Use of a micro-encapsulated eucalyptus-medium chain fatty acid product as an alternative to zinc oxide and antibiotics for weaned pigs

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Summary

Objective: To compare the effects of eucalyptus-medium chain fatty acids (E-MCFAs), zinc oxide (ZnO), and antibiotics on performance, nutrient digestibility, and serum chemistry parameters of nursery pigs.

Materials and methods: Three experiments were conducted. Recently weaned barrows, weighing approximately 7 kg, were allotted to five treatments consisting of a basal diet or the basal diet supplemented with antibiotics (33 mg per kg tiamulin and 44 mg per kg lincomycin), ZnO (1500 or 2500 mg per kg), or 0.1% E-MCFAs (Experiments One and Two). In Experiment Three, 1% diatomaceous earth was added as a digestibility marker and the negative control was not used.

Results: In Experiment One (n = 24), average daily gain (ADG) and average daily feed intake (ADFI) were lower ($P < .05$), while in Experiment Two (n = 18), ADG was lower ($P < .05$) for pigs fed the basal diet than for pigs fed any of the supplemented diets. In all three experiments, performance of pigs fed the four supplemented diets did not differ ($P > .05$). Apparent fecal digestibility of crude protein, calcium, phosphorus, energy, lysine, histidine, phenylalanine, and threonine was higher ($P < .05$) in the diet supplemented with E-MCFAs than in diets supplemented with ZnO or antibiotics (n = 6). Serum zinc, glutamic-oxaloacetic transferase, and glutamic-pyruvic transferase were higher for pigs fed the ZnO-supplemented diets than for pigs fed the other two treatments (n = 9).

Implication: Eucalyptus-MCFAs can be successfully used as a growth promoter in diets fed to nursery pigs.

Keywords: swine, performance, zinc oxide, antibiotics, eucalyptus-medium chain fatty acids

Received: February 16, 2010
Accepted: May 25, 2010

Resumen - Utilización de un producto de eucalipto microencapsulado de ácido graso de cadena media como una alternativa del óxido de zinc y antibióticos para cerdos destetados

Objetivo: Comparar los efectos de los ácido graso de cadena media de eucalipto (E-MCFAs), óxido de zinc (ZnO), y antibióticos en el desempeño, digestibilidad de nutrientes, y parámetros químicos del suero en cerdos de destete.

Materiales y métodos: Se realizaron tres experimentos. Se asignaron machos castrados recién destetados que pesaban aproximadamente 7 kg, a cinco tratamientos consistentes en una dieta basal ó en una dieta basal suplementada con antibióticos (33 mg por kg de tiamulina y 44 mg por kg de lincomicina), ZnO (1500 ó 2500 mg por kg), ó 0.1% E-MCFAs (Experimentos Uno y Dos). En el Experimento Tres, se agregó un 1% de tierra diatomaceous como marcador de digestibilidad y no se utilizó un control negativo.

Resultados: En el Experimento Uno (n = 24), la ganancia diaria promedio (ADG por sus siglas en inglés) y el consumo de alimento diario promedio (ADFI por sus siglas en inglés) fueron más bajos ($P < .05$), mientras que en el Experimento Dos (n = 18), la ADG fue más baja ($P < .05$) en los corrales alimentados con la dieta basal que en los corrales alimentados con cualquiera de las dietas suplementadas. En los tres experimentos, el desempeño de los cerdos alimentados con las cuatro dietas suplementadas no difirió ($P > .05$). La aparente digestibilidad fecal de proteína cruda, calcio, fósforo, energía, lisina, histidina, fenilalanina, y treonina fue más alta ($P < .05$) en la dieta suplementada con E-MCFAs que en las dietas suplementadas con ZnO ó antibióticos (n = 6). El zinc sérico, la transferasa glutámico-oxaloacética, y la transferasa glutámico-pirúvica fueron más altas en los cerdos alimentados con las dietas suplementadas con ZnO que en los cerdos alimentados con los otros dos tratamientos (n = 9).

Implicación: Los MCFAs de eucalipto pueden utilizarse exitosamente como un promotor de crecimiento en dietas alimentadas a cerdos en el destete.

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This article is available online at http://www.aasv.org/shap.html.

Han Y-K, Hwan Hwang IL, Thacker PA. Use of a micro-encapsulated eucalyptus-medium chain fatty acid product as an alternative to zinc oxide and antibiotics for weaned pigs. *J Swine Health Prod.* 2011;19(1):34–43.

Résumé - Utilisation d'un produit de chaînes moyennes d'acides gras d'eucalyptus micro-encapsulées comme alternative à l'oxyde de zinc et aux antibiotiques pour les porcs sevrés

Objectif: Comparer les effets de chaînes moyennes d'acides gras d'eucalyptus (E-MCFAs), d'oxyde de zinc (ZnO), et

d'antibiotiques sur la performance, la digestibilité des nutriments, et les paramètres chimiques sériques de porcelets en pouponnière.

Matériels et méthodes: Trois expériences ont été menées. Des castrats récemment sevrés, pesant approximativement 7 kg, ont été répartis en cinq groupes de traitement: ration de base, ration de base supplémentée d'antibiotiques (33 mg/kg de tiamuline et 44 mg/kg de lincomycine), ZnO (1500 ou 2500 mg/kg), ou 0,1% d'E-MCFAs (Expériences 1 et 2). Pour l'Expérience 3, de la terre diatomée 1% a été ajoutée à titre de marqueur de digestibilité et le groupe témoin négatif n'a pas été utilisé.

