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Supplemental nucleotides high in inosine 5′-monophosphate to improve the growth and health of nursery pigs[1]

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ABSTRACT: This study was conducted to determine the ability of a supplemental nucleotide mixture high in inosine 5′-monophosphate (5′IMP) to enhance pig growth and health after weaning. Pigs (n = 120 and 7.3 ± 0.1 kg) were allotted at weaning to phase 1 diets (3.3 Mcal ME/kg, 22.4% CP, and 1.34% standardize ileal digestible [SID] Lys) supplemented with 0.0, 0.2, 0.5, or 1.0 g/kg of a nucleotide additive. After 7 d, pigs were fed phase 2 diets (3.3 Mcal ME/kg, 21.3% CP, and 1.20% SID Lys) for 21 d with the same additive levels. Growth performance was measured, blood samples were collected for analysis of immune responses and oxidative stress, and fecal scoring was completed. During phase 1, ADG, ADFI, and G:F linearly increased ($P < 0.05$) as dietary nucleotides increased. During phase 2, ADFI increased linearly ($P < 0.05$). Over the entire 28-d trial, ADG and ADFI increased linearly ($P < 0.05$) as nucleotide content increased. Immune responses were not altered during phase 1. At the end of phase 2, IgA showed a quadratic effect ($P < 0.05$) with the lowest concentrations at 0.2 and 0.5 g/kg of the nucleotide additive whereas IgM changed cubically ($P < 0.05$) with the lowest concentration at 0.5 g/kg. The cytokine tumor necrosis factor-α tended to decrease linearly ($P = 0.093$) as nucleotide content increased whereas the marker for oxidative DNA damage, 8-hydroxy-deoxyguanosine, tended to have a quadratic effect ($P = 0.064$) with the lowest levels of damage in pigs fed 0.5 g/kg. On d 8 after changing from the phase 1 to phase 2 diets, fecal diarrhea scores tended to be lowest ($P = 0.072$) when pigs were fed 0.5 g/kg of the nucleotide additive. Overall, 1.0 g/kg of the nucleotide additive provided the most benefit to the growth performance of nursery pigs. However, 0.5 g/kg of the nucleotide additive reduced immune responses and oxidative stress. In conclusion, the addition of a nucleotide mixture high in 5′IMP to the diet of young pigs may be beneficial to enhance growth performance and reduce postweaning stress.

Key words: nucleotides, oxidative stress, pigs, weaning

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INTRODUCTION

Weaning is a stressful event for piglets. Social and dietary stressors can reduce digestion and absorption of nutrients and increase immune challenges, oxidative stress, or diarrhea, which in turn reduces feed intake and growth performance (Salobir et al., 2005; Kim et al., 2010). Dietary nucleotides may be one way to reduce weaning stress. Nucleotides act as bioactive molecules that play a role in metabolic, structural, and regulatory functions (Sauer et al., 2012). Nucleotides are also important in immune system maintenance and may prevent oxidative stress (Salobir et al., 2005). Normally, substantial amounts of nucleotides are obtained through de novo synthesis, but supplemental nucleotides may be beneficial during times of rapid growth or stress (Carver and Walker, 1995; Frankič et al., 2006).

Before weaning, piglets consume high levels of nucleotides in sow milk (Mateo et al., 2004). However, weaning diets may have insufficient nucleotide concentrations (Martinez-Puig et al., 2007). Therefore, dietary nucleotides could benefit the health of newly weaned pigs. One specific nucleotide that may play a valuable role in nursery diets is inosine 5′-monophosphate (**5′IMP**). This particular nucleotide is a major form produced during de novo synthesis (Mateo, 2005). Once formed, 5′IMP then serves as a precursor

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for other nucleotides used for metabolic functions (Stein and Kil, 2006). Dietary 5′IMP may not only reduce the burden of de novo synthesis, but 5′IMP is also shown to increase feed intake by stimulating taste receptors (Kubitza et al., 1997).

