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Effects of a Silicic Acid and Fructo-oligosaccharide Feed Additive With or Without Pharmacological Levels of Zinc on Growth Performance, Fecal Dry Matter, and Blood Biomarkers of Weanling Pigs Experimentally Infected with Enterotoxigenic *Escherichia coli*

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Summary

A total of 88 weanling pigs (241 × 600 DNA; initially 14.0 lb) were used in a 28-d study using two groups of pigs (44 pigs/group) to evaluate the effects of a silicic acid (SA) and short-chain fructo-oligosaccharide (FOS) feed additive with or without pharmacological levels of zinc (Zn) from zinc oxide on growth performance and fecal dry matter (DM) in enterotoxigenic *Escherichia coli* F18 (ETEC) challenged nursery pigs. Within group, pigs were weaned and randomly allotted to one of four dietary treatments in a completely randomized design. There were 22 pigs per dietary treatment, and diets were fed in two phases with phase 1 being fed from d 0 to 10 after weaning, and phase 2 being fed from d 10 after weaning until the conclusion of the trial on d 28 after weaning. The four dietary treatments were arranged in a 2 × 2 factorial with main effects of SA/FOS feed additive (none or 0.5 lb/ton of complete feed; Improx, Addix Biotech, Weston, FL) and pharmacological levels of Zn from ZnO (no supplemental Zn from ZnO or 2,990 mg/kg added in phase 1 and 2,018 mg/kg in phase 2). All diets contained 110 mg/kg Zn from the base trace mineral premix. Pigs were group-housed for a 14-d acclimation period after weaning, then moved to individual pens and inoculated with 6 mL of solution containing approximately 10^7 CFU/mL of ETEC F18 administered via orogastric gavage with a rubber catheter. During period 1 after inoculation (d 14 to 17 after weaning), an SA/FOS × pharmacological Zn interaction was observed for ADG ($P = 0.027$), resulting from no difference

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when pigs were fed pharmacological levels of Zn with or without SA/FOS; however, without pharmacological levels of Zn, supplementing SA/FOS improved ($P < 0.05$) ADG. Overall, pharmacological levels of Zn improved d 28 BW, ADG, and ADFI ($P < 0.001$). A SA/FOS × day interaction was observed ($P = 0.050$) for fecal DM, with a significant decrease in fecal DM on d 21 ($P = 0.023$) in pigs fed SA/FOS, but no significant differences on other days. There was a significant Zn × day interactive effect ($P = 0.034$) for fecal DM with an increase in fecal DM on d 17, 21, and 28 ($P \leq 0.009$) in pigs fed pharmacological levels of Zn but no significant differences on d 10 or 14. For the cytokine analysis, a significant SA/FOS × *pharmacological Zn* × *day interaction was observed* ($P = 0.032$; Table 4) for IL-1β, where an SA/FOS × *pharmacological Zn* interaction was observed on d 21 ($P = 0.030$), resulting from a reduction when pigs were fed pharmacological levels of Zn without SA/FOS; however, with SA/FOS, pharmacological levels of Zn increased IL-1β, with no significant differences observed on other days. In conclusion, an interactive effect was observed in period 1 on ADG, resulting from no difference in ADG when pigs were fed pharmacological levels of Zn with or without SA/FOS; however, without pharmacological levels of Zn, supplementing SA/FOS improved ADG. The combination of SA/FOS and Zn marginally increased pro-inflammatory and anti-inflammatory cytokines during the study. Treatment differences were observed in survival probability by day after pigs were inoculated with enterotoxigenic Escherichia coli, with survival probability lower for pigs fed the control diet compared with other treatments. Overall, pigs fed pharmacological levels of Zn had improved ADG, ADFI, and fecal DM throughout the study.

Introduction

In the swine industry, pathogenic infections are major challenges to both gut health and growth performance in nursery pigs. After weaning, enterotoxigenic *E. coli* (ETEC) is a primary cause of postweaning diarrhea (PWD), resulting in dehydration, reduced weight gain, and mortality. Antibiotics and inorganic metals have been the primary solution to ETEC infections in the early nursery period. However, research for alternative ingredients has been conducted due to microbial resistance and environmental regulations by the European Union.

