

# Effects of encapsulated sodium butyrate and phytogenic on growth performance, carcass traits and health of growing-finishing pigs

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**ABSTRACT**: The aim of this study was to evaluate two feed additives, one based on encapsulated sodium butyrate ( $Adimix^{\text{®}}$  Precision) (AD) and the other, a phytogenic( $Apex^{\text{®}}$  5) (AX), associated or not with an antimicrobial growth promoter (tylosin) during the growth and finishing phases on performance, carcass characteristics and health conditions. A total of 300 barrows and females were distributed in six treatments in a randomized block design with ten replicates. The treatments consisted of a negative control (NC), positive control (PC) (tylosin), AD (encapsulated sodium butyrate), AX (phytogenic), PC+AD (tylosin+encapsulated sodium butyrate), and PC+AX (tylosin+phytogenic). The performance (live weight, daily feed intake, average daily gain and feed conversion) and carcass data (carcass weight, backfat thickness, loin depth, lean meat on the carcass) were submitted to ANOVA plus Tukey's test, and the health conditions (occurrence of diseases, culling, and spontaneous deaths) were analyzed by  $\chi$ 2. Animals of the AD group had the highest carcass weight compared to NC and PC groups. The AX treatment increased the ADG in growth phase II and the live weight at 120 and 140 days of age in relation to the NC. The PC+AX group had a higher final live weight compared to the NC and PC groups and higher carcass, or occurrence of diseases and deaths. The inclusion of encapsulated sodium butyrate (AD treatment) was effective in increasing ADG, final live weight, and carcass weight compared to supplementation with tylosin (PC treatment), as was the inclusion of a phytogenic carcas weight in relation to the PC. Key words: acidifiers, botanical product, essential oil, feed additive, plant extract.

# Efeitos do butirato de sódio encapsulado e fitogênico sobre o desempenho, características da carcaça e saúde de suínos em fase de crescimento e terminação

RESUMO: O objetivo deste estudo foi avaliar dois aditivos alimentares, um a base de butirato de sódio encapsulado (Adimix® Precision) (AD) e outro a base de um fitogênico (Apex® 5) (AX), associados ou não a um antibiótico promotor de crescimento (tilosina), durante as fases de crescimento e terminação, sobre o desempenho, características da carcaça e status de saúde. Foram utilizados 300 suínos machos castrados e fêmeas distribuídos em seis tratamentos em um delineamento em blocos casualizados com dez repetições. Os tratamentos consistiram em um controle negativo (CN), controle positivo (CP) (tilosina), AD (butirato de sódio encapsulado), AX (fitogênico), CP+AD (tilosina+butirato de sódio encapsulado) e CP+AX (tilosina+fitogênico). Os dados de desempenho (peso vivo, consumo diário de ração, ganho de peso médio diário e conversão alimentar) e de carcaça (peso de carcaça, espessura de toucinho, profundidade do lombo e carne magra na carcaça) foram submetidos à ANOVA seguido por teste de Tukey, e os dados de condição de saúde (ocorrência de doenças, animais eutanasiados e mortos espontaneamente) foram analisados pelo teste de  $\chi$ 2. Os animais do grupo AD apresentaram maior ganho de peso diário (GPD) durante o período de avaliação e maior peso vivo aos 120, 140 e 164 dias de idade, além de maior peso de carcaça em comparação aos grupos CN e CP. O tratamento AX aumentou o GPD na fase crescimento II e o peso vivo aos 120 e 140 dias de idade em relação ao CN. O grupo CP+AX apresentou maior peso final em relação aos grupos CN e CP e maior peso de carcaça em relação ao CN. Não houve diferença entre os tratamentos para espessura de toucinho, porcentagem de carne magra na carcaca e ocorrência de doencas e óbitos. A inclusão de butirato de sódio encapsulado (tratamento AD) foi efetiva no aumento de GPD, peso final e peso de carcaça em comparação à suplementação com tilosina (tratamento CP), assim como a inclusão fitogênico (tratamento AX) melhorou a conversão alimentar em comparação ao grupo CP. Palavras-chave: acidificantes, aditivo alimentar, extrato vegetal, óleo essencial, produto botânico.

