Original Article. May-August 2018; 8(2): 68-80. Received: 2018/02/ 27Accepted: 2018/03/28.
http://dx.doi.org/10.21929/abavet2018.82.6

Method of supplementation of organic zinc and productive response of pigs in initiation stage in warm weather

Método de suplementación de zinc orgánico y respuesta productiva de cerdos en etapa de iniciación en clima cálido

Romo-Valdez Juan romo_14@hotmail.com, Barajas-Cruz Rubén rubar@uas.edu.mx, Silva-Hidalgo Gabriela gabsilhid@uas.edu.mx, Enríquez-Verdugo Idalia idaliaenver@yahoo.com, Güémez-Gaxiola Héctor hectorguem@gmail.com, *Romo-Rubio Javier romo60@uas.edu.mx

Faculty of Veterinary Medicine and Zootechnics of the Autonomous University of Sinaloa. Mexico. * Responsible and correspondence author: Romo-Rubio Javier. Boulevard San Angel s / n, Colonia San Benito, Culiacán, Sinaloa, Mexico, CP 80246.romo60@uas.edu.mx

ABSTRACT

In order to evaluate the productive response of pigs in initiation under conditions of high environmental heat load to organic zinc additional supplementation, 816 piglets (21 days of age and 6.280 ± 0.817 kg of body weight) were used, born of mothers who were supplemented with 0 or 100 mg Zn / kg of diet during pregnancy and lactation, under a randomized complete block design with a 2 x 2 x 2 factorial arrangement. The experiment was carried out during two periods: 1) May-July and 2) September-November; each with duration of 49 days. In each period, 408 piglets were grouped by weight in 3 uniform groups, distributed in 12 pens (6 repetitions / treatment). The levels of additional supplementation tested were 0 and 100 mg Zn/kg of diet and the treatments were: 1) Mothers not supplemented-piglets not supplemented (Control); 2) Mothers not supplemented-supplemented piglets (ZnC); 3) Mothers supplemented-piglets not supplemented (ZnGL) and 4) Mothers supplemented-piglets supplemented (ZnGL + ZnC). The pigs were fed diets that met their nutritional requirements during the experiment. The average THI was 78.19 ± 2.9 during the test period. There was no interaction between treatments on the variables evaluated. Supplementing Zn during the gestation-lactation period tended (P = 0.06) to decrease mortality; however, continuing with additional supplementation during the initiation phase offered no advantage. There were no differences in the other variables evaluated in the supplemented group due to the supplementation method. It is concluded that additional supplementation with 100 mg of Zn from Zn during the gestation-lactation phase help to reduce the mortality in the initiation stage, in piglets bred in warm weather.

Keywords: Zinc methionine, piglets, mortality, productive performance.

RESUMEN

Con el objetivo de evaluar la respuesta productiva de cerdos en etapa de iniciación bajo condiciones de alta carga de calor ambiental a la suplementación adicional con zinc orgánico, se usaron 816 lechones (21 días de edad y 6.280 ±0.817 kg de peso corporal), nacidos de madres que fueron suplementadas con 0 ó 100 mg Zn/kg de dieta durante la gestación y lactación, bajo un diseño de bloques completos al azar con arreglo factorial 2 x 2 x 2. El experimento se realizó en dos periodos: 1) Mayo-julio y 2) Septiembre-noviembre; cada uno con una duración de 49 días. En cada periodo, 408 lechones fueron agruparon por peso en 3 grupos uniformes, distribuidos en 12 corraletas (6 repeticiones/tratamiento). Los niveles de suplementación adicional probados fueron de 0 y 100 mg Zn/kg de dieta y los tratamientos consistieron en: 1) Madres no suplementadas-lechones no suplementados (Testigo); 2) Madres no suplementadas-lechones suplementados (ZnC); 3) Madres suplementadas-lechones no suplementados (ZnGL) y 4) Madres suplementadas-lechones suplementados (ZnGL + ZnC). Los cerdos se alimentaron con dietas que cubrieron sus requerimientos nutrimentales durante el experimento. El THI promedio fue de 78.19±2.9 durante el periodo de prueba. No existió interacción entre tratamientos sobre las variables evaluadas. El suplementar Zn orgánico durante el periodo de gestación-lactación tendió (P=0.06) a disminuir la mortalidad; sin embargo, el continuar con la suplementación adicional durante la fase de iniciación no ofreció ventaja. No existieron diferencias en las otras variables evaluadas en el grupo suplementado debido al método de suplementación. Se concluye que la suplementación adicional con 100 mg de Zn a partir de Metionina de Zinc durante la fase de gestación-lactación ayuda a disminuir la mortalidad en la etapa de iniciación, en lechones criados en clima cálido.

Palabras clave: Metionina de Zinc, lechones, mortalidad, desempeño productivo.