Résultats: Au cours de l'Expérience 1 (n = 24), le gain quotidien moyen (ADG) et la consommation journalière de nourriture moyenne (ADFI) étaient inférieures ($P < .05$), alors qu'au cours de l'Expérience 2 (n = 18), l'ADG était inférieur ($P < .05$) pour les parcs où les animaux étaient nourris avec la ration de base comparativement aux parcs où les animaux étaient nourris avec la ration de base et n'importe lequel des suppléments. Au cours des trois expériences, les performances des porcs nourris avec les quatre rations supplémentées n'étaient pas différentes ($P > .05$). La digestibilité fécale apparente des protéines brutes, du calcium, du phosphore, de l'énergie, de la lysine, de l'histidine, de la phénylalanine, et de la thréonine était plus grande ($P < .05$) dans la ration supplémentée avec E-MCFAs comparativement aux rations supplémentées avec du ZnO ou des antibiotiques (n = 6). Les concentrations sériques de zinc, de glutamate-oxaloacétate transférase, et de glutamate-pyruvate transférase étaient plus élevées chez les porcs nourris avec la ration supplémentée avec du ZnO que chez les porcs nourris avec les deux autres traitements (n = 9).

Implication: Des MCFAs d'eucalyptus peuvent être utilisés avec succès comme agent de promotion de croissance dans les rations données aux porcelets en pouponnière.

Weaning at 3 to 4 weeks of age exposes piglets to nutritional and environmental stresses, often resulting in suboptimal performance, increased risk of diarrhea, and sometimes death.[1] In order to prevent diarrhea or poor performance, antimicrobial feed additives are often supplied in nursery pig diets.[2] However, due to concerns about residues in meat and the potential for development of microbial resistance to antibiotics, government agencies in many pig-producing countries are considering implementation of a complete ban in the use of antibiotics in animal feeds.[3] As a consequence, development of alternatives to antibiotics is receiving considerable attention.[4]

High levels of zinc in the form of zinc oxide (ZnO) are commonly added to nursery pig diets because they improve performance[5-7] and reduce the incidence of diarrhea after weaning.[8] However, a concern with feeding pharmacological levels of ZnO to pigs is that application of manure containing high levels of ZnO to agricultural lands has the potential to negatively impact the environment.[9] Therefore, it would be desirable if the beneficial effects of feeding ZnO could be obtained at lower levels of supplementation,[10] or if alternative growth promoters could be developed.

Eucalyptus oil is obtained from the leaves of the eucalyptus, a tree which belongs to the plant family Myrtaceae and is cultivated worldwide. In humans, eucalyptus oil has antibacterial effects on pathogenic bacteria in the respiratory tract.[11] Eucalyptus oil also stimulates the immune system by affecting the phagocytic ability of monocyte-derived macrophages.[12] Dietary inclusion of eucalyptus improves production performance and stimulates the immunity of commercial laying hens.[13] However, the effect of eucalyptus on pig performance or immunity has not been determined.

Medium-chain fatty acids (MFCAs) have been suggested as an alternative feed additive to antibiotics for piglets.[1,14] Unfortunately, MCFAs are a strong stimulus for the release of cholecystokinin, which has a pronounced satiating activity that could interfere with feed intake.[14] In addition, MCFAs may reduce feed intake simply because of their unpleasant taste.[15] To avoid these adverse side effects, Dierick et al[14] attempted to use in situ generation of MCFAs by feeding a combination of triacylglycerol-containing MCFAs and exogenous lipolytic enzymes.

Micro-encapsulation of MCFAs is an alternative to in situ generation, which could be used to avoid the adverse effects of MCFAs on feed intake. In this process, the MCFAs are nano-micronized to extremely small particles to facilitate absorption and then encapsulated so that the negative effects on feed intake are avoided. A eucalyptus-MCFAs product (E-MCFAs) has recently been developed using this technology, but its effects on nursery pig performance have not been reported. Therefore, the objective of the present study was to compare the effects of feeding micro-encapsulated E-MCFAs, ZnO, and antibiotics on the performance, nutrient digestibility, and serum chemistry of weaned pigs.

Materials and methods

All procedures used in this experiment were approved by the Animal Ethics Committee of Sungkyunkwan University in Korea following the *Guidelines for the Care and Use of Animals in Research*[16] published by the Korean Ministry for Food, Agriculture, Forestry and Fisheries.

Production of micro-encapsulated E-MCFAs

The process used to produce the micro-encapsulated E-MCFAs product has been patented by the Korean Intellectual Property Office (Daejeon, Korea) under patent number 10-2009-0025329. Briefly, the product was produced by mixing eucalyptus extract (Desert King International, San Diego, California), caprylic acid (C8:0), and carpric acid (C10:0) in a ratio of 2:1:1 and then subjecting the mixture to micronization (Ultra-Micro Pulverizer; GR Engineering Company, Seoul, Korea). Palm oil was then sprayed onto the extract and the two MCFAs, and the entire mixture was diluted 50:50 with a carrier consisting of calcium carbonate, rice-husk powder, and wheat powder (20:40:40). The product is marketed as a dry powder under the name Bye All CT and was obtained from Easybio Systems (Seoul, Korea).