### **1 INTRODUCTION**

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3 For decades, the inclusion of sub-4 therapeutic doses of antibiotics in livestock farming has been used as an effective resource in improving the health, animal performance, and quality of products for human consumption (HASHEMI & DAVOODI, 2011). However, the detection of antibiotic 1

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1 residues in animal products and in the environment 2 (RONQUILLO & HERNANDEZ, 2017), microbial 3 antibiotic resistance (HUYGHEBAERT et al., 2011), 4 and the possibility of transmission of this resistance 5 to humans through the food chain (ZENG et al., 6 2015) have led to the banning of these antibiotics in 7 several countries (Kim et al., 2016). Therefore, some additives, such as organic acids and phytogenics, 8 9 which are alternatives to antimicrobial growth 10 promoters (AGPs) (FRANZ et al., 2010; HASHEMI 11 & DAVOODI, 2011; ZENG et al., 2015), have the 12 same purposes, besides modulating the intestinal 13 microbiota and improving health and animal 14 performance (HUYGHEBAERT et al., 2011).

15 Butyrate is a salt of an acid (butyric acid), 16 but the active ingredient itself is not an acid or acidifier 17 (e.g., lowering the pH and direct antibacterial effects). 18 Butyrate favors gene expression, cell differentiation, 19 immune modulation, oxidative stress reduction, 20 and diarrhea control (BEDFORD & GONG, 2018), 21 supporting energy for the cells of the colon mucosa 22 (LE GALL et al., 2009) and consequently promoting 23 the development of the gastrointestinal mucosa 24 (HUYGHEBAERT et al., 2011). In its free form as 25 butyric acid, butyrate absorption occurs mostly in the 26 upper portion of the gastrointestinal tract, limiting 27 its actions in the large intestine (PITUCH et al., 28 2013). Nonetheless, butyrate is easily digested in the 29 stomach and therefore it needs protection to reach 30 the large intestine. Protecting sodium butyrate with 31 a triglyceride matrix results in slower release of the 32 principle in the lower gastrointestinal tract, favoring its action (BEDFORD & GONG, 2018). 33

34 In turn, phytogenics include products based on different active plant components, including 35 cinnamaldehyde, eugenol, thymol, and carvacrol, 36 37 which are digestive stimulants (FRANKIČ et al., 38 2009) and mainly modulate the intestinal microbiota 39 (HASHEMI & DAVOODI, 2011). Some phytogenics 40 may also improve food palatability, increasing feed 41 intake and weight gain (ZENG et al., 2015) as well 42 as stimulating endogenous secretion and acting as 43 anthelmintics and coccidiostats (TAJODINI et al., 44 2015). Nevertheless, the improvement in nutrient 45 digestibility also manifests as an indirect effect of eubiosis improvement on the diversity and population 46 47 of the microbiota in the intestinal tract (HASHEMI & 48 DAVOODI, 2011).

49 Most studies involving organic acids 50 are about propionic, lactic, citric, and butyric 51 acids and their corresponding salts (CHIOFALO 52 et al., 2014), although the main challenge of these 53 evaluations is the lack of consistency of positive results on animal performance (LE GALL et al., 2009; LIU et al., 2018). As for phytogenics, studies evaluating different levels and principles in the diets of growing and finishing pigs have shown benefits over performance, despite the difficulty of comparing their efficiency due to the wide variation of compositions employed (LIU et al., 2018).

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In face of the demand for alternative products to AGPs and considering the need for more evaluations of the benefits of these additives, the aim of this study was to evaluate the inclusion of encapsulated sodium butyrate (Adimix® Precision) and a phytogenic (Apex<sup>®</sup> 5), associated or not with tylosin, on the performance, carcass characteristics, and health conditions of pigs in the growing and finishing phases.

## MATERIALS AND METHODS

A total of 300 PIC (Camborough x Ag 337) pigs, being 150 barrows and 150 females, with an initial weight of  $21.78 \pm 2.45$  kg and mean age of 63 days, were used. The animals were housed in a barn with 60 pens of 5.0 m<sup>2</sup> each equipped with a Dutch model feeder, nipple drinking through, and partially slatted floor. The temperature in the barn was regulated by curtain control. The experimental period comprised the growth and finishing phases (63 to 164 days of age). Animals were distributed into five blocks by initial body weight and by sex, with six treatments involving the use of additives, with ten replicates, being the pen the experimental unit.

The treatments, doses, and the period of use (Table 1) were defined by the use, combined or not, of three performance-enhancing additives, i.e. 30% encapsulated sodium butyrate (Adimix<sup>®</sup> Precision), a phytogenic composed of a blend of components from essential oils, mixed with dry herbs (Apex® 5)—a mixture of garlic oil (41%) and an essential oil component core (6%), with cinnamic aldehyde, thymol, carvacrol and eugenol-and a antimicrobial growth promoter (tylosin). The nutritional program had four phases: growth I (63-100 days of age), growth II (100-120 of age), finishing I (120-140 of age), and finishing II (140-164 of age) (Table 2). All diets were based on ground corn and soybean meal and were provided ad libitum throughout the experimental period.

