Asian Journal of Animal and Veterinary Advances 8 (3): 502-510, 2013
ISSN 1683-9919 / DOI: 10.3923/ajava.2013.502.510

Effects of Dietary Capsulated Zinc Oxide on Growth Performance, Blood Metabolism and Mineral Concentrations in Weaning Piglets

C. Wang, P. Xie, L.L. Liu, J.J. Lu and X.T. Zou

Institute of Feed Science, College of Animal Science, Zhejiang University, Key Laboratory of Molecular Animal Nutrition, Ministry of Education, NO. 388 Yuhang Tang Road Hangzhou Zhejiang Province, 310058, China

Corresponding Authors: Jian-Jun Lu and Xiao-Ting Zou, Institute of Feed Science, College of Animal Science, Zhejiang University, Key Laboratory of Molecular Animal Nutrition, Ministry of Education, NO. 388 Yuhang Tang Road Hangzhou Zhejiang Province, 310058, China Tel: +86-571-88982729 Fax: 86-571-88982650

ABSTRACT

The objective of this study was to evaluate effects of various dietary concentrations of capsulated zinc oxide (C-ZnO) on growth performance, blood metabolism and mineral concentrations in weaning piglets. In this study, a total of 144 crossbred piglets (Duroc×Landrance×Yorkshire) were randomly assigned into 6 groups. One of six treatments was fed the basal diet supplemented with 0 (the control), 281.25, 562.5, 1125 and 2250 mg kg^{-1} zinc as C-ZnO and 2250 mg kg^{-1} zinc as zinc oxide (ZnO) for 21 days. Results indicated that compared to the control, dietary supplementation of C-ZnO (≥562.5 mg kg^{-1} zinc) and ZnO (2250 mg kg^{-1} zinc) increased ($p<0.05$) the average daily gain, decreased ($p<0.05$) the feed: gain ratio as well as serum urea nitrogen concentration. Lower levels of zinc as C-ZnO (281.25-1125 mg kg^{-1} zinc) decreased ($p<0.05$) the zinc concentrations in liver, kidney and feces compared with 2250 mg kg^{-1} zinc as ZnO. These results showed that lower levels (281.25-1125 mg kg^{-1}) of zinc as C-ZnO enhanced growth performance, altered blood metabolism and decreased fecal zinc excretion in weaning piglets compared to pharmacological concentration of zinc as ZnO.

Key words: Capsulated zinc oxide, weaning piglet, growth performance, blood metabolism, mineral concentration

INTRODUCTION

Zinc is an important trace element in animals and human and participates in many enzymes to modulate the metabolism (O'Dell, 2000). The requirement of zinc for nursery pigs is 100 mg kg^{-1} (NRC, 1998). However, it was reported that pharmacological concentrations of zinc as zinc oxide (ZnO) could improve growth performance of weaning piglets (Hahn and Baker, 1993; Poulsen, 1995). Subsequently, the efficacy of 2000-4000 mg kg^{-1} zinc from ZnO was further documented by the results of Smith *et al.* (1997), Hill *et al.* (2000) and Carlson *et al.* (2004). It was believed that ZnO was the only inorganic form of zinc known to improve the growth performance in early weaning piglets as fed on diets supplemented with pharmacological doses (Hahn and Baker, 1993; McCully *et al.*, 1995; Smith *et al.*, 1997). However, large quantities of zinc were found in feces resulted from high dietary ZnO, which could cause increased zinc in soil when the manure was applied as the crop fertilizer and produced metal toxicity to plants and soil microorganisms (Jongbloed and Lenis, 1998; Jondreville *et al.*, 2003; Carlson *et al.*, 2004).

Recent studies has documented that dietary supplementation with lower levels of organic zinc and Capsulated Zinc Oxide (C-ZnO) maintained the growth performance in weaning piglets compared with supplementation with pharmacological concentrations of zinc as ZnO (Case and Carlson, 2002; Wang *et al*., 2009, 2012a; Kim *et al*., 2010). Case and Carlson (2002) and Wang *et al*. (2009) reported that lower concentrations of organic zinc could markedly reduce the fecal zinc concentrations compared to pharmacological concentrations of zinc as ZnO. However, experiments about the fecal mineral concentrations in weaning piglets fed with lower levels of zinc from C-ZnO have not been conducted.