Silicic acid (SA) is the monomeric active form of silicon, contributing to bone mineralization, collagen synthesis, homeostasis, and immune status. A study evaluating pigs fed sodium silicate, a mineral complex originating from SA, observed a significant reduction in the proportion of antigen-presenting cells (MHC-II+), T-cell populations (CD2+, CD4+, and CD8+), and IgM+ B lymphocytes following vaccination with an attenuated live hog cholera virus.[5]

Fructo-oligosaccharides (FOS) are prebiotics composed of non-digestible fibers that stimulate beneficial bacteria growth in the gastrointestinal tract through fermentation. In previous research evaluating FOS in pigs inoculated with ETEC, supplementing with FOS reduced the incidence of diarrhea, decreased the concentrations of IL-1β and TNF-α, and downregulated the expression of IL-6 and TNF-α in the jejunum and ileum. Pigs fed FOS had increased ADG, villus height, and villus height:crypt depth

[5] Park, B., Y. H. Park, and K. Seo. 2000. Relation between lymphocyte subpopulations of peripheral blood and immune responses of modified live hog cholera virus vaccine in pigs treated with an ionized alkali mineral complex. J. Vet. Sci. 1:49–52. doi:I410-ECN-0102-2009-520-006631291.

ratio compared with control pigs.[6] This suggests FOS could improve growth performance and intestinal health in weaned pigs infected with ETEC.

Improx (Addix Biotech, Weston, FL) is a dried *Aspergillus niger* fermentation product composed of a combination of silicic acid and a short-chain fructo-oligosaccharide. Improx is identified as a prebiotic additive for pork and poultry production, using calcium carbonate as a carrier; however, data are not available to determine its response in pigs challenged with E. *coli*. Therefore, the objective of this study was to evaluate the effects of silicic acid (SA) and a short-chain fructo-oligosaccharide (FOS) feed additive with or without pharmacological levels of zinc on growth performance and fecal DM in weanling pigs experimentally infected with enterotoxigenic *Escherichia coli.*

Procedures

The protocol used in this experiment was approved by the Kansas State University Institutional Animal Care and Use Committee and Institutional Biosafety Committee. This study was conducted at the K-State Swine Enteric Health Research Center facility in Manhattan, KS. Each pen had metal tri-bar flooring, a stainless-steel self-feeder, and nipple waterer to provide *ad libitum* access to feed and water. Pigs were placed in solid-sided pens to prevent cross-contamination between adjacent pens.

Animal selection criteria

Selected piglets came from sows not previously vaccinated for *E. coli* F18. Piglets were confirmed for genetic susceptibility to the F18 strain of ETEC by sequencing the (1,2) fucosyltransferase-1 (FUT1) gene via PCR at the Iowa State University Veterinary Diagnostic Laboratory (VDL). To identify susceptible piglets, an initial group of 104 piglets with similar BW, age, and an equal distribution of litters were selected within each group of pigs used in the experiment. A tail sample was collected at litter processing from the selected piglets. Samples were frozen and shipped on dry ice to the ISU VDL for analysis. Only fully susceptible piglets were used in the study.

Animals and diets

A total of 88 weanling pigs (241 × 600 DNA; initially 14.0 lb) were used in a 28-d study using two groups of pigs (44 pigs/group). Within group, pigs were randomly allotted to one of four dietary treatments in a completely randomized design and grouped with five or six pigs per pen for a 14-d adaptation period. There were 22 pigs per dietary treatment, and diets were fed in two phases with phase 1 being fed from d 0 to 10 after weaning, and phase 2 being fed from d 10 after weaning until the conclusion of the trial on d 28 after weaning. Pigs were group-housed for a 14-d acclimation period after weaning, then moved to individual pens and inoculated on d 14. Diets were corn-soybean meal-based and were arranged in a 2 × 2 factorial with main effects of SA/FOS feed additive (none or 0.5 lb/ton of complete feed; Improx, Addix Biotech, Weston, FL) and pharmacological levels of Zn from ZnO (no supplemental Zn from ZnO or 2,990 mg/kg added in phase 1 and 2,018 mg/kg in phase 2; Table 1). All diets contained 110 mg/kg Zn from the base trace mineral premix. Treatment diets were manufactured at the Kansas State University O.H. Kruse Feed Technology Innovation Center in Manhattan, KS, and fed in meal form. Pig weights and feed disappear-

[6] Liu, L., D. Chen, B. Yu, H. Yin, Z. Huang, Y. Luo, P. Zheng, X. Mao, J. Yu, J. Luo, H. Yan, and J. He. 2020. Fructooligosaccharides improve growth performance and intestinal epithelium function in weaned pigs exposed to enterotoxigenic *Escherichia coli*. Food Funct. 11:9599–9612. doi:10.1039/D0FO01998D.

ance were measured on d 14, 17, 21, and 28 to determine ADG, ADFI, and G:F. All instances of mortality were recorded to determine the percentage of mortality per treatment before necropsy of d 28 .