Experiment One

In Experiment One, 120 pens were used to house 640 crossbred barrows (Landrace-Yorkshire female × Duroc sire), averaging 24 ± 3 days of age and 6.04 ± 0.88 kg. The pigs were blocked on the basis of initial weight and litter of origin and allotted to five dietary treatments in a randomized block design. The basal diet formula was based on corn (extruded and expanded), soybean meal (regular and fermented), milk-based products (lactose powder, whey powder, and milk powder complex), and spray-dried porcine plasma (Table 1). The five dietary treatments consisted of the basal diet fed without supplementation (negative control) or the basal diet supplemented with antibiotics (33 mg per kg tiamulin and 44 mg per kg lincomycin; positive control), ZnO (1500 or 2500 mg per kg), or 0.1% micro-encapsulated E-MCFAs (Easybio Systems). Prior to mixing

Table 1: Ingredient composition (% as fed) of the basal diet used to determine the effects of antibiotics (tiamulin 33 mg/kg and lincomycin 44 mg/kg), zinc oxide (1500 or 2500 mg/kg), and eucalyptus-medium chain fatty acids (E-MCFAs; 0.1%) on performance, nutrient digestibility, and serum chemistry parameters in nursery pigs*

Component	Phase 1	Phase 2	Phase 3
Yellow corn, extruded (%)	11.00	0.00	0.00
Yellow corn, expanded (%)	3.50	36.28	47.78
Bakery by-product (%)	5.00	7.00	9.00
Lactose (%)	10.00	0.00	0.00
Soybean meal, 48% (%)	8.00	0.00	0.00
Soybean meal, 44% (%)	0.00	16.50	30.00
Soybean meal, fermented (%)	10.00	3.75	0.00
Whey powder (%)	20.76	10.00	5.00
Milk powder (%)	10.00	7.50	0.00
Spray-dried plasma (%)	5.00	2.50	0.00
Fishmeal (%)	2.50	0.00	0.00
Lard (%)	0.00	2.00	2.50
Soybean oil (%)	4.50	3.00	0.00
Limestone (%)	0.00	0.30	0.13
Salt (%)	0.00	0.20	0.30
Tricalcium phosphate (%)	0.00	0.00	0.60
Monocalcium phosphate (%)	1.32	0.64	0.00
Sodium propionate (%)	1.05	0.73	1.25
Sucrose (%)	3.00	3.00	0.00
DL-methionine (%)	0.26	0.16	0.18
L-lysine HCl (%)	0.06	0.25	0.31
Threonine (%)	0.04	0.00	0.12
Choline chloride, 50% (%)	0.20	0.20	0.20
Vitamin-mineral premix (%)†	0.30	0.30	0.30
Cellulose powder+treatment(%)‡	3.51	3.19	2.33

* Pigs were weaned and assigned to treatment at 24 days of age in Experiment One and 28 days of age in Experiments Two and Three. Experiment One: phase 1 diet fed Days 0 to 7, phase 2 diet fed Days 8 to 21, phase 3 diet fed Days 22 to 28. Experiment Two: phase 1 diet fed Days 0 to 14, phase 2 diet fed Days 15 to 28. Experiment Three: a 50:50 blend of phase 1 and 2 diets fed for 14 days.

† Vitamin-trace mineral premix provided the following per kg of diet: vitamin A, 20,000 IU; vitamin D3, 2000 IU; vitamin E, 100 mg; vitamin K, 3 mg; thiamin, 4 mg; riboflavin, 7.0 mg; pyridoxine, 5 mg; vitamin B12, 0.05 mg; pantothenic acid, 16 mg; niacin, 35 mg; biotin, 0.18 mg; folic acid 1.3 mg; choline, 350 mg; Fe, 100 mg; Cu, 10 mg; Mn, 20 mg; Zn, 100 mg; I, 0.35 mg; Se, 0.20 mg.

‡ Cellulose powder was mixed with antibiotics, zinc oxide, or micro-encapsulated E-MCFAs.

in the diet, the antibiotics, ZnO, or micro-encapulated E-MCFAs were premixed with cellulose (Sigma, St Louis, Missouri) and were then added to the feed mixer.

The experiment was conducted in three phases, with the phase 1 diet (Days 0 to 7) formulated to provide 1.72% lysine, 1.06% methionine plus cystine, and 1.18% threonine; the phase 2 diet (Days 8 to 21) was formulated to provide 1.56% lysine, 0.89% methionine plus cystine, and 1.10% threonine; while the phase 3 diet (Days 22 to 28) was formulated to provide 1.49% lysine, 0.79% methionine plus cystine, and 0.99% threonine (Table 2). All amino acid levels reported are total, not digestible levels. All diets were fed in crumbled form and all nutrient levels met or exceeded NRC[17] requirements for the nursery pig. The basal diet contained 100 mg per kg Zn as $ZnSO_4$ (35.5% Zn).

The experiment was conducted on six separate commercial pig farms located in the provinces of Hallim, Icheon, Illzug, Namwon, Pocheon, and Seoguipo in South Korea. The piglets were housed in environmentally regulated barns in 1.2 × 1.4-m pens located over a plastic slatted floor. Air temperature was controlled at 30°C during the first 7 days, and the temperature was decreased by 1°C every 3 days until it reached 23°C at the end of the experiment. There were four replicate pens per treatment in each of the six commercial pig farms (n = 24), and each pen housed four barrows (provinces of Hallim, Icheon, Illzug, and Seoguipo) or eight barrows (provinces of Namwon and Pocheon). Each pen had two feeders and two nipple waterers to provide free access to feed and water. Individual pig weights and pen feed disappearance were measured weekly and used to calculate average daily gain (ADG), average daily feed intake (ADFI), and feed conversion efficiency (FCE) on a pen basis. Feed wastage was negligible and was not considered.

Experiment Two

This experiment was conducted to further evaluate the effects of treatment with micro-encapsulated E-MCFAs, antibiotics, and ZnO addition on nursery pig performance. In Experiment Two, 90 pens were used to house 360 crossbred barrows (Landrace-Yorkshire × Duroc sire), averaging 28 ± 3 days of age and 7.34 ± 0.47 kg BW. The barrows were blocked on the basis of initial weight and litter of origin, and allotted to the five dietary treatments used in Experiment One in a randomized block design. The pigs were fed the phase 1 diets from Day 0 to 14 and the phase 2 diets from Day 15 to 28.