Therefore, objectives of the present study were to determine the fecal, blood and tissues mineral (Zn, Cu, Fe and Mn) concentrations and further to evaluate the growth performance and blood metabolism in weaning piglets fed various levels of zinc as C-ZnO.

MATERIALS AND METHODS

During this 21st day trial (from 6th December 2011 to 27th December 2011), all the experimental procedures were approved by the Zhejiang University Animal Care and Use Committee (Zhejiang, China).

Animals and experimental design: A total of 144 piglets (Duroc×Landrance×Yorkshire) with an average body weight of 8.46 kg (SEM = 0.23) were randomly allotted into 6 groups on the basis of weight and sex. Each group had 3 replicates, 8 piglets per replicate. This trial lasted for 21 days. During this trial, piglets were fed with different diets as follows: (1) The control (base diet), (2) Basal diet+281.25 mg kg^{-1} zinc as C-ZnO, (3) Basal diet+562.5 mg kg^{-1} zinc as C-ZnO, (4) Basal diet+1125 mg kg^{-1} zinc as C-ZnO, (5) Basal diet+2250 mg kg^{-1} zinc as C-ZnO and (6) ZnO group (supplementation with 2250 mg kg^{-1} zinc as ZnO). The ZnO and C-ZnO were both provided by Hangzhou King Techina Technology CO., Ltd. (Zhejiang, China). The basal diet was corn-soybean meal-based diet, which was formulated to meet or exceed the requirement of nutrients as recommended by NRC (1998) as shown in Table 1.

Pigs were housed on the concrete floors and had *ad libitum* access to water and feed. Body weight and feed consumption were weighed to evaluate the Average Daily Gain (ADG), Average Daily Intake (ADFI) and feed: Gain ratio (F:G).

Sample collection: At the end of 21-day trial, 6 pigs (fasted for 12 h) from each treatment (2 pigs per replicate) were randomly selected to draw blood samples by jugular vein using heparinized and plain vacutainer tubes and then were slaughtered humanely to collect tissue samples. Blood samples were centrifuged at 3000×g for 15 min at 4°C to obtain the serum. The serum samples were stored at -80°C until needed for analysis. The tissues, including liver, kidney and longissimus muscle and fecal samples were collected, weighed, dried and stored at -80°C until for the determination of mineral concentration.

Analysis of blood metabolism: The serum concentrations of Total Protein (TP), Urea Nitrogen (UN), Albumin (ALB), Ca and P, Zn Cu, Fe and Mn and activities of Glutamic-Oxalacetic Transaminase (GOT) and Glutamic-Pyruvic Transaminase (GPT) in serum were determined by corresponding commercial kits provided by Nanjing Jiancheng Bioengineering Institute (Nanjing, China). These concentrations were analyzed with the corresponded procedure of each kit as recommended by the manufacturers.

Table 1: Chemical composition of the basal diet

Item	%
Ingredient	
Corn	54.27
Soybean meal (45% CP)	19.0
Soybean oil	1.6
Extruded full-fat soybean	12.0
Fish meal (63% CP)	4.0
Dried whey	4.0
Dicalcium phosphate	2.0
Limestone	1.0
Sodium chloride	0.25
L-lysine HCl (78%)	0.28
Methionine (98.5%)	0.6
Vitamin-mineral premix[1]	1.0
Analysed chemical composition as feed	
DE, MJ kg^{-2}	14.40
Crude protein	20.39
Lysine	1.30
Met.+Cyst.	0.82
Threonine	0.90
Calcium	0.90
Total phosphorus	0.63

