic
Initial wt, kg	100.1	100.0	100.1	100.1	103.3	103.4	103.3	103.4	1.37	0.99	0.002	0.99	0.98	0.98
Initial pen head count	20.4	20.2	20.4	20.6	22.6	22.2	22.4	22.4	0.69	0.99	0.001	0.97	0.93	0.69
ADG, kg	0.74	0.83	0.84	0.82	0.76	0.84	0.84	0.87	0.027	0.79	0.24	0.005	0.003	0.05
ADFI, kg	2.72	2.71	2.62	2.59	2.68	2.68	2.56	2.64	0.061	0.79	0.60	0.21	0.09	0.75
G:F	0.27	0.31	0.32	0.32	0.29	0.31	0.33	0.33	0.006	0.91	0.02	0.001	0.001	0.001
Final wt, kg	120.7	123.2	123.5	123.1	125.0	126.8	126.9	127.8	1.46	0.97	0.001	0.27	0.10	0.36
Final pen head count	20.4	20.2	20.4	20.4	22.2	22.2	22.4	22.4	0.70	0.99	0.001	0.99	0.83	0.92
Daily SID lysine intake, g	14.14	17.64	20.44	23.56	13.91	17.39	19.94	24.0	0.44	0.72	0.70	0.001	0.001	0.86
SID lysine intake/kg gain, g	19.37	21.31	24.47	28.92	18.28	20.82	23.76	27.67	0.470	0.85	0.02	0.001	0.001	0.007
Carcass measurements														
Backfat, mm	16.0	15.4	14.9	15.8	16.5	16.5	16.3	16.4	0.66	0.84	0.03	0.67	0.62	0.32
Lean, %	56.4	55.9	56.5	56.0	56.3	56.5	56.4	56.4	0.70	0.91	0.71	0.97	0.89	0.91
Loin depth, cm	6.13	6.22	6.27	6.19	6.27	6.43	6.23	6.28	0.177	0.86	0.35	0.87	0.95	0.51
Yield, %	75.6	75.7	75.9	75.5	76.4	75.6	75.5	75.4	0.50	0.54	0.87	0.67	0.25	0.94
FFLI, %[3]	50.9	51.1	51.4	51.0	50.8	50.9	50.9	50.9	0.28	0.86	0.18	0.67	0.54	0.35

[1]A total of 930 gilts (PIC 337 × 1050) were used in this 28-d trial with 5 replications per PCV2 vaccination and diet combination.
[2]Vaccination for PCV2 was administered at placement into the wean-to-finish facility and again 3 wk later.
[3]Fat-free lean index.

Table 2-12. Effects of SID lysine:ME ratio and PCV2 vaccination on 97 to 118 kg barrows (Exp. 4)[1]

	PCV2 vaccine[2]									Probability, $P <$				
	No				Yes					Vaccine			Lysine	
SID lysine:ME, g/Mcal:	1.49	1.86	2.23	2.61	1.49	1.86	2.23	2.61	SEM	× lysine	Vaccine	Lysine	Linear	Quadratic
Initial wt, kg	97.6	97.6	97.4	97.6	97.8	97.8	97.8	97.8	1.97	1.00	0.86	1.00	0.99	0.99
Initial day pen head count	18.2	19.0	19.2	18.2	22.8	22.6	22.6	22.4	0.89	0.91	0.001	0.91	0.86	0.48
ADG, kg	0.92	0.97	0.97	1.02	0.86	0.91	0.95	1.02	0.019	0.36	0.02	0.001	0.001	0.81
ADFI, kg	3.04	3.24	3.23	3.08	2.94	2.98	3.11	3.04	0.083	0.62	0.04	0.19	0.31	0.06
G:F	0.30	0.30	0.30	0.33	0.30	0.31	0.31	0.34	0.008	0.81	0.70	0.001	0.001	0.03
Final wt, kg	117.5	118.0	117.9	119.0	116.1	117.0	117.8	119.3	1.81	0.96	0.68	0.63	0.21	0.84
Final pen head count	18.0	19.0	19.0	18.2	22.4	22.6	22.4	22.4	0.90	0.94	0.001	0.89	0.95	0.44
Daily SID lysine intake, g	15.80	21.07	25.20	28.07	15.29	19.38	24.25	27.65	0.583	0.69	0.04	0.001	0.001	0.07
SID lysine intake/kg gain, g	17.28	21.72	25.89	27.58	17.78	21.25	25.66	27.04	0.561	0.79	0.65	0.001	0.001	0.005
Carcass measurements														
Backfat, mm	19.5	19.1	19.3	19.5	20.5	20.1	19.5	19.3	0.61	0.74	0.24	0.70	0.29	0.63
Lean, %	54.0	54.1	54.0	53.8	53.0	53.4	53.9	54.0	0.48	0.59	0.29	0.79	0.37	0.66
Loin depth, cm	5.84	5.73	5.72	5.63	5.44	5.62	5.79	5.77	0.164	0.38	0.52	0.92	0.63	0.72
Yield, %	74.3	74.6	74.6	74.1	74.8	74.8	74.8	74.8	0.51	0.95	0.25	0.96	0.93	0.60
FFLI, %[3]	48.8	49.1	49.0	48.9	48.2	48.5	48.8	49.0	0.28	0.55	0.11	0.47	0.16	0.48

[1]A total of 825 barrows (PIC 337 × 1050) were used in this 21-d trial with 5 replications per PCV2 vaccination and diet combination.
[2]Vaccination for PCV2 was administered at placement into the wean-to-finish facility and again 3 wk later.
[3]Fat-free lean index.

CHAPTER 3 - Effects of copper sulfate, tri-basic copper chloride, and zinc oxide on weanling pig performance

Abstract

Three experiments were conducted to evaluate the effects of increasing dietary Cu and Zn concentrations on weanling pig performance. Diets were fed in 2 phases: phase 1 from d 0 to 14 post-weaning and phase 2 from d 14 to 28 in Exp. 1 and 2 and d 14 to 42 in Exp. 3. The trace mineral premix, included in all diets, provided 165 ppm Zn and 16.5 ppm Cu. In Exp. 1, treatments were arranged in a 2 × 3 factorial with main effects of added Cu from tri-basic copper chloride (TBCC; 0 or 150 ppm) and added Zn from zinc oxide (ZnO; 0, 1,500, or 3,000 ppm from d 0 to 14 and 0, 1,000, or 2,000 ppm from d 14 to 28). No Cu × Zn interactions were observed ($P > 0.10$) for any of the growth data. Adding TBCC increased ($P < 0.03$) ADG and ADFI during each phase. Increasing dietary Zn also increased (linear, $P < 0.04$) ADG and ADFI during each phase. In Exp. 2, treatments were arranged in a 2 × 3 factorial with main effects of added Zn from ZnO (0 or 3,000 ppm from d 0 to 14 and 0 or 2,000 ppm from d 14 to 28) and Cu (control, 125 ppm Cu from TBCC, or 125 ppm Cu from copper sulfate; $CuSO_4$). No Cu × Zn interactions ($P > 0.10$) were observed for any performance data. Adding ZnO improved ($P < 0.02$) ADG and ADFI from d 0 to 14 and overall. From d 0 to 28, supplementing $CuSO_4$ increased ($P < 0.02$) ADG, ADFI, and G:F, and TBCC improved (P = 0.006) ADG. In Exp. 3, the 6 dietary treatments were arranged in a 2 × 2 factorial with main effects of added Cu from $CuSO_4$ (0 or 125 ppm) and added Zn from ZnO (0 or 3,000 ppm from d 0 to 14 and 0 or 2,000 ppm from d 14 to 42). The final 2 treatments were feeding added ZnO alone or in combination with $CuSO_4$ from d 0 to 14 and adding $CuSO_4$ from d 14 to 42. Adding ZnO increased ($P < 0.04$) ADG, ADFI, and G:F from d 0 to 14 and ADG from d 0 to 42. Dietary $CuSO_4$ increased ($P < 0.004$) ADG and ADFI from d 14 to 42 and d 0 to 42. From d 28 to 42, a trend for a Cu × Zn interaction was observed ($P = 0.06$) for ADG. This interaction was reflective of the numeric decrease in ADG for pigs when Cu and Zn were used in combination compared with each used alone. Also, numerical advantages were observed when supplementing Zn from d 0 to 14 and Cu from d 14 to 42 compared with all other Cu and Zn regimens. These 3 experiments show advantages to including both Cu and Zn in the diet for 28 d post-weaning; however, as evident in

Exp. 3, when Zn was added early and Cu was added late, performance was similar or numerically greater than when both were used for 42 d.
Key Words: copper, growth, weanling pig, zinc

Introduction

Zinc and Cu are two minerals commonly added at pharmacological concentrations to weanling pig diets to serve as growth promoters. Nursery studies have demonstrated that increased dietary concentrations of Zn can promote growth rates (Hahn and Baker, 1993; Smith et al., 1997; Carlson et al., 1999; Hill et al., 2001; Williams et al., 2005;) and increase stool firmness (Hill et al., 2000). The greatest response to pharmacological concentrations of Zn is observed when 3,000 ppm is provided for the first 2 to 4 wk postweaning (Carlson et al., 1999; Woodworth et al., 2005). Zinc oxide (ZnO) is the most common form used to increase growth (Hahn and Baker, 1993; Schell and Kornegay, 1996; Hollis et al., 2005).

Dietary Cu also has been shown to enhance growth rates in weanling pigs (Stahly et al., 1980; Cromwell et al., 1989; 1998; Hill et al., 2000). Supplemental Cu is most efficacious for weanling pigs at 200 to 250 ppm (Cromwell, 2001), and 125 ppm offers 75% of the growth response achieved with 250 ppm (Cromwell et al., 1989). The sulfate form of Cu historically has been used because of its improved performance compared with the oxide form (Cromwell et al., 1989). However, Cromwell et al. (1998) observed similar growth-promoting effects when adding Cu from either tri-basic copper chloride (TBCC) or copper sulfate ($CuSO_4$) and showed that TBCC may be more efficacious at lower levels than $CuSO_4$.

Historically, use of high concentrations of both Zn (3,000 ppm) and Cu (250 ppm) has not shown additive effects (Smith et al., 1997; Hill et al., 2000). However, Perez-Mendoza et al. (2008) observed improved growth when nursery pigs were fed supplemental $CuSO_4$ along with pharmacological Zn at 3,000 ppm. Also, the effect of moderate concentrations of Cu (100 to 150 ppm) combined with high pharmacological Zn has not been evaluated. Therefore, the objective of these experiments was to characterize the effect of combining ZnO with moderate concentrations of TBCC or $CuSO_4$ on nursery pig growth performance and blood plasma minerals.

Materials and Methods

General

Protocols used in these experiments were approved by the Kansas State University Institutional Animal Care and Use Committee. Experiments 1 and 3 were conducted at the Kansas State University Swine Teaching and Research Center, and Exp. 2 was conducted at the Kansas State University Segregated Early Weaning Facility.

