

2017

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Recommended Citation

Menegat, M. B.; Capps, K.; Williams, H.; Woodworth, J. C.; Dritz, S. S.; Amachawadi, R. G.; Nagaraja, T. G.; Tokach, M. D.; DeRouchey, J. M.; and Goodband, R. D. (2017) "Impact of Added Copper and Chlortetracycline on Growth Performance of Nursery Pigs," *Kansas Agricultural Experiment Station Research Reports*: Vol. 3: Iss. 7. <https://doi.org/10.4148/2378-5977.7481>

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Funding Source

Appreciation is expressed to Micronutrients (Indianapolis, IN) for financial support.

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Impact of Added Copper and Chlortetracycline on Growth Performance of Nursery Pigs¹

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Summary

A total of 320 nursery pigs (DNA 200 × 400 barrows; initially 16.3 lb BW) were used in a 28-d trial to determine the effect of copper (Cu) and chlortetracycline (CTC), fed alone or in combination, on growth performance of weanling pigs. Pigs were weaned at approximately 21 d of age and fed a common pelleted starter diet (non-medicated) for 7 d after weaning. Pigs were allotted to dietary treatments based on BW and location in a randomized complete block design. Dietary treatments were arranged as a 2 × 2 factorial with main effects of added Cu (0 vs. 200 ppm Cu from copper sulfate) and CTC (0 vs. 440 ppm CTC). Experimental diets were corn-soybean meal-based and were fed in one phase for 28 d in meal form. There were 5 pigs per pen and 8 replications per treatment with each replication consisting of a pair of adjoining pens. The results showed no evidence for an interactive effect of Cu and CTC for any of the performance and economic variables ($P > 0.05$). From d 0 to 14, added Cu increased ($P < 0.05$) ADG and ADFI and added CTC improved ($P < 0.05$) ADG, ADFI, and F/G. From d 14 to 28, the addition of CTC to the diet improved ($P < 0.05$) ADG and ADFI, but there was no evidence for a Cu effect. For the overall experimental period (d 0 to 28), pigs fed diets with CTC had improved ($P < 0.05$) ADG, ADFI, and F/G, but there was no evidence for a Cu effect. The inclusion of either Cu or CTC increased ($P < 0.05$) BW on d 14 and 28. Regarding the economics, added dietary Cu increased ($P < 0.05$) feed cost per pig and value of gain per pig, but not income over feed cost (IOFC). The addition of CTC to the diet increased ($P < 0.05$) feed cost per pig, value of gain per pig, and IOFC. In conclusion, the findings of the present study characterize a beneficial effect of feeding Cu for 14 d on growth performance of young pigs (16 to 25 lb) and a positive effect of including CTC in nursery diets. The lack of interactive effects between Cu and CTC suggests that the responses of Cu and CTC on growth performance of nursery pigs are as efficacious when fed alone or in combination.

¹ Appreciation is expressed to Micronutrients (Indianapolis, IN) for financial support.

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Introduction

Copper (Cu) is supplemented in nursery diets at concentrations of 100 to 250 ppm for growth promotion.⁴ The potential effect of Cu is suggested to be similar to that of antimicrobials regarding the regulation of microbial flora for nutrient utilization and suppression of pathogens.⁵ However, the exact mode of action of Cu remains unclear. Studies performed in the 1980s have shown that supplementation of Cu is effective even in combination with feed-grade antimicrobials.^{6,7} This suggests that differences in the modes of action of Cu and antimicrobials might have led to additive effects on growth promotion.^{6,7} Recent studies on Cu supplementation have focused on different sources of Cu,^{8,9} the interactive effect of Cu and Zn,^{7,10} and antimicrobial resistance.¹¹ However, studies on the supplementation of Cu in combination with feed-grade antimicrobials are scarce.

In view of the potential similarity of modes of action and the perspectives on limiting the use of feed-grade antimicrobials, it is of interest to compare the effects of Cu and antimicrobials and to determine whether there is an additive response on growth performance of nursery pigs. The main objective of this study was to determine the impact of Cu and CTC, fed alone or in combination, on prevalence and quantification of Cu resistance and antimicrobial resistance in fecal enterococci of weaned piglets.¹¹ This report describes the effect of treatments on growth performance, whereas the impact on Cu and antimicrobial resistance will be reported elsewhere. Therefore, the objective of this study was to characterize the effect of Cu and CTC, fed alone or in combination, on growth performance of weanling pigs.