Pen feed intake and live weight (LW) were recorded at the end of each production phase (at 100, 120, 140, and 164 days of average age). These values were used in the calculation of daily feed intake (DFI), average daily gain (ADG), and feed conversion (FC).

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Treatment	Inclusion of additive in the basal diet					
	Growth I and II (63 to 120 days)	Finishing I and II (120 to 164 days)				
NC	No inclusion	No inclusion				
PC	22 ppm of tylosin	11 ppm of tylosin				
AD	500 ppm of Adimix <sup>®</sup> Precision	250 ppm of Adimix <sup>®</sup> Precision				
AX	150 ppm of Apex <sup>®</sup> 5	150 ppm of Apex <sup>®</sup> 5				
PC+AD	22 ppm of tylosin + 500 ppm of Adimix <sup>®</sup> Precision	11 ppm of tylosin + 250 ppm of Adimix <sup>®</sup> Precision				
PC+AX	22 ppm of tylosin + 150 ppm of Apex <sup>®</sup> 5	11 ppm of tylosin + 150 ppm of Apex <sup>®</sup> 5				

Table 1 – 16 Description of treatments, doses, and supplementation periods.

NC = negative control; PC = positive control (tylosin; T-Grow<sup>®</sup>); AD = encapsulated sodium butyrate (Adimix<sup>®</sup> Precision); AX = phytogenic (Apex<sup>®</sup> 5).

The animals were slaughtered at an 1 2 average age of 164 days and after being stunned 3 by the three-point electron-accumulation method. 4 The carcasses were submitted to electronic grading 5 (Hennessy Grade Probe, Hennessy Grading Systems, 6 Auckland, NZ) by measuring backfat thickness (BT) and Longissimus thoracis et lumborum depth (LD) 7 8 at point P2 (59 mm lateral to the carcass dorsal line, 9 immediately caudal to the last rib, left half carcass), 10 according NPPC (1991). The carcasses were weighed (CW), and the values of percentage and content 11 of lean meat in the carcass (LM) were obtained. 12 13 The percentage of LM was calculated based on the 14 equation proposed by the Hennessy Grading Systems 15 (% LM = 61.33 - [0.76 x BT] + [0.1 x LD]), and the content of LM was calculated by multiplying the 16 17 carcass weight by LM percentage.

The occurrence of diseases requiring 18 19 therapeutic treatment, as well as the number of 20 outliers that died spontaneously, were recorded daily 21 throughout the experimental period. In the first two 22 weeks of the study (63 to 77 days of age), fecal 23 consistency was assessed individually, and feces were 24 classified as normal, pasty, doughy fluid, and diarrhea 25 (Liu et al., 2010). The score was calculated by dividing the number of days the animals had diarrhea 26 27 by the total number of days evaluated.

28 Each pen with five animals of the same sex 29 was an experimental unit for the growth performance 30 parameters (LW, DFI, ADG, FC), whereas each 31 individual animal was the experimental unit for carcass traits (CW, BT, LD, LM) and health. The 32 growth performance and carcass data were submitted 33 to ANOVA, and the means were compared by 34 the Tukey's test using the statistical program R 35 version 3.5.0. The occurrences of diarrhea and other

conditions, as well as of dead and culled animals, were analyzed by  $\chi 2$ . For both tests, a P value of 0.05 was used as the significance threshold.

#### RESULTS

In growth phase I (63 to 100 days of age), no differences (P>0.05) were found among treatments for the parameters evaluated (Table 3). In growth phase II (100 to 120 days of age), no differences (P>0.05) were found among treatments for DFI. The animals of the negative control (NC) treatment had worse ADG (P<0.05) in relation to treatments of encapsulated sodium butyrate—Adimix® Precision (AD) and a positive control-tylosin plus phytogenic-Apex® 5 (PC+AX), but no differences (P>0.05) were seen between this treatment and PC, AX, or PC+AD. The LW at the end of the period (LW120) was higher (P<0.01) for pigs in groups AD, AX, and PC+AX compared to the NC treatment.