Each pen contained a 4-hole, dry self-feeder and either a cup or nipple waterer, depending on facility, to provide ad libitum access to feed and water. Pens had metal woven-wire flooring in Exp. 1 and 3 and metal tri-bar flooring in Exp. 2 while allowing 0.30 m^2 per pig. Weights and feed disappearance were measured weekly to determine ADG, ADFI, and G:F.

Similar diets were used in each of the 3 experiments (Table 1). The phase 1 diet was fed for the first 14 d postweaning, and the phase 2 diet was fed for the remainder of the trial (14 d in Exp. 1 and 2 and 28 d in Exp. 3). Diets were fed in meal form and were formulated to contain 1.41 and 1.31% standardized ileal digestible lysine, respectively. Phase 1 diets contained 15% spray-dried whey and 3.75% fish meal. Phase 2 diets were corn-soybean meal based without specialty protein sources. All diets contained a trace mineral premix that supplied 165 ppm Zn from zinc sulfate ($ZnSO_4$) and 16.5 ppm Cu from $CuSO_4$. All other nutrients were formulated to meet or exceed NRC (1998) requirements. To generate treatment diets, ZnO, TBCC, and $CuSO_4$ were added in place of corn starch to achieve the desired Zn and Cu concentrations. Treatment diets were sampled in each experiment and analyzed for Cu and Zn concentrations. Samples were digested with HNO_3 and H_2O_2 and then analyzed for Cu and Zn by the atomic absorption spectrophotometric method. Calculated values were determined using the amount added from the trace mineral premix, any added Cu or Zn supplementation based on treatment, and the amount provided by other dietary ingredients using values from NRC (1998).

Blood samples were collected from 2 pigs per pen (d 14 in Exp. 1, d 14 and 28 in Exp. 2, and d 14 and 42 in Exp. 3) by jugular venapuncture. On d 14, pigs were weighed and diets were changed at approximately 0800 h, and blood was collected at 1300 h. On d 28 in Exp. 2 and d 42 in Exp. 3, pigs were again weighed at 0800 h, and blood was collected at 1300 h. However, on the final day of the trial, pigs were provided the same diet that was offered prior to weighing. Blood samples were stored on ice for approximately 1 h until they were centrifuged at 1,600 × *g* for 20 min at 4°C. Plasma was then collected from each blood sample, frozen, and sent to Michigan State University (East Lansing, MI) for mineral analysis. Copper and Zn

concentrations were determined by flame atomic absorption spectrophotometry (Smith-Hieftje 4000, Thermo Jarrell Ash Corp., Franklin, MA), and P was measured by color spectrophotometry.

Experiment 1

Weanling pigs (n=180; TR4 ×1050; PIC, Hendersonville, TN; initially 5.7 kg and 21 d of age) were allotted by initial BW in a RCBD. There were 5 pens per treatment with 6 pigs per pen. Treatments were arranged in a 2 × 3 factorial with main effects of added Cu from TBCC (0 or 150 ppm) and added Zn from ZnO (0, 1,500, or 3,000 ppm from d 0 to 14 and 0, 1,000, or 2,000 ppm from d 14 to 28).

Experiment 2

Weanling pigs (n=180; PIC 1050; initially 6.0 kg and 21 d of age) were allotted by initial BW in a RCBD for this 28-d trial. There were 6 pens per treatment with 5 pigs per pen. Treatments were arranged in a 2 × 3 factorial with main effects of added Zn from ZnO (0 or 3,000 ppm from d 0 to 14 and 0 or 2,000 ppm from d 14 to 28) and added Cu sources (0, 125 ppm Cu from TBCC, or 125 ppm Cu from $CuSO_4$).

Experiment 3

Weanling pigs (n=216; PIC TR4 ×1050, initially 6.2 kg and 21 d of age) were fed in a 42-d growth trial to compare the effects of supplemental Zn and Cu and observe the effects of changing mineral regimens. Pigs were allotted by initial BW in a RCBD. There were 6 pens per treatment with 6 pigs per pen. Treatments were arranged in a 2 × 2 factorial with main effects of added Cu from $CuSO_4$ (0 or 125 ppm) and added Zn from ZnO (0 or 3,000 ppm from d 0 to 14 and 0 or 2,000 ppm from d 14 to 42). Two additional treatments were included in which the added ZnO or ZnO and $CuSO_4$ diet was fed from d 0 to 14 with added $CuSO_4$ fed from d 14 to 42.

Statistical Analysis

Pen was the experimental unit for all analysis, and data from each experiment were analyzed using the MIXED procedure in SAS (SAS Institute Inc., Cary, NC). Each study was analyzed as a RCBD, and initial BW was used to establish blocks. Blocks were treated as

random effects in the model. Also in each model, Cu and Zn effects were treated as fixed effects. Experiment 1 was analyzed in a 2 × 3 factorial arrangement with 2 Cu and 3 Zn concentrations. Contrast statements were used to evaluate linear and quadratic polynomial effects associated with increasing dietary Zn. Experiment 2 also was analyzed in a 2 × 3 factorial arrangement with main effects of 2 Zn concentrations and 3 sources of added Cu. Contrast statements were used to separate differences between Cu sources. In Exp. 3, main effects and potential interactions for added Cu and Zn were tested using contrast statements. For Phase 1, growth performance was similar between both dietary treatments that were fed either the high Zn or high Cu and Zn diet; therefore, results were pooled to determine the main effects of Cu and Zn. For plasma mineral results, concentrations were not similar between the 2 treatments receiving the same mineral regimen in both phases; therefore, only pigs remaining on the same regimen for both phases were used to test for main effects of Cu and Zn. In Phase 2 as well as for the overall trial, only treatments that remained on the same mineral regimen for the entire trial were used to determine the main effects of Cu and Zn. Effects were considered significant if their *P*-values were < 0.05 and trends if their *P*-values were < 0.10.

Results

Laboratory analysis of the diets indicated that Cu and Zn concentrations were similar to calculated values in Exp. 1, 2, and 3 (Tables 2, 3, and 4, respectively).

Experiment 1

No Cu × Zn interactions were observed ($P > 0.10$) for any of the performance criteria in Exp. 1 (Table 5). Increasing dietary Zn increased (linear, $P < 0.003$) both ADG and ADFI from d 0 to 14. Dietary Cu from TBCC also increased ($P < 0.02$) ADG and ADFI compared with non-Cu-supplemented treatments. However, dietary Cu and Zn additions did not influence G:F ($P > 0.10$).

From d 14 to 28, the addition of Cu from TBCC increased ($P < 0.03$) both ADG and ADFI. Also, increasing dietary Zn increased (linear, $P < 0.04$) both ADG and ADFI from d 14 to 28. Feed efficiency was not influenced (P > 0.10) by adding Cu or Zn.

Overall (d 0 to 28), adding Cu from TBCC improved ($P < 0.007$) both ADG and ADFI. The additions of dietary Zn from ZnO resulted in (linear, $P < 0.003$) improvements in ADG and

ADFI. Pigs that were fed both added Cu and pharmacological Zn had the greatest numerical ADG and ADFI, and no interactions were observed.

Inclusion of ZnO or TBCC had no effect ($P > 0.10$) on plasma Cu concentrations (Table 6). However, Cu × Zn interactions were detected ($P < 0.03$) for both plasma Zn and P concentrations. The interaction for plasma Zn occurred because a greater increase in plasma Zn was observed as dietary Zn increased for pigs fed diets containing no added Cu compared to the response when TBCC was incorporated into the diet with increasing dietary Zn. The P interaction was due to plasma P increasing in pigs fed increasing dietary Zn without added Cu, but decreased as Zn concentration increased in diets with supplemental Cu.

Experiment 2

No Cu × Zn interactions were observed ($P > 0.10$) for any of the growth criteria in Exp. 2 (Table 7). From d 0 to 14, adding dietary Zn increased ($P < 0.02$) ADG, ADFI, and G:F. A main effect of Cu also was observed ($P < 0.01$) from d 0 to 14 for ADG, ADFI, and G:F. Pigs supplemented with Cu from $CuSO_4$ had greater ($P < 0.04$) ADG, ADFI, and G:F than pigs supplemented with no Cu or with Cu from TBCC.

From d 14 to 28, adding Cu from either $CuSO_4$ or TBCC tended to increase ($P < 0.08$) ADG. Daily feed intake increased ($P = 0.01$) in pigs that were supplemented with Zn. Also, supplementing Cu from $CuSO_4$ improved ($P = 0.02$) and from TBCC tended to improve ($P = 0.08$) G:F compared with not adding supplemental Cu.

Over the entire 28-d trial, pharmacological Zn increased ($P < 0.01$) ADG and ADFI. Pigs fed added $CuSO_4$ had increased ($P < 0.02$) ADG, ADFI, and G:F compared with control pigs. Also, pig fed supplemental TBCC had greater ($P = 0.006$) ADG than control pigs. Pigs fed both pharmacological ZnO and $CuSO_4$ had the greatest numeric ADG and ADFI.

No Cu or Zn effects were observed for plasma Cu on d 14; however, plasma Zn concentrations increased ($P = 0.001$) on d 14 and tended ($P = 0.09$) to be higher at d 28 for pigs supplemented with ZnO (Table 8). A Cu × Zn interaction was detected ($P = 0.02$) on d 28. In diets containing no added Zn, plasma Cu numerically increased when TBCC was added to the diet but decreased when $CuSO_4$ was added to the diet. The opposite was true in diets containing supplemental Zn, with plasma Cu numerically decreasing as TBCC was added to the diet and

increasing when $CuSO_4$ was added to the diet. Unlike Exp. 1, no dietary effects were observed ($P > 0.10$) for plasma P at either bleeding time.

Experiment 3

Pharmacological Zn improved ($P < 0.04$) ADG, ADFI, and G:F (Table 9), during phase 1 (d 0 to 14). The addition of Cu did not improve ($P > 0.10$) ADG or G:F compared to pigs fed the control diet, but tended to increase ($P = 0.07$) ADFI. The numerically greatest ADG and ADFI responses were seen when pigs were fed both added Zn and Cu; however, these responses were only numerically greater (3%) than Zn used alone.

From d 14 to 28, pharmacological Zn increased ($P = 0.04$) ADFI but had no effect on ADG ($P = 0.10$). Thus, G:F became worse ($P = 0.02$) when Zn was added to the diet. Added dietary Cu also increased ($P < 0.003$) ADG and ADFI and tended to improve ($P = 0.06$) G:F. As pigs were switched from supplemental Zn in phase 1 to added Cu, ADG improved ($P < 0.05$) compared with maintaining a high concentration of Zn. Conversely, when pigs were switched from high concentrations of added Cu and Zn to added Cu alone, performance was not improved ($P > 0.05$) compared with adding both minerals.