Bacterial strains, culture preparations, and inoculation methods

The ETEC F18 strain was obtained and cultured at the Kansas State University College of Veterinary Medicine. The isolate used was an F18 fimbrial type, with genes for heat-labile enterotoxin (LT), heat-stable toxin A (STa), heat-stable toxin B (STb), and Shiga toxin type 2e (Stx2e) as determined via PCR and was derived from a field clinical case submission. On d 14, all pigs were inoculated with 6 mL of solution containing approximately 10^7 CFU/mL of ETEC F18. The inoculum was administered via orogastric gavage with a rubber catheter. Briefly, the pig was manually restrained in an upright position with an open mouth and the head elevated compared with the abdomen. The catheter was gently maneuvered into the caudal aspect of the oropharynx. A swallow reflex was stimulated, and when visually observed, the tube was slowly introduced into the esophagus. Once the inoculum was dispensed, the catheter was kinked during the removal process to ensure no residual material was deposited in the oropharynx.

Plasma cytokines

On d 14 (before challenge), 21, and 28, a blood sample was collected via jugular venipuncture into a 10-mL vacutainer tube. Aliquots of plasma were obtained through centrifugation, and samples were stored at -4°F before being sent to Eve Technologies, Calgary, AB, Canada, for analysis using a multiplex immunoassay that quantified 13 cytokines (GM-CSF, IFN-γ, IL-1α, IL-1β, IL-1RA, IL-2, IL-4, IL-6, IL-8, IL-10, IL-12, IL-18, and TNF-α).

Fecal consistency

On d 10, 14, 17, 21, and 28, fecal samples were collected from each pig for an objective measure of fecal consistency using DM analysis. Using a cotton-tipped applicator to stimulate defecation, fecal samples were collected into plastic bags and frozen at -112°F until fecal DM analysis. Fecal samples were dried at 131°F in a forced-air oven for 48 h, and the ratio of dried-to-wet fecal weight determined the percentage fecal DM.

Statistical analysis

Experimental data were analyzed using the GLIMMIX procedure of SAS OnDemand for Academics (SAS Institute Inc., Cary, NC). Individual pig served as the experimental unit, with dietary treatment as a fixed effect and group included as a random intercept. Fecal DM samples were analyzed using the fixed effects of day, treatment, and the associated interaction, accounting for repeated measures over time. Mortality rate was analyzed using a Kaplan-Meier survival curve using the ggplot procedure in R Studio (Version 4.5.0, R Core Team, Vienna, Austria) with days post-inoculation and survival probability serving as the x- and y-axes, respectively. Observations with studentized residuals > 4 were considered outliers and removed from statistical analysis. When treatment was a significant source of variation, differences were determined by pairwise comparison using the Tukey-Kramer multiplicity adjustment to control for type I error. Results were considered significant at P 0.05 and were considered marginally significant at 0.05 < P 0.10.

Results and Discussion

Growth performance

At weaning, pigs were allotted to dietary treatment for a 14-d adaptation period with an average weight of 14.0 lb. On inoculation day (d 14), a tendency for a main effect of pharmacological levels of Zn was observed ($P = 0.095$), with pigs fed pharmacological Zn resulting in increased BW (Table 2). During period 1 after inoculation (d 14 to 17), an SA/FOS × pharmacological Zn interaction was observed for ADG ($P = 0.027$), resulting from no difference when pigs were fed pharmacological levels of Zn with or without SA/FOS; however, without pharmacological levels of Zn, supplementing SA/FOS improved ($P < 0.05$) ADG. In period 1 (d 14 to 17), pigs fed pharmacological levels of Zn had improved d 17 BW, ADG, ADFI, and G:F compared with pigs fed without pharmacological levels of Zn ($P \leq 0.013$; Table 3). In period 2 (d 17 to 21), pharmacological levels of Zn improved d 21 BW, ADG, ADFI, and G:F ($P \leq 0.007$). In period 3 (d 21 to 28), pigs fed pharmacological levels of Zn had greater ADFI compared with pigs fed without pharmacological levels of Zn ($P = 0.002$); however, pigs fed without pharmacological levels of Zn had improved G:F compared with pigs fed with pharmacological levels of Zn ($P < 0.001$). Overall, pharmacological levels of Zn improved d 28 BW, ADG, and ADFI ($P < 0.001$).