We hypothesize that dietary supplementation of nucleotides with a high concentration of 5′IMP will enhance pig growth and health during the nursery period. To test this hypothesis, this study was conducted to 1) determine the impact of increasing concentrations of dietary 5′IMP on piglet growth performance and 2) measure the impact of nucleotides on blood levels of immunological and oxidative stress parameters.

MATERIALS AND METHODS

A protocol for the use of animals in this study was approved by the North Carolina State University animal care and use committee.

Animals and Experimental Diets

One hundred twenty piglets (7.27 ± 0.07 kg) were weaned at 22.1 ± 0.3 d old. Pigs were housed in temperature controlled, raised-deck nursery pens (0.91 by 1.52 m) at the North Carolina State University Swine Educational Unit (Raleigh, NC). Each pen had a double space feeder and 2 nipple water drinker. Pigs were blocked by BW (5 groups) and sex (2 groups) and randomly allotted to 4 treatments. Each treatment had 10 replicates with 3 pigs per pen for a total of 30 pigs per treatment. During the entire trial period, pigs were provided with feed and water ad libitum. Body weight and feed intake were measured every 7 d for 28 d.

After weaning, a standard phase 1 diet was fed for 7 d (Table 1). Diets were supplemented with 0.0, 0.2, 0.5, or 1.0 g/kg of a nucleotide additive (Inotide; CJ Corp, Seoul, Korea). This additive contains 53.0% total nucleotides (51.0% 5′IMP and 2.0% other nucleotides), 16.8% crude ash, 11.2% total sugars, 9.3% water, 4.1% phosphorus, 3.2% total AA, and 2.4% compounds containing nonprotein nitrogen. The addition of the nucleotide additive replaced an equal amount of soybean meal in each diet to maintain equal CP and Lys concentrations. After phase 1, pigs were fed a phase 2 diet for 21 d (Table 1). Pigs were fed the same nucleotide additive supplementation received during phase 1 (0.0, 0.2, 0.5, or 1.0 g/kg).

Table 1. Composition of experimental diets, as-fed basis

	Dietary composition[1]	
Item	Phase 1	Phase 2
Ingredient, %		
Yellow corn, ground	45.0	50.5
Soybean meal, dehulled	23.9	27.9
Dried whey	20.0	15.0
Plasma protein	2.00	0.00
Fish meal	5.00	3.00
L-Lys HCl	0.10	0.10
DL-Met	0.08	0.06
L-Thr	0.02	0.00
Salt	0.22	0.26
Vitamin premix[2]	0.03	0.03
Trace mineral premix[3]	0.15	0.15
Dicalcium phosphate	1.15	0.80
Ground limestone	0.25	0.60
Poultry fat	2.00	1.5
Calculated composition		
DM, %	91.3	90.8
ME, kcal/kg	3,269	3,313
CP, %	22.4	21.3
Lys, %	1.34	1.20
Cys + Met, %	0.76	0.70
Trp, %	0.25	0.23
Thr, %	0.84	0.73
Ca, %	0.91	0.82
Available P, %	0.55	0.40
Total P, %	0.82	0.68
Analyzed composition[4]		
DM, %	90.8	90.3
CP, %	22.9	22.2

[1]Diets in each phase supplemented with 0.0, 0.2, 0.5, or 1.0 g/kg of a nucleotide additive (Inotide; CJ Corp, Seoul, Korea) for a total of 4 diets per phase. This additive contains 53% total nucleotides, with 51% of these as inosine 5′-monophosphate. The addition of the nucleotide additive replaced an equal amount of soybean meal in each diet.

[2]The vitamin premix provided per kilogram of complete diet: 6,614 IU of vitamin A as vitamin A acetate, 992 IU of vitamin D_3, 19.8 IU of vitamin E, 2.64 mg of vitamin K as menadione sodium bisulfate, 0.03 mg of vitamin B_{12}, 4.63 mg of riboflavin, 18.52 mg of D-pantothenic acid as calcium panthonate, 24.96 mg of niacin, and 0.07 mg of biotin.

[3]The trace mineral premix provided per kilogram of complete diet: 4.0 mg of Mn as manganous oxide, 165 mg of Fe as ferrous sulfate, 165 mg of Zn as zinc sulfate, 16.5 mg of Cu as copper sulfate, 0.30 mg of I as ethylenediamine dihydroiodide, and 0.30 mg of Se as sodium selenite.