From d 28 to 42, a trend for a Cu × Zn interaction was observed ($P = 0.06$) for ADG. This interaction was reflective of the numeric decrease in ADG for pigs fed pharmacological Cu and Zn in combination compared with each fed separately. Pigs fed pharmacological Cu had increased ($P < 0.04$) ADFI and lower G:F than pigs not supplemented with Cu for this 2 wk period.

During dietary phase 2 (d 14 to 42), pigs fed pharmacological Cu had increased ($P < 0.003$) ADG and ADFI. Pigs fed added Zn had lower ($P = 0.04$) G:F compared with those not supplemented with Zn. Pigs that were fed pharmacological concentrations of Zn from d 0 to 14 and then fed pharmacological Cu for d 14 to 42 had increased ($P < 0.05$) ADG compared with pigs fed pharmacological Zn in both phases.

For the entire study (d 0 to 42), pharmacological Zn and pharmacological Cu improved ($P < 0.03$) ADG, with no interaction ($P > 0.10$). Feed intake was greater (P = 0.004) for pigs fed pharmacological Cu compared with those not receiving supplemental Cu. Final body weights were increased (P < 0.05) for each of the 5 regimens of pharmacological Cu and Zn compared with the control.

For blood plasma on d 14, no dietary effects were observed ($P > 0.10$) for plasma Cu concentration (Table 10). Plasma Zn concentrations increased ($P = 0.001$) when pharmacological Zn was fed in phase 1 but not phase 2. Pigs whose mineral regimens were changed on d 14 from pharmacological Zn or Zn and Cu to only Cu had decreased ($P < 0.05$) plasma Zn compared with pigs remaining on the same regimen. The 5-h period in which pigs were allowed to eat the phase 2 diet may have generated the decrease in plasma Zn. No dietary main effects were observed ($P > 0.10$) for plasma P at either d 14 or 42. On d 42, trends for a Cu × Zn interaction were detected ($P < 0.08$) for both plasma Cu and Zn. The plasma Cu interaction was due to a numeric increase in plasma Cu compared with the control diet when Cu was added to the diet alone; no difference in plasma Cu was observed when Cu and Zn were added together. The plasma Zn interaction was due to a greater increase in plasma Zn when Zn was added alone in the diet compared with adding both Cu and Zn.

Discussion

Zinc supplementation in each of these 3 experiments increased feed intake, which resulted in increased overall ADG of 12.6, 10.8, and 7.0% for Exp. 1, 2, and 3, respectively compared to pigs not supplemented with Zn. Each of the experiments showed an advantage to supplementing 3,000 ppm Zn in the first 2 wk postweaning, similar to Carlson et al. (1999). Hahn and Baker (1993) observed 14.5 and 12.4% improvements in daily gain with 3,000 ppm Zn supplementation that were related to 13.5 and 12.8% increases in feed intake, in 35-d and 28-d old pigs after they had been placed on common diets for 7-d post-weaning . Hollis et al. (2005) observed an 11.9% improvement in ADG when adding 2,500 ppm Zn from ZnO for 28 d post-weaning compared with no supplemental Zn. Hill et al. (2001) reported that improvements in growth from adding high concentrations of Zn were additive to effects of antimicrobial agents (carbadox).

The source of added Zn seems to be an important factor in observing positive responses in pig performance. Hahn and Baker (1993) showed that $ZnSO_4$ and a Zn-Met complex increased plasma Zn concentrations much greater than ZnO, which suggests an increase in the uptake of Zn from the small intestine. The sulfate and amino acid forms of Zn are absorbed at a greater rate than ZnO (Wedekind et al., 1994; Schell and Kornegay, 1996), and other researchers have hypothesized that lower concentrations of $ZnSO_4$ or Zn amino acid complexes (ZnAA) could be

included in the diet to elicit a growth response while reducing Zn excretion. Hollis et al. (2005) showed that an additional 500 ppm Zn from either ZnO or organic sources of Zn did not improve ADG compared with normal values; however 3,000 ppm Zn from ZnO increased performance. Woodworth (1999) also showed that pigs fed 100 to 500 ppm of either $ZnSO_4$ or a ZnAA complex had intermediate growth rates to the pigs fed 165 or 3,165 ppm Zn from ZnO. Therefore, ZnO is the only form used to achieve pharmacological levels of Zn in the diet to improve growth in nursery pigs.

Copper supplementation also improved ADG in these experiments; TBCC improved daily gain by 9.0 and 9.7% in Exp. 1 and 2, respectively, and $CuSO_4$ improved ADG by 17.9 and 7.1% in Exp. 2 and 3, respectively. These increases were primarily due to increases in feed intake. Hence, Cu supplementation also improved G:F (Exp. 2). Cromwell (2001) summarized 23 studies on the influence of adding 200 to 250 ppm Cu from $CuSO_4$ on pig performance from 8 to 20 kg. In this text, he calculated an 11.9% improvement in growth and a 4.5% improvement in feed efficiency due to $CuSO_4$ addition. Perez-Mendoza et al. (2008) also observed increases in growth through 6 wk post-weaning with 315 ppm supplemental Cu from $CuSO_4$. In addition, Stahly et al. (1980) pooled the results of 4 trials comparing the use of $CuSO_4$ and antibiotic supplementation and determined that the effect of Cu supplementation was independent of the response of growth-promoting levels of antibiotics.

The concentration and source of added Cu also affect the response. Cromwell et al. (1989) observed a curvilinear response in gain to increasing concentrations of dietary Cu from $CuSO_4$ and, on the basis of the inflection point, calculated the greatest response at 242 ppm. Additional studies have shown the ideal amount of added Cu from $CuSO_4$ to promote growth is between 125 and 250 ppm (Stahly et al., 1980; Roof and Mahan, 1982; Coffey et al., 1994). Cuprous oxide added at either 125 or 250 ppm does not elicit a growth response (Cromwell et al., 1989); however, a Cu-Lys complex has shown similar growth responses when compared with $CuSO_4$ (Coffey et al. 1994; Apgar et al. 1995). Using liver concentrations as the response criteria, Apgar and Kornegay (1996) determined that absorption of Cu from a Cu-Lys was similar to that of Cu from $CuSO_4$. Cromwell et al. (1998) also observed similar performance in weanling pigs that were supplemented with Cu from either TBCC or $CuSO_4$. Therefore, it appears that under some conditions, pharmacological concentrations of Cu from $CuSO_4$, a Cu-lysine complex, or TBCC can be added to pig diets to promote growth.

Contrary to our results, inclusion of both Cu and Zn at pharmacological concentrations does not always show additive effects in weanling pigs (Smith et al., 1997; Hill et al. 2000). In previous experiments, Cu and Zn were added to diets that contained growth-promoting levels of antibiotics, whereas in our experiment, diets contained no additional antimicrobials. Responses of Zn or Cu have been shown to be additive to other antimicrobial agents (Stahly et al., 1980; Hill et al., 2001; Woodworth et al., 2005); however, the combination of all 3 may not be additive in nature. Perez-Mendoza et al. (2008) observed a 15.6% improvement in growth in the first 2 wk postweaning when supplemental Cu was added to diets containing 3,000 ppm of added Zn, but the effect of Zn supplementation was not tested.

Little research has been done to examine the effect of changing mineral regimens to validate the influence of switching from feeding Zn in the initial diets after weaning to feeding Cu in later diets. Numerical benefits to this approach were found in Exp. 3. Switching mineral regimens can reduce diet cost because Zn is removed from diets fed later in the nursery period. Another major benefit of this approach is decreased excretion of Zn in manure. Zinc accumulation in soil has been shown to hinder some crop production (Takkar and Mann, 1978; Chaney, 1993). Rincker et al. (2005) showed that Zn excretion increases after approximately 9 d of feeding pharmacological Zn as the body stores become maximized. Therefore, adding Zn in the initial post-weaning diets followed by supplementing Cu in later diets may be a way to obtain the desired growth-promoting effects while limiting costs and minimizing the concentration of Zn excreted in manure.

The mode or modes of action for adding Cu to weanling pig diets are unknown. Pharmacological Cu has not been shown to improve intestinal morphology (Hedemann et al., 2006). Copper supplementation also has shown been shown to promote growth independently of antibiotic additions (Stahly et al., 1980; Roof and Mahan, 1982), indicating it may have a different mode of action than antibiotics.

Modes of action for Zn supplementation also are unknown; however, several hypotheses have been generated. Poulsen (1989) suggested that pharmacological Zn prevented *Escherichia coli* diarrhea in weanling pigs. Pharmacological Zn from ZnO does not alter the level of *E. coli* excreted in fecal material (Jensen-Waern et al., 1998; Pulz and Carlson, 2007). Woodworth (1999) suggested that added Zn prevents *E. coli* from creating a toxic environment in the

digestive system, possibly by preventing *E. coli* attachment and invasion of the enteric epithelium. Zinc does not appear to inhibit *E. coli* multiplication within the intestinal lumen.

While Hahn and Baker (1993) suggested the mode of action for increased growth was related to plasma Zn concentrations. Pharmacological Zn increased plasma Zn on d 14 in our 3 experiments, but our values did not approach the concentrations observed by Hahn and Baker (1993). Perhaps this may be due to the use of older pigs in that particular study compared with ours. Carlson et al. (1999) observed increased metallothionein concentration in the liver, kidney, and intestinal mucosa cells with pharmacological Zn supplementation. Metallothionein is a metal-binding protein associated with maintaining Zn homeostasis that is found throughout the body (Richards and Cousins, 1975) and is related to Zn absorption. Carlson et al. (1999) concluded that metallothionein synthesis in intestinal mucosal cells may facilitate Zn uptake into the body, resulting in improved growth performance.

A third proposed mode of action for Zn supplementation is the potential for improved intestinal morphology (Carlson et al., 1999). Villus atrophy is a physiological event that occurs in newly weaned pigs (Hampson, 1986). Li et al. (2001) validated the previous report of Carlson et al. (1998) showing that pharmacological concentrations of Zn fed to weanling pig diets increased villus height and decreased crypt depth at 11 d post-weaning compared with not supplementing Zn. In contrast, Hedemann et al. (2006) observed no improvements in villus height of pigs weaned at 28-d of age with 2,500 ppm Zn supplementation for 14 d post-weaning. One factor that should be considered when interpreting those results is the timing of intestinal sample collection. Villus height has been shown to increase back to preweaning values as quickly as 9 d after weaning (Hedemann et al., 2003).

In each of our 3 experiments, plasma Zn on d 14 increased linearly as Zn increased in the diet. Carlson et al. (1999) observed similar increases in plasma Zn when pigs of early and traditional weaning ages were fed 3,000 ppm Zn for 14 d post-weaning. Hahn and Baker (1993) also showed an increase in plasma Zn with supplementation of Zn from several sources. Hill et al. (2000) also observed increased plasma Zn concentrations with Zn supplementation; however, plasma Zn concentration was greater when dietary Cu and Zn were combined than when high concentrations of Zn were fed without Cu. This same numerical pattern was observed in Exp. 2, but the opposite was observed in Exp. 1 and 3. Also in Exp. 3, pigs switched from either high Zn or high Cu and Zn to high Cu on d 14 had decreased plasma Zn concentrations compared with

pigs that remained on the same mineral regimen in both phases. The 5-h period in which pigs were allowed to eat the phase 2 diet may have generated the decrease in plasma Zn. However, interaction of these 2 minerals in the liver and intestine could also alter this response.