INTRODUCTION

The heat stress induces alterations in the metabolic system (Baumgard and Rhoads, 2013), which includes the decrease in the release of growth hormone and thyroid, causing a reduction in the basal metabolic rate (Aggarwal and Upadhyay, 2013), affecting the expression of genes and proteins involved in the metabolism of energy and nutrients (Sanz *et al*., 2015). Zinc in the form of divalent metal ion, Zn^{2+}, is nutritionally essential for all living organisms (Maret, 2013); it is a trace mineral with proven importance for the function of more than 300 enzymes (Chasapis *et al*., 2012). The metabolic action of Zn includes energy metabolism, protein synthesis, nucleic acid metabolism, epithelial tissue integrity, repair and cell division, transport and utilization of vitamin A and vitamin E absorption (Borah *et al*., 2014).

It has been suggested that Zn is required by the fetus to support cell proliferation, and tissue differentiation in developing organs (Terrin *et al*., 2015). Supplementation with Zn in the diet of the sow during pregnancy and lactation reduces pre-weaning mortality (Payne *et al*., 2006; Romo *et al*., 2017), improves the condition of piglets during lactation (Caine *et al*., 2009) and the immune function of piglets (Romo *et al*., 2017). It has also been suggested that the addition of Zn to the diet prevents reduction and improves intestinal integrity during heat stress (Sanz *et al*., 2014), decreases intestinal permeability in piglets during weaning (Zhang and Guo, 2009).), promotes the restoration of intestinal epithelium (Song *et al*., 2015) and improves protein metabolism in pigs (Pearce *et al.,* 2015).

Because of Zn requirements are increased during heat stress (Lagana *et al*., 2007), it has been suggested that the Zn addition to the diet can be used to attenuate the serum Zn decrease during periods with high environmental temperatures (Li *et al*., 2015). Diets for pigs are generally supplemented with inorganic Zn ($ZnSO_4$ or ZnO) to ensure the required consumption; being $ZnSO_4$ the inorganic source with the highest bioavailability (NRC, 2012). In recent years, the use of organic sources has been explored due to its greater bioavailability (Star *et al*., 2012).

The objective of the present study was to evaluate the effect of supplemental supplementation of organic zinc in the productive response of pigs under initiation, under conditions of high environmental heat load, born to mothers supplemented or not with organic Zn during gestation and lactation.

MATERIAL AND METHODS

The experiment was carried out in the pig farm "La Huerta", located in the Sindicatura de Culiacancito, Culiacán, Sinaloa., with geographic coordinates: 24o

49 '38' North latitude and 107º 22 '47' West longitude. The place has an altitude of 60 meters above sea level (m a.s.l); the climate is classified as very warm semi-dry (BS1 (h ')), with an average annual temperature of 24.9 °C, with maximum temperatures of 45 ºC in the months of July and August and minimums of 7 ºC in December and January. The average rainfall is 671.4 mm, with maximum rainfall in the months of July, August and September.

The work was carried out during the months of May-July (first period) and September to November 2015 (second period); the average temperature during these periods was 28.68 °C and relative humidity 63% (CIAD, 2015). During the test period the pigs were exposed to a temperature and humidity index (THI) of 78.19 ± 2.9, according to Mader *et al*. (2006).

Experimental design. 816 piglets were used with an average age of 21 days and 6,280 ± 0.817 kg of body weight, from a previous study (Romo *et al*., 2017), carried out in sows that received or not food added with 100 mg of organic Zn from zinc methionine (MetZn) / kg of food from 35 days of gestation to the moment of weaning. The piglets were assigned to one of four treatments in an BCA´s experimental design with a 2 x 2 x 2 factorial arrangement, to receive or not, food additionally supplemented with 100 mg of Zn / kg; where the factors were: the method of supplementation (1- supplementation in pregnancy-lactation and 2- supplementation during the period of initiation), the level of additional supplementation of Zn (0 and 100 mg / kg of food) and the study period (1. May-July and 2. September-November).

The treatments were: 1) Mothers not supplemented-piglets not supplemented (control, n = 204); 2) Mothers not supplemented-supplemented piglets (ZnC, n = 204); 3) Mothers supplemented-piglets not supplemented (ZnGL, n = 204) and 4) Mothers supplemented-supplemented piglets (ZnGL + ZnC, n = 204). During the first two weeks after weaning the pigs received commercial feed, Vimifos Fase 1® and Vimifos Fase 2®, to which 100 mg Zn organic / kg was added; the pre-initiation and initiation diets were elaborated in the corn-soybean paste farm. The diets contained the nutritional contribution for each physiological stage (see Tables 3 and 4).

Management of animals. In each study period, the piglets previously weighed and identified were housed in 12 corrals, each with a space of 12 m^2 (8 x 1.5 m); the corral was divided with a feeder of steel type hopper to the center, in such a way that in one of the halves (4 x 1.5 m) 17 females were lodged and in the other 17 males. The corral had steel grid floor, in closed rooms totally roofed and with forced ventilation. Each of the divisions had two metallic pacifier drinking troughs. The pigs had permanent access to drinking water and food at free access. On day

49 after the start of the study the pigs were weighed. The experimental unit was the complete corral.