In finishing phase I (120 to 140 days of age), no difference (P>0.05) was found among the treatments for the parameters evaluated. In finishing phase II (140 to 164 days of age), the lowest ADG results were seen in treatments PC and NC, being significantly different (P<0.001) in relation to treatment AD. Furthermore, PC+AD and PC+AX treatments had better ADG (P<0.001) than NC treatment. The LW at the end of the period (LW164) was higher (P=0.05) for the pigs of the treatments AD and PC+AX compared to those of the treatments NC and PC. No differences (P>0.05) were seen among 32 the treatments for DFI. 33

Considering the total period of the study 34 (63 to 164 days of age), differences (P<0.05) were 35 found for ADG among treatments, with the lowest 36

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Table 2 - Ingredientsand calculated composition in the experimental diets.

	Phases					
	Growth I	Growth II	Finishing I	Finishing II		
	(63-100 days)	(100-120 days)	(120-140 days)	(140–164 days)		
Ingredients (%)						
Corn	68.54	72.46	77.09	81.76		
Soybean meal 45%	28.10	24.72	20.39	15.90		
Dicalcium phosphate	1.14	0.93	0.86	0.79		
Limestone	0.69	0.64	0.60	0.56		
Soybean oil	0.58	0.27	0.02	0.00		
L-lysine	0.12	0.15	0.20	0.24		
DL-methionine	0.03	0.02	0.03	0.02		
L-threonine	0.02	0.03	0.03	0.03		
L-tryptophan	0.00	0.00	0.00	0.02		
Vitamin premix <sup>1</sup>	0.10	0.10	0.10	0.08		
Mineral premix <sup>2</sup>	0.10	0.10	0.10	0.10		
Sodium chloride	0.38	0.38	0.38	0.38		
Calcium aluminosilicate	0.15	0.15	0.15	0.15		
Premix with products <sup>3</sup>	0.05	0.05	0.05	0.05		
Total	100.00	100.00	100.00	100.00		
	Calculated com	position (%)				
Metabolizable energy (MJ/kg)	13.4	3,212	3,215	3,230		
Crude protein	18.35	17.16	15.60	14.00		
Calcium	0.67	0.58	0.54	0.49		
Total phosphorus	0.52	0.48	0.46	0.43		
Available phosphorus	0.30	0.26	0.24	0.22		
Sodium	0.19	0.19	0.18	0.19		
Potassium	0.49	0.47	0.44	0.40		
Total lysine	1.04	0.97	0.90	0.82		
Digestible lysine	0.94	0.88	0.82	0.82		
Total methionine	0.31	0.28	0.28	0.25		
Digestible methionine	0.29	0.27	0.26	0.23		
Total Met. + cyst.	0.62	0.58	0.55	0.49		
Digestible Met. + cyst.	0.55	0.52	0.49	0.44		
Total threonine	0.74	0.70	0.64	0.57		
Digestible threonine	0.64	0.61	0.55	0.49		
Total tryptophan	0.22	0.20	0.17	0.17		
Digestible tryptophan	0.19	0.17	0.15	0.15		
Total valine	0.87	0.81	0.74	0.62		
Digestible valine	0.77	0.72	0.65	0.58		

<sup>1</sup>Vitamin premix provided per kg of diet: 6,000 IU vitamin A; 1,500 IU vitamin D<sub>3</sub>; 15 mg vitamin E; 1.5 mg vitamin K<sub>3</sub>; 1.35 mg vitamin B<sub>1</sub>; 4 mg vitamin B<sub>2</sub>; 2 mg vitamin B<sub>6</sub>; 20 µg vitamin B<sub>12</sub>; 20 mg niacin; 9.35 mg pantothenic acid; 600 µg folic acid; 80 µg biotin; 300 µg Se.

<sup>2</sup>Mineral premix provided per kg of diet: 100 mg Fe; 10 mg Cu; 40 mg Mn; 1 mg Co; 100 mg Zn; 1.5 mg I. <sup>3</sup>Caulim/Adimix<sup>®</sup> Precision/Apex<sup>®</sup> 5/tylosin.

Table 3 - Effect of encapsulated sodium butyrate and essential oils, alone or in combination with a growth-promoting antibiotic, on growth performance of growing-finishing pigs (n = 50/treatment).