If pharmacological Zn is provided in weanling pig diets, metallothionein will increase in intestinal cells (Carlson et al., 1999). Then, Cu may be bound by metallothionein, limiting the amount of Zn that can be absorbed (Hill and Spears, 2001). This may be why plasma Zn increased to a greater degree in diets with no added Cu compared with diets containing added $CuSO_4$. Hill et al. (2000) also observed an increase in plasma Cu concentration with Cu supplementation. Plasma Cu did not differ on d 14 in any of our experiments; however, interactions between Cu and Zn supplementation for plasma Cu at the end of Exp. 2 and 3 were observed. Interestingly, in Exp. 2, a numerical decrease in plasma Cu was observed for Cu from $CuSO_4$ compared with other treatments. In Exp. 3, the Cu plasma concentration was increased with either Zn or Cu supplementation; however, when both minerals were combined, plasma Cu concentration was similar to that of the control.

In conclusion, these experiments showed additive growth responses to supplementing Cu and Zn in the diet of weanling pigs for 28-d in these experiments. However, performance was numerically greater when mineral regimens were switched from feeding pharmacological Zn (3,000 ppm) for the first 14 d and moderate Cu (125 ppm) in later nursery phases than when both minerals were fed for the entire 42-d period. Also, removing Zn from later diets would decrease the amount of Zn excreted in manure (Rincker et al., 2005).

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Figures and Tables

Table 3-1. Composition of diets (as-fed basis)

Item	Phase 1[1]	Phase 2[2]
Ingredient, %		
Corn	48.72	60.74
Soybean meal (46.5% CP)	29.01	35.00
Spray-dried whey	15.00	---
Select menhaden fish meal	3.75	---
Monocalcium P (21% P)	1.05	1.60
Limestone	0.70	1.10
Salt	0.33	0.33
Vitamin premix[3]	0.25	0.25
Trace mineral premix[4]	0.15	0.15
L-Lys HCl	0.30	0.30
DL-Met	0.175	0.125
L-Thr	0.125	0.110
Cornstarch[5]	0.435	0.307
Total	100	100
Calculated analysis		
SID[6] amino acids, %		
Lys	1.41	1.31
Ile:Lys	60	63
Leu:Lys	120	129
Met:Lys	36	33
Met & Cys:Lys	58	58
Thr:Lys	62	62
Trp:Lys	17	18
Val:Lys	65	69
Total Lys, %	1.55	1.45
ME, kcal/kg	3,296	3,296
SID Lys:ME, g/Mcal	4.28	3.97
CP, %	22.3	21.9
Ca, %	0.88	0.85
P, %	0.78	0.75
Available P, %	0.50	0.42

[1]Pigs were fed Phase 1 from d 0 to 14 (Exp. 1, 2, and 3).
[2]Pigs were fed Phase 2 from d 14 to 28 in Exp. 1 and 2 and from d 14 to 42 in Exp. 3.
[3]Vitamin premix provided per kg of complete feed: 11,023 IU of vitamin A, 1,377 IU of vitamin D, 44.1 IU of vitamin E, 4.4 mg of vitamin K, 0.04 mg of vitamin B_{12}, 50.0 mg of niacin, 27.6 mg of pantothenic acid, and 8.3 mg of riboflavin.
[4]Trace mineral premix provided per kg of complete feed: 16.5 mg of Cu from $CuSO_4 \cdot 5H_20$, 0.30 mg of I as $C_2H_2(NH_2)_2 \cdot 2HI$, 165 mg of Fe as $FeSO_4H_2O$, 39.7 mg of Mn as $MnSO_4 \cdot H_20$, 0.30 mg of Se as Na_2SeO_3, and 165 mg of Zn as $ZnSO_4$.
[5]Cornstarch was replaced with zinc oxide, tri-basic copper chloride, and copper sulfate to formulate treatment diets.
[6]Standardized ileal digestible.

Table 3-2. Analyzed chemical composition of diets (Exp. 1)[1]

Added Cu[2]:	No	No	No	Yes	Yes	Yes
Added Zn[3]:	No	Medium	High	No	Medium	High
Phase 1[4]						
Zn, ppm	212 (196)[6]	1,472 (1,696)	2,519 (3,196)	190 (196)	1,431 (1,696)	2,831 (3,196)
Cu, ppm	23 (25)	22 (25)	24 (25)	196 (175)	170 (175)	191 (175)
Phase 2[5]						
Zn, ppm	217 (194)	1,201 (1,194)	1,993 (2,194)	427 (194)	840 (1,194)	1,713 (2,194)
Cu, ppm	26 (25)	19 (25)	63 (25)	124 (175)	137 (175)	169 (175)

[1]A total of 180 weanling pigs (initially 5.7 kg and 21 d of age, PIC TR4 × 1050) were used in a 28-d experiment.
[2]Added Cu from tri-basic copper chloride was supplied at no (0 ppm) or yes (150 ppm) levels above that provided by the trace mineral premix (16.5 ppm Cu).
[3]Added Zn from zinc oxide was supplied at no (0 ppm), medium (1,500 ppm in phase 1 and 1,000 in phase 2), or high (3,000 ppm in phase 1 and 2,000 in phase 2) levels above the 165 ppm Zn provided by trace mineral premix.
[4]Pigs were fed phase 1 from d 0 to 14.
[5]Pigs were fed phase 2 from d 14 to 28.
[6]Values in parentheses indicate the calculated value.

Table 3-3. Analyzed chemical composition of diets (Exp. 2)[1]

Added Zn[2]:	No	No	No	Yes	Yes	Yes
Cu source[3]:	None	TBCC	$CuSO_4$	None	TBCC	$CuSO_4$
Phase 1[4]						
Zn, ppm	286 (196)[6]	183 (196)	197 (196)	2,798 (3,196)	2,721 (3,196)	2,599 (3,196)
Cu, ppm	28 (25)	152 (150)	149 (150)	27 (25)	156 (150)	141 (150)
Phase 2[5]						
Zn, ppm	183 (194)	229 (194)	176 (194)	2,360 (2,194)	1,897 (2,194)	1,930 (2,194)
Cu, ppm	25 (25)	178 (150)	188 (150)	48 (25)	140 (150)	144 (150)

[1]A total of 180 weanling pigs (initially 6.0 kg and 21 d of age, PIC 1050) were used in this 28-d experiment.
[2]Added Zn from zinc oxide was supplied at no (0 ppm) or yes (3,000 ppm in phase 1 and 2,000 ppm in phase 2) levels above the 165 ppm Zn provided by the trace mineral premix.
[3]Copper sources were none, tri-basic copper chloride (TBCC, 125 ppm Cu), and copper sulfate ($CuSO_4$, 125 ppm Cu) and were supplemented above the 16.5 ppm Cu provided by the trace mineral premix.
[4]Pigs were fed phase 1 from d 0 to 14.
[5]Pigs were fed phase 2 from d 14 to 28.
[6]Values in parentheses indicate the calculated value.

Table 3-4. Analyzed chemical composition of diets (Exp. 3)[1]

Added Cu[2]:	No	Yes	No	Yes
Added Zn[3]:	No	No	Yes	Yes
Phase 1[4]				
Zn, ppm	69 (196)[6]	286 (196)	3,031 (3,196)	3,099 (3,196)
Cu, ppm	74 (26)	161 (151)	11 (26)	183 (151)
Phase 2[5]				
Zn, ppm	204 (194)	256 (194)	1,823 (2,194)	1,819 (2,194)
Cu, ppm	19 (25)	162 (150)	26 (25)	180 (150)

[1]A total of 216 weanling pigs (PIC, initially 6.2 kg and 21 d of age, PIC TR4 × 1050) were used in a 42-d experiment.
[2]Added Cu from copper sulfate was supplied at no (0 ppm) or yes (125 ppm) levels above the 16.5 ppm Cu provided by the trace mineral premix.
[3]Added Zn from zinc oxide was supplied at no (0 ppm) or yes (3,000 ppm in phase 1 and 2,000 in phase 2) levels above the 165 ppm Zn provided by the trace mineral premix.
[4]Pigs were fed Phase 1 from d 0 to 14.
[5]Pigs were fed Phase 2 from d 14 to 42.
[6]Values in parentheses indicate the calculated value.

Table 3-5. Effects of zinc oxide and tri-basic copper chloride on weanling pig performance (Exp. 1)[1]

								Probability, $P <$				
Added Cu[2]:	No	No	No	Yes	Yes	Yes		Zinc ×			Zinc	
Added Zn[3]:	No	Medium	High	No	Medium	High	SEM	Copper	Copper	Zinc	linear	quadratic
Initial wt, kg	5.6	5.7	5.7	5.7	5.7	5.7	0.34	0.45	0.29	0.40	0.26	0.45
d 0 to 14												
ADG, g	157	180	226	212	205	239	18.7	0.30	0.01	0.004	0.002	0.18
ADFI, g	198	220	276	254	257	281	18.3	0.26	0.02	0.006	0.003	0.29
G:F	0.79	0.80	0.82	0.83	0.79	0.85	0.035	0.60	0.36	0.44	0.42	0.32
d 14 to 28												
ADG, g	475	500	526	523	525	552	25.7	0.78	0.03	0.10	0.04	0.68
ADFI, g	670	697	755	731	742	795	37.9	0.87	0.008	0.005	0.002	0.32
G:F	0.71	0.72	0.70	0.72	0.71	0.70	0.012	0.71	0.90	0.23	0.17	0.30
d 0 to 28												
ADG, g	316	340	376	367	365	393	20.6	0.38	0.007	0.008	0.003	0.34
ADFI, g	434	458	515	492	500	534	26.7	0.43	0.005	0.002	0.001	0.26
G:F	0.73	0.74	0.73	0.75	0.73	0.74	0.009	0.29	0.49	0.94	0.75	0.89
Final wt, kg	14.5	15.2	16.2	15.9	15.9	17.0	0.85	0.61	0.006	0.006	0.003	0.29

[1]A total of 180 weanling pigs (initially 5.7 kg and 21 d of age, PIC TR4 × 1050) were used in this 28-d experiment.
[2]Added Cu from tri-basic copper chloride was supplied at no (0 ppm) or yes (150 ppm) levels above the 16.5 ppm Cu provided by the trace mineral premix.
[3]Added Zn from zinc oxide was supplied at no (0 ppm), medium (1,500 ppm in phase 1 and 1,000 in phase 2), or high (3,000 ppm in phase 1 and 2,000 in phase 2) levels above the 165 ppm Zn provided by trace mineral premix.