The 28-day experiment was conducted at two commercial farms located in the provinces of Namwon and Pocheon in South Korea. The pigs were housed in environmentally regulated barns in 1.0 × 1.2-m pens located over a slatted wire floor. There were nine pens per treatment in each of the two commercial farms (n = 18), and each pen housed four barrows. Each pen had two feeders and a nipple waterer to provide free

Table 2: Chemical analysis (as fed) of diets fed to determine the effects of antibiotics, zinc oxide (ZnO), and eucalyptus-medium chain fatty acids (E-MCFAs) on performance, nutrient digestibility, and serum chemistry parameters in nursery pigs*

	Phase 1	Phase 2	Phase 3
Chemical analysis			
Crude protein (%)	24.89	23.14	23.01
Crude fiber (%)	1.51	2.88	3.33
Ether extract (%)	6.51	6.81	6.73
Ash (%)	7.01	6.91	7.00
Calcium (%)	0.89	0.86	0.85
Phosphorus (%)	0.68	0.67	0.66
Total essential amino acids			
Arginine (%)	1.35	1.18	1.15
Histidine (%)	0.69	0.54	0.54
Isoleucine (%)	1.06	0.98	0.81
Leucine (%)	2.00	1.90	1.80
Lysine (%)	1.72	1.56	1.49
Methionine + cystine (%)	1.06	0.89	0.79
Phenylalanine (%)	1.15	1.11	1.02
Threonine (%)	1.18	1.10	0.99
Valine (%)	1.20	1.10	0.98

* Pigs were weaned and assigned to treatment at 24 days of age in Experiment One and 28 days of age in Experiments Two and Three. Experiment One: phase 1 diet fed Days 0 to 7, phase 2 diet fed Days 8 to 21, phase 3 diet fed Days 22 to 28. Experiment Two: phase 1 diet fed Days 0 to 14, phase 2 diet fed Days 15 to 28. Experiment Three: a 50:50 blend of phase 1 and 2 diets fed for 14 days. Diets were either unsupplemented (control) or supplemented with antibiotics (tiamulin 33 mg/kg and lincomycin 44 mg/kg), ZnO (1500 or 2500 mg/kg), or eucalyptus-MCFAs (0.1%). Chemically determined zinc concentrations: 98, 101, 1465, 2480, and 101 mg/kg for the control, antibiotic, 1500 mg/kg ZnO, 2500 mg/kg ZnO, and E-MCFAs diets, respectively. All analyses conducted in triplicate.

access to feed and water. Air temperature in the barn was controlled at 32°C during the first 7 days, and the temperature was decreased by 1°C every 3 days until it reached 25°C at the end of the experiment. Individual pig weights and pen feed disappearance were measured weekly and used to calculate ADG, ADFI, and FCE.

Experiment Three

This 14-day experiment was set up at a commercial farm in the province of Hallim and was conducted to evaluate the effects of treatment with microencapsulated E-MCFAs, antibiotics, and ZnO addition on performance, nutrient digestibility, and serum chemistry parameters of nursery pigs. In Experiment Three, 36 pens were used to house 504 crossbred barrows (Landrace-Yorkshire × Duroc sire), averaging 28 ± 3 days of age and 7.68 ± 0.64 kg. The barrows were blocked on the basis of initial weight and litter of origin and allotted to four dietary treatments in a randomized block design. The pigs were fed a mixture of the phase 1 and 2 diets (50:50) used in Experiment One. Because of severe diarrhea, feeding of the negative control diet was stopped after 10 days and all pigs on this treatment were removed from the experiment. All diets contained 1.0% diatomaceous earth (Celite 545, Fluka Chemika/Biochemika, Buchs, Switzerland) as a digestibility marker.

During the experiment, the pigs were housed in an environmentally regulated barn in 2.0 × 2.4-m pens located over a slatted wire floor. There were nine pens per treatment (n = 9), and each pen housed 14 barrows. Each pen had a three-hole feeder and two nipple waterers to provide free access to feed and water. Air temperature in the house was controlled at 32°C during the first 7 days and the temperature was decreased by 1°C every day until it reached 25°C at the end of the experiment. Individual pig weights and pen feed disappearance were measured weekly and used to calculate ADG, ADFI, and FCE.

Fecal samples were collected from each pen on Days 11, 12, 13, and 14. The fecal samples from the four collections from each pen were pooled by placing the feces into a stainless steel pan and stirring with a teflon spatula so that there was a single sample from each pen representing the four collections. All fecal samples were stored in sealed plastic bags at -60°C. Prior to analysis, the fecal samples were freeze-dried for 72 hours, allowed to equilibrate for 24 hours at room temperature, and then ground through a 1.0-mm screen with a Cyclotec Grinder (Model 1093; Foss Group, Hillerod, Denmark). Digestibility coefficients for nutrients were calculated using the equations for the indicator method described by Schneider and Flatt.[18] Digestibility data was obtained from six randomly chosen pens per treatment.

On Day 14, one pig in each pen (n = 9), closest to the average body weight for that pen, was chosen for blood sampling. Blood samples (approximately 7 mL per sample) were collected by anterior vena cava puncture after a 6-hour fast, using plain vacuum-filled blood collection tubes (21-gauge × 1.5 inches; Serum Clot Activator; Greiner Bio-one, Kremsmunster, Austria). The samples were then centrifuged (Model VS-5000N; Vision Scientific, Bucheon, Korea) at 415*g* at 4°C for 15 minutes. Serum was collected and stored at -25°C until needed for analysis of serum parameters.