Fecal dry matter

No significant interactive effect of SA/FOS × *pharmacological Zn* × *day was observed during the experiment; however, an SA/FOS* × *day interaction was observed* ($P = 0.050$), with a significant decrease in fecal DM on d 21 ($P = 0.023$) in pigs fed SA/FOS, but no significant differences on other days. There was a significant Zn × day interactive effect ($P = 0.034$) with an increase in fecal DM on d 17, 21, and 28 ($P \leq 0.009$) in pigs fed pharmacological levels of Zn but no significant differences on d 10 or 14. On d 17, a tendency for an SA/FOS × pharmacological Zn interaction was observed for fecal DM ($P = 0.066$), resulting from no difference when pigs were fed pharmacological levels of Zn with or without SA/FOS; however, without pharmacological levels of Zn, supplementing SA/FOS decreased fecal DM. A main effect of pharmacological Zn was observed ($P < 0.001$), with pigs fed pharmacological Zn having greater fecal DM compared with pigs without pharmacological Zn. A main effect of timepoint on fecal DM was observed ($P < 0.001$), with fecal DM decreasing and then increasing as time changed, aligning with the expected progression of the ETEC challenge.

Plasma cytokine panel

A significant SA/FOS × *pharmacological Zn* × *day interaction was observed* ($P = 0.032$; Table 4) for IL-1β, where an SA/FOS × *pharmacological Zn* interaction was observed on d 21 ($P = 0.030$), resulting from a reduction when pigs were fed pharmacological levels of Zn without SA/FOS; however, with SA/FOS, pharmacological levels of Zn increased IL-1β, with no significant differences observed on other days. Tendencies for SA/FOS × *pharmacological Zn* × *day interactions were observed* ($P \leq 0.092$) for IL-10 and IL-18. Tendencies for SA/FOS × *pharmacological Zn interactions were observed on d 21* ($P \leq 0.097$) for IL-12 and IL-18, where in pigs fed diets without SA/FOS, Zn reduced IL-12 and IL-18; however, with SA/FOS, pharmacological levels of Zn increased IL-12 and IL-18. A tendency for SA/FOS × *pharmacological Zn interaction was observed on d 14* ($P = 0.076$) for IL-8, resulting from an increase when pigs were fed pharmacological levels of Zn without SA/FOS; however, with SA/FOS, pharmacological levels of Zn reduced IL-8.

Survivability curve

After inoculation (d 14 to 28), a treatment difference was observed ($P \leq 0.001$; Figure 1), resulting in a difference in the survival probability by day after pigs were inoculated with enterotoxigenic *Escherichia coli* with survival probability being lower for pigs fed the control diet compared with pigs fed pharmacological Zn from ZnO, SA/FOS, or the combination.

In conclusion, an interactive effect was observed in period 1 on ADG, resulting from no difference in ADG when pigs were fed pharmacological levels of Zn with or without SA/FOS; however, without pharmacological levels of Zn, supplementing SA/FOS improved ADG. The combination of SA/FOS and Zn marginally increased pro-inflammatory and anti-inflammatory cytokines during the study. Treatment differences were observed in survival probability by day after pigs were inoculated with enterotoxigenic Escherichia coli, with survival probability lower for pigs fed the control diet compared with other treatments. Overall, pigs fed pharmacological levels of Zn had improved ADG, ADFI, and fecal DM throughout the study.

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Table 1. Ingredient composition of experimental diets (as-fed basis)[1]

	Phase 1		Phase 2	
Added Zn, mg/kg[2]	0	2,990	0	2,018
Ingredients, %				
Corn	43.49	43.09	57.29	57.00
Soybean meal, 47.7% CP	20.89	20.89	24.25	24.25
Whey powder	15.00	15.00	10.00	10.00
Whey permeate	9.00	9.00	---	---
Microbial enhanced SBM[3]	6.25	6.25	3.75	3.75
Soybean oil	2.00	2.00	1.00	1.00
Calcium carbonate	0.38	0.38	0.58	0.58
Monocalcium phosphate, 21% P	1.10	1.10	0.95	0.95
Sodium chloride	0.35	0.35	0.56	0.56
L-Lys-HCl	0.45	0.45	0.49	0.49
DL-Met	0.28	0.28	0.26	0.26
L-Thr	0.20	0.20	0.22	0.22
L-Trp	0.04	0.04	0.06	0.06
L-Val	0.11	0.11	0.13	0.13
Trace mineral premix	0.15	0.15	0.15	0.15
Vitamin premix	0.25	0.25	0.25	0.25
Copper sulfate	0.02	0.02	0.02	0.02
Phytase[4]	0.06	0.06	0.06	0.06
Zinc oxide[2]	0.00	0.40	0.00	0.29
SA/FOS[5]	+/-	+/-	+/-	+/-
Total	100	100	100	100
Calculated analysis				
Standardized ileal digestible (SID) amino acids, %				
Lys	1.35	1.35	1.35	1.35
Ile:Lys	59	59	57	57
Leu:Lys	113	113	115	115
Met:Lys	41	41	39	39
Met and Cys:Lys	58	58	58	58
Thr:Lys	65	65	65	65
Trp:Lys	21	21	21	21
Val:Lys	70	70	70	70
His:Lys	34	34	35	35
Total Lys, %	1.49	1.49	1.49	1.49
NE, kcal/lb	1,177	1,172	1,137	1,134
SID Lys:CP	6.49	6.49	6.43	6.43
Ca, %	0.66	0.66	0.66	0.66
STTD P, %	0.58	0.58	0.51	0.51
Ca:P	1.01	1.01	1.09	1.09