Measurement. The food served in each corral was registered. At the end of each test period, the pigs of each corral were weighed and with the information of feed consumption and weight gain, the average daily gain in weight and daily feed intake was obtained, as well as the feed conversion. Mortality was also recorded during each study period.

Statistical Analysis. To the variables of food consumption, daily weight gain and feed conversion, an analysis of variance was applied for a randomized complete block design with a 2 x 2 x 2 factorial arrangement. The values of number of deaths and mortality were analyzed by nonparametric statistics with the Kruskall-Wallis test. Contrast analysis was performed to determine the effect of the supplementation method on the variables under study; the contrasts were: Control vs. Treatment 2 (Mothers not supplemented-piglets supplemented) and Treatment 4 (Mothers supplemented-piglets supplemented) and Control vs. Treatment 3 (Mothers supplemented-piglets not supplemented) and Treatment 4 (Mothers supplemented-piglets supplemented). The alpha to accept statistical difference was $P < 0.05$.

RESULTS AND DISCUSSION

The climate conditions during the experiment are shown in Tables 1 and 2. The maximum daily THI exceeded the limit thermo neutral value for the pigs, which is from a THI of 74 (Mader *et al*., 2006) for each day of the study. During period1 (May-July) the pigs were exposed to an average environmental temperature of 29.66 °C and relative humidity of 54.45 %; what according to Mader *et al*. (2006) were in an average THI of 78.49, which indicates a state of physiological alertness; however, during most of the time the experiment lasted they were at a THI higher than 80; which indicates that the pigs were exposed to heat stress. During period 2 (September-November), the pigs were exposed to an average environmental temperature of 27.7 °C and relative humidity of 70.39% (THI = 77.9, physiological alert).

In growing pigs, constant exposure to heat stress markedly increases respiration rates and body temperature, decreases body weight gains and significantly reduces feed intake (Pearce *et al*., 2013b); likewise, it causes a redistribution of blood to the periphery in an attempt to maximize the dissipation of radiant heat; while at the gastrointestinal level vasoconstriction occurs to redefine the blood flow (Lambert, 2008); consequently, the reduction of blood flow and nutrients to the intestinal epithelium compromises the integrity of the intestinal barrier (Yan *et al*., 2006). Pearce *et al*. (2013a) indicated that both caloric stress and reduced food intake decrease intestinal integrity and increase the permeability to endotoxins.

Table 1. Weekly average of relative humidity, room temperature and THI for period 1 (May-July 2015) of the experiment

Week	Aver. RH	Aver.T (°C)	Min T (°C)	Max T (°C)	Aver. THI[1]	Min THI	Max THI
1	52.52	26.48	17.36	37.69	73.92	61.83	88.77
2	47.67	26.89	16.31	38.56	73.88	60.44	88.68
3	57.05	30.60	24.17	39.14	80.13	71.32	91.83
4	56.14	30.84	24.66	39.00	80.31	71.90	91.41
5	55.24	30.81	23.79	39.59	80.12	70.69	91.97
6	55.24	30.81	23.79	39.59	80.12	70.69	91.97
7	57.29	31.20	25.14	39.57	80.94	72.64	92.42
Average	54.45	29.66	22.17	39.02	78.49	68.50	91.01

[1]Temperature and humidity index (THI) = 0.8 × Room temperature + [(% relative humidity ÷ 100) × (Room temperature − 14.4)] + 46.4. THI ranges (normal THI <74; alert 75 a 79; danger 79 a 84; and emergency >84).

Table 2. Weekly average of relative humidity, room temperature and THI for period 2 (September-November 2015) of the experiment

Week	Aver. HR	Aver.T (°C)	Min T (°C)	Max T (°C)	Aver. THI[1]	Min THI	Max THI
1	71.84	30.68	25.51	38.80	82.63	74.81	94.97
2	77.41	27.20	23.16	33.91	77.89	71.60	88.36
3	75.56	28.02	23.50	34.89	79.06	72.05	89.73
4	67.60	28.97	23.16	37.43	79.46	70.89	91.94
5	65.16	27.17	21.00	35.70	76.46	67.55	88.80
6	65.16	27.17	21.00	35.70	76.46	67.55	88.80
7	70.02	24.70	19.57	33.03	73.37	65.69	85.81
Average	70.39	27.70	22.41	35.64	77.90	70.02	89.77

[1]Temperature and humidity index (THI) = 0.8 × Room temperature + [(% relative humidity ÷ 100) × (Room temperature − 14.4)] + 46.4. THI ranges (normal THI <74; alert 75 a 79; danger 79 a 84; and emergency >84).