[1]The vitamin-mineral premix provided, per kg feed: Vitamin A 4000 IU, vitamin, D_3 800 IU, vitamin. E 10 IU, vitamin. K_3 0.5 mg, biotin 0.05 mg, folic acid 0.3 mg, niacin 10 mg, d-pantothenic acid 10 mg, riboflavin 3.6 mg thiamine 1.0 mg, pyridoxine 1.5 mg, cobalamin 15 mg, Mn ($MnSO_4 \cdot H_2O$) 10 mg, Zn ($ZnSO_4 \cdot 7H_2O$) 80 mg, Fe ($FeSO_4 \cdot 7H_2O$) 80 mg, Cu ($CuSO_4 \cdot 5H_2O$) 15.0 mg, I (KI) 0.14 mg and Se (Na_2SeO_3) 0.15 mg, [2]DE (digestible energy) was based on calculated values

Determination of tissue and fecal mineral concentration: The tissue samples were prepared from the selected liver, kidney and muscle as described by Hill *et al.* (1983). Briefly, uniform samples were cut from the tissues and were wet-digested using nitric and perchloric acids and were diluted with deionized-distilled water. For fecal samples, dried fecal sample was dissolved with nitric acid and was digested using a microwave digestion system (Armstrong *et al.*, 2004). The mineral concentrations of Zn, Cu, Fe and Mn were determined with the Flame Atomic Absorption spectrophotometry (AA-6300, Shimadzu, Tokyo, Japan).

Statistical analysis: The data were analyzed by using the ANOVA procedures of the SPSS statistical package for Windows 16.0 (SPSS Inc., Chicago, IL). The replicate was considered as the experimental unit for growth performance analysis and the individual pig was the unit for determination of blood metabolism and mineral concentration. The p-value below 0.05 was considered as significant differences among treatments.

RESULTS

Growth performance: Table 2 displayed the effects of C-ZnO on growth performance. The results indicated that compared to the control, dietary supplementation of C-ZnO (≥562.5 mg kg^{-1} zinc) increased the ADG ($p<0.05$) and decreased the F/G ($p<0.05$), but did not affect the ADFI ($p>0.05$). There was no significant difference between pigs fed pharmacological dose of zinc as ZnO and those fed with additional zinc as C-ZnO ($p>0.05$).

Table 2: Effects of different levels of C-ZnO on growth performance of weaning piglets

	C-ZnO (mg kg^{-1})					ZnO (mg kg^{-1})	p-value*			
Item	0	281.25	562.5	1125	2250	2250	Control vs. C-ZnO	ZnO vs. C-ZnO	Linear	Quadratic
Initial weight (kg)	8.59	08.038	08.030	08.062	08.031	08.055	0.490	0.032	0.053	0.72
Final weight (kg)	11.75	11.084	12.024	12.071	12.036	12.068	0.040	0.012	0.008	0.30
ADG (kg)	0.150	00.165	00.188	00.195	00.193	00.196	0.004	0.058	<0.001	0.09
ADFI (kg)	0.295	00.297	00.322	00.316	00.322	00.340	0.051	0.056	0.009	0.42
F:G	1.965	01.806	01.713	01.562	01.676	01.072	0.002	0.124	<0.001	0.27

Each least squares mean represents 3 pens of 8 pig/pen, *Control vs Cr-CNP treated represents the contrast between pigs in control group with pigs fed 281.25, 562.5, 1125 and 2250 mg kg^{-1} C-ZnO, ZnO vs Cr-CNP treated represents the contrast between pigs in ZnO group with pigs fed 281.25, 562.5, 1125 and 2250 mg kg^{-1} C-ZnO , **ADG: Average daily gain, ADFI: Average daily feed, intake, F: G: Feed: Gain ratio

Table 3: Effects of different levels of C-ZnO on blood metabolism of weaning piglets

