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Performance and intestinal health of weanling pigs fed with dietary nucleotides

Desempenho e saúde intestinal de leitões recém-desmamados suplementados com nucleotídeos

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Abstract

Previous studies reported benefits to growth performance, intestinal histology and reduced diarrhea for pigs supplemented with nucleotide additive as a replacement to antimicrobial growth promoters. The purpose of this study was to evaluate the effects of nucleotide levels on performance, occurrence of diarrhea, relative weight of organs, intestinal histology, and intestinal microbiota of weanling pigs. One hundred and sixty 21-d weaned pigs (6.43 ± 0.71 kg BW) were used in a randomized complete block design experiment with five treatments, eight replications per treatment and four animals per pen (experimental unit). The treatments were basal diet with 120 ppm of chloro-hydroxyquinoline (antimicrobial), and basal diet with 0 (control), 100, 150, or 200 ppm of nucleotides. The average daily gain (ADG), average daily feed intake (ADFI), gain to feed ratio (G:F), and occurrence of diarrhea were calculated from day 1 to 14, day 14 to 34, and day 1 to 34 of the experiment. A day after the end of the experiment, one animal from each pen was slaughtered to evaluate the relative weight of organs, intestinal histology, and intestinal microbiota. From day 1-14 and day 14-34 of the experiment, performance was not affected by the treatments. For the total experimental period (day 1-34), increasing the dietary concentrations of nucleotides linearly improved the final body weight and average daily gain. *Salmonella* spp. was detected only in the control treatment, without affecting the other microorganisms. Pigs fed with antibiotic had a lower occurrence of diarrhea from day 1-14 compared to pigs fed with nucleotide treatments. Although increasing the occurrence of diarrhea in the first 14 days, dietary nucleotides added up to 200 ppm, improve the final body weight and average daily gain at 34 days post weaning. Nucleotides and antimicrobial not shown beneficial effects on organ weights, and intestinal histology of nursery pig, however, are able to decrease the population of *Salmonella* spp. at small intestine.

Key words: Diarrhea. Feed additives. Growth promoter. Histology. Microbiota. Swine.

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Resumo

Benefícios ao desempenho zotécnico, histologia intestinal e menor incidencia de diarreia têm sido observados em suínos suplementados com nucleotídeos como alternativa aos antibióticos melhores de desempenho. O objetivo deste estudo foi avaliar os efeitos de níveis de nucleotídeos sobre o desempenho, ocorrência de diarreia, peso relativo de órgãos, histologia e microbiota intestinal de leitões recém-desmamados. Cento e sessenta leitões desmamados aos 21 dias (6,43 ± 0,71 kg) foram distribuídos em blocos casualizados com cinco tratamentos, oito repetições por tratamento e quatro animais por baia (unidade experimental). Os tratamentos foram dieta basal com 120 ppm de cloro-hidroxiquinolina (antimicrobiano) e dieta basal com 0 (controle), 100, 150 ou 200 ppm de nucleotídeos. O ganho diário de peso, o consumo diário de ração, a eficiência alimentar e a ocorrência de diarreia foram calculadas nos períodos de 1 a 14, 14 a 34 e 1 a 34 dias de experimentação. Um dia após o final do período experimental, um animal de cada baia foi abatido para avaliar o peso relativo dos órgãos, a histologia e a microbiota intestinal. No período de 1-14 e 14-34 dias, o desempenho dos animais não foi afetado pelos tratamentos. No período total (1-34 dias), com o aumento dos níveis de nucleotídeos na dieta, houve melhora no peso final e no ganho diário de peso. *Salmonella* spp. foi detectada apenas no tratamento controle, sem afetar os demais micro-organismos. Leitões alimentados com o antimicrobiano apresentaram menor ocorrência de diarreia de 1-14 dias, comparados aos animais suplementados com nucleotídeos. Embora aumente a ocorrência de diarreia no primeiros 14 dias, a inclusão de até 200 ppm de nucleotídeos aumenta o peso final e o ganho diário de peso dos leitões aos 34 dias pós-desmame. Nucleotídeos e antibiótico não mostram efeitos no peso dos órgãos e na histologia intestinal de leitões na fase de creche, entretanto, podem diminuir a população de *Salmonella* spp. no intestino delgado.