[4]The analyzed compositions of DM and CP for phase 1 and 2 were determined by averaging the values obtained from the analyzed levels of the 4 diets in each respective phase.

Blood Sampling

Blood samples (7 mL) were collected aseptically from the jugular vein from 1 pig per pen (pig with median initial BW) at the end of each phase (d 7 and 28). Blood was collected in vacutainer tubes containing dipotassium EDTA (BD, Franklin Lakes, NJ). Plasma samples were separated by centrifuging (3,000 × *g* for 15 min at 4°C) and stored at –80°C until analyzed for immune and oxidative stress responses.

Plasma samples were used to measure the immunological responses, IgA, IgG, IgM, and the cytokine tumor necrosis factor α (**TNFα**), as indicators of health status. Total concentrations of immunoglobulins were measured using a ELISA kit (Bethyl Laboratories, Mont-

gomery, TX) as previously described by Chaytor et al. (2011). Plasma samples were diluted 1:2,000, 1:80,000, or 1:4,000 for determination of IgA, IgG, and IgM, respectively. Absorbance was read at 450 nm using a plate reader (Synergy HT Plate Reader; BioTek Instruments, Inc., Winooski, VT) and Gen5 data analysis software (BioTek Instruments). Samples were quantified relative to a standard curve constructed with known amounts of pig immunoglobulin subset. Detection limits were 15.6 to 1,000 ng/mL for IgA, 7.8 to 500 ng/mL for IgG, and 15.6 to 1,000 ng/mL for IgM.

Plasma TNFα concentration was measured using a ELISA kit (R&D Systems, Minneapolis, MN) as previous described by Weaver et al. (2013). A total of 50 μL of standard, control, or plasma sample were added to separate microplate wells coated with a monoclonal antibody for porcine TNFα. After incubation, wells were washed and porcine TNFα conjugate was added. Following a second incubation period, plates were again washed and a color reagent substrate solution was added followed by a stop solution of diluted hydrochloric acid. Absorbance was read at 450 and 540 nm as described previously. The detection limit range for this TNFα ELISA was 2.8 to 5.0 pg/mL.

Oxidative DNA damage was estimated by determining the concentration of plasma 8-hydroxy-deoxyguanosine (**8-OHdG**), a metabolite of DNA breakdown. Total 8-OHdG was measured using a ELISA kit (Cell Bio Labs, San Diego, CA) as previous described by Zhao et al. (2013). Plasma samples and 8-OHdG standards were added to an 8-OHdG/BSA precoated microplate. After incubation, an anti-8-OHdG monoclonal antibody was added to wells followed by a conjugated secondary antibody. After washing, a substrate solution was added followed by a stop solution. The 8-OHdG content in the samples is determined by comparison to the standard curve read at 450 nm. The detection range for this ELISA is 100 pg/mL to 20 ng/mL.

Diarrhea Scoring

Fecal scores of all pigs were determined at 3 time points during this experiment on d 5, 8, and 15. To determine the severity of postweaning diarrhea, feces were scored by determining the moisture content as described by Liu et al. (2008). Scores were 1 = normal, firm feces, 1.5 = looser feces leading to possible slight diarrhea, 2 = moderate liquid consistency, 2.5 = definite diarrhea with unformed, fluid feces, or 3 = severe diarrhea with very watery and frothy feces. An overall diarrhea score per diet and sampling day was then calculated.

Statistical Analysis

Data were analyzed using SAS (SAS Inst., Inc., Cary, NC) following a randomized block design. The pen was considered as the experimental unit. Polynomial contrasts for linear, quadratic, and cubic effects were determined using the Interactive Matrix Language (**IML**) procedure of SAS to generate coefficients for the unevenly spaced orthogonal contrasts. These coefficients generated by the IML procedure were then used in the Mixed Model statement to determine polynomial contrasts. Fixed effects were the treatment and sex and a random effect was initial BW. Probability values less than 0.05 were considered statistically significant and between 0.05 and 0.10 as trends.