	C-ZnO (mg kg^{-1})					ZnO (mg kg^{-1})	p-value*			
Item	0	281.25	562.5	1125	2250	2250	Control vs. C-ZnO	ZnO vs. C-ZnO	Linear	Quadratic
TP (g L^{-1})	56.05	57.15	60.32	58.68	58.56	60.77	0.75	0.75	0.43	0.21
ALB (g L^{-1})	39.4	35.55	37.35	37.35	37.37	39.94	0.85	0.79	0.61	0.86
UN (mmol L^{-1})	4.20	3.44	3.40	3.39	3.57	3.48	0.001	0.91	0.005	0.315
GOT (IU L^{-1})	70.84	70.68	69.95	72.26	72.87	73.22	0.74	0.72	0.35	0.44
GPT (IU L^{-1})	23.54	24.28	23.69	22.91	24.16	25.11	0.95	0.81	0.97	0.99
Ca (mmol L^{-1})	1.25	1.32	1.23	1.26	1.20	1.26	0.94	0.90	0.59	0.66
P (mmol L^{-1})	2.77	2.94	2.82	2.91	2.95	3.00	0.89	0.91	0.54	0.90

Each least squares mean represents 6 pigs, *Control vs Cr-CNP treated represents the contrast between pigs in control group with pigs fed 281.25, 562.5, 1125 and 2250 mg kg^{-1} C-ZnO, ZnO vs Cr-CNP treated represents the contrast between pigs in ZnO group with pigs fed 281.25, 562.5, 1125 and 2250 mg kg^{-1} C-ZnO, **TP: Total proteinm ALB: Albumin, UN: Urea Nitrogen, OT: Glutamic-oxalacetic transaminase, GPT: Glutamic-pyruvic transaminase

Blood metabolism: Effects of C-ZnO on blood metabolism are shown in Table 3, which showed that the concentrations of TP, ALB, Ca and P and activities of GOT and GPT in serum were not affected by additional ZnO and C-ZnO ($p>0.05$). However, pigs fed diets supplemented with ZnO and C-ZnO decreased serum urea nitrogen concentration ($p<0.05$).

Serum and tissue mineral concentration: Effects of C-ZnO on serum and tissue mineral concentration are presented in Table 4. These results indicated that compared with those of the control, pigs fed diets with additional 2250 mg kg^{-1} zinc as ZnO and ≥1125 mg kg^{-1} zinc as C-ZnO increased serum zinc concentrations ($p<0.05$). However, the serum concentrations of Cu, Fe and Mn were not affected by dietary supplemental zinc ($p>0.05$).

In addition, Table 4 also showed that the contents of Cu, Fe and Mn in liver, kidney and muscle were not altered by supplemental zinc ($p>0.05$). Compared with the pigs of the control, dietary supplemental zinc as ZnO and C-ZnO increased ($p<0.05$) the zinc concentrations in liver and kidney, but did not affect ($p>0.05$) zinc concentration in muscle.

Feces mineral concentration: Effects of C-ZnO on feces mineral concentration are shown in Table 5. Results showed that additional zinc from both ZnO and C-ZnO increased fecal zinc

Table 4: Effects of different levels of C-ZnO on mineral concentrations in serum, liver, kidney and muscle of weaning piglets