Palavras-chave: Aditivos alimentares. Diarreia. Histologia. Melhorador de desempenho. Microbiota. Suínos.

Introduction

The post-weaning period is considered stressful for pigs due to changes in behavior, environment, health, nutrition, and immunology. Nutritionally, a diet consisting exclusively of sow milk is replaced by dry diets based on vegetable ingredients and is given to young pigs with a limited digestive capacity. As an adaptive response to this new condition, morphological changes occur in the gastrointestinal tract of animals, such as a shortening of intestinal villi, deepening of crypts, and changes in organ weights, such as the small intestine. These changes may reduce the ability of weanling pigs to digest food and to absorb nutrients, thereby increasing the occurrence of diarrhea (LALLÈS et al., 2007) and a reduction in weight gain (BIAGI et al., 2007; SANTOS et al., 2010).

A number of strategies are used in pig feeding to minimize the negative effects of stressful factors during the nursery phase. These include the addition of antimicrobial growth promoters in the feed. However, their use has been banned in several countries due to the potential of cross-resistance development. Consequently, numerous studies have been performed to identify alternative feed additives for weanling pigs.

Nucleotides are composed of a nitrogenous base (purine or pyrimidine) linked to a pentose (2-deoxyribose in DNA and ribose for RNA) sugar to which one or more phosphate group are attached (SAUER et al, 2011). Nucleotides and their related metabolic products play key roles in many biological processes and become essential dietary components when endogenous supply is insufficient for normal function. Nucleotides as feed additives have shown positive effects on the health of young animals (ANDRÉS-ELIAS et al., 2007). They have been reported to improve the performance and intestinal morphology of weanling pigs (ANDRADE et al., 2011). Moore et al. (2011) demonstrated that the intestinal villus height was higher for pigs receiving nucleotides, suggesting a beneficial effect on the growth of intestinal cells. Superchi et al. (2012) also reported reduced cortisol levels in weaned pigs fed with diets supplemented with nucleotides and suggested that they may improve growth by modulating the adaptive response to weaning. Thus, the objective of this study was to evaluate the effects of dietary nucleotide levels on performance, the occurrence of diarrhea, relative weight of organs, intestinal histology, and intestinal microbiota of nursery pigs.

Material and Methods

All procedures using animals were approved by the "Committee of Ethics for the Use of Animals of the 'Luiz de Queiroz' College of Agriculture – CEUA / ESALQ / USP."

Animals and experimental design

One hundred and sixty 21-d weaned pigs (6.43 ± 0.71 kg BW), castrated males and females, were used in a randomized complete block design experiment consisting of five treatments, with eight replications per treatment, and four pigs per experimental unit (pen). The pigs were blocked based on the initial BW and sex and housed in 1.20 × 1.50 m pens with a partially slatted floor in a naturally ventilated building. Each pen was equipped with a feeder and a nipple drinker, which provided *ad libitum* access to feed and water throughout the entire experimental period, and a complementary heat source.

Experimental diets

Experimental diets (Table 1) were formulated based on the nutrient requirements of weanling pigs as described by Rostagno et al. (2011). A 2-phase feeding program was used, which consisted of a pre-starter diet from day 1 to 14 and a starter diet from day 14 to 34. The complex diets containing corn, soybean meal, milk products, spray-dried plasma and 3,000 ppm of ZnO (ZnO acts similarly to an antimicrobial agent and preventative of diarrhea) was included throughout the entire experiment.