RESULTS

Growth Performance

During phase 1, there was a linear increase in BW ($P = 0.008$), ADG ($P = 0.007$), ADFI ($P = 0.005$), and G:F ($P = 0.015$) as dietary nucleotides increased from 0.0 to 1.0 g/kg (Table 2). During phase 2, growth performance traits were not altered from d 7 to 14, but ADG increased during d 14 to 21 and tended to increase from d 21 to 28 ($P = 0.043$ and $P = 0.053$, respectively). Throughout phase 2, ADFI increased ($P < 0.001$) as nucleotide supplementation increased. Throughout the entire study, the ADG and ADFI increased ($P = 0.031$ and $P < 0.001$, respectively) with increasing nucleotide supplementation to the diet.

Immune Function and Oxidative Stress

Immunological and oxidative stress measurements were not different among treatments at the end of phase 1. However, at the end of phase 2, the immune system was altered by nucleotide supplementation (Table 3). The IgA had a quadratic effect ($P = 0.019$) with the lowest levels at 0.2 and 0.5 g/kg of the nucleotide additive. The levels of IgG were not altered by treatment; however, IgM was lowest at 0.5 g/kg ($P = 0.036$). The plasma levels of TNFα tended to decrease linearly ($P = 0.093$) as nucleotide level was increased in the diet. Finally, the amount of 8-OHdG tended to have a quadratic effect ($P = 0.064$) with the lowest levels of 8-OHdG in pigs fed 0.5 g/kg of the nucleotide additive.

Fecal Scores

Fecal scores of diarrhea severity were not different among treatments on d 5 during phase 1 or on d 15 during phase 2 (Table 4). However, fecal scores tended ($P = 0.072$) to be lowest from pigs fed 0.5 g/kg of the nucleotide additive on d 8. This difference occurred when pigs were switched from the phase 1 to phase 2 diets.

Table 2. Growth performance of nursery pigs fed supplemental nucleotides for 28 d

	Treatment[1]					*P*-value		
Item	0.0	0.2	0.5	1.0	SEM	Linear	Quadratic	Cubic
Age at wean, d	21.9	21.8	22.2	22.6	0.3	0.046	0.653	0.634
BW, kg								
d 0	7.25	7.27	7.27	7.27	0.07	0.887	0.824	0.927
d 0 to 7	7.46	7.66	7.66	7.95	0.12	0.008	0.978	0.428
d 7 to 14	8.93	8.70	8.91	8.88	0.21	0.894	0.820	0.408
d 14 to 21	11.40	11.30	11.53	11.82	0.27	0.178	0.704	0.678
d 21 to 28	15.10	14.87	15.43	16.03	0.37	0.035	0.603	0.489
ADG, g/d								
d 0 to 7	25.7	45.6	43.5	83.7	14.3	0.007	0.658	0.417
d 7 to 14	210.2	148.2	178.0	136.9	28.5	0.160	0.776	0.170
d 14 to 21	353.2	371.4	374.8	420.6	23.3	0.043	0.752	0.677
d 21 to 28	528.3	510.5	556.4	600.4	32.0	0.053	0.679	0.507
d 7 to 28	363.9	343.4	369.7	386.0	16.0	0.148	0.549	0.294
d 0 to 28	270.9	261.2	279.1	301.8	12.4	0.031	0.499	0.465
ADFI, g/d								
d 0 to 7	150.9	193.7	172.8	197.1	8.6	0.005	0.406	0.002
d 7 to 14	288.8	266.0	281.1	279.3	11.2	0.913	0.533	0.187
d 14 to 21	526.2	542.0	538.5	605.6	13.6	<0.001	0.161	0.315
d 21 to 28	721.4	766.3	792.1	879.3	18.7	<0.001	0.888	0.439
d 7 to 28	512.1	524.8	537.3	588.0	9.5	<0.001	0.317	0.642
d 0 to 28	412.5	433.5	436.7	480.2	7.8	<0.001	0.525	0.174
G:F, g/g								
d 0 to 7	0.014	0.268	0.232	0.401	0.098	0.015	0.548	0.206
d 7 to 14	0.702	0.507	0.611	0.439	0.098	0.128	0.956	0.182
d 14 to 21	0.674	0.686	0.702	0.701	0.042	0.640	0.783	0.957
d 21 to 28	0.730	0.666	0.690	0.688	0.036	0.639	0.459	0.341
d 7 to 28	0.712	0.655	0.684	0.657	0.026	0.300	0.679	0.179
d 0 to 28	0.656	0.602	0.637	0.629	0.025	0.800	0.537	0.158