	C-ZnO (mg kg^{-1})					ZnO (mg kg^{-1})	p-value*			
Item	0	281.25	562.5	1125	2250	2250	Control vs. C-ZnO	ZnO vs. C-ZnO	Linear	Quadratic
Serum										
Zn (μmol L^{-1})	20.85	23.01	27.33	28.49	30.37	28.32	0.004	0.07	<0.001	0.28
Cu (μmol L^{-1})	29.26	29.32	29.33	28.47	28.31	28.06	0.92	0.86	0.39	0.55
Fe (μmol L^{-1})	29.80	28.27	25.44	26.37	25.92	26.98	0.76	0.96	0.23	0.65
Mn (mg L^{-1})	1.10	1.08	1.03	1.16	1.05	0.95	0.66	0.46	0.59	0.66
Liver										
Zn (mg L^{-1})	58.50	64.50	106.4	254.48	433.4	471.47	<0.001	<0.001	<0.001	<0.001
Cu (mg L^{-1})	12.98	13.38	13.13	12.63	12.09	12.69	0.24	0.19	0.09	0.23
Fe (mg L^{-1})	75.09	69.05	70.86	70.16	72.95	72.74	0.18	0.56	0.59	0.06
Mn (mg L^{-1})	2.06	1.99	2.05	1.99	2.02	1.99	0.85	0.91	0.63	0.82
Kidney										
Zn (mg L^{-1})	18.78	19.15	24.67	43.21	62.16	59.08	<0.001	<0.001	<0.001	<0.001
Cu (mg L^{-1})	5.19	5.05	6.04	5.78	5.24	5.08	0.07	0.11	0.34	0.06
Fe (mg L^{-1})	56.13	58.65	52.14	53.16	51.35	51.13	0.30	0.13	0.10	0.82
Mn (mg L^{-1})	2.12	2.23	2.16	2.12	2.07	2.09	0.68	0.59	0.37	0.29
Muscle										
Zn (mg L^{-1})	18.87	19.93	19.82	19.76	19.37	19.55	0.65	0.96	0.52	0.34
Cu (mg L^{-1})	1.35	1.36	1.30	1.28	1.32	1.31	0.51	0.79	0.22	0.57
Fe (mg L^{-1})	69.27	71.06	67.65	67.91	69.32	69.68	0.82	0.84	0.69	0.65
Mn (mg L^{-1})	1.09	1.17	1.18	1.19	1.16	1.11	0.48	0.68	0.27	0.18

Each least squares mean represents 6 pigs, *Control vs Cr-CNP treated represents the contrast between pigs in control group with pigs fed 281.25, 562.5, 1125 and 2250 mg kg^{-1} C-ZnO; ZnO vs Cr-CNP treated represents the contrast between pigs in ZnO group with pigs fed 281.25, 562.5, 1125 and 2250 mg kg^{-1} C-ZnO

Table 5: Effects of different levels of C-ZnO on fecal mineral concentration of weaning piglets

	C-ZnO (mg kg^{-1})					ZnO (mg kg^{-1})	p-value *			
Item	0	281.25	562.5	1125	2250	2250	Control vs. C-ZnO	ZnO vs. C-ZnO	Linear	Quadratic
Zn (mg L^{-1})	2350.1	3664.9	7147.6	10767.0	17324.0	16092.0	<0.001	<0.001	<0.01	<0.01
Cu (mg L^{-1})	319.5	0305.0	0304.0	00306.7	00319.5	00310.9	0.024	0.032	0.42	0.69
Fe (mg L^{-1})	2843	2932.0	2865.0	02890.0	02908.0	02887.0	0.087	0.094	0.66	0.91
Mn (mg L^{-1})	339.5	0305.7	0323.5	00333.8	00322.7	00320.8	0.014	0.040	0.85	0.62

Each least squares mean represents 6 pigs, *Control vs Cr-CNP treated represents the contrast between pigs in control group with pigs fed 281.25, 562.5, 1125 and 2250 mg kg^{-1} C-ZnO, ZnO vs Cr-CNP treated represents the contrast between pigs in ZnO group with pigs fed 281.25, 562.5, 1125 and 2250 mg kg^{-1} C-ZnO

concentration ($p<0.05$), but did not change fecal concentrations of Cu, Fe and Mn ($p>0.05$). Compared with the pig in the ZnO group, supplemental C-ZnO (≥1125 mg kg^{-1} zinc) decreased the fecal zinc concentrations ($p<0.05$).

DISCUSSION

The efficacy of pharmacological of dietary zinc on weaning pig's growth performance has been documented by previous researches (Hahn and Baker, 1993; Smith *et al*., 1997; Hill *et al*., 2000). High doses (2000-3000 mg kg^{-1}) zinc as ZnO are widely used in nursery pigs as growth promotants, although, Hill *et al*. (2001) and Case and Carlson (2002) reported 1500 mg kg^{-1} zinc had the similar

growth response Results of present study indicated that feeding pharmacological concentration (2250 mg kg^{-1}) zinc as ZnO and concentrations (≥562.5 mg kg^{-1}) of zinc as C-ZnO improved growth performance in weaning piglets compared with the pigs receiving the control diet, which supported the previous findings (Case and Carlson, 2002; Kim *et al*., 2010). Kim *et al*. (2010) reported that lower level of zinc from C-ZnO could enhance growth performance and may be an alternation to pharmacological concentration of ZnO, but the level for enhanced growth response was different from our present study. The reason for the difference in levels for enhanced growth performance may contribute to different sources of C-ZnO. At mean while, the authors speculated that one of the possible mechanisms for the beneficial effects of C-ZnO on growth was that zinc was delivered to the ideal location in gastrointestinal tract for maximum effectiveness (Kim *et al*., 2010). However, more researches are still needed in future.