The treatments (Table 2) consisted of a basal diet with 120 ppm of chloro-hydroxyquinoline (antimicrobial treatment) and basal diets supplemented with 0 (control), 100, 150, or 200 ppm of nucleotides. One commercial product containing approximately 60% of free nucleotides and 25% of intact RNA extracted from yeast (ICC, São Paulo, Brazil) was added on top of diets of up to 200 ppm of nucleotides.

Growth performance

Considering the effects of nucleotides on the performance of animals associated with a change in diet (from complex for 1 to 14 days, to less complex for 14 to 34 days of the experimental period), individual pig body weight and feed intake per pen were registered on day 1, 14, and 34 to determine the average daily gain, average daily feed intake, and feed:gain.

The occurrence of diarrhea

The occurrence of diarrhea was monitored every day for all pigs (defining diarrhea to be liquid stool), in the presence or absence of diarrhea in each pen, independent of the number of animals with diarrhea. The percentage of days with diarrhea was calculated from 1 to 14 days, and from 1 to 34 days of the experimental period.

Table 1. Composition of the basal pre-starter and starter diets[a].

Item	Pre-starter diet	Starter diet
Ingredient, %		
Corn	54.19	65.97
Soybean meal, 46% CP	18.00	20.00
Spray-dried whey	11.40	4.74
Spray-dried whole milk	5.16	0.36
Spray-dried plasma	5.00	3.00
Sugar	3.00	3.00
Dicalcium phosphate	1.32	1.43
Limestone	0.84	0.69
Salt	0.10	0.13
Mineral premix[b]	0.10	0.10
Vitamin premix[c]	0.05	0.05
L-Lysine·HCl, 78%	0.28	0.15
DL-Methionine, 99%	0.12	0.02
L-Threonine, 98.5%	0.08	0.00
ZnO	0.30	0.30
Ethoxyquin	0.025	0.025
Kaolin	0.035	0.035
Total	100.00	100.00
Calculated composition		
ME, Mcal/kg	3.32	3.23
CP, %	19.12	17.45
Ca, %	0.82	0.72
Available P, %	0.45	0.40
Lactose, %	10.00	3.50
Digestible lysine, %	1.33	0.99
Digestible methionine, %	0.42	0.28
Digestible threonine, %	0.84	0.63
Digestible tryptophan, %	0.23	0.19

[a]120 ppm of antimicrobial chloro-hydroxyquinoline (60%) and 0, 100, 150, and 200 ppm of nucleotides (ICC, São Paulo, Brazil) were included in the diets replacing Kaolin. [b]Provided per kilogram of diet: Mg, 60 mg; Zn, 150 mg; Fe, 100 mg; Cu, 10 mg; and I, 1.2 mg. [c]Provided per kilogram of diet: vitamin A, 11,500 IU; vitamin D_3, 5,850 IU; vitamin E, 45 IU; vitamin K_3, 3.0 mg; thiamine, 1.80 mg; riboflavin, 5.1 mg; pyridoxine, 3.5 mg; vitamin B_{12}, 24.0 µg, niacin, 37.5 mg; folic acid, 0.82 mg; biotin, 0.14 mg; pantothenic acid, 18.0 mg; Se, 0.35 mg; and ethoxyquin, 0.042 mg.

Table 2. The treatments used for pigs during 34 days post-weaning.

Treatment	Description
Antimicrobial	Basal diet with 120 ppm of chloro-hydroxyquinoline (Positive control)
0	Basal diet without nucleotide or antibiotic (Negative control)
100	Basal diet supplemented with 100 ppm of nucleotides[a]
150	Basal diet supplemented with 150 ppm of nucleotides[a]
200	Basal diet supplemented with 200 ppm of nucleotides[a]

[a]One commercial product containing approximately 60% of free nucleotides and 25% of intact RNA extracted from yeast (ICC, São Paulo, Brazil) was added on top of diets of up to 200 ppm of nucleotides.