Chemical analysis

Samples of the diets and feces were analyzed in triplicate according to the methods of the Association of Official Analytical Chemists.[19] Analyses were conducted for moisture (method 930.15), crude protein (method 984.13), ash (method 942.05), crude fiber (method 978.10), and ether extract (method 920.39). Calcium was determined by a Shimazu AA625 Atomic Absorption Spectrophotometer (Shimazu, Kyoto, Japan), and phosphorus was analyzed using a UV-Vis Spectrophotometer (Hitachi, Tokyo, Japan). An amino-acid analysis of the feeds and feces was performed using an L8500-Hitachi Amino Acid Analyzer (Hitachi) after hydro-

lysis for 24 hours in 6M HCl. Performic acid (85%) hydrolysis was performed prior to analysis of the sulfur-containing amino acids. Gross energy was measured using an Adiabatic Oxygen Bomb Calorimeter (Model 1241; Parr Instrument Co, Moline, Illinois). Diatomaceous earth (Acid Insoluble Ash) analysis was conducted according to the description provided by Prabucki et al.[20] The analyzed chemical composition of the experimental diets is shown in Table 2.

The serum concentrations of total protein, albumin, glutamic-oxaloacetic transferase (GOT), glutamic-pyruvic transferase (GPT), urea nitrogen, total cholesterol, high density lipoprotein, low density lipoprotein, and triglyceride were determined using commercial kits (Bayer, Terrytown, New York) following the procedures recommended for an Automatic Biochemical Analyzer (Model ADVIA 1650, Bayer, Terrytown, New York). The concentration of immunoglobulin G was analyzed with a commercially available Nephelometry kit (Bade Behring, Schwalbach, Germany) and a Model BN II Nephelometer (Bade Behring). Zinc was analyzed using inductively coupled plasma mass spectrometry (ICP-MS Model Elan DRCe; Perkin Elmer, Wiesbaden, Germany). Serum cortisol, somatomedin-C, and tumor necrosis factor were analyzed using radioimmunoassay (Diagnostic Products Corporation, Los Angeles, California), chemiluminescent immunoassay (Diagnostic Products Corporation), and enzyme-linked immunosorbent assay (R&D Systems, Minneapolis, Minnesota), respectively.

Statistical analysis

The performance and digestibility data were analyzed as a randomized block design using the analysis of variance procedures of the Statistix for Windows program (Analytical Software, Tallahassee, Florida). Pen was considered the experimental unit for analyses of performance and digestibility data. The animal was considered the experimental unit for analyses of data regarding serum parameters. Because of the severe diarrhea in Experiment Three, the data for the negative control group were deleted from the data set. The model included the effects of farm, treatment, farm × treatment, and error. There were no significant differences between the farms for any of the parameters measured. The significance of differences between means was determined by Student Newman Keul's test for performance, digestibility, and serum parameters with the significance level set at $\alpha = .05$.

Results

In Experiment One, ADG Days 8 to 21 and Days 0 to 28, and ADFI Days 8 to 21 and Days 0 to 28, were lower ($P < .05$) for pigs fed the negative control diet than for pigs fed diets supplemented with any of the four treatments (Table 3). However, during all experimental periods, ADG and ADFI did not differ for pigs fed diets supplemented with antibiotics, ZnO, or micro-encapsulated E-MCFAs ($P > .05$). There were no treatment effects on FCE during any experimental period ($P > .05$).

In Experiment Two, ADG (Days 0 to 14 and Days 0 to 28) was lower ($P < .05$) for pigs fed the negative control diet than for pigs fed diets supplemented with antibiotics, ZnO, or micro-encapsulated E-MCFAs (Table 4). The FCE of the negative control

Table 3: Effects of antibiotics, zinc oxide, and eucalyptus-medium chain fatty acids on nursery pig performance (Experiment One)*

Parameter	Control	Antibiotics	ZnO 1500 mg/kg	ZnO 2500 mg/kg	E-MCFAs	SEM	*P*
Days 0-7 (phase 1 diet)							
ADG (g/day)	209	240	248	258	242	17.7	.06
ADFI (g/day)	268	286	302	305	282	12.9	.22
FCE	1.44	1.24	1.24	1.29	1.25	0.08	.30
Days 8-21 (phase 2 diet)							
ADG (g/day)	223[a]	316[b]	284[b]	299[b]	319[b]	21.8	.02
ADFI (g/day)	343[a]	407[b]	412[b]	437[b]	457[b]	22.9	.01
FCE	1.69	1.57	1.49	2.12	1.52	0.24	.31
Days 22-28 (phase 3 diet)							
ADG (g/day)	316	389	377	375	363	22.5	.18
ADFI (g/day)	492[a]	625[b]	570[ab]	538[ab]	597[b]	32.0	.04
FCE	1.62	1.68	1.52	1.62	1.76	0.10	.59
Days 0-28							
ADG (g/day)	243[a]	315[b]	298[b]	308[b]	310[b]	13.6	< .01
ADFI (g/day)	361[a]	431[b]	426[b]	429[b]	448[b]	18.1	.01
FCE	1.53	1.41	1.44	1.41	1.46	0.05	.35

* Mean of 24 pens of four or eight pigs per pen (n = 24). Pigs were weaned at 24 days of age and immediately placed on test (Day 0). Diets described in Tables 1 and 2.

[ab] Means in the same row with different superscripts are statistically different (ANOVA; $P < .05$).

ADG = average daily gain; ADFI = average daily feed intake; FCE = feed conversion efficiency; ZnO = zinc oxide; E-MCFA = eucalyptus-medium chain fatty acids.