[1]Diets were supplemented with 0.0, 0.2, 0.5, or 1.0 g/kg of a nucleotide additive (Inotide; CJ Corp, Seoul, Korea). Pigs were fed a phase 1 diet for the first 7 d followed by a phase 2 diet from d 7 to 28.

DISCUSSION

For young pigs, the composition of sow's milk may represent the most accurate nutrient requirements needed for adequate growth and health. Nutrients provided to the piglet through the milk include the nucleotides cytidine 5′-monophosphate (**5′CMP**), adenosine 5′-monophosphate (**5′AMP**), guanosine 5′-monophosphate (**5′GMP**), uridine 5′-monophosphate (**5′UMP**), and 5′IMP (Mateo, 2005). These nucleotides are used for maintenance and growth, intestinal development, immune system support, and reducing oxidative stress (Mateo, 2005; Salobir et al., 2005; Sauer et al., 2012).

Nucleotide demand increases during periods of stress and rapid growth, such as when piglets are weaned. At this point, piglets no longer receive a nucleotide source from their mother's milk but demand remains high so a dietary source is required (Mateo et al., 2004). Despite this dietary need, typical starter feeds for nursery pigs often have low nucleotide concentrations compared with the young pig's requirements (Stein and Kil, 2006). Although research indicates that 5′CMP is provided in weaning diets, other nucleotides including 5′AMP, 5′GMP, 5′IMP, and 5′UMP are not provided in adequate levels by the common feedstuffs used in nursery pig diets (Mateo, 2005). As a result, newly weaned pigs may not be able to synthesize or consume enough nucleotides to meet the demand for growth and health.

In our current study, dietary nucleotide supplementation benefited pigs immediately after weaning, that is, improved growth and feed intake. During phase 1, ADG was increased by 72% whereas ADFI was increased by 25% compared to the control group. Although ADG was low for all treatments due to a post-weaning growth lag, a considerable increase in gain was observed as the nucleotide content in the diet increase. The greatest increase was observed when 1.0 g/kg of the nucleotide additive was included in the diet; however, supplementation levels of 0.2 and 0.5 g/kg also resulted in a linear increase in the performance traits. During phase 2, nucleotide supplementation did

Table 3. Plasma immune and oxidative stress parameters of nursery pigs fed supplemental nucleotides for 28 d

	Treatment[2]					*P*-value		
Item[1]	0.0	0.2	0.5	1.0	SEM	Linear	Quadratic	Cubic
Phase 1[2]								
IgA, mg/mL	0.15	0.14	0.13	0.14	0.01	0.757	0.179	0.903
IgG, mg/mL	7.89	7.59	6.23	7.67	1.65	0.885	0.493	0.733
IgM, mg/mL	0.82	0.74	0.80	0.83	0.10	0.717	0.722	0.581
TNFα, pg/mL	94.42	91.17	81.67	89.92	7.45	0.620	0.297	0.652
8-OHdG, ng/mL	1.44	1.65	1.29	1.29	0.14	0.204	0.959	0.134
Phase 2[2]								
IgA, mg/mL	0.63	0.48	0.48	0.63	0.06	0.657	0.019	0.489
IgG, mg/mL	6.32	6.61	6.43	7.00	1.25	0.724	0.921	0.850
IgM, mg/mL	1.55	1.95	1.39	1.80	0.19	0.770	0.556	0.036
TNFα, pg/mL	126.67	99.58	98.17	85.58	14.99	0.093	0.508	0.481
8-OHdG, ng/mL	0.54	0.40	0.36	0.41	0.06	0.157	0.064	0.576

[1]Phase 1 concentrations measured in plasma collected on d 7, and phase 2 concentrations measured in plasma collected on d 28. TNFα = tumor necrosis factor-alpha; 8-OHdG = 8-hydroxy-deoxyguanosine.