Variable			Treatn	nent			CV	P-value
	NC	PC	AD	AX	PC+AD	PC+AX		
			Growing I (63-	-100 days of ag	e)			
LW63 (kg)	21.72	21.63	21.95	21.96	21.70	21.77	7.82	0.720
DFI (kg)	1.61	1.58	1.56	1.59	1.64	1.62	6.67	0.621
ADG (kg)	0.77	0.77	0.80	0.80	0.80	0.80	10.32	0.081
FC (kg/kg)	2.09	2.07	1.97	2.05	2.08	2.02	6.33	0.311
LW100 (kg)	50.12	50.29	51.63	51.61	51.50	51.53	7.16	0.129
			-Growing II (1	00–120 days of	age)			
DFI (kg)	2.18	2.29	2.41	2.27	2.33	2.29	8.15	0.178
ADG (kg)	0.93 <sup>b</sup>	$0.98^{ab}$	1.02ª	$1.00^{ab}$	$0.98^{ab}$	1.03 <sup>a</sup>	13.99	0.014
FC (kg/kg)	2.33	2.38	2.36	2.29	2.40	2.28	7.32	0.592
LW120 (kg)	68.79 <sup>b</sup>	69.85 <sup>ab</sup>	71.96 <sup>a</sup>	71.67 <sup>a</sup>	71.19 <sup>ab</sup>	72.15 <sup>a</sup>	7.31	0.009
			Finishing I (1	20–140 days of	age)			
DFI (kg)	2.68	2.72	2.71	2.72	2.65	2.73	10.28	0.986
ADG (kg)	1.08	1.07	1.08	1.05	1.06	1.05	13.78	0.449
FC (kg/kg)	2.56	2.57	2.50	2.50	2.51	2.50	8.94	0.948
LW140 (kg)	89.77	91.32	92.59	93.72	92.38	93.21	6.68	0.057
			-Finishing II (1	40-164 days of	age)			
DFI (kg)	2.78	2.84	2.96	2.74	2.78	2.83	9.13	0.497
ADG (kg)	0.93 <sup>b</sup>	0.90°	1.03 <sup>a</sup>	$0.95^{\mathrm{abc}}$	$0.99^{ab}$	$0.99^{ab}$	13.55	0.000
FC (kg/kg)	3.02	3.26	3.00	2.91	2.98	2.93	10.20	0.165
LW164 (kg)	112.55 <sup>b</sup>	112.79 <sup>b</sup>	117.45 <sup>a</sup>	115.20 <sup>ab</sup>	115.55 <sup>ab</sup>	116.31ª	6.68	0.021
Total period (63–164 days of age)								
DFI (kg)	2.21	2.24	2.29	2.21	2.25	2.26	6.33	0.848
ADG (kg)	$0.90^{\rm b}$	0.91 <sup>b</sup>	0.95ª	$0.92^{ab}$	0.93 <sup>ab</sup>	0.94 <sup>a</sup>	7.90	0.013
FC (kg/kg)	2.45 <sup>ab</sup>	2.51 <sup>b</sup>	2.40 <sup>ab</sup>	2.38 <sup>a</sup>	2.44 <sup>ab</sup>	2.38ª	4.17	0.047

NC = negative control; PC = positive control (tylosin; T-Grow<sup>®</sup>); AD = encapsulated sodium butyrate (Adimix<sup>®</sup> Precision); AX = phytogenic (Apex<sup>®</sup> 5); LW = live weight (the number on the side corresponds to the average age of the animals; 63, 100, 120, 140, and 164 days of age); DFI = daily feed intake; ADG = average daily gain; FC = feed conversion.

<sup>a,b,c</sup>Means within a row with different superscript letters significantly differ at  $P \le 0.05$ .

results being presented by treatments NC and PC in 1 2 relation to treatments AD and PC+AX. The animals 3 of treatments AX and PC+AD did not differ from the 4 others (P>0.05). Considering each evaluation period 5 separately, no differences (P>0.05) were found among treatments for FC, yet, over the total period (63 to 6 164 days of age), worse FC (P<0.05) was observed 7 8 for the PC treatment in relation to AX and PC+AX. 9 Treatments NC, AD, and PC+AD did not differ from 0 the others (P>0.05).

A difference (P=0.001) was found in CW (Table 4) between the NC and PC treatments and the AD treatment, with advantages for the latter. Furthermore, the PC+AX treatment was better than the NC treatment (P=0.001). Treatments PC, AX, and PC+AD had intermediate results for this parameter, not differing among each other (P>0.05). The AD treatment resulted in an increase in CW by 4.86 kg (+6.01%) and 4.52 kg (+5.57%), respectively, compared to NC and PC. Furthermore, supplementation with PC+AX resulted in an increase by 3.78 kg (+4.68%) in CW compared to NC.