Table 3. Proximal chemical analysis of the commercial foods offered to weaned piglets in the first 14 days of the study period

Ingredients	[1]Vimifos Fase 1® (7 days)	[2]Vimifos Fase 2® (7 days)
Crude protein (%; minimum)	20	18
Crude fat (%;minimum)	4	3
Crude fiber (%; maximum)	3	3
Humidity (%;maximum)	12	12
Ash (%;maximum)	8	9
E.L.N.	53	55

[1]Control diet (commercial) containing 2064 mg of Zn / kg from an inorganic source; [2]Control diet (commercial) containing 2395 mg of Zn / kg from an inorganic source. To each of the test diets was added 100 mg of Zn from MetZn.

Table 4. Composition and nutritional contribution of the diets offered to the initiation pigs from the 14 post-weaning.

Ingredients	[1]Pre-iniciator (14 days)	[2]Iniciator (21 days)
Maize	603	738
Soybean paste	206	218
Oil	16	12
Vimifos Baby Pig Mix	175	
Mineral premix		32
Nutritional contribution		
E.M.(Mcal Kg^{-1})	3.304	3.355
Protein (%)	18.700	16.949
Lysine (%)	1.271	1.177
Fiber (%)	2.266	2.499
Phosphorus (%)	0.691	0.599
Calcium (%)	0.938	0.693

[1]Control diet containing 1251 mg of Zn/kg from a mineral premix; [2]Control diet that contained 173 mg of Zn/kg from a mineral premix. To each of the test diets was added 100 mg of Zn from MetZn.

Zinc is essential for the normal function of the intestinal barrier and for the regeneration of damaged intestinal epithelium (Zhong *et al*., 2010); Zinc supplementation reduces the intestinal permeability of piglets during weaning (Zhang and Guo, 2009). In addition, Zn participates in the antioxidant defense system of the animal organism and Zn deficiency increases the oxidative damage in the cell membrane, caused by free radicals (Waeytens *et al*., 2009; Wang *et al*., 2013).

The effect of food intake added with Zn methionine during the gestation and lactation stage (GL), by the sow and the piglets during the initiation stage is shown in Table 5. Mortality tended to be lower (P = 0.06) in weaned pigs from sows that consumed food added with 100 mg of Zn / kg of feed during the GL stage.

In a previous work Romo *et al*. (2017), observed that the additional consumption of 100 mg of Zn during the gestation and lactation period, decreased (P = 0.006) the mortality of piglets during lactation (11 vs. 26%); similar results reported Payne *et al*. (2006), who offered food with 100 ppm of $ZnSO_4$ plus the addition of 100 ppm of an organic source of Zn-amino acids (ZnAA), from 15 d of gestation; and during lactation observed a greater survival of piglets during lactation and more piglets weaned per litter. Also, Caine *et al*. (2009), reported that the consumption of diets added with 250 mg / kg of ZnAA by the sows during the last third of gestation, as well as the gastric administration by intubation of 40 mg Zn, from zinc methionine (MetZn) to the lactating piglets at the time of birth, at 7 and 14 d of age, improved the condition of the piglets during lactation.

Table 5. Effect of food consumption added with 100 ppm of organic zinc during the gestation and lactation period, and in the stage of initiation in the productive performance of growing pigs under heat stress, in two periods of the year (May-July and September-November 2015).

Variable	[1] Treatments				Standard error	[2] Main factors			Interaction			[3]Contrasts	
	Control	ZnC	ZnGL	ZnGL + ZnC		P	ZnGL	ZnC	Px ZnGL	Px ZnC	ZnGLx ZnC	1	2
Initial weight, kg	6.33	6.28	6.26	6.27	0.366	0.81	0.91	0.97	0.91	0.87	0.92	0.90	0.88
Final weight, kg	21.00	21.53	21.22	21.78	0.963	0.94	0.82	0.56	0.73	0.60	0.99	0.58	0.68
[4] GDP, kg/day	0.30	0.31	0.31	0.32	0.016	0.97	0.76	0.53	0.72	0.60	0.99	0.50	0.59
Consumption kg/day	0.60	0.59	0.57	0.58	0.034	0.15	0.55	0.90	0.63	0.89	0.84	0.83	0.61
Comsumption/gain	1.99	1.90	1.88	1.83	0.075	0.05	0.24	0.35	0.95	0.73	0.76	0.18	0.15
[5] Deads, n	0.93	0.67	0.17	0.17	0.308	0.18	0.07	0.78	-	-	-	0.29	0.09
[5] Mortality, %	2.33	2.00	0.50	0.50	0.869	0.18	0.06	0.85	-	-	-	0.32	0.10

[1]Treatments: Control= mothers not supplemented-piglets not supplemented, ZnC = Mothers not supplemented-supplemented piglets; ZnGL = supplemented mothers-piglets not supplemented; ZnGL + ZnC = supplemented mothers-supplemented piglets. Supplement of 100 mg of Zn / kg of food, provided from zinc methionine (Zinpro 100, Zinpro, Eden Praire, MN). [2]Factors: P = Period (1,2), supplementation method = ZnGL and ZnC, Zn addition level (0 and 100 mg / kg food); [3]Contrasts: 1 = Control vs. ZnC and ZnGL + ZnC; 2 = Control vs. ZnGL and ZnGL + ZnC; [4]GDP = Daily gain of body weight; [5]The values of number of deaths and mortality were analyzed by nonparametric statistics with the Kruskall-Wallis test. Conversion/gain: Period 1 = 1,824, period 2 = 1,978, standard error 0.051; Dead: ZnGL = 0.17, ZnC = 0.75, standard error 0.213; Mortality ZnGL = 0.50; ZnC = 2.17, standard error 0.599.