Procedures

This trial was conducted in collaboration with the Department of Clinical Sciences and the Department of Diagnostic Medicine/Pathobiology, College of Veterinary Medicine, Kansas State University. The Kansas State University Institutional Care and Use Committee approved the protocol used in this experiment. The experiment was conducted at the Kansas State University Segregated Early Weaning Facility in Manhattan,

⁴ NRC, 2012. Nutrient requirements of swine. 11th rev. ed. Natl. Acad. Press, Washington, DC.

⁵ Højberg, O., Canibe, N., Poulsen, H. D., Hedemann, M. S., and Jensen, B.B. 2005. Influence of dietary zinc oxide and copper sulfate on the gastrointestinal ecosystem in newly weaned piglets. *Appl. Environ. Microbiol.* 71:2267–2277.

⁶ Stahly, T. S., Cromwell, G. L., and Monegue, H. J. 1980. Effect of single additions and combinations of copper and antibiotics on the performance of weanling pigs. *J. Anim. Sci.* 51:1347–1351.

⁷ Burnell, T. W., Cromwell, G. L., and Stahly, T. S. 1988. Effects of dried whey and copper sulfate on the growth responses to organic acid in diets for weanling pigs. *J. Anim. Sci.* 66:1100–1108.

⁸ Shelton, N. W., Tokach, M. D., Nelssen, J. L., Goodband, R. D., Dritz, S. S., DeRouchey, J. M., Hill, G. M. 2011 Effects of copper sulfate, tri-basic copper chloride, and zinc oxide on weanling pig performance. *J. Anim. Sci.* 89:2440–2451.

⁹ Ma, Y. L., Zanton, G. I., Zhao, J., Wedekind, K., Escobar, J., and M. Vazquez-Añón. 2015. Multitrial analysis of the effects of copper level and source on performance in nursery pigs. *J. Anim. Sci.* 93:606–614.

¹⁰ Pérez, V. G., Waguespack, A. M., Bidner, T. D., Southern, L. L., Fakler, T. M., Ward, T. L., Steidinger, M. and Pettigrew, J. E. 2011. Additivity of effects from dietary copper and zinc on growth performance and fecal microbiota of pigs after weaning. *J. Anim. Sci.* 89:414–425.

¹¹ Amachawadi, R. G., Scott, H. M., Vinasco, J., Tokach, M. D., Dritz, S. S., Nelssen, J. L. and Nagaraja, T. G. 2015. Effects of in-feed copper, chlortetracycline, and tylosin on the prevalence of transferable copper resistance gene, *tcpB*, among fecal enterococci of weaned piglets. *Foodborne Pathog. Dis.* 12(8):670–678.

KS. Each pen (4×4 ft) contained a four-hole dry self-feeder and one cup waterer to provide ad libitum access to feed and water. All diets were manufactured at the Kansas State University O.H. Kruse Feed Technology Innovation Center in Manhattan, KS.

A total of 320 nursery pigs (DNA 200 $\times$ 400, Columbus, NE; initially 16.3 lb BW) were used in a 28-d trial with 5 pigs per pen and 8 replicates per treatment. Each replicate consisted of a pair of adjoining pens of the same treatment and were separated from adjacent pens by a solid panel. Pigs were weaned at approximately 21 d of age and allotted to pens in a completely randomized design based on initial BW. Pigs were fed a common, non-medicated, pelleted starter diet for 7 d after weaning and then allotted to dietary treatments based on BW and location in a randomized complete block design.

The dietary treatments were arranged as a 2×2 factorial with main effects of Cu (0 vs. 200 ppm from Cu sulfate) and antibiotic (0 vs. 440 ppm CTC; Zoetis Services, LLC., Florham Park, NJ). The experimental diets were corn-soybean meal-based and were fed in meal form. The treatment ingredients (Cu and CTC) were included in the diet at the expense of corn (Table 1). The dietary treatments were fed in one phase for 28 d. On d 14, CTC was removed from the diets to comply with FDA guidelines and resumed feeding on d 15.

Pigs were weighed and feed disappearance was recorded on d 0, 7, 14, 21, and 28 to determine ADG, ADFI, and F/G. Diet samples were collected from each treatment and composite samples were submitted for analysis of DM, CP, Ca, P, and Cu (Cumberland Valley Analytical Services, Inc., Waynesboro, PA). In addition, diet samples were submitted for CTC quantification (Midwest Laboratories, Omaha, NE).