Table 3-6. Effects of zinc oxide and tri-basic copper chloride on plasma mineral concentrations of weanling pigs (Exp. 1)[1]

								Probability, *P* <				
Added Cu[2]:	No	No	No	Yes	Yes	Yes		Zinc ×			Zinc	
Added Zn[3]:	No	Medium	High	No	Medium	High	SEM	Copper	Copper	Zinc	Linear	Quadratic
Plasma mineral concentrations[4], µg/mL												
Cu	1.88	1.88	1.81	1.81	1.98	1.89	0.102	0.58	0.63	0.57	0.97	0.30
Zn	0.64	0.77	1.08	0.81	0.81	0.93	0.063	0.03	0.68	0.001	0.001	0.14
P	0.070	0.083	0.085	0.081	0.080	0.077	0.0024	0.003	0.95	0.05	0.03	0.21

[1]A total of 180 weanling pigs (initially 5.7 kg and 21 d of age, PIC TR4 × 1050) were used in this 28-d experiment.
[2]Added Cu from tri-basic copper chloride was supplied at no (0 ppm) or yes (150 ppm) levels above the 16.5 ppm Cu provided by the trace mineral premix.
[3]Added Zn from zinc oxide was supplied at no (0 ppm), medium (1,500 ppm in phase 1 and 1,000 in phase 2), or high (3,000 ppm in phase 1 and 2,000 in phase 2) levels above the 165 ppm Zn provided by trace mineral premix.
[4]Plasma was collected on d 14 from 2 pigs per pen (10 pigs/trt).

Table 3-7. Effects of zinc oxide, tri-basic copper chloride, and copper sulfate on weanling pig performance (Exp. 2)[1]

								Probability, $P <$					
											Copper effects		
Added Zn[2]:	No	No	No	Yes	Yes	Yes		Zinc ×			None vs.		$CuSO_4$ vs.
Cu source[3]:	None	TBCC	$CuSO_4$	None	TBCC	$CuSO_4$	SEM	Copper	Zinc	Copper	$CuSO_4$	TBCC	TBCC
Initial wt, kg	6.0	6.0	6.0	6.0	6.0	6.0	0.31	0.89	0.94	0.95	0.78	0.78	0.99
d 0 to 14													
ADG, g	149	168	209	205	208	261	18.3	0.86	0.001	0.002	0.001	0.49	0.004
ADFI, g	214	217	251	237	243	283	18.1	0.95	0.02	0.01	0.007	0.77	0.01
G:F	0.69	0.77	0.83	0.86	0.85	0.92	0.027	0.21	0.001	0.01	0.002	0.22	0.04
d 14 to 28													
ADG, g	443	471	468	440	487	496	22.1	0.74	0.40	0.11	0.06	0.08	0.88
ADFI, g	714	734	697	733	767	791	25.8	0.21	0.01	0.47	0.37	0.24	0.78
G:F	0.62	0.64	0.67	0.60	0.64	0.63	0.017	0.56	0.10	0.05	0.02	0.08	0.57
d 0 to 28													
ADG, g	288	319	338	320	348	379	18.3	0.92	0.01	0.01	0.001	0.006	0.11
ADFI, g	450	475	474	480	505	537	20.6	0.46	0.004	0.05	0.02	0.12	0.33
G:F	0.64	0.67	0.71	0.66	0.69	0.70	0.017	0.54	0.45	0.01	0.002	0.09	0.11
Final wt, kg	14.4	14.9	15.4	15.1	15.7	16.6	0.70	0.85	0.02	0.03	0.01	0.22	0.11

[1]A total of 180 weanling pigs (initially 6.0 kg and 21 d of age, PIC 1050) were used in this 28-d experiment.

[2]Added Zn from zinc oxide was supplied at no (0 ppm) or yes (3,000 ppm in phase 1 and 2,000 ppm in phase 2) levels above the 165 ppm Zn provided by the trace mineral premix.

[3]Copper sources were none, tri-basic copper chloride (TBCC, 125 ppm Cu), and copper sulfate ($CuSO_4$, 125 ppm Cu) and were supplemented above the 16.5 ppm Cu provided by the trace mineral premix.

Table 3-8. Effects of zinc oxide, tri-basic copper chloride, and copper sulfate on plasma mineral concentrations of weanling pigs (Exp. 2)[1]

								Probability, *P* <					
											Copper effects		
											None vs.		
Added Zn[2]:	No	No	No	Yes	Yes	Yes		Zinc ×					$CuSO_4$ vs.
Cu source[3]:	None	TBCC	$CuSO_4$	None	TBCC	$CuSO_4$	SEM	Copper	Zinc	Copper	$CuSO_4$	TBCC	TBCC
Plasma mineral concentrations[4], µg/mL													
d 14													
Cu	1.73	1.68	1.47	1.66	1.60	1.61	0.072	0.26	0.99	0.12	0.05	0.49	0.18
Zn	0.68	0.63	0.60	1.11	1.12	1.21	0.059	0.31	0.001	0.88	0.84	0.77	0.62
P	0.064	0.063	0.063	0.061	0.063	0.065	0.0024	0.67	0.82	0.69	0.42	0.87	0.52
d 28													
Cu	1.78	1.88	1.56	1.75	1.61	1.82	0.085	0.02	0.86	0.71	0.42	0.83	0.56
Zn	0.87	0.89	0.87	0.90	0.95	0.96	0.040	0.72	0.09	0.69	0.50	0.42	0.90
P	0.074	0.073	0.073	0.072	0.075	0.070	0.0021	0.48	0.42	0.52	0.48	0.68	0.26

[1]A total of 180 weanling pigs (initially 13.2 lb and 21 d of age, PIC) were used in this 28-d experiment.
[2]Added Zn from zinc oxide was supplied at no (0 ppm) or yes (3,000 ppm from d 0 to 14 and 2,000 from d 14 to 28) levels to the basal diet (165 ppm Zn).
[3]Copper sources were none, tri-basic copper chloride (TBCC, 125 ppm Cu), and copper sulfate ($CuSO_4$, 125 ppm Cu).
[4]Plasma was collected from the same two pigs on d 14 and 28 (12 pigs/trt).

Table 3-9. Effects of zinc oxide and copper sulfate on weanling pig growth performance (Exp. 3)[1]

Phase 1 diet[2]:	Control	Cu	Zn	Cu and Zn	Zn	Cu and Zn		Probability, $P<$		
Phase 2 diet[3]:	Control	Cu	Zn	Cu and Zn	Cu	Cu	SEM	Zinc × Copper	Zinc	Copper
Initial wt, kg	6.2	6.2	6.2	6.2	6.2	6.2	0.33	0.12	0.49	0.59
d 0 to 14										
ADG, g	146^{a}	182^{b}	212^{bc}	222^{c}	217^{bc}	222^{c}	13.3	0.23	0.001	0.14
ADFI, g	220^{a}	261^{b}	256^{ab}	274^{b}	267^{b}	274^{b}	14.7	0.25	0.04	0.07
G:F	0.67^{a}	0.70^{a}	0.82^{b}	0.81^{b}	0.81^{b}	0.81^{b}	0.022	0.35	0.001	0.73
wt on d 14, kg	8.2^{a}	8.7^{ab}	9.2^{bc}	9.3^{c}	9.2^{bc}	9.3^{c}	0.43	0.22	0.001	0.14
d 14 to 28										
ADG, g	468^{a}	533^{c}	481^{ab}	551^{c}	544^{c}	512^{bc}	21.3	0.85	0.29	0.001
ADFI, g	656^{a}	729^{bc}	705^{ab}	779^{c}	749^{bc}	717^{abc}	31.2	0.99	0.04	0.003
G:F	0.72^{a}	0.73^{a}	0.68^{b}	0.71^{ab}	0.73^{a}	0.71^{a}	0.010	0.74	0.02	0.06
d 28 to 42										
ADG, g	705^{a}	734^{ab}	733^{ab}	713^{ab}	743^{b}	725^{ab}	18.4	0.06	0.77	0.69
ADFI, g	1163^{a}	1243^{b}	1214^{ab}	1231^{b}	1247^{b}	1233^{b}	40.9	0.17	0.40	0.04
G:F	0.61^{a}	0.59	0.60^{ab}	0.58^{c}	0.60^{abc}	0.59^{bc}	0.010	0.66	0.22	0.004
d 14 to 42										
ADG, g	586^{a}	634^{c}	605^{ab}	632^{bc}	643^{c}	618^{bc}	17.9	0.32	0.39	0.001
ADFI, g	910^{a}	986^{b}	956^{ab}	1005^{b}	998^{b}	975^{b}	34.3	0.47	0.10	0.003
G:F	0.65	0.64	0.63	0.63	0.65	0.64	0.008	0.97	0.04	0.55
d 0 to 42										
ADG, g	440^{a}	483^{bc}	473^{b}	495^{bc}	501^{c}	486^{bc}	14.9	0.30	0.03	0.003
ADFI, g	680^{a}	745^{b}	720^{ab}	761^{b}	754^{b}	741^{b}	27.0	0.47	0.09	0.004
G:F	0.65	0.65	0.66	0.65	0.67	0.66	0.008	0.65	0.46	0.68
Final wt, kg	24.6^{a}	26.5^{b}	26.2^{b}	27.0^{b}	27.2^{b}	26.9^{b}	0.86	0.19	0.02	0.004

[1]A total of 216 weanling pigs (PIC, initially 13.6 lb and 21 d of age) were used in a 42-d experiment with 6 pens per treatment.
[2]Phase 1 diets were fed from d 0 to 14 after weaning: control (basal diet with no added Cu or Zn), Cu (125 ppm added Cu from copper sulfate), Zn (3,000 ppm added Zn from zinc oxide), and Cu and Zn (125 ppm added Cu from copper sulfate and 3,000 ppm added Zn from zinc oxide).
[3]Phase 2 diets were fed from d 14 to 42 after weaning: control (basal diet with no added Cu or Zn), Cu (125 ppm added Cu from copper sulfate), Zn (2,000 ppm added Zn from zinc oxide), and Cu and Zn (125 ppm added Cu from copper sulfate and 2,000 ppm added Zn from zinc oxide).
[abc]Within a row, means without a common superscript differ ($P < 0.05$).