Table 4: Effects of antibiotics, zinc oxide, and eucalyptus-medium chain fatty acids on nursery pig performance (Experiment Two)*

Parameter	Control	Antibiotics	ZnO 1500 mg/kg	ZnO 2500 mg/kg	E-MCFAs	SEM	*P*
Days 0-14 (Phase 1)							
ADG (g/day)	272[a]	330[b]	335[b]	342[b]	330[b]	16.8	.03
ADFI (g/day)	399	417	428	427	451	14.3	.16
FCE	1.50	1.44	1.29	1.28	1.43	0.09	.37
Days 15-28 (Phase 2)							
ADG (g/day)	395	436	404	414	431	13.2	.14
ADFI (g/day)	638	659	620	652	651	24.2	.82
FCE	1.62	1.51	1.53	1.58	1.52	0.04	.22
Days 0-28							
ADG (g/day)	334[a]	383[b]	370[b]	378[b]	381[b]	12.1	.03
ADFI (g/day)	519	538	524	540	551	14.5	.54
FCE	1.56[a]	1.43[b]	1.42[b]	1.44[b]	1.46[ab]	0.04	.05

* Pen means, four pigs per pen (n = 18). Pigs were weaned at 28 days of age and immediately placed on test (Day 0). Diets described in Tables 1 and 2.

[ab] Means in the same row with different superscripts are statistically different (ANOVA; $P < .05$).

ADG = average daily gain; ADFI = average daily feed intake; FCE = feed conversion efficiency; ZnO = zinc oxide; E-MCFAs = eucalyptus-medium chain fatty acids.

Table 5: Effects of antibiotics, zinc oxide, and eucalyptus-medium chain fatty acids on nursery pig performance (Experiment Three)*

Parameter	Antibiotics	ZnO 1500 mg/kg	ZnO 2500 mg/kg	E-MCFAs	SEM	*P*†
Days 0-14 (50:50 blend of phase 1 and 2 diets)						
ADG (g/day)	293	300	302	313	21.2	.96
ADFI (g/day)	526	517	525	547	27.8	.91
FCE	1.83	1.78	1.76	1.76	0.08	.67

* Pen means, 14 pigs per pen (n = 9). Pigs were weaned at 28 days of age and immediately placed on test (Day 0). Diets described in Tables 1 and 2.

† ANOVA.

ADG = average daily gain; ADFI = average daily feed intake; FCE = feed conversion efficiency; ZnO = zinc oxide; E-MCFAs = eucalyptus-medium chain fatty acids.

group measured Days 0 to 28 was higher ($P < .05$) than that of pigs fed diets supplemented with antibiotics or either of the ZnO supplemented diets, but did not differ from that of pigs fed the E-MCFA-supplemented diet. There were no treatment effects on ADFI during phases 1 and 2 or over the entire experimental period ($P > .05$).

In Experiment Three, there were no differences ($P > .05$) in ADG, ADFI, or FCE between pigs fed diets supplemented with antibiotics, ZnO, or E-MCFAs (Table 5).

The apparent fecal digestibility coefficients for various nutrients contained in the experimental diets are shown in Table 6. Digestibility coefficients of dry matter, calcium, phosphorus, energy, and methionine were lower ($P < .05$) in pigs fed the diets supplemented with ZnO than in pigs fed the diet supplemented with antibiotics. In contrast, digestibility coefficients for crude protein, calcium, phosphorus, energy, histidine, leucine, lysine, phenylalanine, and threonine were higher ($P < .05$) for pigs fed the diet supplemented with E-MCFAs than for pigs fed the diet supplemented with antibiotics. In addition, digestibility coefficients for dry matter, crude protein, calcium, phosphorus, energy, histidine, lysine, methionine, phenylalanine, threonine, and valine were higher in pigs fed the diet supplemented with E-MCFAs than in pigs fed the ZnO-supplemented diets ($P < .05$).

There were no differences ($P > .05$) between the treatments for serum concentrations of total protein, albumin, blood urea nitrogen, triglyceride, high-density lipoprotein cho-

Table 6: Effects of diets supplemented with antibiotics, zinc oxide (ZnO), and eucalyptus-medium chain fatty acids (E-MCFAs) on nutrient digestibility coefficients (%) for nursery pigs (Experiment Three)*

Parameter	Digestibility coefficient (%)				SEM	*P*
	Antibiotics	ZnO 1500 mg/kg	ZnO 2500 mg/kg	E-MCFAs		
Dry matter	91.74[a]	90.58[b]	90.44[b]	92.17[a]	0.26	< .01
Crude protein	74.18[a]	72.01[a]	71.23[a]	78.93[b]	1.13	< .01
Calcium	56.31[a]	48.26[b]	46.75[b]	65.93[c]	1.56	< .01
Phosphorus	54.48[a]	38.25[b]	42.77[b]	66.10[b]	2.01	< .01
Energy	82.92[a]	81.60[b]	81.00[b]	86.00[c]	0.61	< .01
Essential amino acids						
Arginine	85.64	85.44	83.69	84.44	1.24	.66
Histidine	77.19[a]	74.32[b]	74.34[b]	82.05[c]	0.97	< .01
Isoleucine	71.45	71.78	64.33	76.57	2.95	.06
Leucine	77.24[a]	77.30[ab]	73.69[b]	80.58[c]	1.39	.02
Lysine	79.13[a]	80.25[b]	78.25[a]	83.80[b]	0.88	< .01
Methionine	83.94[a]	80.95[b]	80.78[b]	84.23[a]	0.63	< .01
Phenylalanine	73.39[a]	74.58[a]	72.93[a]	79.14[b]	1.12	< .03
Threonine	73.56[a]	73.57[a]	73.43[a]	79.40[b]	1.40	.02
Valine	65.96[ab]	61.39[a]	58.66[a]	74.20[b]	3.25	.02