[2]Diets supplemented with 0.0, 0.2, 0.5, or 1.0 g/kg of a nucleotide additive (Inotide; CJ Corp, Seoul, Korea).

not further improve pig ADG but did increase ADFI by 13% when pigs consumed the diet with 1.0 g/kg of nucleotides. Previous research showed varied effects of nucleotides to improve growth performance and feed intake. These variations may relate directly to the type and levels of nucleotides supplemented in the diet. Zomborszky-Kovács et al. (2000) found that supplementation of the synthetic nucleotide bases adenine and uracil at 0.5 g/kg to weanling pig diets improved growth performance. Sauer et al. (2012) found that feeding a mixture of pure nucleotides (5′AMP, 5′CMP, 5′GMP, 5′IMP, and 5′UMP) to weanling pigs increased ADFI but did not improve gain or feed efficiency. However, another study showed that a mixture of nucleotides added to the diet at 0.1 g/kg did not improve weanling pig growth performance, which was speculated to have occurred due to an insufficient dosage of nucleotides (Lee et al., 2007).

Improvements in growth performance may be a result of increased feed intake or it may also be due to improved immune health and reduced oxidative stress. It is speculated that nucleotides act on the immune system through their interaction with T cells (Carver and Walker, 1995). In the current study, the immune system responses measured were not different among treatments in phase 1 despite the improvements in growth performance by nucleotide supplementation during this time period. However, during phase 2, some immune responses were altered in a dose-dependent manner. The IgA was lowered in pigs fed 0.2 and 0.5 g/kg compared with pigs fed no supplemental nucleotides or 1.0 g/kg. This result is in contrast to Sauer et al. (2012) who indicated that nucleotides will elevate IgA as a result of an increase in number of lymphocyte Peyer's patches caused by the nucleotide interaction, which causes IgA producing cells of the intestine to increase. The concentration of IgM was increased in our current study by feeding of the nucleotides, except at 0.5 g/kg supplementation, which was lower than the control. Previous research also indicated that nucleotides supplementation to pig diets will increase IgM (Lee et al., 2007; Sauer et al., 2012). In the current study, it is not determined if lower or higher levels of IgA or IgM are beneficial in this situation; however, it is apparent that 0.5 g/kg of the nucleotide additive had the greatest effect on the pig immune system.

Feeding of nucleotides also tended to linearly decrease TNFα levels during phase 2. The cytokine TNFα is a proinflammatory cytokine produced early in an immune response by macrophages (van Reeth and Nauwynck, 2000). This early cytokine is responsible for local and systemic inflammatory effects. Thus, pigs not receiving dietary nucleotides had an increased inflammatory response compared to pigs consuming the nucleotide additive. Oxidative stress results from an imbalance between reactive oxygen species and antioxidant substances (Valavanidis et al., 2009). This imbalance can result in damage to many macromolecules, including DNA. Previous research has shown that dietary nucleotide supplementation can reduce DNA damage caused by oxidative stress (Frankič et al., 2006). In the current study, 8-OHdG was measured as an indicator of DNA damage. Results showed that increasing the nucleotide additive level tended to lower 8-OHdG observed in pigs at the end of phase 2. Therefore, nucleotides may be important in reducing stress during the nursery phase by reducing inflammation and DNA damage.

The final aspect of the current study was to determine the ability of nucleotides to reduce diarrhea of

Table 4. Fecal scores as a measure of diarrhea of nursery pigs fed supplemental nucleotides for 28 d

	Treatment[1]					*P*-value		
Item	0.0	0.2	0.5	1.0	SEM	Linear	Quadratic	Cubic
Fecal score[2]								
d 5	1.07	1.11	1.11	1.15	0.09	0.555	0.949	0.835
d 8	1.33	1.12	1.03	1.26	0.12	0.870	0.072	0.870
d 15	1.48	1.26	1.35	1.45	0.15	0.843	0.386	0.471

[1]Diets supplemented with 0.0, 0.2, 0.5, or 1.0 g/kg of a nucleotide additive (Inotide; CJ Corp, Seoul, Korea).