Table 3-10. Effects of zinc oxide and copper sulfate on plasma mineral concentrations of weanling pigs (Exp. 3)[1]

								Probability, *P*<		
Phase 1 diet[2]:	Control	Cu	Zn	Cu and Zn	Zn	Cu and Zn		Zinc ×		
Phase 2 diet[3]:	Control	Cu	Zn	Cu and Zn	Cu	Cu	SEM	Copper	Zinc	Copper
Plasma mineral concentrations, µg/mL										
d 14										
Cu	1.87	1.89	1.86	1.88	1.75	1.86	0.082	0.68	0.51	0.42
Zn	0.53[a]	0.55[a]	0.95[c]	0.93[c]	0.74[b]	0.73[b]	0.066	0.81	0.001	0.92
P	0.084[ab]	0.083[a]	0.086[ab]	0.086[ab]	0.094[b]	0.086[ab]	0.0042	0.71	0.17	0.28
d 42										
Cu	1.94	2.13	2.06	1.97	1.97	2.10	0.077	0.08	0.78	0.54
Zn	1.04[a]	1.08[a]	1.24[b]	1.12[ab]	1.13[ab]	1.06[a]	0.043	0.07	0.01	0.42
P	0.092[a]	0.089[a]	0.092[a]	0.092[a]	0.098[b]	0.088[a]	0.0022	0.42	0.38	0.38

[1]A total of 216 weanling pigs (PIC, initially 13.6 lb and 21 d of age) were used in a 42-d experiment with 6 pens per treatment.
[2]Phase 1 diets were fed from d 0 to 14 after weaning: control (basal diet with no added Cu or Zn), Cu (125 ppm added Cu from copper sulfate), Zn (3,000 ppm added Zn from zinc oxide), and Cu and Zn (125 ppm added Cu from copper sulfate and 3,000 ppm added Zn from zinc oxide).
[3]Phase 2 diets were fed from d 14 to 42 after weaning: control (basal diet with no added Cu or Zn), Cu (125 ppm added Cu from copper sulfate), Zn (2,000 ppm added Zn from zinc oxide), and Cu and Zn (125 ppm added Cu from copper sulfate and 2,000 ppm added Zn from zinc oxide).
[abc]Within a row, means without a common superscript differ ($P < 0.05$).

CHAPTER 4 - Effects of copper sulfate, zinc oxide, and an in-feed antibiotic combination on weanling pig growth and antibiotic resistance rate for fecal *Escherichia coli*

Abstract

A total of 180 weanling pigs (PIC TR4 ×1050, initially 5.0 kg and 21 d of age) were used in a 42-d growth trial to compare the effects of supplemental Zn, Cu, and in-feed antimicrobial combination on weanling pig growth and *Escherichia coli* excretion and antibiotic resistance. There were 5 dietary treatments with 6 pens per treatments and 5 pigs per pen. Treatments were arranged as a 2 × 2 factorial with main effects of added Cu from $CuSO_4$ (0 or 125 ppm) and added Zn from ZnO (0 or 3,000 ppm from d 0 to 14 and 0 or 2,000 ppm from d 14 to 42) along with an additional treatment of an in-feed antibiotic that provided neomycin (55 ppm) and oxytetracycline (55 ppm). The trace mineral premix added to all diets provided 165 ppm Zn from zinc sulfate and 16.5 ppm Cu from $CuSO_4$. Fecal samples were collected from 3 pigs per pen on d 14 and 42 to determine total coliform and *E. coli* counts as well as *E. coli* antibiotic resistance rates. Pigs fed added ZnO had increased ($P < 0.05$) ADG, G:F, and tended to have improved ($P < 0.09$) ADFI from d 0 to 14. From d 14 to 42, pigs fed added ZnO had poorer ($P = 0.006$) G:F than pigs fed no added ZnO, and pigs fed added $CuSO_4$ had improved ($P < 0.04$) G:F compared with those fed no added $CuSO_4$. From d 14 to 42 and over the entire trial, a trend for a Cu × Zn interaction was observed ($P < 0.10$) for ADG as pigs fed added $CuSO_4$ or ZnO had increased ADG over the control; however, when Zn and Cu were combined, growth rate was similar to that when each was added alone. No additive effects were observed in this experiment from feeding a combination of high dietary Cu and Zn. Addition of $CuSO_4$, ZnO, or in-feed antibiotic had no effect ($P > 0.22$) on total coliform or *E. coli* concentrations on d 14 or 42. For d 14 isolates, Zn supplementation had no effect ($P > 0.10$) on *E. coli* resistance rate to chlortetracycline, neomycin, oxytetracycline, or tiamulin; however, Cu supplementation tended to increase ($P < 0.10$) resistance to chlortetracycline and oxytetracycline. A Cu × Zn interaction was detected ($P < 0.02$) for *E. coli* resistance to chlortetracycline and neomycin from isolates on d 42. These interactions were caused by a decrease in resistance when $CuSO_4$ was fed alone. High concentrations of ZnO improved performance in the early post-weaning period, whereas high

concentrations of $CuSO_4$ increased growth in the later phase of the nursery. Although the resistance rate varied with dietary treatment, no clear pattern was detected.

Key words: bacterial sensitivity, copper, growth, weanling pig, zinc

Introduction

Growth promoting or subtherapeutic levels of antibiotics are often added to nursery diets to increase growth rates (Cromwell, 2001). The use of antibiotics to promote growth has been controversial, due to the increased potential for antibiotic resistant bacteria. One alternative to antibiotics, would be to include pharmacological concentrations of either Zn or Cu in the diets of nursery pigs. Pharmacological Zn has been shown to increase growth rate (Hahn and Baker, 1993; Smith et al., 1997; Carlson et al., 1999; Hill et al., 2001; Williams et al., 2005;) as well as increase stool firmness (Hill et al., 2000). Adding Cu to weanling pig diets also has been shown to enhance growth rates (Stahly et al., 1980; Cromwell et al., 1989; 1998; Hill et al., 2000). Historically, the use of high levels of both ZnO (3,000 ppm Zn) and $CuSO_4$ (250 ppm Cu) has not shown additive effects (Smith et al., 1997; Hill et al., 2000). However, Shelton et al. (2008) observed additive effects to supplementing pharmacological Zn and moderate concentrations of Cu (125 to 150 ppm) for 28-d post-weaning. Perez-Mendoza et al. (2008) also observed an improvement in growth the first 2 wk post-weaning with Cu supplementation in diets containing 3,000 ppm of added Zn.

Originally, it was thought pharmacological Cu or Zn could replace antibiotics and reduce the potential for antibiotic resistance bacteria. However, recent research has shown links between feeding increased concentrations of Cu and the development of *Enterococci* resistant to Cu as well as to the antibiotics vancomycin and erythromycin (Hasman and Aarestrup, 2002). In addition, Cu resistant *E. coli* isolates have been collected from pigs fed $CuSO_4$ by Tetaz and Luke (1983). Therefore, our objective was to evaluate the growth effects of Cu, Zn, and antibiotic supplementation during the nursery stage, as well as determine differences in antibiotic sensitivity and excretion of fecal *E. coli*.

Materials and Methods

General

The protocol used in this experiment was approved by the Kansas State University Institutional Animal Care and Use Committee. The study was conducted at the Kansas State University Swine Teaching and Research Center, Manhattan.

Animals

A total of 180 weanling pigs (PIC, Hendersonville, TN, TR4 ×1050, initially 5.0 kg and 21 d of age) were used in a 42-d growth trial. Pigs were allotted to pens by initial BW, and pens were assigned to treatments in a randomized complete block design with initial body weight used to establish blocks. There were 6 pens per treatment with 5 pigs per pen. Treatments were arranged as a 2 × 2 factorial with main effects of added Cu from $CuSO_4$ (0 or 125 ppm) and added Zn from ZnO (0 or 3,000 ppm from d 0 to 14 and 0 or 2,000 ppm from d 14 to 42) along with an additional treatment of an in-feed antibiotic that provided 55 ppm of neomycin and oxytetracycline (Penfield Animal Health, Omaha, NE). The trace mineral premix used in all diets supplied a base level of 165 ppm Zn from zinc sulfate and 16.5 ppm Cu from $CuSO_4$. The diets were fed in 2 phases: Phase 1 from d 0 to 14 and Phase 2 from d 14 to 42 (Table 1). Phase 1 and 2 diets were fed in meal form and formulated to contain 1.41% and 1.31% standardized ileal digestible lysine, respectively. Phase 1 diets contained 15% spray-dried whey and 3.75% fish meal, and Phase 2 diets were corn-soybean meal based without any specialty protein sources. All other nutrients were formulated to meet or exceed NRC (1998) requirements. Treatment diets were prepared by replacing corn starch with ZnO, $CuSO_4$, or in-feed antibiotic. Diets samples were taken and analyzed for Cu and Zn concentrations (Table 2). Samples were digested with HNO_3 and H_2O_2 and then analyzed for Cu and Zn by the atomic absorption spectrophotometric method (AOAC, 2000). Calculated dietary Cu and Zn concentrations were determined using amounts added by the trace mineral premix, values for dietary ingredients from NRC (1998), and any added Cu or Zn based on dietary treatment.

Weights and feed disappearance were measured every 14 d to determine ADG, ADFI, and G:F. Each pen contained a 4-hole dry self-feeder and a nipple waterer to provide ad libitum access to feed and water. Pens had wire-mesh floor and allowed for approximately 0.36 m^2 per pig.

Fecal collection and analysis

On d 14 and 42, fecal samples were collected by rectal massage from 3 randomly selected pigs per pen. Fecal samples were diluted within a gram-negative broth, and then plated on MacConkey agar. Plates were placed in an incubator at 37°C for 6 h and then counted to determine the number of colony forming units per g of sample for both *E. coli* and total coliforms. One *E. coli* colony per sample was then isolated and retained for further analysis. Minimum inhibitory concentrations (MIC) of antibiotics were then determined on each isolate by the micro-broth dilution method (CLSI, 2002). The antibiotics evaluated included chlortetracycline, neomycin, oxytetracycline, and tiamulin. The MIC for each isolate was compared with published MIC values to determine whether each isolate was resistant or susceptible. Isolates were classified as resistant if the MIC was 16 µg/mL or higher for oxytetracycline, chlortetracycline, and neomycin and 32 µg/mL or higher for tiamulin. Finally, a pen resistant rate was calculated on the basis of the resistance for each pen's 3 isolates.

Statistical Analysis

Pen was used as the experimental unit for all analyses, and data were analyzed using the MIXED procedure in SAS (SAS Institute Inc., Cary, NC). Main effects and potential interactions for added dietary Cu and Zn were tested using contrast statements. Bacterial counts were log transformed to achieve normality. Individual treatments were compared using the least square means differences. Pair-wise comparison was also used to test the difference between treatment means. Main effects and treatment comparisons were considered significant if their *P*-values were < 0.05 and trends if their *P*-values were < 0.10.

Results

Over the first phase (d 0 to 14), pigs fed added dietary ZnO had improved ($P < 0.05$) ADG and G:F (Table 3). Dietary Zn additions also tended to increase ($P = 0.09$) ADFI. The addition of $CuSO_4$ did not affect ($P > 0.10$) ADG or ADFI; however, G:F was reduced ($P = 0.05$) from d 0 to 14 compared with pigs fed no added Cu. Also, no improvements ($P > 0.59$) in ADG, ADFI, or G:F were observed for pigs supplemented with in-feed antibiotics compared with pigs fed no added Zn or Cu.