Activities of GOT and GPT and concentrations of Ca and P in serum were determined to get an indication of possible zinc toxicity (Wang *et al*., 2012b). However, their concentrations and activities were not affected by zinc from ZnO or C-ZnO. Serum UN concentration was decreased by dietary ZnO and C-ZnO, which supported the previous finding that zinc could modulate the protein metabolism (O'Dell, 2000).

Serum zinc concentration were increased by dietary ZnO (2250 mg kg^{-1} zinc) and C-ZnO (2250 and 1125 mg kg^{-1} zinc) in present study, which partly supported the positive relationship between serum zinc and ADG when zinc concentrations were below 38 μmoL L^{-1} (Hahn and Baker, 1993; Carlson *et al*., 1999). However, the biological mechanisms behind the increased serum zinc concentration are still not clear. Carlson *et al*. (1999) reported that dietary supplementation with zinc could significantly increase the intestinal mucosa metallothionein concentration and further affect the amount of zinc that is transferred across the basolateral membrane into circulation (Richards and Cousins, 1975). Serum Cu, Fe and Mn concentrations were unaffected by additional zinc, which were in line with results of (Carlson *et al*., 1999 and Wang *et al*., 2012a). However, Wang *et al*. (2009) reported that 3000 mg kg^{-1} zinc as ZnO could increase the serum Cu concentration.

In present study, concentrations of zinc in liver and kidney were increased by dietary supplemental zinc, which supported the previous studies conducted by (Schell and Kornegay, 1996; Carlson *et al*., 1999; Case and Carlson, 2002). They reported that levels of zinc in liver and kidney in pigs fed 2000-3000 mg kg^{-1} zinc as ZnO were higher than those in pigs receiving the adequate zinc. Results of Schell and Kornegay (1996) also indicated that feeding 2000 mg kg^{-1} zinc as Zn-methionine, Zn-lysine, or ZnSO4 significantly increased the liver and kidney zinc concentration compared with pigs fed basal diet containing 105 mg kg^{-1} zinc. These results indicate that liver and kidney play an important role in homeostatic regulation of zinc. In our present study, the zinc concentration in muscle was not altered by additional zinc as ZnO or C-ZnO, which was consistent with the work of Schell and Kornegay (1996) and Ansari *et al*. (1976), who reported that the degree of variation in the muscle zinc concentration was not large. These results indicated that the muscle tissue may be a poor indicator for zinc status.

Feeding pharmacological concentrations of zinc as ZnO could enhance the growth in nursery pigs. However, the increased fecal zinc will produce metal toxicity to plants and soil microorganisms as the mature is applied (L'Herroux *et al*., 1997; Jondreville *et al*., 2003). Carlson *et al*. (2004) reported that fecal excretion of zinc was directly related to the amount of zinc consumed regardless of zinc source. Therefore, many researches were conducted to decrease fecal zinc concentration by replacing dietary high zinc as ZnO with lower zinc from other zinc sources, including organic zinc

and C-ZnO (Case and Carlson, 2002; Kim *et al*., 2010). Results of Buff *et al*. (2005) showed that fecal zinc concentration was reduced 76% by feeding 300 mg kg^{-1} zinc as zinc-polysaccharide compared with 2000 mg kg^{-1} zinc as ZnO. Here we showed that the fecal zinc concentrations in pigs fed lower levels of C-ZnO (281.25-1125 mg kg^{-1} zinc) were lower than those in pigs receiving pharmacological concentration of zinc as ZnO, which were similar to the work of Wang *et al*., 2012a).