For the economic analysis, feed cost per pig, feed cost per lb of gain, value of gain per pig, and IOFC were calculated on a pig basis. The basal diet cost was \$333.91/ton with corn valued at \$3.30/bu (\$118/ton), soybean meal at \$290/ton, L-lysine at \$0.75/lb, DL-methionine at \$1.30/lb, L-threonine at \$1.10/lb, and L-tryptophan at \$4.75/lb. The price of Cu sulfate was \$1.02/lb and CTC was \$1.65/lb. Feed cost per pig was calculated by multiplying the feed cost per lb by ADFI and by the number of days on the diet. Feed cost per lb of gain was calculated by dividing the feed cost per pig by the overall weight gain. Value of gain was calculated by subtracting body weight on d 0 from body weight on d 28 and multiplying by an assumed live price of \$0.42 per lb. The IOFC was calculated by subtracting the feed cost per pig from value of gain per pig.

Data were analyzed using a linear mixed model with treatment as fixed effect and block as random effect. The experimental unit was defined as the combination of two adjoining pens assigned to the same treatment within a location block. Preplanned contrast statements were built to evaluate the main effects and interactions of Cu and CTC. Statistical models were fitted using the GLIMMIX procedure of SAS version 9.4 (SAS Institute Inc., Cary, NC). Results were considered significant at $P \leq 0.05$ and marginally significant at $0.05 < P \leq 0.10$.

Results and Discussion

The analyzed DM, CP, Ca, P, Cu, and CTC contents of experimental diets (Table 2) were similar to formulated estimates.

There was no evidence for an interactive effect of Cu and CTC for any of the performance and economic variables throughout the trial ($P > 0.10$; Table 3). Therefore, the interaction was removed from the statistical model and the main effects of Cu and CTC on growth performance were analyzed (Table 4). From d 0 to 14, the addition of Cu to the diet increased ADG ($P = 0.025$) and ADFI ($P = 0.011$), while the addition of CTC to the diet improved ($P < 0.05$) ADG, ADFI, and F/G. From d 14 to 28, the addition of CTC to the diet increased ($P < 0.001$) ADG and ADFI. There was no evidence for a Cu effect ($P > 0.05$) on ADG, ADFI, and F/G in this period.

For the overall experimental period (d 0 to 28), pigs fed diets with CTC had improved ($P < 0.05$) ADG, ADFI, and F/G. There was no evidence for a Cu effect ($P > 0.10$) on ADG, ADFI, and F/G in the overall period. The inclusion of either Cu or CTC increased ($P < 0.05$) BW on d 14 and 28.

For the economic analysis, the addition of Cu to the diet increased ($P < 0.05$) feed cost per pig and value of gain per pig, but there was no evidence for differences in IOFC. The inclusion of CTC to the diet increased ($P < 0.001$) feed cost per pig and value of gain per pig, and it also resulted in improved ($P = 0.014$) IOFC.

In conclusion, the findings of the present study characterize a beneficial effect of feeding Cu for 14 d on growth performance of young pigs (16 to 25 lb) and a positive effect of including CTC in nursery diets. The lack of interactive effects between Cu and CTC suggests that the responses of Cu and CTC on growth performance of nursery pigs are as efficacious when fed alone or in combination.

Table 1. Diet composition (as-fed basis)¹

Item	Control	Cu ²	CTC ³	Cu + CTC
Ingredient, %				
Corn	56.05	55.97	55.62	55.54
Soybean meal, 47% CP	24.76	24.77	24.79	24.80
Dried whey	10.00	10.00	10.00	10.00
HP 300 ⁴	5.00	5.00	5.00	5.00
Monocalcium phosphate	1.20	1.20	1.20	1.20
Limestone	1.05	1.05	1.05	1.05
Sodium chloride	0.60	0.60	0.60	0.60
L-Lys HCl	0.45	0.45	0.45	0.45
DL-Met	0.20	0.20	0.20	0.20
L-Thr	0.20	0.20	0.20	0.20
L-Trp	0.02	0.02	0.02	0.02
L-Val	0.05	0.05	0.05	0.05
Trace mineral premix ⁵	0.15	0.15	0.15	0.15
Vitamin premix	0.25	0.25	0.25	0.25
Phytase ⁶	0.02	0.02	0.02	0.02
Copper sulfate	---	0.08	---	0.08
CTC-50	---	---	0.40	0.40
Total	100	100	100	100