Analyzed composition				
CP[6]	20.3	20.1	19.8	19.6
Zn[7]	209.1	2,039.2	245.8	1,666.7

[1] Phase 1 diets were fed from d 0 to 10 during the adaptation period after weaning before inoculation, and phase 2 diets were fed from d 10 in the adaptation period to d 28 in the experimental period after inoculation.

[2] Zinc oxide was added to corresponding treatment diets to provide 2,990 mg/kg Zn in phase 1 and 2,018 mg/kg Zn in phase 2. All diets contained 110 mg/kg Zn from $ZnSO_4$ in the trace mineral premix.

[3] Access starter protein (Prairie Aquatech, Brookings, SD).

[4] HiPhorius 2400 (Novonesis, Kongens Lyngby, Denmark), which provided an estimated release of 0.12% STTD P with 1,500 FYT/kg.

[5] Improx (Addix Biotech, Weston, FL) was added at 0.5 lb/ton in phases 1 and 2 for the corresponding treatment diets.

[6] Nitrogen was estimated by N combustion, using the Dumas methodology, and then multiplied by a factor of 6.25 to obtain the CP values.

[7] Samples were analyzed for zinc analysis using ICP-OES at the University of Missouri Agricultural Experiment Station Chemical Laboratory.

Table 2. Interactive effects of a silicic acid (SA)/fructo-oligosaccharide (FOS) feed additive with or without pharmacological levels of zinc from zinc oxide on growth performance and fecal dry matter of weanling pigs[1]

	SA/FOS[2]							
	No		Yes			*P* =		
Pharmacological Zn[3]:	-	+	-	+	SEM	Zn × SA/FOS	Zn	SA/FOS
BW, lb								
d 0 (Weaning)	14.0	13.9	13.9	14.0	---	---	---	---
d 14 (Inoculation)	19.5	19.9	17.9	19.9	0.71	0.274	0.095	0.289
d 17	19.8	22.3	19.2	22.1	1.03	0.786	0.001	0.606
d 21	22.8	27.0	20.7	26.9	1.48	0.327	< 0.001	0.277
d 28	31.3	35.8	29.8	35.8	2.07	0.559	< 0.001	0.593
Period 1 (d 14 to 17)								
ADG, lb	0.06[c]	0.81[a]	0.43[b]	0.73[a]	0.184	0.027	< 0.001	0.152
ADFI, lb	1.18	1.93	1.50	1.67	0.671	0.114	0.013	0.861
G:F	0.07	0.56	0.31	0.54	0.114	0.226	0.001	0.332
Period 2 (d 17 to 21)								
ADG, lb	0.39	1.17	0.41	1.19	0.147	0.996	< 0.001	0.902
ADFI, lb	0.78	1.43	0.90	1.44	0.104	0.577	< 0.001	0.515
G:F	0.69	0.83	0.59	0.83	0.080	0.460	0.007	0.488
Period 3 (d 21 to 28)								
ADG, lb	1.21	1.25	1.37	1.28	0.109	0.293	0.694	0.146
ADFI, lb	1.48	1.72	1.42	1.77	0.104	0.552	0.002	0.928
G:F	0.83	0.73	0.90	0.73	0.032	0.205	< 0.001	0.137
Overall (d 14 to 28)								
ADG, lb	0.81	1.14	0.92	1.14	0.106	0.371	< 0.001	0.361
ADFI, lb	1.30	1.68	1.29	1.65	0.195	0.921	< 0.001	0.817
G:F	0.66	0.69	0.66	0.70	0.042	0.980	0.200	0.769
Fecal DM, %[4]								
d 10	20.1	21.5	19.0	22.0	1.68	0.590	0.147	0.823
d 14	20.6	22.0	22.1	23.7	1.49	0.933	0.248	0.209
d 17	15.6	19.6	14.0	23.3	1.64	0.066	< 0.001	0.458
d 21	17.5	20.4	12.6	18.0	2.02	0.430	0.009	0.023
d 28	19.0	22.3	19.1	23.2	1.73	0.788	0.008	0.728