From d 14 to 28, no improvements in ADG or G:F were observed ($P > 0.10$) from supplementing dietary Cu or Zn. However, a trend for a Cu × Zn interaction was detected ($P = 0.07$) for ADFI. This interaction was due to increased ADFI when either Cu or Zn were used independently over the control; however, when Cu and Zn were used in combination, feed intake was intermediate to that of each used singularly. Pigs fed in-feed antibiotics had increased ($P = 0.01$) ADFI and tended to have increased ($P = 0.10$) ADG over that of pigs fed no added Zn or Cu.

From d 28 to 42, supplemental ZnO and/or $CuSO_4$ did not influence ($P > 0.10$) ADG or ADFI. However, a trend for improved G:F was observed ($P < 0.06$) with $CuSO_4$ addition, and a trend for worse G:F was observed ($P < 0.08$) with ZnO addition. The in-feed antibiotic had no effect ($P > 0.10$) on ADG, ADFI, or G:F compared with pigs fed the control diet.

Over the entire Phase 2 (d 14 to 42), a trend ($P = 0.10$) for a Cu × Zn interaction was detected for ADG. Pigs fed supplemental $CuSO_4$ or ZnO had increased ADG compared to pigs fed the control and the combination of minerals had reduced performance compared to the use of each independently. Pigs fed additional ZnO had poorer ($P = 0.006$) G:F and a trend for increased ($P = 0.07$) ADFI compared to pigs not receiving additional ZnO. Pigs fed supplemental $CuSO_4$ had improved ($P = 0.04$) G:F but ADG and ADFI ($P > 0.10$) were not influenced. Antibiotic addition did not improve ($P > 0.10$) ADG, ADFI, or G:F compared with control pigs.

Overall, a trend for a Cu × Zn interaction was detected ($P = 0.09$) for ADG. The addition of supplemental Cu or Zn increased ADG over the control; however, when Cu and Zn were combined, pigs had reduced growth compared with that achieved when feeding each independently. Pharmacological concentrations of Zn also increased ($P = 0.04$) ADFI. However, pigs fed the in-feed antimicrobial did not have improved ($P > 0.10$) ADG, ADFI, or G:F.

Fecal coliform and *E. coli* counts in feces were not affected ($P > 0.10$) by dietary addition of $CuSO_4$, ZnO, or in-feed antimicrobials (Table 3). For d 14 isolates, dietary ZnO supplementation had no effect ($P > 0.10$) on the percentage of *E. coli* isolates classified as resistant for chlortetracycline, neomycin, oxytetracycline, or tiamulin. However, from d 14 isolates, $CuSO_4$ tended to increase ($P < 0.10$) the percentage of isolates resistant to chlortetracycline and oxytetracycline. Also, the in-feed antimicrobial tended to increase ($P < 0.10$) the percentage of isolates resistant to chlortetracycline and oxytetracycline compared with

the controls. For d 42 isolates, a copper × zinc interaction was detected ($P < 0.02$) for *E. coli* resistance to chlortetracycline and neomycin. These interactions were related to a decrease in the percentage of isolates classified as resistant when Cu was fed alone. In-feed antibiotic and $CuSO_4$ dietary additions also tended to increase ($P < 0.09$) the percentage of *E. coli* isolates resistant to tiamulin on d 42.

Discussion

In this study, from d 0 to 14, Zn supplementation increased ADG by 21.2 %. The increased growth was due to a 12.4 % increase in feed intake and a 7.4 % increase in G:F. Carlson et al. (1999) also observed increased growth rate when supplementing 3,000 ppm Zn from ZnO for the first 2 wk post-weaning in pigs of either traditional or early weaning ages. During the second phase of our trial, numerical increases in growth and feed intake were observed with Zn supplementation; yet they were not significant. In two studies published by Hahn and Baker (1993), ADG increased by 14.5 and 12.4 % with supplementation of 3,000 ppm Zn from ZnO, after weanling pigs had been placed on common starter diets for 7 d. Shelton et al. (2008) also observed increases in ADG of 12.6 and 10.8 % when supplementing pharmacological concentrations of Zn for 28-d. In contrast to the positive responses, Tokach et al. (1992), Hedemann et al. (2006), and two studies by Smith et al. (1997) observed no effect of supplementing pharmacological concentrations of Zn for 14-d post-weaning.

In this trial, Cu supplementation at 125 ppm from $CuSO_4$ had no effect on ADG or ADFI during the initial phase. Likewise, Roof and Mahan (1982) also no growth promotion from adding 125 ppm Cu for the first 14-d post-weaning. During the second phase (d 14 to 42), feeding added $CuSO_4$ alone increased ADG as compared with the control and the combination of Zn and Cu produced intermediate results to Cu alone and the control. Smith et al. (1997) observed similar results where $CuSO_4$ added alone or in combination with ZnO increased growth rate as compared to control pigs; however, growth from adding either $CuSO_4$ treatments were lower than the performance of the treatment containing ZnO alone. However, the optimal level of added Cu in weanling pig diets has varied between trials. Cromwell (2001) concluded the most efficacious level for weanling pigs is 200 to 250 ppm Cu from $CuSO_4$ by pooling results from 23 studies at the University of Kentucky with pigs weighing from 8 to 20 kg. Cromwell (2001) reported 11.9% improvement in growth and a 4.5% improvement in G:F with added Cu at

200 to 250 ppm from $CuSO_4$. However, adding Cu as 125 ppm from $CuSO_4$ produced 75% the growth response achieved with 250 ppm (Cromwell et al., 1989).

Minimal advantages were observed in this study for adding an in-feed antibiotic combination. Other studies have shown much greater responses to additions of growth promoting concentrations of antibiotics (Cromwell, 2001). Woodworth et al. (2005) observed a 7.2% increase in ADG in weanling pigs provided the same level of 55 ppm neomycin and oxytetracycline. Frantz et al. (2004) also observed increased performance in supplementing this in-feed antibiotic combination to weanling pigs; however, 154 ppm of neomycin and oxytetracycline was used in their study. Cromwell et al. (2001) also showed that pigs housed in research stations have a lower response to including in-feed antimicrobials, which may have limited the response in this study.

This study did not show additive effects of adding ZnO and $CuSO_4$ on the growth performance of weanling pigs. Similar to Hill et al. (2000) and Smith et al. (1997), adding ZnO or $CuSO_4$ alone improved ADG compared with the control; however, the combination showed similar performance compared with the use of each singularly in these studies. This is in contrast with the additive effects of added Cu and Zn observed by Shelton et al. (2008). Perez-Mendoza et al. (2008) also observed an improvement in growth the first 2 wk post-weaning with Cu supplementation in diets containing 3,000 ppm of added Zn. The results from this present trial also showed optimal responses to added Zn- in initial diets post-weaning, followed by added Cu in later diets. This would minimize any excess feed costs economics costs from Cu and Zn supplementation that do not offer growth advantages. A second benefit would be to minimize the level of excreted Zn and Cu. Rincker et al. (2005) showed that Zn excretion increases after approximately 9 d of feeding pharmacological Zn as the body stores become maximized. The accumulation of Zn in soil has been shown to hinder crop production (Takkar and Mann, 1978; Chaney, 1993). DeRouchey et al. (2002) evaluated nutrient contents of swine lagoons in Kansas and showed that while Zn concentrations are increased in lagoons from nursery facilities, the concentration is only 2.5 times greater than from finishing lagoons. Therefore, by only supplementing Zn in the early diets and Cu in later diets, producers can take advantage of the growth promotion effects, remove the added diet costs, and minimize Zn excretions.

The modes of action for Zn supplementation are unknown; however, several hypotheses have been proposed. Poulsen (1989) showed that pharmacological concentrations of Zn

prevented *E. coli* diarrhea in the weanling pigs. However, research has shown adding ZnO in the diet does not alter the level of *E. coli* excreted in fecal material (Jensen-Waern et al., 1998; Pulz and Carlson, 2007). This would be in agreement with our study where neither Cu or Zn supplementation affected the number of either *E. coli* or coliforms excreted in feces. Woodworth (1999) suggested that while Zn does not affect the number of *E. coli*, instead it may prevent E. coli from adhering to the gut wall and allowing for greater absorption of nutrients. Diarrhea was not observed for any pigs in the present study.

The modes of action for adding Cu have not been defined. Hedemann et al. (2006) showed that dietary added Cu had no effect on intestinal morphology. It has also been shown that Cu supplementation promotes growth independently of antibiotic additions (Stahly et al., 1980; Roof and Mahan, 1982), indicating it may have a different mode of action than antibiotics.

Bacterial resistance can be expressed either intrinsically or by acquired resistance. Each bacterial species has particular antibiotics that it is intrinsically resistant to (Klare et al., 2003). For example, E. coli are intrinsically resistant to glycopeptide antibiotics due to their outer membrane being impermeable to the glycopeptides, such as vancomycin (Quintiliani and Courvan, 1995). Acquired resistance is achieved from either the mutation of a certain gene within that microorganism or by horizontal gene transfer (Catry et al., 2003). Horizontal gene transfer occurs when genes are transferred from a donor to recipient bacterium by either conjugation, transformation, or transduction. The mechanisms associated with resistance are varied and may differ depending on antibiotic; however, the same resistance mechanism may also be applicable for several antibiotics (Catry et al., 2003). For example, Danish research has shown a correlation between copper resistance and vancomycin and erythromycin resistance (Hasman and Aarestrup, 2002) in *Enterococcus faecium*. The plasmid associated with Cu resistance can also initiate resistance for vancomycin and erythromycin in *Enterococci*.

The impact of Cu and Zn supplementation on *E. coli* resistance to antibiotics has not been well defined. Overall, there was a high prevalence of antibiotic resistant *E. coli* throughout our study. Our study was conducted at a site where feed grade antibiotics are commonly utilized in nursery diets to improve growth performance, which could have induced the overall high level or resistance. At the same time antibiotics are produced by microorganisms and antibiotic resistance may occur even without their inclusion in the feed (Mathew, 2003). The Cu × Zn interaction for *E. coli* resistance to chlortetracycline and neomycin from isolates on d 42 is an interesting

observation from this study. There is not a biological reason why resistance would drop dramatically when additional dietary copper was fed alone. It may have been an effect of sampling, as only 3 isolates per pen were used to determine resistance rate. Holt (2008) observed no resistant *E. coli* isolates to neomycin when either pharmacological Zn or Cu were provided. They utilized pigs from a herd where antibiotics had been discontinued for 32 years and therefore fecal *E. coli* were sensitive to most gram-negative antibiotics. Holt (2008) did detect an increase in the proportion of resistant *E. coli* isolates to tylosin when Cu was added to nursery pig diets at 240 ppm compared with pigs fed control diets or those with pharmalogical levels of Zn. Although the resistance rate to some antibiotics tended to increase with Cu supplementation in our study, no clear pattern was detected.