Relative weight of organs, intestinal histology, and intestinal microbiota

One day after the end of the experiment, one animal per experimental unit was slaughtered and tissue samples were collected to evaluate intestinal histology, intestinal microbiota, and relative weight of organs. From each pig, 3-cm samples of the duodenum (resected 15 cm from the gastric pyloric valve) and jejunum (resected 150 cm from the ileo-cecal junction) were fixed in formalin 24 h prior to staining for intestinal histology. Each histological sample was prepared in paraffin and four sections of tissue (6 μm thick) were cut and colored by the method of hematoxylin-eosin staining. The villus height, villus width and crypt depth were then measured in five villi per section using optical microscopy (AFIP, 1994). The relative weights of the digestive organs (empty stomach, pancreas, liver, and empty small intestine) and spleen were calculated based on the slaughter body weight and the weight-to-length ratio of the small intestine was determined. For intestinal microbiota analysis, the intestine was cut longitudinally, and the contents of the duodenum and jejunum were collected by scraping with a spatula. Afterwards, the samples were placed in identified plastic bags and sent to a commercial laboratory (CBO laboratory, Campinas, Brazil) for quantification of mesophiles, gram-positive bacteria, gram-negative bacteria, *Lactobacillus* spp., *Escherichia coli*, *Salmonella* spp., *Staphylococcus* spp., and *Clostridium perfringens*. Twenty-five grams of sample were weighed, placed into 225 mL of peptone water (BPW) 0.1%, and homogenized and incubated for 24 h at 36 ± 1°C according to the procedures described by AOAC (2005). These results were expressed in colony-forming units per gram of sample (CFU g^{-1}).

Statistical analysis

For the statistical analysis, data were submitted to analysis of variance, considering a randomized block design experiment, using the GLM procedure of SAS (SAS, 2009). All data were tested for normality, homogeneity of residual variances, and outliers. The model included the treatment as the fixed effect and the block as the random effect, as follows:

$$Y(ij) = \mu + t(i) + b(j) + \varepsilon(ij), \text{ where:}$$

Y(ij) is the dependent response, μ is the overall mean, t (i) is the fixed effect of treatments (i=1,…5), b (j) is the effect of block (j=1,…8), and ε (ij) is the residual error.

The degrees of freedom of dietary nucleotide levels were decomposed in individual components (linear and quadratic) by orthogonal polynomials. Specific orthogonal contrasts were performed to compare antimicrobial treatment *vs*. 100, 150, and 200 ppm of nucleotides (C1) and antimicrobial *vs*. control (C2). The alpha level for the determination of significance was ≤ 0.05.

Results and Discussion

During the first 14 days of the experimental period, the treatments did not affect (P > 0.05) the body weight, average daily gain, average daily feed intake, and gain:feed (Table 3). This finding was consistent with previous studies, which showed that 375 ppm (ANDRÉS-ELIAS et al., 2007) and 500 ppm (DOMENEGHINI et al., 2004) of dietary nucleotide supplementations did not affect the growth performance of weanling pigs. Nucleotides and other feed additives, such as antimicrobial agents, may not demonstrate beneficial effects to weanling pigs fed with complex diets without exposure to stressful conditions. The efficacy of antimicrobials in improving the growth performance of weanling pigs has been well documented (CROMWELL, 2002; BOSI et al., 2011). However, these responses were greater in pigs raised under farm conditions compared to experimental conditions (NRC, 1998).

Table 3. The performance of pigs fed with diets containing antimicrobial or different levels of nucleotides for 34 days post-weaning[(a)].