[1] A total of 88 pigs were used in two groups (44 pigs/group) for a 28-d growth study with 1 pig per pen and 22 replicates per treatment. On d 14 (14 d after weaning), pigs were placed in individual pens and inoculated with 6 mL of solution containing approximately 10^7 CFU/mL of ETEC F18 via orogastric gavage.

[2] Improx was supplied from Addix Biotech, Weston, FL. The silicic acid (SA)/fructo-oligosaccharide (FOS) feed additive was added to the diet at the recommended level of 0.5 lb/ton in phases 1 and 2.

[3] Zn from ZnO was added at 2,990 mg/kg and 2,018 mg/kg from d 0 to 10 and d 10 to 28, respectively. All diets contained 110 mg/kg Zn from the trace mineral premix.

[4] SA/FOS × Zn × day interaction, $P = 0.613$; SA/FOS × day interaction, $P = 0.050$; Zn × day interaction, $P = 0.034$. SA/FOS × Zn, $P = 0.244$. SA/FOS, $P = 0.825$. Zn, $P < 0.001$. Time, $P < 0.001$.

Table 3. Main effects of a silicic acid (SA)/fructo-oligosaccharide (FOS) feed additive or pharmacological levels of zinc from zinc oxide on growth performance and fecal dry matter of weanling pigs[1]

	SA/FOS[2]				Pharmacological Zn[3]			
Item:	-	+	SEM	*P* =	-	+	SEM	*P* =
BW, lb								
d 0 (Weaning)	14.0	13.9	---	---	13.9	13.9	---	---
d 14 (Inoculation)	19.7	18.9	0.51	0.289	18.7	19.9	0.51	0.095
d 17	21.1	20.7	0.87	0.606	19.5	22.2	1.55	0.001
d 21	23.8	24.9	1.19	0.277	21.8	26.9	1.13	< 0.001
d 28	33.5	32.8	1.68	0.593	30.5	35.8	1.68	< 0.001
d 14 to 17								
ADG, lb	0.44	0.58	0.169	0.152	0.24	0.77	0.169	< 0.001
ADFI, lb	1.55	1.58	0.657	0.861	1.34	1.80	0.657	0.013
G:F	0.31	0.42	0.079	0.332	0.19	0.55	0.078	0.001
d 17 to 21								
ADG, lb	0.78	0.80	0.098	0.902	0.40	1.18	0.098	< 0.001
ADFI, lb	1.11	1.17	0.070	0.515	0.84	1.44	0.070	< 0.001
G:F	0.76	0.71	0.050	0.488	0.64	0.83	0.053	0.007
d 21 to 28								
ADG, lb	1.23	1.33	0.093	0.146	1.29	1.27	0.093	0.694
ADFI, lb	1.60	1.59	0.067	0.928	1.45	1.74	0.067	0.002
G:F	0.78	0.81	0.022	0.137	0.86	0.73	0.023	< 0.001
d 14 to 28 (Post-inoculation)								
ADG, lb	0.97	1.03	0.091	0.361	0.87	1.14	0.091	< 0.001
ADFI, lb	1.49	1.47	0.178	0.817	1.29	1.67	0.178	< 0.001
G:F	0.67	0.68	0.034	0.769	0.66	0.69	0.035	0.200
Fecal DM, %[4]								
d 10	20.8	20.5	1.28	0.823	19.5	21.7	1.29	0.147
d 14	21.3	22.9	1.17	0.209	21.3	22.8	1.16	0.248
d 17	17.6	18.7	1.25	0.458	14.8	21.4	1.25	< 0.001
d 21	19.0	15.3	1.40	0.023	15.0	19.2	1.41	0.009
d 28	20.6	21.1	1.27	0.728	19.0	22.7	1.26	0.008

[1] A total of 88 pigs were used in two groups (44 pigs/group) for a 28-d growth study with 1 pig per pen and 22 replicates per treatment. On d 14 (14 d after weaning), pigs were placed in individual pens and inoculated with 6 mL of solution containing approximately 10^7 CFU/mL of ETEC F18 via orogastric gavage.