It has been suggested that Zn is required by the fetus to support cell proliferation, and tissue differentiation in developing organs (Terrin *et al*., 2015). These effects of Zn during gestation and lactation are especially important because the sow can provide the necessary nutrients to support the growth and development of the fetus and the piglet; in addition, the body reserves of the trace elements have been shown to serve as a source for meeting the nutritional requirements of the fetus (Mahan and Vallet, 1997).

There are several reports regarding the effect of Zn in pigs, but there are few studies conducted with organic sources of Zn in pregnant and lactating sows, and the subsequent effects on the growing pig. In this regard, Caine *et al*. (2009) suggested that the consumption of diets added with 250 mg/kg of Zn from ZnAA, during the last trimester of gestation of the sows, raised the serum concentration of Zn in the suckling piglets, but did not report on the performance of the piglets during the initiation stage. Romo *et al*. (2017) indicated that piglets weaned from sows that consumed food supplemented with Zn from 35 days of gestation and during lactation had a higher (P = 0.001) plasma concentration of IgG (267 vs. 390.8 ng / ml) at 14 days post-weaning. It has also been reported that in broilers supplementation with Zn increases the IgM and IgG titers (Sunder *et al*., 2008).

The consumption of food added with 100 mg of Zn / kg of feed, from zinc methionine, during GL and 49 days post-weaning, did not improve (p> 0.05) the productive behavior of the pigs in initiation. It is known that weaned piglets are subjected to important nutritional and environmental changes, which dramatically alter the balance of the microbiota of the gastrointestinal tract; which provides an opportunity for pathogens to colonize and cause disease, and cause poor performance in growth and even death. It has also been reported that heat stress damages the integrity of the intestinal barrier, which can increase the circulation of endotoxins (Pearce *et al*., 2012).

It has been suggested that supplementation with Zn at the appropriate dose could improve aspects of the integrity of the small intestine and attenuate intestinal damage (Ineu *et al*., 2013, Sanz *et al*., 2014). However, pharmacological levels of Zn (between 300 to 3000 ppm) are often used in the pig industry in the diets of pigs in initiation, immediately after weaning; and it has been reported that they increase growth performance (Morales *et al*., 2012).

In this study the inorganic Zn content of the control diets used was 2064 mg of Zn / kg in the commercial food Vimifos Fase 1® and 2395 mg / kg in Vimifos Fase 2®, consumed during a period of seven days after weaning each one; in the pre-starter food that was offered during a period of 14 days, the content was 1251 mg of Zn / kg and the initiation food contained 173 mg of Zn / kg, which was offered for a period of 21 days; levels that are above the nutritional requirements of the pig

(NRC, 2012). To the control diets were added 100 mg of organic Zn / kg, from zinc methionine; additional level that did not improve the productive response of the pigs in the initiation stage.

Pharmacological levels of inorganic zinc prevent diarrheal diseases in piglets; in this regard it has been shown that zinc oxide has antimicrobial properties, causing changes in the gastrointestinal ecosystem of the piglet (Molist *et al*., 2011, Slade *et al*., 2011, Pieper *et al*., 2012, Hu *et al*., 2013); which led to the assumption that high levels of zinc oxide in the diet, increases the growth of weaned pigs by controlling the population of bacterial pathogens at the intestinal level. In this regard, Zhang and Guo (2009) indicated that high concentrations of Zn in the diet decrease intestinal permeability by preventing the transfer of pathogenic bacteria through the intestinal barrier; in this sense, Debski (2016) suggested that for the treatment of diarrhea, only pharmacological doses of 2000-3000 mg of ZnO/kg of food are beneficial during the first 2-3 weeks after weaning; although other researchers have reported that pharmacological doses of 1000 to 3000 mg of zinc/kg of food can be administered to piglets for up to five weeks, to prevent or overcome post-weaning diarrhea and improve the performance of pigs (ANSES, 2013; , 2013).

It has been shown that the stress of weaning causes Zn deficiencies in piglets (Davin *et al.*, 2013), which can affect their productive behavior; however, the replenishment of these losses does not justify supplementation with pharmacological doses, because zinc homeostasis is a "closed system", and only about 0.1% of total zinc needs to be replenished daily (Maret and Sandstead, 2006).; for what seems to be, that for pigs raised in environments with high sanitary status, Zn supplementation should be done at low levels. In this regard, it has been proposed in the European community that the maximum concentration of Zn in the piglet and sow feed should be 150 mg / kg of feed (EFSA, 2014).