Item[(b)]	Antimicrobial	Dietary nucleotide level, ppm				SEM[(c)]	P-value
		0	100	150	200		
BW, kg							
d 0	6.43	6.40	6.45	6.41	6.45	0.11	0.429
d 14	12.70	12.30	12.80	12.65	12.66	0.21	0.336
d 34[(d)]	23.08	23.58	24.13	24.18	24.23	0.33	0.026
ADG, kg							
d 1 to 14	0.447	0.422	0.454	0.446	0.444	0.01	0.367
d 14 to 34	0.558	0.525	0.566	0.577	0.578	8.85	0.080
d 1 to34[(d)]	0.491	0.504	0.520	0.523	0.523	0.01	0.045
ADFI, kg							
d 1 to 14	0.610	0.588	0.626	0.626	0.623	0.01	0.254
d 14 to 34	1.099	1.102	1.154	1.041	1.137	0.20	0.609
d 1 to 34	0.901	0.887	0.937	0.870	0.925	0.03	0.801
G:F							
d 1 to 14	0.738	0.717	0.724	0.711	0.712	0.01	0.598
d 14 to 34	0.510	0.479	0.495	0.568	0.523	11.45	0.127
d 1 to 34	0.574	0.545	0.558	0.591	0.574	0.01	0.305

[(a)]Values are the least square means of eight replicates per treatment and four pigs per pen. [(b)]BW = body weight; ADG = average daily gain; ADFI = average daily feed intake; G:F = gain:feed. [(c)]The standard error of the mean. [(d)]Positive linear effect ($P < 0.05$) of nucleotides on BW and ADG at 34 days.

From day 14 to 34 of the experiment, growth performance was not affected ($P > 0.05$) by the treatments. For the total experimental period (day 1 to 34), increasing concentrations of dietary nucleotides linearly improved the final body weight ($P = 0.005$) and average daily gain ($P = 0.008$), but did not affect ($P > 0.05$) the average feed intake and gain:feed (Table 2). No effects of the antimicrobial treatment were observed on animal performance compared to the control treatment. Previous studies with weanling pigs have shown that the inclusion of 150 ppm of dietary nucleotide (ANDRADE et al., 2011), 1,000 ppm of yeast extract nucleotides (SUPERCHI et al., 2012), and 2,000 ppm of yeast supplement as a source of nucleotide (BONTEMPO et al., 2006) was effective in improving the body weight and average daily gain. Edwards et al. (2013) and Weaver and Kim (2014) also reported beneficial effects of nucleotides on the growth performance and health of weaned pigs fed with diets containing 3.5% of yeast protein meal and up to 1,000 ppm of nucleotides, respectively. Similarly, broilers supplemented with 2 or 6% of a commercial nucleotide product were heavier and showed improved gain:feed compared to the control diet (JUNG; BATAL, 2012). It is important to highlight that the dietary nucleotide levels used in this experiment were lower compared to other studies, due to the high concentrations of free nucleotides in the product used.

Pigs fed with an antimicrobial treatment demonstrated a lower ($P = 0.049$) occurrence of diarrhea compared to pigs fed with dietary nucleotide for the first 14 days of the experimental period (Table 4). Although 3,000 ppm of ZnO were included in all the diets, protective role in the prevention of diarrhea were not observed to animals fed nucleotides. A negative effect of supplementation of nucleotides on this parameter (diarrhea) it was evidenced, but the biological explanation was not found. However, for the total experimental period (from day 1 to 34), no effects of the treatments were observed on the occurrence of diarrhea, suggesting that the critical period for pigs are the first two weeks after weaning.

Table 4. The occurrence of diarrhea (%) in pigs fed with diets containing antimicrobial or different levels of nucleotides for 34 days post-weaning[(a)].

Period	Am[(b)]	Dietary nucleotide level, ppm				SEM[(c)]	P-value	Contrast P-value[(d)]	
		0	100	150	200			C1	C2
d 1 to 14	0.89	1.78	1.78	3.57	5.36	0.84	0.0002	0.049	0.142
d 14 to 34	1.25	1.25	0.00	0.62	0.00	0.74	0.999	0.983	1.000
d 1 to 34	1.47	1.10	0.73	1.84	2.20	0.43	0.1704	0.951	0.524

[(a)]Values are the least square means of eight replicates per treatment and four pigs per pen. [(b)]Am = basal diet with 120 ppm of chloro-hydroxyquinoline (antimicrobial treatment). [(c)]The standard error of the mean. [(d)]C1 = Antimicrobial vs. nucleotide (100, 150, and 200 ppm); C2 = Antimicrobial vs. 0 (control).