[2] Improx was supplied by Addix Biotech, Weston, FL. The silicic acid (SA)/fructo-oligosaccharide (FOS) feed additive was added to the diet at the recommended level of 0.5 lb/ton in phases 1 and 2.

[3] Zn from ZnO was added at 2,990 mg/kg and 2,018 mg/kg from d 0 to 10 and d 10 to 28, respectively. All diets contained 110 mg/kg Zn from the trace mineral premix.

[4S] A/FOS × Zn × day interaction, $P = 0.613$; SA/FOS × day interaction, $P = 0.050$; Zn × day interaction, $P = 0.034$. SA/FOS × Zn, $P = 0.244$. SA/FOS, $P = 0.825$. Zn, $P < 0.001$. Time, $P < 0.001$.

Table 4. Effects of a silicic acid (SA)/fructo-oligosaccharide (FOS) feed additive with or without pharmacological levels of zinc from zinc oxide on plasma cytokine concentrations (fluorescence intensity values) of F18 *E. coli* challenged nursery pigs[1]

	SA/FOS[2]							
	No		Yes			*P* =		
Pharmacological Zn[3]:	-	+	-	+	SEM	SA/FOS Zn	SA/FOS	Zn
GM-CSF								
d 14	2.45	2.77	2.53	2.75	0.176	0.780	0.890	0.123
d 21	2.52	2.64	2.53	2.62	0.197	0.915	0.977	0.581
d 28	2.43	2.57	2.55	2.61	0.197	0.840	0.666	0.580
IFN-γ								
d 14	3.99	4.05	4.05	3.96	0.272	0.604	0.923	0.930
d 21	3.70	3.57	3.80	3.73	0.288	0.831	0.394	0.514
d 28	3.51	3.54	3.72	3.75	0.286	0.992	0.187	0.838
IL-1α								
d 14	4.20	4.37	4.17	4.32	0.296	0.970	0.866	0.536
d 21	4.09	4.13	4.07	4.24	0.330	0.816	0.875	0.684
d 28	3.84	4.25	4.21	4.43	0.330	0.717	0.315	0.238
IL-1β[4]								
d 14	4.79	4.69	4.54	4.80	0.176	0.309	0.684	0.653
d 21	4.92	4.51	4.43	4.84	0.215	0.030	0.686	0.992
d 28	4.53	4.70	4.79	4.79	0.209	0.664	0.341	0.651
IL-1RA								
d 14	5.49	5.53	5.35	5.45	0.127	0.777	0.386	0.578
d 21	5.33	5.24	5.82	5.36	0.237	0.356	0.139	0.178
d 28	5.24	5.53	5.53	5.45	0.140	0.148	0.386	0.393
IL-2								
d 14	4.12	4.22	3.96	4.24	0.309	0.724	0.799	0.466
d 21	3.92	3.91	3.91	4.11	0.349	0.705	0.726	0.733
d 28	3.62	4.04	4.06	4.26	0.344	0.684	0.236	0.252
IL-4								
d 14	4.31	4.40	4.13	4.13	0.262	0.781	0.613	0.481
d 21	4.13	4.17	4.12	4.27	0.293	0.824	0.858	0.675
d 28	3.92	4.23	4.20	4.43	0.293	0.861	0.311	0.247
IL-6								
d 14	4.29	4.50	4.15	4.53	0.252	0.694	0.810	0.198
d 21	4.05	4.26	4.11	4.46	0.284	0.783	0.574	0.244
d 28	4.07	4.21	4.30	4.51	0.284	0.894	0.271	0.465
IL-8								
d 14	2.88	3.15	3.44	3.12	0.168	0.076	0.111	0.842
d 21	3.18	2.99	3.15	3.11	0.202	0.647	0.795	0.527
d 28	2.90	2.88	3.13	2.96	0.202	0.672	0.362	0.588