* Pigs were weaned at 28 days of age and immediately placed on test (Day 0). Diets are described in Tables 1 and 2. All diets contained 1.0% diatomaceous earth (Celite 545; Fluka Chemika/Biochemika, Buchs, Switzerland) as a digestibility marker. Fecal samples were collected from each pen (14 pigs per pen) on Days 11, 12, 13, and 14. For digestibility determinations, only six of the nine pens per treatment were used (n = 6). Digestibility coefficients for nutrients calculated using the equations for the indicator method described by Schneider and Flatt.[18]

[abc] Means in the same row with no common superscript are statistically different (ANOVA; $P < .05$).

lesterol, low-density lipoprotein cholesterol, cortisol, somatomedin-C, immunoglobulin G, and tumor necrosis factor-α (Table 7). Serum zinc, glutamic-oxaloacetic transferase, and glutamic-pyruvic transferase concentrations were higher ($P < .05$) in pigs fed the diets supplemented with ZnO than in pigs fed the diets supplemented with antibiotics or E-MCFAs.

Discussion

The overall performance data (Days 0 to 28) demonstrated higher ADG and ADFI in Experiment One and higher ADG and FCE in Experiment Two for pigs fed ZnO-supplemented diets than for the negative control pigs. In both experiments, performance of the ZnO-supplemented pigs did not differ from that of the antibiotic-supplemented pigs, indicating that ZnO can substitute for antibiotics in diets fed to nursery pigs. Previous studies have also indicated that pharmacological doses of ZnO stimulate performance in weaned pigs,[7,21,22] although there are some reports in which no growth-promoting benefits were observed.[23,24]

Our data indicate that the higher ADG due to ZnO supplementation can be at least partially attributed to an increase in voluntary ADFI. In a recent study by Yin et al,[25] it was observed that ZnO supplementation stimulates ghrelin secretion from the stomach of young pigs, and ghrelin has been shown to act on the small intestine and the brain to stimulate feed intake via an unknown mechanism.[25] Therefore, increased ghrelin secretion may explain the higher feed intake of the ZnO-supplemented pigs observed in Experiment One of the present study.

It has previously been suggested that ZnO promotes the growth of weaned pigs by controlling pathogenic bacterial scours.[26-28] However, other work has indicated that ZnO promotes growth in early and conventionally weaned pigs regardless of diarrhea incidence or effects on intestinal microbial numbers.[21,29] There was no evidence of diarrhea in Experiments One and Two, while severe diarrhea was observed in the control group in Experiment Three, to the extent that feeding of the control diet had to be terminated.

In comparison to the antibiotic treatment, lower digestibility of dry matter, calcium, phosphorus, energy, and methionine digestibility was observed as a result of feeding ZnO at either 1500 or 2500 mg per kg, while digestibility of histidine was lower for pigs fed ZnO at 1500 mg per kg but not at 2500 mg per kg. These findings are somewhat surprising, given the fact that Li et al[29] and Li et al[30] have shown that zinc supplementation improves gut morphology by increasing villous height and reducing crypt depth in the small intestine, thus potentially increasing the absorptive capacity of the small intestine. In addition, Hedemann et al[31] reported that high dietary zinc increased the activity of several enzymes in the pancreatic tissue (amylase, carboxypeptidase, chymotrypsin, trypsin, and lipase) and it might reasonably be expected that such an increase would result in improvements in nutrient digestibility. However, in the present experiment, nutrient digestibility was either unaffected or reduced by zinc supplementation.

Table 7: Effects of antibiotics, zinc oxide (ZnO), and eucalyptus-medium chain fatty acids (E-MCFAs) on serum chemistry parameters of nursery pigs (Experiment Three)*

Parameter	Antibiotics	ZnO 1500 mg/kg	ZnO 2500 mg/kg	E-MCFAs	SEM	*P*
Protein (g/dL)	4.63	4.73	4.69	4.61	0.16	.95
Albumin (g/dL)	2.93	3.09	2.99	3.07	0.12	.76
Blood urea nitrogen (mg/dL)	11.80	11.37	11.33	11.25	0.59	.91
Triglyceride (mg/dL)	56.3	57.8	63.7	59.0	5.2	.77
Total cholesterol (mg/dL)	83.13	88.04	87.02	92.26	3.22	.27
HDL cholesterol (mg/dL)	37.12	38.97	41.27	41.14	1.94	.39
LDL cholesterol (mg/dL)	35.95	40.84	46.52	41.98	3.07	.13
Zinc (µg/dL)	103[a]	232[b]	313[c]	111[a]	21	< .01
Cortisol (µg/dL)	3.46	2.15	1.78	2.86	0.48	.08
Somatomedin-C (ng/mL)	104	83	109	121	12	.19
Immunoglobulin G (mg/dL)	242	218	277	210	36	.56
Tumor necrosis factor-α (pg/mL)	123	127	135	103	12	.30
Glutamic-oxaloacetic transferase (U/L)	53.9[a]	70.5[b]	80.2[b]	51.1[a]	5.4	< .01
Glutamic-pyruvic transferase (U/L)	40.8[a]	58.6[b]	58.1[b]	36.2[a]	2.9	< .01

* Pigs were weaned at 28 days of age and immediately placed on test (Day 0). Diets are described in Tables 1 and 2. Blood samples were obtained at Day 14. There were nine pens per treatment, with blood collection from one pig per pen (n = 9), selected as closest to the average body weight in that pen.