The results obtained in the productive behavior of the pigs at the beginning of the present study were predictable; however, the decrease in mortality in pigs during this stage, from sows that received diets supplemented with Zn during pregnancy and lactation, suggests that this method of supplementation may improve the immune response and physiological adaptation capacity of piglets to stressful events during the initiation period.

CONCLUSION

The supplementation with 100 mg of organic Zn/kg of food from zinc methionine during pregnancy and lactation can be a useful method to reduce the mortality of piglets during the initiation stage, reared under conditions of high heat load.

BIBLIOGRAPHY

AGGARWAL A, Upadhyay R. 2013. Thermoregulation. In: A. Aggarwal, editor, Heat stress and animal productivity. Springer Press, New Delhi, India. p. 27–42. ISBN: 978-81-322-0879-2

ANSES (French Agency for Food, Environmental and Occupational Health & Safety). 2013. Opinion of the on the use of zinc oxide in the diet of piglets at weaning to reduce the use of antibiotics. *ANSES Opinion*. Request No. 2012-SA-0067 Available online: http://www.anses.fr/sites/default/files/documents/ALAN2012sa0067Ra.pdf

BAUMGARD LH, Rhoads Jr. RP. 2013. Effects of heat stress on postabsorptive metabolism and energetics. *Annual Review of Animal Biosciences*. 1:311–337. ISSN: 2165-8102. http://dx.doi.org/10.1146/annurev-animal-031412-103644

BORAH S, Sarmah BC, Chakravarty P, Naskar S, Dutta DJ, Kalita D. 2014. Effect of zinc supplementation on serum biochemicals in grower pig. *Journal of Applied Animal Research*. 42 (2): 244- 248. ISSN: 0971-2119. http://dx.doi.org/10.1080/09712119.2013.824888

CAINE WR, Metzler-Zebeli BU, McFall M, Miller B, Ward TL, Kirkwood RN, Mosenthin R. 2009. Supplementation of diets for gestating sows with zinc amino acid complex and gastric intubation of suckling pigs with zinc-methionine on mineral status, intestinal morphology and bacterial translocation in lipopolysaccharide-challenged early-weaned pigs. *Research in Veterinary Science*. ISSN: 0034-5288. 86(3):453–462. http://dx.doi.org/10.1016/j.rvsc.2008.10.005. Epub 2008 Dec 4

CHASAPIS CT, Loutsidou AC, Spiliopoulou CA, Stefanidou ME. 2012. Zinc and human health: an update. *Archives of Toxicology*. 86(4):521–534. ISSN: 0340-5761. http://dx.doi.org/10.1007/s00204-011-0775-1

DAVIN R, Manzanilla EG, Klasing KC, Perez JF. 2013. Effect of weaning and in-feed high doses of zinc oxide on zinc levels in different body compartments of piglets. *Journal of Animal Physiology and Animal Nutrition*. 97, (Suppl. s1): 6-12. ISSN:0931-2439. http://dx.doi.org/10.1111/jpn.12046.

DEBSKI B. 2016. Supplementation of pigs diet with zinc and copper as alternative to conventional antimicrobials. *Polish Journal of Veterinary Sciences.* 19 (4): 917–924. ISSN: 2300-2557. http://dx.doi.org/10.1515/pjvs-2016-0113

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed). 2014. Scientific Opinion on the potential reduction of the currently authorised maximum zinc content in complete feed. *EFSA Journal*. 12(5):3668-3677. ISSN 1831 – 4732. http://dx.doi.org/10.2903/j.efsa.2014.3668

HU CH, Xiao K, Song J and Luan ZS. 2013. Effects of zinc oxide supported on zeolite on growth performance, intestinal microflora and permeability, and cytokines expression of weaned pigs. *Animal Feed Science and Technology*. 181:65–71. ISSN: 0377-8401. Disponible en:

https://www.sciencedirect.com/science/article/pii/S0377840113000539?via%3Dihub

INEU RP, Oliveira CS, Oliveira VA, Moraes-Silva L, da Luz SCA, and Pereira ME. 2013. Antioxidant effect of zinc chloride against ethanol-induced gastrointestinal lesions in rats. *Food and Chemical Toxicology*. 58:522–529. ISSN:0278-6915. Disponible en: https://ac.els-cdn.com/S0278691513003268/1-s2.0-S0278691513003268-main.pdf?_tid=spdf-ddb64d0c-4bd4-4a3a-9a00-202221d993a4&acdnat=1519702406_629c8214116f88bad65642b760dc3ff1

LAGANA C, Ribeiro AML, Kessler A, Kratz LR, Pinheiro CC. 2007. Effect of the supplementation of vitamins and organic minerals on the performance of broilers under heat stress. *Brazilian Journal of Poultry Science*. 9(1):39–43. ISSN 1516-635X. http://dx.doi.org/10.1590/S1516-635X2007000100006