In conclusion, this trial did not show additive effects to supplementing Cu and Zn in weanling pig diets. We observed minimal increases in the proportion of resistant *E. coli* isolates when pharmacological Cu and/or Zn were provided in the diet; however, that may be masked due to the high proportion of resistant bacteria for all animals. Fecal *E. coli* concentrations were unaltered by pharmacological Cu or Zn. Zinc additions increased growth primarily in the early period after weaning, and Cu supplementation improved performance in later periods. This suggests that growth performance may be affected even greater if pharmacological Zn was provided in the early weaning rations, followed by supplemental Cu during later portions in the nursery.

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Figures and Tables

Table 4-1. Composition of diets (as-fed basis)[1]

Item	Phase 1[2]	Phase 2[3]
Ingredient, %		
Corn	48.72	60.74
Soybean meal (46.5% CP)	29.01	35.00
Spray-dried whey	15.00	---
Select menhaden fish meal	3.75	---
Monocalcium P (21% P)	1.05	1.60
Limestone	0.70	1.10
Salt	0.33	0.33
Vitamin premix[4]	0.25	0.25
Trace mineral premix[5]	0.15	0.15
L-Lys HCl	0.30	0.30
DL-Met	0.175	0.125
L-Thr	0.125	0.110
Corn starch[6]	0.435	0.307
Total	100	100
Calculated analysis		
SID[7] amino acids, %		
Lys	1.41	1.31
Ile:Lys	60	63
Leu:Lys	120	129
Met:Lys	36	33
Met & Cys:Lys	58	58
Thr:lys	62	62
Trp:Lys	17	18
Val:Lys	65	69
Total lysine, %	1.55	1.45
ME, kcal/kg	3,296	3,296
SID lysine:ME ratio, g/Mcal	4.28	3.97
CP, %	22.3	21.9
Ca, %	0.88	0.85
P, %	0.78	0.75
Available P, %	0.50	0.42

[1]A total of 180 weanling pigs (PIC, initially 5.0 kg and 21 d of age) were used in a 42-d experiment with 6 pens per treatment and 5 pigs per pen.
[2]Pigs were fed Phase 1 from d 0 to 14.
[3]Pigs were fed Phase 2 from d 14 to 42.
[4]Vitamin premix provided per kg of complete feed: 11,023 IU of vitamin A, 1,377 IU of vitamin D, 44.1 IU of vitamin E, 4.4 mg of vitamin K, 0.04 mg of vitamin B_{12}, 50.0 mg of niacin, 27.6 mg of pantothenic acid, and 8.3 mg of riboflavin.
[5]Trace mineral premix provided per kg of complete feed: 16.5 mg of Cu from $CuSO_4 \cdot 5H_20$, 0.30 mg of I as $C_2H_2(NH_2)_2 \cdot 2HI$, 165 mg of Fe as $FeSO_4H_2O$, 39.7 mg of Mn as $MnSO_4 \cdot H_20$, 0.30 mg of Se as Na_2SeO_3, and 165 mg of Zn as $ZnSO_4$
[6]Cornstarch was replaced with ZnO, $CuSO_4$, or Neo/Oxy 10/10 (Penfield Animal Health, Omaha, NE) to create treatment diets.
[7]Standardized ileal digestible.

Table 4-2. Analyzed chemical composition of diets, ppm[1]

	Treatment[2]				
	Control	Cu	Zn	Cu + Zn	Antibiotic
Phase 1[3]					
Zn	196 (196)[5]	215 (196)	2,750 (3,196)	3,246 (3,196)	223 (196)
Cu	25 (26)	179 (151)	48 (26)	198 (151)	41 (26)
Phase 2[4]					
Zn	254 (194)	228 (194)	1,836 (2,194)	1,958 (2,194)	316 (194)
Cu	28 (25)	178 (150)	35 (25)	169 (150)	36 (25)

[1]A total of 180 weanling pigs (PIC, initially 5.0 kg and 21 d of age) were used in a 42-d experiment with 6 pens per treatment and 5 pigs per pen.
[2]Treatments included: control (basal diet with no added Cu or Zn), Cu (125 ppm of added Cu from $CuSO_4$), Zn (3,000 ppm from d 0 to 14 and 2,000 ppm from d 14 to 28 of added Zn from ZnO), Cu and Zn (125 ppm of added Cu from $CuSO_4$ and 3,000 ppm from d 0 to 14 and 2,000 ppm from d 14 to 28 of added Zn from ZnO), and antibiotic (55 ppm of neomycin and oxytetracycline from Neo/Oxy 10/10; Penfield Animal Health, Omaha, NE).
[3]Pigs were fed Phase 1 from d 0 to 14.
[4]Pigs were fed Phase 2 from d 14 to 42.
[5]Values in parentheses indicate the calculated value.

Table 4-3. Effects of zinc oxide, copper sulfate, and antibiotic combination on weanling pig growth performance[1]

	Treatment[2]						Probability, $P<$			
	Control	Cu	Zn	Cu + Zn	Antibiotic	SEM	Zinc × Copper	Zinc	Copper	Antibiotic vs. control
Initial wt, kg	5.0	5.0	5.0	5.0	5.0	0.02	0.82	0.86	0.91	0.89
D0 to 14										
ADG, g	169[a]	184[ab]	218[b]	210[b]	180[ab]	18.7	0.45	0.02	0.84	0.60
ADFI, g	191[a]	220[ab]	227[ab]	235[b]	199[ab]	17.7	0.46	0.09	0.20	0.71
G:F	0.90[ab]	0.85[b]	0.98[a]	0.90[ab]	0.92[ab]	0.030	0.70	0.05	0.05	0.70
wt on d 14, kg	7.3[a]	7.5[ab]	8.0[b]	7.9[ab]	7.5[ab]	0.29	0.45	0.03	0.86	0.60
D 14 to 28										
ADG, g	419	460	455	450	454	17.9	0.13	0.38	0.24	0.10
ADFI, g	571[a]	615[ab]	643[b]	621[b]	637[b]	21.8	0.07	0.03	0.52	0.01
G:F	0.71	0.73	0.69	0.70	0.69	0.014	0.97	0.15	0.33	0.42
D 28 to 42										
ADG, g	685	727	704	713	675	25.1	0.40	0.89	0.19	0.72
ADFI, g	1,018	1,043	1,077	1,057	1,009	39.3	0.45	0.23	0.93	0.83
G:F	0.67[ab]	0.69[a]	0.65[b]	0.67[ab]	0.66[ab]	0.013	0.85	0.08	0.06	0.93
D 14 to 42										
ADG, g	547[a]	591[b]	577[ab]	574[ab]	562[ab]	17.9	0.10	0.63	0.14	0.45
ADFI, g	790[a]	828[ab]	858[b]	836[ab]	819[ab]	27.0	0.15	0.07	0.69	0.29
G:F	0.69[ab]	0.71[a]	0.67[b]	0.68[b]	0.68[b]	0.010	0.60	0.006	0.04	0.56
D 0 to 42										
ADG, g	418[a]	454[b]	456[b]	450[ab]	432[ab]	15.3	0.09	0.15	0.21	0.39
ADFI, g	586[a]	623[ab]	646[b]	635[b]	609[ab]	21.1	0.14	0.04	0.41	0.29
G:F	0.71	0.72	0.70	0.70	0.70	0.009	0.47	0.12	0.30	0.75
Final wt, kg	22.7	24.1	24.2	23.9	23.5	0.72	0.15	0.24	0.32	0.30

[1]A total of 180 weanling pigs (PIC, initially 5.0 kg and 21 d of age) were used in a 42-d experiment with 6 pens per treatment and 5 pigs per pen.
[2]Treatments included: control (basal diet with no added Cu or Zn), Cu (125 ppm of added Cu from $CuSO_4$), Zn (3,000 ppm from d 0 to 14 and 2,000 ppm from d 14 to 28 of added Zn from ZnO), Cu and Zn (125 ppm of added Cu from $CuSO_4$ and 3,000 ppm from d 0 to 14 and 2,000 ppm from d 14 to 28 of added Zn from ZnO), and antibiotic (55 ppm of neomycin and oxytetracycline from Neo/Oxy 10/10; Penfield Animal Health, Omaha, NE).
[ab]Within a row, means without a common superscript differ ($P < 0.05$).

Table 4-4. Effects of zinc oxide, copper sulfate, and antibiotic combination on fecal bacteria counts and E. coli antibiotic resistance[1]

	Treatment[2]						Probability, $P<$			
	Control	Cu	Zn	Cu + Zn	Antibiotic	SEM	Zinc × Copper	Zinc	Copper	Antibiotic vs. control
Coliform counts, Log_{10} CFU/g										
D 14	6.2	5.8	6.2	5.6	6.0	0.50	0.82	0.81	0.25	0.68
D 42	5.5	4.9	5.1	5.0	4.9	0.49	0.52	0.72	0.30	0.23
E. coli count, Log_{10} CFU/g										
D 14	5.9	5.3	5.9	5.4	5.6	0.53	0.91	0.95	0.25	0.62
D 42	4.7	4.2	4.8	4.6	4.3	0.52	0.78	0.59	0.38	0.49
Antibiotic-resistant *E. coli* isolates, %										
D 14 isolates										
Chlortetracycline[3]	56	89	61	78	92	14.1	0.57	0.85	0.10	0.09
Neomycin[3]	33	33	28	28	44	15.0	1.00	0.68	1.00	0.56
Oxytetracycline[3]	72^{ab}	94^{ab}	67^{a}	89^{ab}	100^{b}	11.2	1.00	0.63	0.07	0.10
Tiamulin[4]	100	94	100	100	94	3.5	0.44	0.44	0.44	0.28
D 42 isolates										
Chlortetracycline[3]	83^{b}	47^{a}	81^{b}	89^{b}	81^{b}	9.6	0.02	0.03	0.10	0.81
Neomycin[3]	78^{b}	25^{a}	67^{b}	83^{b}	81^{b}	11.2	0.01	0.05	0.13	0.87
Oxytetracycline[3]	94	72	86	89	94	8.4	0.16	0.63	0.27	1.00
Tiamulin[4]	90	100	94	100	100	3.7	0.59	0.59	0.06	0.09

[1]A total of 180 weanling pigs (PIC, initially 5.0 kg and 21 d of age) were used in a 42-d experiment with 6 pens per treatment and 5 pigs per pen.
[2]Treatments included: control (basal diet with no added Cu or Zn), Cu (125 ppm of added Cu from $CuSO_4$), Zn (3,000 ppm from d 0 to 14 and 2,000 ppm from d 14 to 28 of added Zn from ZnO), Cu and Zn (125 ppm of added Cu from $CuSO_4$ and 3,000 ppm from d 0 to 14 and 2,000 ppm from d 14 to 28 of added Zn from ZnO), and antibiotic (55 ppm of neomycin and oxytetracycline from Neo/Oxy 10/10; Penfield Animal Health, Omaha, NE).
[3]Isolates with a minimum inhibitory concentration of 16 µg/mL or higher for this antibiotic were considered resistant.
[4]Isolates with a minimum inhibitory concentration of 32 µg/mL or higher for this antibiotic were considered resistant.
[ab]Within a row, means without a common superscript differ ($P < 0.05$).