[2]Fecal scores were determined based on the following scoring values: 1 = normal, firm feces, 1.5 = looser feces leading to possible slight diarrhea, 2 = moderate liquid consistency, 2.5 = definite diarrhea with unformed, fluid feces, or 3 = severe diarrhea with very watery and frothy feces. d 5: during phase 1, d 8: after the transition from a phase 1 to 2 diet, and d 15: during consumption of the phase 2 diet.

newly weaned pigs. Previously, dietary nucleotides have shown an ability to reduce diarrhea. In a study by Martinez-Puiget al. (2007), nucleotide supplementation was able to reduce the number of pigs treated with antibiotics as a result of a reduction in diarrhea occurrence. Nucleotides are also shown to reduce the incidence of diarrhea in human infants (Carver et al., 1991). In the current study, pigs did not appear to have a problem with diarrhea directly after weaning. However, the incidence of diarrhea increased when pigs were switched from the phase 1 to phase 2 diets. In that instance, pigs fed supplemental nucleotides at 0.5 g/kg tended to have the lowest occurrence of diarrhea. Thus, during the nursery period, dietary supplementation of nucleotides showed some ability to reduce diarrhea and this may be important in maintaining piglet health.

Although each of the nucleotides present in the dietary additive may have benefited the young pigs, the nucleotide 5′IMP may have had a stronger role in the current study. The nucleotide source used in this experiment had a high total nucleotide content of 53%, but over half of this total nucleotide concentration was as 5′IMP. Inosine 5′-monophosphate is a nucleotide that is the first purine to be synthesized by the liver during de novo synthesis (Mateo, 2005). Once 5′IMP is formed, it serves as a precursor for the formation of other nucleotides such as 5′AMP and 5′GMP. Together, these nucleotides are used within the animal for many metabolic and cellular functions (Carver and Walker, 1995; Mateo, 2005). Therefore, it is speculated that the addition of a nucleotide additive high in 5′IMP directly to the diet of young pigs may not only improve 5′IMP consumption but may also increase total nucleotide concentrations because of the metabolic conversions of 5′IMP. As a result, the observed benefits of feeding dietary nucleotides to newly weaned pigs in this current study may be attributed to the high 5′IMP concentration. Prior research shows that dietary 5′IMP has a strong impact on feed intake. In fish, 5′IMP appears to improve feed intake by stimulating taste receptors (Kubitza et al., 1997; Miyasaki and Harada, 2003). In these studies, 5′IMP had a stronger ability to stimulate feed intake than other nucleotides. The ability of 5′IMP to improve feed intake is also shown in primates (Rolls et al., 1996). It is speculated that intake is stimulated because 5′IMP provides umami sensation and activates taste neurons. In our current study, a diet supplemented with a nucleotide additive composed highly of 5′IMP improved feed intake and subsequently growth performance. There seem to be no other studies that determined the individual benefits of 5′IMP in pigs; however, based on our results, a mixture of nucleotides high in 5′IMP may play a valuable role in improving feed intake in pigs when consumed after weaning. Further studies are necessary to determine how 5′IMP specifically improves growth performance, gut health, and immune status compared to other nucleotides.

In summary, dietary supplementation of 0.2 to 1.0 g/kg of the nucleotide additive improved gain and feed intake of the newly weaned pigs. Consumption of the nucleotides also resulted in a tendency for decreased systemic inflammation and oxidative stress as measured by TNFα and 8-OHdG. Overall, 1.0 g/kg of the nucleotide additive provided the most benefits to the growth performance of nursery pigs. However, 0.5 g/kg of the nucleotide additive had the greatest effect on the immune responses and oxidative stress. The results of this study demonstrate the importance of increased levels of total nucleotides in the diet of young pigs to improve pig growth performance and minimize weaning stress. Together, these improvements in pig health could benefit pig producers by reducing piglet weaning stress and in turn improving pig growth performance.

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