continued

Table 1, continued. Diet composition (as-fed basis)¹

Item	Control	Cu ²	CTC ³	Cu + CTC
Calculated analysis				
Standardized ileal digestible (SID) amino acids, %				
Lys	1.35	1.35	1.35	1.35
Ile:Lys	57	57	57	57
Leu:Lys	115	115	115	115
Met:Lys	36	36	35	35
Met and Cys:Lys	57	57	57	57
Thr:Lys	64	64	64	64
Trp:Lys	18.5	18.5	18.5	18.5
Val:Lys	65	65	65	65
Total Lys, %	1.48	1.48	1.48	1.48
ME, kcal/lb	1,491	1,490	1,485	1,484
SID Lys:ME, g/Mcal	4.11	4.11	4.12	4.13
CP, %	21.1	21.1	21.1	21.1
Ca, %	0.79	0.79	0.79	0.79
P, %	0.69	0.69	0.69	0.69
Available P, %	0.50	0.50	0.50	0.50

¹ Diets were fed in meal form from d 0 to 28 (~16.0 to 43.0 lb BW). A common starter pelleted diet was fed for 7 d after weaning. The treatment ingredients (Cu and CTC) were included in the diet at the expense of corn.

² The basal diet with 200 ppm of added copper (Cu) from copper sulfate.

³ The basal diet with 440 ppm of added CTC (Zoetis Services, LLC., Florham Park, NJ).

⁴ Hamlet Protein, Inc., Findlay, OH.

⁵ Trace mineral premix containing 17 ppm Cu and 165 ppm Zn.

⁶ HiPhos 2700 (DSM Nutritional Products, Inc., Parsippany, NJ), providing 184.3 phytase units (FTU)/lb and an estimated release of 0.10% available P.

Table 2. Chemical analysis of experimental diets (as-fed basis)¹

Item	Control	Cu ²	CTC ³	Cu + CTC
Proximate analysis, %				
DM	88.2	88.1	88.1	88.2
CP	20.6	20.7	20.9	21.1
Ca	0.85	0.91	0.93	0.91
P	0.63	0.65	0.69	0.66
Cu, ppm	24	202	31	194
CTC, ppm	n.d. ⁴	0.06	539	309

¹ Diet samples were collected from each treatment and composite samples were submitted to Cumberland Valley Analytical Services, Inc. (Waynesboro, PA) for analysis of DM, CP, Ca, P, and Cu, and to Midwest Laboratories (Omaha, NE) for analysis of CTC.

² The basal diet with 200 ppm of added copper (Cu) from copper sulfate.

³ The basal diet with 440 ppm of added chlortetracycline (CTC).

⁴ Not detected.

Table 3. Interactive effects of Cu and CTC level on growth performance of nursery pigs^{1,2,3}

	Cu, ppm ⁴ :	0	200	0	200		Probability, $P <$	
	CTC, ppm ⁵ :	0	0	440	440	SEM	Cu	CTC
d 0 to 14								
ADG, lb		0.55	0.61	0.65	0.69	0.023	0.029	0.001
ADFI, lb		0.76	0.82	0.83	0.88	0.022	0.013	0.005
F/G		1.39	1.37	1.29	1.28	0.022	0.520	0.001
d 14 to 28								
ADG, lb		1.27	1.26	1.36	1.38	0.023	0.697	0.001
ADFI, lb		1.89	1.89	2.01	2.06	0.032	0.386	0.001
F/G		1.49	1.49	1.48	1.49	0.013	0.551	0.496
d 0 to 28								
ADG, lb		0.91	0.93	1.01	1.03	0.020	0.171	0.001
ADFI, lb		1.33	1.35	1.43	1.47	0.024	0.121	0.001
F/G		1.46	1.45	1.42	1.42	0.010	0.784	0.001
BW, lb								
d 0		16.3	16.3	16.3	16.3	0.144	0.717	0.262
d 14		23.9	24.8	25.3	26.0	0.335	0.011	0.001
d 28		41.7	42.8	44.3	45.3	0.554	0.035	0.001
Economics ⁶								
Feed cost per pig, \$		6.15	6.36	6.85	7.17	0.113	0.013	0.001
Feed cost per lb gain, ⁷ \$		0.245	0.244	0.246	0.247	0.002	1.000	0.157
Value of gain per pig, ⁸ \$		10.65	11.12	11.76	12.17	0.238	0.035	0.001
IOFC, ⁹ \$		4.50	4.76	4.91	5.00	0.144	0.168	0.015

¹ A total of 320 pigs (DNA 200 × 400, Columbus, NE; 16.3 lb BW) were used in a 28-d nursery trial with 5 pigs per pen and 8 replicates (pair of pens) per treatment.