It's well known that there is antagonism between zinc and Cu (Van Campen and Scaife, 1967; Hall *et al*., 1979; Fischer *et al*., 1981). However, the Cu, Fe and Mn concentrations in liver, kidney, muscle and feces were unaffected by supplemental zinc in present study. As speculated by Klevay *et al*. (1994) and Buff *et al*. (2005), no Zn-Cu antagonism in present study may be due to the high level of copper (at approximately 300% of NRC, 1998) requirement) in our basal diet.

CONCLUSION

Results of present study indicated that diets supplemented with 562.5, 1125 and 2250 mg kg^{-1} of zinc as C-ZnO and 2250 mg kg^{-1} zinc as ZnO could enhance growth performance and alter blood metabolism compared to the basal diet. Pigs fed lower level of zinc (562.5, 1125 and 2250 mg kg^{-1}) as C-ZnO had lower fecal zinc concentration than those receiving pharmacological level of zinc as ZnO. These results suggested that C-ZnO could be a good source of zinc for weanling piglets.

ACKNOWLEDGMENT

This work was financially supported by Hangzhou King Techina Technology CO., Ltd and National Natural Funds of China (No. 31072038).

REFERENCES

Ansari, M.S., W.J. Miller, M.W. Neathery, J.W. Lassiter, R.P. Gentry and R.L. Kincaid, 1976. Zinc metabolism and homeostasis in rats fed a wide range of high dietary zinc levels. Proc. Soc. Exp. Biol. Med., 152: 192-194.

Armstrong, T.A., D.R. Cook, M.M. Ward, C.M. Williams and J.W. Spears, 2004. Effect of dietary copper source (cupric citrate and cupric sulfate) and concentration on growth performance and fecal copper excretion in weanling pigs. J. Anim. Sci., 82: 1234-1240.

Buff, C.E., D.W. Bollinger, M.R. Ellersieck, W.A. Brommelsiek and T.L. Veum, 2005. Comparison of growth performance and zinc absorption, retention and excretion in weanling pigs fed diets supplemented with zinc-polysaccharide or zinc oxide. J. Anim. Sci., 83: 2380-2386.

Carlson, M.S., C.A. Boren, C. Wu, C.E. Huntington, D.W. Bollinger and T.L. Veum, 2004. Evaluation of various inclusion rates of organic zinc either as polysaccharide or proteinate complex on the growth performance, plasma and excretion of nursery pigs. J. Anim. Sci., 82: 1359-1366.

Carlson, M.S., G.M. Hill and J.E. Link, 1999. Early-and traditionally weaned nursery pigs benefit from phase-feeding pharmacological concentrations of zinc oxide: Effect on metallothionein and mineral concentrations. J. Anim. Sci., 77: 1199-1207.

Case, C.L. and M.S. Carlson, 2002. Effect of feeding organic and inorganic sources of additional zinc on growth performance and zinc balance in nursery pigs. J. Anim. Sci., 80: 1917-1924.

Fischer, P.W., A. Giroux and M.R. L'Abbe, 1981. The effect of dietary zinc on intestinal copper absorption. Am. J. Clin. Nutr., 34: 1670-1675.

Hahn, J.D. and D.H. Baker, 1993. Growth and plasma zinc responses of young pigs fed pharmacologic levels of zinc. J. Anim. Sci., 71: 3020-3024.

Hall, A.C., B.W. Young and I. Bremner, 1979. Intestinal metallothionein and the mutual antagonism between copper and zinc in the rat. J. Inorg. Biochem., 11: 57-66.

Hill, G.M., D.C. Mahan, S.D. Carter, G.L. Cromwell and R.C. Ewan *et al*., 2001. Effect of pharmacological concentrations of zinc oxide with or without the inclusion of an antibacterial agent on nursery pig performance. J. Anim. Sci., 79: 934-941.

Hill, G.M., E.R. Miller, P.A. Whetter and D.E. Ullrey, 1983. Concentration of minerals in tissues of pigs from dams fed different levels of dietary zinc. J. Anim. Sci., 57: 130-138.