[abc] Means in the same row with different superscripts are statistically different (ANOVA; $P < .05$).

Serum zinc concentrations were elevated for pigs fed diets supplemented with ZnO at 1500 or 2500 mg per kg. This supports previous studies which have also reported elevated levels of serum zinc for zinc-supplemented pigs.[21,32,33] Serum glutamic-oxaloacetic transferase and glutamic-pyruvic transferase concentrations were higher in ZnO-supplemented pigs, which supports our previous work.[34] Elevated levels of these enzymes are typically associated with liver damage,[35] and therefore future work should be conducted to determine whether or not pharmacological levels of dietary ZnO alter liver function.

The overall pig performance data from Experiments One and Two showed higher ADG and ADFI in Experiment One and higher ADG in Experiment Two for nursery pigs fed the diet supplemented with micro-encapsulated E-MCFAs than for pigs fed the negative control diet. In both experiments, the performance of pigs fed micro-encapsulated E-MCFAs did not differ from that of pigs fed antibiotics or pharmacological levels of ZnO, indicating that E-MCFAs can substitute for antibiotics or pharmacological levels of ZnO in diets fed to nursery pigs.

The performance-enhancing effects of micro-encapsulated E-MCFAs could be due to beneficial effects arising from inclusion of eucalyptus or MCFAs either alone or in combination. In poultry, dietary inclusion of eucalyptus has been shown to improve the production performance of commercial laying hens through mechanisms involving stimulation of the immune system.[13] In humans, eucalyptus oil has been shown to stimulate the immune system by affecting the phagocytic ability of monocyte-derived macrophages.[12] However, in the present study, there were no changes in serum parameters such as immunoglobulin G, tumor necrosis factor-α, or cortisol, suggesting that mechanisms other than immune-system stimulation are responsible for the performance enhancement observed in pigs fed eucalyptus. In humans, eucalyptus oil has been shown to have antibacterial effects on pathogenic bacteria in the respiratory tract,[11] and it is possible that antibacterial effects of eucalyptus are responsible for at least some of the performance enhancement observed for pigs fed E-MCFAs.

Another possible explanation for the performance enhancement resulting from feeding E-MCFAs is direct effects of MCFAs. There is some evidence[36] that their use in diets modulates antibacterial responses in pigs. Dierick et al[1,14] showed strong in vitro and in vivo antibacterial effects of MCFAs in the pig proximal small intestine in the absence of growth-promoting antibiotics. It has been estimated that as much as 6% of the net energy in pig diets may be lost due to microbial fermentation in the intestine,[37] and therefore a reduction in bacterial populations could leave more energy available for animal growth. In addition, caprylic acid has been used in the treatment of some bacterial infections. As a result of its relatively short chain length, it can penetrate fatty cell-wall membranes and is therefore effective in combating certain lipid-coated bacteria, such as *Staphylococcus aureus* and various species of *Streptococcus*.[38]

Our data suggest that the superior pig performance associated with supplementing the diet with micro-encapsulated E-MCFAs was primarily the result of higher nutrient digestibility. The results of Experiment Three demonstrated better digestibility of most major nutrients, including crude protein, calcium, phosphorus, and energy, as well as the amino acids histidine, lysine, phenyalanine, and

threonine in the pigs supplemented with micro-encapsulated E-MCFAs. It has been reported that lipid may influence nutrient digestibility by altering intestinal morphology of young pigs.[39-42]

One concern with using MCFAs for growth promotion is that they are a strong stimulus for the release of cholecystokinin, which has a pronounced satiating activity that could interfere with feed intake.[14] In addition, MCFAs are reported to be unpalatable.[15] However, the results of the current experiment indicate that the process of micro-encapsulation overcomes any negative effects of E-MCFAs on feed intake, which was not adversely affected by dietary inclusion of E-MCFAs in any of the three experiments. The overall results of this study indicate that E-MCFAs may be an effective substitute for antibiotics and ZnO as a means of growth promotion in diets fed to weanling pigs.

An issue with feeding pharmacological levels of zinc to pigs is that application of their manure to soil can negatively impact the environment.[9] Pigs fed zinc at 3000 mg per kg of feed excreted almost four times more zinc in their feces as pigs fed zinc at 500 mg per kg.[33] Zinc accumulation in the soil has been implicated in reducing plant growth,[43] while leaching of zinc from soils treated with swine manure may lead to pollution of lakes, streams, and coastal waters.[44,45] The fact that 250 mg per kg of caprylic and carpric acids produced similar levels of growth promotion as 1500 or 2500 mg per kg zinc suggests that the use of E-MCFAs as a growth promoter could minimize the environmental impact of intensive swine operations and reduce the amount of minerals in swine manure that could potentially pollute the environment.

In conclusion, the performance of pigs fed diets supplemented with antibiotics or pharmacological levels of ZnO was better than that of pigs fed a negative control (unsupplemented) diet. The performance of pigs fed a diet supplemented with microencapsulated E-MCFAs did not differ from that of pigs fed diets supplemented with either antibiotics or pharmacological levels of ZnO, indicating that E-MCFAs can also be used as a growth promoter in diets fed to nursery pigs. The effects of E-MCFAs appeared to be mediated through greater nutrient digestibility.

Implications

- Under the conditions of this study, growth performance of pigs supplemented with microencapsulated E-MCFAs did not differ from that of pigs supplemented with antibiotics or pharmacological levels of ZnO.
- Eucalyptus-MCFAs can be used as a growth promoter in diets fed to nursery pigs.

Acknowledgments

This study was supported by the Technology Development Program for Agriculture and Forestry, Ministry for Food, Agriculture, Forestry and Fisheries, Republic of Korea.

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