² Pigs were weaned at approximately 21 d of age, a common starter diet was fed for 7 d after weaning, and dietary treatments were fed in one phase for the following 28 d. On d 14 of trial, CTC was removed from the diets to comply with FDA guidelines and resumed feeding on d 15.

³ There was no evidence for an interactive effect of Cu and CTC for any of the performance and economic variables throughout the trial ($P > 0.10$).

⁴ Copper (Cu) as Cu sulfate.

⁵ Chlortetracycline (CTC) as CTC-50 (Zoetis Services, LLC., Florham Park, NJ).

⁶ Corn was valued at \$3.30/bu (\$118/ton), soybean meal at \$290/ton, Cu sulfate at \$1.02/lb, and CTC at \$1.65/lb.

⁷ Feed cost per lb gain = total feed cost/total gain per pig.

⁸ Value of gain per pig = (BW d 28 – BW d 0) × \$0.42.

⁹ Income over feed cost = value of gain per pig – feed cost per pig.

Table 4. Main effects of Cu and CTC level on growth performance of nursery pigs^{1,2}

Item	Cu, ppm ³		SEM	Probability, <i>P</i> <	CTC, ppm ⁴		SEM	Probability, <i>P</i> <
	0	200			0	440		
d 0 to 14								
ADG, lb	0.60	0.65	0.017	0.025	0.58	0.67	0.017	0.001
ADFI, lb	0.80	0.85	0.016	0.011	0.79	0.86	0.016	0.004
F/G	1.34	1.32	0.016	0.507	1.38	1.29	0.015	0.001
d 14 to 28								
ADG, lb	1.31	1.32	0.017	0.693	1.27	1.37	0.017	0.001
ADFI, lb	1.95	1.97	0.026	0.386	1.89	2.03	0.026	0.001
F/G	1.48	1.49	0.009	0.545	1.49	1.48	0.009	0.490
d 0 to 28								
ADG, lb	0.96	0.98	0.014	0.168	0.92	1.02	0.013	0.001
ADFI, lb	1.38	1.41	0.018	0.111	1.34	1.45	0.017	0.001
F/G	1.44	1.44	0.007	0.782	1.46	1.42	0.007	0.001
BW, lb								
d 0	16.3	16.3	0.143	0.710	16.3	16.3	0.143	0.251
d 14	24.6	25.4	0.268	0.009	24.4	25.6	0.268	0.001
d 28	43.0	44.1	0.444	0.030	42.3	44.8	0.444	0.001
Economics ⁵								
Feed cost per pig, \$	6.50	6.77	0.089	0.012	6.25	7.01	0.089	0.001
Feed cost per lb gain, ⁶ \$	0.246	0.246	0.001	1.000	0.244	0.247	0.001	0.152
Value of gain per pig, ⁷ \$	11.21	11.65	0.192	0.031	10.88	11.97	0.192	0.001
IOFC, ⁸ \$	4.71	4.88	0.114	0.163	4.63	4.96	0.114	0.014

¹ A total of 320 pigs (DNA 200 × 400, Columbus, NE; 16.3 lb BW) were used in a 28-d nursery trial with 5 pigs per pen and 8 replicates (pair of pens) per treatment. Thus, there were 16 replicates for main effects.

² Pigs were weaned at approximately 21 d of age, a common starter diet was fed for 7 d after weaning, and dietary treatments were fed in one phase for the following 28 d. On d 14 of trial, CTC was removed from the diets to comply with FDA guidelines and resumed feeding on d 15.

³ Copper (Cu) as Cu sulfate.

⁴ Chlortetracycline (CTC) as CTC-50 (Zoetis Services, LLC., Florham Park, NJ).

⁵ Corn was valued at \$3.30/bu (\$118/ton), soybean meal at \$290/ton, Cu sulfate at \$1.02/lb, and CTC at \$1.65/lb.

⁶ Feed cost per lb gain = total feed cost/total gain per pig.

⁷ Value of gain per pig = (BW d 28 – BW d 0) × \$0.42.

⁸ Income over feed cost = value of gain per pig – feed cost per pig.