Hill, G.M., G.L. Cromwell, T.D. Crenshaw, C.R. Dove and R.C. Ewan *et al*., 2000. Growth promotion effects and plasma changes from feeding high dietary concentrations of zinc and copper to weanling pigs (regional study). J. Anim. Sci., 78: 1010-1016.

Jondreville, C., P.S. Revy and J.Y. Dourmand, 2003. Dietary means to better control the environmental impact of copper and zinc by pigs from weaning to slaughter. Livest. Prod. Sci., 84: 147-156.

Jongbloed, A.W. and N.P. Lenis, 1998. Environmental concerns about animal manure. J. Anim. Sci., 76: 2641-2648.

Kim, J.C., C.F. Hansen, J.R. Pluske and B.P. Mullan, 2010. Evaluating the replacement of zinc oxide with an encapsulated zinc oxide product as a means of controlling post-weaning diarrhoea in piglets. Project 2C-114, Co-Operative Research Centre for an Internationally Competitive Pork Industry, pp: 1-16.

Klevay, L., W. Pond and D. Medeiros, 1994. Decreased high density lipoprotein cholesterol and apoprotein A-1 in plasma and ultra structural pathology in cardiac muscle of young pigs fed a diet high in zinc. Nutr. Res., 14: 1227-1239.

L'Herroux, L., S. Le Roux, P. Appriou and J. Martinez, 1997. Behaviour of metals following intensive pig slurry applications to a natural field treatment process in Brittany (France). Environ. Pollut., 97: 119-130.

McCully, G.A., G.M. Hill, J.E. Link, R.L. Weaver, M.S. Carlson and D.W. Rozeboom, 1995. Evaluation of zinc sources for the newly weaned pig. J. Anim. Sci., 73: 72-72.

NRC, 1998. Nutrient Requirements of Swine. 10th Edn., National Academy Press, National Research Council, Washington, DC., USA.

O'Dell, B.L., 2000. Role of zinc in plasma membrane function. J. Nutr., 130: 1432S-1436S.

Poulsen, H.D., 1995. Zinc oxide for weanling piglets. Acta Agric. Scand. Sect. A-Anim. Sci., 45: 159-167.

Richards, M.P. and R.J. Cousins, 1975. Mammalian zinc homeostasis: Requirement for RNA and metallothionein synthesis. Biochem. Biophys. Res. Commun., 64: 1215-1223.

Schell, T.C. and E.T. Kornegay, 1996. Zinc concentration in tissues and performance of weanling pigs fed pharmacological levels of zinc from ZnO, Zn-methionine, Zn-lysine, or $ZnSO_4$. J. Anim. Sci., 74: 1584-1593.

Smith, J.W., M.D. Tokach, R.D. Goodband, J.L. Nelssen and B.T. Richert, 1997. Effets of the interrelationships between zinc oxide and copper sulfate on growth performance of early-weaned pigs. J. Anim. Sci., 75: 1861-1866.

Van Campen, D.R. and P.U. Scaife, 1967. Zinc interference with copper absorption in rats. J. Nutr., 91: 473-476.

Wang, C., P. Xie, L.L. Liu, X.Y. Dong, J.J. Lu and X.T. Zou, 2012a. Use of lower level of capsulated zinc oxide as an alternative to pharmacological dose of zinc oxide for weaned piglets. Asian J. Anim. Vet. Adv., 7: 1290-1300.

Wang, M.Q., C. Wang, H. Li, Y.J. Du, W.J. Tao, S.S. Ye and Y.D. He, 2012b. Effects of chromium-loaded chitosan nanoparticles on growth, blood metabolites, immune traits and tissue chromium in finishing pigs. Biol. Trace. Elem. Res., 149: 197-203.

Wang, Y., J.W. Tang, W.Q. Ma, J. Feng and J. Feng, 2009. Dietary zinc glycine chelate on growth performance, tissue mineral concentrations and serum enzyme activity in weanling piglets. Biol. Trace Elem. Res., 133: 325-334.