LAMBERT GP. 2008. Intestinal barrier dysfunction, endotoxemia, and gastrointestinal symptoms: The 'canary in the coal mine' during exercise heat-stress. Medicine and Sport Science. 53:61–73. ISSN, 02545020. http://dx.doi.org/10.1159/000151550

LI Y, Cao Y, Zhou X, Wang F, Shan T, Li Z, Xu W, Li C. 2015. Effects of zinc sulfate pretreatment on heat tolerance of Bama miniature pig under high ambient temperature. *Journal of Animal Science*. 93(7):3421–3430. ISSN: 0021-8812. https://doi.org/10.2527/jas.2015-8910

MADER TL, Davis MS, Brown-Brandl T. 2006. Environmental factors influencing heat stress in feedlot cattle. *Journal of Animal Science*. 84:712-719. ISSN: 0021-8812. Disponible en:http://digitalcommons.unl.edu/cgi/viewcontent.cgi?article=1622&context=animalscifacpub

MAHAN DC, Vallet JL. 1997. Vitamin and mineral transfer during fetal development and the early postnatal period in pigs. *Journal of Animal Science*. 75(10):2731–2738. ISSN: 0021-8812. http://dx.doi.org/10.2527/1997.75102731x

MARET W, Sandstead HH. 2006. Zinc requirements and the risks and benefits of zinc supplementation. *Journal of Trace Elements in Medicine and Biology*. 20(1):3−18. ISSN, 0946672X. https://doi.org/10.1016/j.jtemb.2006.01.006

MARET W. 2013. Zinc biochemistry: From a single zinc enzyme to a key element of life. *Advances in Nutrition*. 4(1):82−91. ISSN: 2161-8313. http://dx.doi.org/10.3945/an.112.003038.

MOLIST F, Hermes RG, Gómez de Segura A, Martín-Orúe SM, Gasa J, Garcia Manzanilla E and Pérez JF, 2011. Effect and interaction between wheat bran and zinc oxide on productive performance and intestinal health in post-weaning piglets. *British Journal of Nutrition.* 105(11):1592−1600. ISSN: 0007-1145. http://doi.org/10.1017/S0007114510004575

MORALES J, Cordero G, Piñeiro C, Durosoy S. 2012. Zinc oxide at low supplementation level improves productive performance and health status of piglets. *Journal of Animal Science*. 90 (suppl. 4): 436–438. ISSN: 0021-8812. https://doi.org/10.2527/jas.53833.

NRC. 2012. Nutrient requirements of swine. 11th rev. ed. Natl. Acad. Press, Washington, DC. ISBN: 978-0-309-22427-7, DOI: https://doi.org/10.17226/13298

PAYNE RL, Bidner TD, Fakler TM and LL Southern. 2006. Growth and intestinal morphology of pigs from sows fed two zinc sources during gestation and lactation. *Journal of Animal Science*. 84:2141-214. ISSN: 0021-8812. https://dx.doi.org/10.2527/jas.2005-627

PEARCE SC, Gabler NK, Ross JW, Escobar J, Patience JF, Rhoads RP, Baumgard LH. 2013b. The effects of heat stress and plane of nutrition on metabolism in growing pigs. *Journal of Animal Science*. 91(5):2108–2118. ISSN: 0021-8812. https://doi.org/10.2527/jas2012-5738

PEARCE SC, Mani V, Boddicker RL, Johnson JS, Weber TE, Ross JW, Baumgard LH, and Gabler NK. 2012. Heat stress reduces barrier function and alters intestinal metabolism in growing pigs. *Journal of Animal Science*. 90(Suppl. 4):257–259. doi: https://dx.doi.org/10.2527/jas.52339.

PEARCE SC, Mani V, Weber TE, Rhoads RP, Patience JF, Baumgard LH, and Gabler NK. 2013a. Heat stress and reduced plane of nutrition decreases intestinal integrity and function in pigs. J. Anim. Sci. 91:5183–5193. ISSN: 0021-8812, https://doi.org/10.2527/jas2013-6759

PEARCE SC, Sanz Fernandez MV, Torrison J, Wilson ME, Baumgard LH, Gabler NK. 2015. Dietary organic zinc attenuates heat stress–induced changes in pig intestinal integrity and metabolism. *Journal of Animal Science*. 93(10):4702–4713. ISSN: 0021-8812. https://dx.doi.org/10.2527/jas2015-9018

PIEPER R, Vahjen W, Neumann K, Van Kessel AG and Zentek J, 2012. Dose-dependent effects of dietary zinc oxide on bacterial communities and metabolic profiles in the ileum of weaned pigs. ISSN:0931-2439. 96(5): 825−833. https://dx.doi.org/10.1111/j.1439-0396.2011.01231.x.