IL-10[5]								
d 14	4.40	4.65	4.21	4.56	0.243	0.825	0.546	0.193
d 21	4.24	4.29	4.17	4.44	0.276	0.652	0.875	0.500
d 28	4.02	4.30	4.43	4.50	0.276	0.667	0.213	0.471
IL-12								
d 14	7.22	7.08	7.09	7.07	0.149	0.230	0.164	0.144
d 21	7.11	6.99	6.95	7.09	0.165	0.096	0.678	0.936
d 28	7.25	7.21	7.28	7.14	0.157	0.454	0.794	0.137
IL-18[5]								
d 14	4.85	4.88	4.59	4.86	0.171	0.465	0.418	0.374
d 21	4.99	4.80	4.58	4.99	0.202	0.097	0.551	0.515
d 28	4.69	4.98	4.97	5.14	0.202	0.746	0.224	0.200
TNF-α								
d 14	3.44	3.54	3.47	3.73	0.154	0.541	0.436	0.196
d 21	3.29	3.45	3.43	3.59	0.170	0.964	0.316	0.262
d 28	3.29	3.38	3.51	3.51	0.170	0.742	0.223	0.740

[1] A total of 88 pigs were used in two groups (44 pigs/group) for a 14-d growth study with 1 pig per pen and 22 replicates per treatment. On d 14 (14 d after weaning), pigs were placed in individual pens and inoculated with 6 mL of solution containing approximately 10^7 CFU/mL of ETEC F18 via orogastric gavage.

[2] Improx was supplied by Addix Biotech, Weston, FL. The silicic acid (SA)/fructooligosaccharide (FOS) feed additive was added to the diet at the recommended level of 0.5 lb/ton in phases 1 and 2.

[3] Zn from ZnO was added at 2,990 mg/kg and 2,018 mg/kg from d 0 to 10 and d 10 to 28, respectively. All diets contained 110 mg/kg Zn from the trace mineral premix.

[4] SA/FOS × Zn × day interaction, $P = 0.032$.

[5] SA/FOS × day interaction, $P \leq 0.092$.

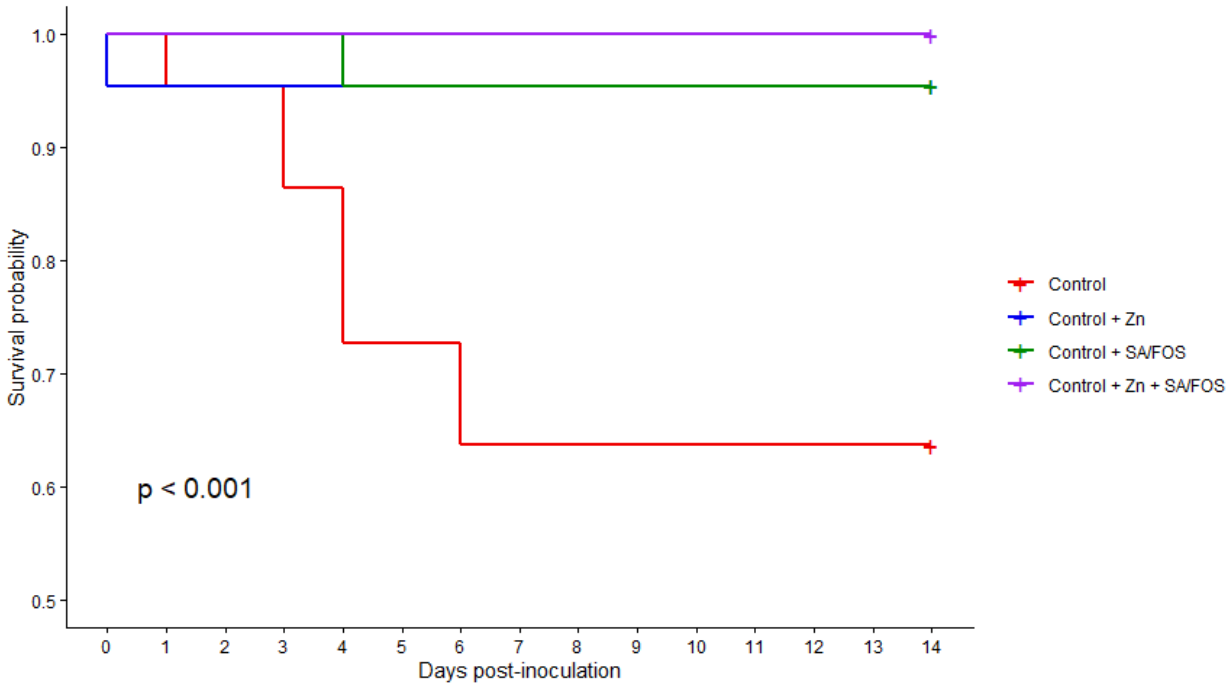


Figure 1. Pig survival probability within treatment by day after inoculation with enterotoxigenic *Escherichia coli.* Individual lines represent each treatment and the survival probability after inoculation.