Supplementation of nucleotides of up to 1,000 ppm of weanling pig diets has shown beneficial effects on reducing diarrhea (MARTINEZ-PUIG et al., 2007). In addition, dietary nucleotide supplementations of 31 mg/L (SINGHAL et al., 2008) in formula-fed human infants showed a reduction in the occurrence of diarrhea, which may positively affect gastrointestinal microbiota. The intestinal pathogens, such as *Salmonella typhimurium* and *Clostridium* spp., are able to use the undigested and unabsorbed nutrients present in the gut as substrates for their growth and can be a major cause of the diarrhea (OETTING et al., 2006).

In this study, the relative weights of the digestive organs and spleen (Table 5), intestinal histology (Table 6) and intestinal microbiota (Table 7) were not affected by the dietary treatments.

Table 5. The relative weight of organs (%) in pigs fed with diets containing antimicrobial or different levels of nucleotides for 34 days post-weaning[(a)].

Item	Antimicrobial	Dietary nucleotide level, ppm				SEM[(b)]	P-value
		0	100	150	200		
Body weight, kg	24.09	23.18	24.05	24.01	25.05	0.40	0.447
Estomach, %	0.69	0.66	0.70	0.68	0.72	0.01	0.462
Pancreas, %	0.14	0.12	0.14	0.14	0.09	0.01	0.108
Liver, %	2.89	2.94	3.15	2.83	3.11	0.04	0.065
Small intestine (SI), %	5.15	4.70	5.33	4.83	4.65	0.02	0.439
Spleen, %	0.25	0.20	0.25	0.21	0.26	0.01	0.225
Length SI, m	15.78	15.80	15.44	16.25	15.75	0.24	0.828
Relative length SI, m/kg body weight	0.66	0.68	0.64	0.67	0.65	0.01	0.628
Weight:length SI, g/m	76.45	72.06	84.24	72.11	72.24	0.01	0.192

SI = small intestine. [(a)]Values are the least square means of eight replicates per treatment and one pig per pen. [(b)]The standard error of the mean.

The increased gastrointestinal weight in relation to body weight, occurs independent of age at weaning and is caused mainly by the change in the type of diet (LE DIVIDICH; SÈVEN, 2000), and by amount of feed intake during the days immediately following weaning (PLUSKE et al., 1997). In the present study, the average daily feed intake was not affected by treatments, which may partially explain no differences on the relative weight of the digestive organs.

For intestinal microbiota, *Clostridium perfringens* was not statistically analyzed because the quantification for all of the samples was less than 10 CFU g^{-1}. *Salmonella* spp. was detected ($P < 0.001$) only in the control treatment, suggesting that nucleotides and antibiotics might be efficient in reducing this microorganism in the weanling pig intestine. In addition, in other study (SAUER et al., 2011), the inclusion of 1,000 ppm of a dried yeast product, which contained free nucleotides, did not affect the total count of *Lactobacillus* spp., *Enterococcus* spp., *Bifidobacterium* spp., and Enterobacteria.

Table 6. The intestinal histology of pigs fed with diets containing antimicrobial or different levels of nucleotides for 34 days post-weaning[(a)].

Item[(b)]	Antimicrobial	Dietary nucleotide level, ppm				P-value
		0	100	150	200	
Duodenum:						
VH (µm)	549.0	537.5	541.9	554.6	553.6	0.401
CD (µm)	480.9	481.3	480.5	479.0	480.9	0.456
VH:CD	1.15	1.12	1.14	1.17	1.16	0.245
VW (µm)	81.85	82.07	81.72	81.97	81.10	0.941
Jejunum:						
VH (µm)	603.0	596.7	590.0	597.1	600.9	0.762
CD (µm)	428.8	431.5	431.4	429.7	429.8	0.386
VH:CD	1.41	1.38	1.37	1.39	1.40	0.532
VW (µm)	72.12	71.40	72.20	71.34	71.32	0.785

[(a)]Values are the least square means of eight replicates per treatment and one pig per pen. [(b)]VH = villus height, CD = crypt depth, VH:CD = villus height: crypt depth ratio, VW = villus width.