ROMO JM, Romo JA, Barajas R, Enríquez I, Silva G, Montero A. 2017. Efecto del consume de zinc orgánico en la respuesta productiva de la cerda y su camada. Abanico veterinario, Mayo-Agosto 2017; 7(2):43-59. ISSN 2448-6132. http://dx.doi.org/10.21929/abavet2017.72.4

SALES J. 2013. Effects of pharmacological concentrations of dietary zinc oxide on growth of post-weaning pigs: A meta-analysis. *Biological Trace Element Research*. 152 (3):343−349. ISSN: 0163-498. http://dx.doi.org/10.1007/s12011-013-9638-3

SANZ FMV, Johnson JS, Abuajamieh M, Stoakes SK, Seibert JT, Cox L, Kahl S, Elsasser TH, Ross JW, Isom SC., Rhoads RP, Baumgard LH. 2015. Effects of heat stress on carbohydrate and lipid metabolism in growing pigs. *Physiological Reports*. 3(2):e12315: 1-17. ISSN 2051-817X. http://dx.doi.org/10.14814/phy2.12315

SANZ FMV, Pearce SC, Gabler NK, Patience JF, Wilson ME, Socha MT, Torrison JL, Rhoads RP, and Baumgard LH. 2014. Effects of supplemental zinc amino acid complex on gut integrity in heat-stressed growing pigs. *Animal*. 8(1):43–50. ISSN: 1751-7311, http://dx.doi.org/10.1017/S1751731113001961

SLADE RD, Kyriazakis I, Carroll SM, Reynolds FH, Wellock IJ, Broom LJ and Miller HM, 2011. Effect of rearing environment and dietary zinc oxide on the response of group-housed weaned pigs to enterotoxigenic *Escherichia coli* O149 challenge. *Animal*. 5 (8): 1170–1178. ISSN: 1751-7311. http://dx.doi.org/10.1017/S1751731111000188

SONG ZH, Ke YL, Xiao K, Jiao LF, Hong QH, Hu CH. 2015. Diosmectite–zinc oxide composite improves intestinal barrier restoration and modulates TGF-β1, ERK1/2, and Akt in piglets after acetic acid challenge. *Journal of Animal Science*. 93:1599–1607. ISSN: 0021-8812. http://dx.doi.org/10.2527/JAS.2014-8580

STAR L, van der Klis JD, Rapp C, Ward TL. 2012. Bioavailability of organic and inorganic zinc sources in male broilers. Poultry Science. 91(12):3115-3120. ISSN: 0032-5791. https://doi.org/10.3382/ps.2012-02314

SUNDER GS, Panda AK, Gopinath NCS, Rama RSV, Raju MVLN, Reddy MR, and Kumar CV. 2008. Effects of higher levels of zinc supplementation on performance, mineral availability, and immune competence in broiler chickens. *The Journal Applied Poultry Research*. 17(1):79–86. ISSN: 1056-6171. https://doi.org/10.3382/japr.2007-00029

TERRIN G, Canani RB, Di Chiara M, Pietravalle A, Aleandri V, Conte F, De Curtis M. 2015. Zinc in Early Life: A Key Element in the Fetus and Preterm Neonate. *Nutrients*. 7(12):10427–10446. ISSN 2072-6643. http://dx.doi.org/doi:10.3390/nu7125542

WAEYTENS A, De Vos M, Laukens D. 2009. Evidence for a Potential Role of Metallothioneins in Inflammatory Bowel Diseases. *Mediators of Inflammation*. Article ID 729172: 9 pages. ISSN: 0962-9351. http://dx.doi.org/10.1155/2009/729172

WANG X, Valenzano MC, Mercado JM, Zurbach EP, Mullin JM. 2013. Zinc supplementation Modifies Tight Junctions and Alters Barrier Function of CACO-2 Human Intestinal Epithelial Layers. *Digestive Diseases and Sciences*. 58(1):77-87. ISSN: 0163-2116. http://dx.doi.org/10.1007/s10620-012-2328-8

YAN Y, Zhao Y, Wang H, and Fan M. 2006. Pathophysiological factors underlying heatstroke. *Medical Hypotheses*. 67(3):609–617. ISSN 0306-9877. https://doi.org/10.1016/j.mehy.2005.12.048

ZHANG B, Guo Y. 2009. Supplemental zinc reduced intestinal permeability by enhancing occludin and zonula occludens protein-1 (ZO-1) expression in weaning piglets. *British Journal of Nutrition*. 102:687–693. ISSN: 0007-1145. https://doi.org/10.1017/S0007114509289033

ZHONG W, McClain CJ, Cave M, Kang J and Zhou Z. 2010. The role of zinc deficiency in alchohol-induced intestinal barrier dysfunction. *American Journal of Physiology, Gastrointestinal Liver Physiology*. 298(5):G625-G633. ISSN: 0193-1857 https://dx.doi.org/10.1152/ajpgi.00350.2009