Table 7. The intestinal microbiota of pigs fed with diets containing antimicrobial or different levels of nucleotides for 34 days post-weaning[(a)].

Microorganism	Antimicrobial	Dietary nucleotide level, ppm				P-value
		0	100	150	200	
Mesophylls	5.39	0.40	6.12	5.83	6.07	0.399
Gram-negative	3.59	0.69	2.71	3.67	3.76	0.695
Gram-positive	5.11	0.17	6.09	5.56	5.55	0.169
Lactobacillus	3.95	0.86	3.50	3.97	4.04	0.861
Staphylococcus	0.76	0.28	1.04	0.00	0.92	0.283
E. coli	1.85	0.96	2.51	3.13	3.11	0.957
Salmonella spp.	-	+	-	-	-	<0.001

+ = present; – = absent. [(a)]Values are the least square means of four replicates per treatment and one pig per pen.

The *Salmonella* population grows to a population size of approximately one billion cells in the gut. From the gut, this bacterium colonizes the cecal lymph node, and subsequently spreads throughout the body (KAISER et al., 2013). Thus, an understanding of how a pathogen colonizes their hosts; which organ it colonizes; and where and how fast it replicates, migrates, and is killed is crucial in the prevention of infection. However, in this study, the *Salmonella* count was performed only in the small intestine, and we were not able to evaluate the *Salmonella* count in other organs.

The beneficial effects of dietary nucleotide on intestinal microbiota has been only detected at approximately six weeks after its supplementation in the diet, as previously reported by Castillo et al. (2007), or under high microbial contamination. However, dietary nucleotides are able to modulate the changes in microbiota composition after weaning, acting specially in the ileum (ANDRÉS-ELIAS et al., 2007). The inclusion of 2,000 ppm of extract of yeast *Saccharomyces cerevisiae*, as a source of nucleotides, increased the population of *Lactobacillus* and Bacteroides, after an oral challenge of the animals with *Salmonella* (PRICE et al., 2010). Similarly, increasing the levels of yeast extract (2,500, 5,0000, 10,000, and 20,000 ppm) depressed the population of *Escherichia coli* and showed beneficial effects on average daily gain and intestinal histology in weanling pigs (SHEN et al., 2009).

In previous studies, the villus height of the duodenum of weanling pigs slaughtered at d 28 (MARTINEZ-PUIG et al., 2007), d 35 (ANDRADE et al., 2011), and d 42 (MOORE et al., 2011) post-weaning increased with dietary nucleotide additions of 500, 600, and 2,000 ppm, respectively. For broilers, dietary supplementation of up to 2,000 ppm of a commercial product providing nucleotides increased the villus height and decreased the villus height-to-crypt depth ratio, compared to the animals fed with the control diet (JUNG; BATAL, 2012). However, some studies have demonstrated that supplementing the diet of weanling pigs with nucleotides does not alter intestinal morphology (NORTON et al., 2011), and the intestinal and fecal bacterial count (SAUER et al., 2011, 2012). These findings suggested that differences in these results were related with diet composition, level of dietary added nucleotides, and their production process, in addition to the nutrition and health conditions of the animals.

Conclusions

Dietary nucleotides added up to 200 ppm improve the final body weight and average daily gain of nursery pigs. Nucleotides and antimicrobial not shown beneficial effects on organ weights, and intestinal histology of weaned pigs, however, are able to decrease the population of *Salmonella* spp. at small intestine.

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