No differences were found among the10treatments (P>0.05) for BT and LD. More LM (kg)11was obtained (P<0.05) for animals from the AD and</td>12PC+AX treatments compared to animals from the13

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Variable	Treatment						CV	P-value
	NC	PC	AD	AX	PC+AD	PC+AX		
CW (kg)	80.82°	81.16 <sup>bc</sup>	85.68ª	84.17 <sup>abc</sup>	83.79 <sup>abc</sup>	$84.60^{ab}$	7.82	< 0.001
BT (mm)	13.57	14.12	14.69	14.69	14.60	14.26	17.30	0.205
LD (mm)	66.03	63.28	64.84	64.43	64.43	65.32	9.40	0.375
LM (%)	57.62	56.93	56.65	56.60	56.68	57.03	3.45	0.124
LM (kg)	46.57 <sup>ab</sup>	46.15 <sup>b</sup>	48.50ª	47.61 <sup>ab</sup>	47.43 <sup>ab</sup>	48.19 <sup>a</sup>	7.56	0.014

Table 4 - Effect of encapsulated sodium butyrate and essential oils, alone or in combination with a growth-promoting antibiotic, on carcass traits of growing-finishing pigs (n = 50/treatment).

NC = negative control; PC = positive control (tylosin; T-Grow<sup>®</sup>); AD = encapsulated sodium butyrate (Adimix<sup>®</sup> Precision); AX = phytogenic (Apex<sup>®</sup> 5); CW = carcass weight; BT = backfat thickness; LD = loin depth; LM = lean meat on the carcass. <sup>a,b,c</sup>Means within a row with different superscript letters significantly differ at P < 0.05.

1 PC treatment. The other treatments did not differ 2 from each other. No differences were observed 3 among treatments (P>0.05) for the occurrence 4 and intensity of diarrhea, sanitary occurrences, 5 or number of animals that were culled or died 6 spontaneously (Table 5).

# 8 **DISCUSSION**

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DISCUSSION

10 The absence of statistical differences 11 among the treatments for daily feed intake (DFI) in 12 all experimental phases shows that the additives did 13 not show any benefit or compromised consumption, 14 contradicting, in the case of essential oils, the improvement that such additives cause in DFI, as reported by ZENG et al. (2015).

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The supplementation of diets with tylosin (positive control - PC) did not result any significant advantages in growth performance. Although tylosin is an antimicrobial growth promoter (AGP), others studies did not report significantly effective results when using tylosin. For example, the use of this growth promoter in pigs between 24–136 days of age at doses of 44, 22, and 11 mg/kg of feed for 21, 21, and 70 days, respectively (HOLMAN & CHÉNIER, 2013), as well as at doses of 40 mg/kg of feed for pigs aged 100–170 days (KIM et al., 2016), did not lead to improvements compared to the performance of the

Table 5 - Effect of encapsulated sodium butyrate and essential oils, alone or in combination with a growth-promoting antibiotic, on the	
occurrence of diseases requiring antibiotic therapy, number of animals culled, and spontaneous deaths of growing-finishing pigs	
(n = 50/treatment).	

Occurrence	Treatment					
	NC	PC	AD	AX	PC+AD	PC+AX
Arthritis (n)	00	00	02	00	00	00
Encephalitis (n)	00	00	00	00	01	01
Pneumonia (n)	02	05	07	01	04	03
Diarrhea (n)	01	00	00	00	00	00
Culled (n)	00	01	03	03	02	02
Death (n)	01	01	03	01	01	01

NC = negative control; PC = positive control (tylosin; T-Grow<sup>®</sup>); AD = encapsulated sodium butyrate (Adimix<sup>®</sup> Precision); AX = phytogenic (Apex<sup>®</sup> 5).

1 control group with antibiotic-free animals. The action 2 of tylosin as a growth promoter is attributed to the 3 modulation of intestinal microbial composition, thus 4 influencing metabolic activity (KIM et al., 2016). 5 Nonetheless, according to HOLMAN & CHÉNIER 6 (2013), when pigs are housed under low densities and 7 under good health conditions, similar to the situation reported in this study, some antimicrobial growth 8 9 promoters (AGPs), including tylosin, do not result in 10 consistent actions on performance.

11 Although the benefits of sodium butyrate for 12 performance and carcass characteristics are considered 13 more evident when it is supplemented in the diet of 14 young animals (BEDFORD & GONG, 2018), in this 15 study, the use of encapsulated sodium butyrate (AD 16 treatment) in the diet of growing and finishing pigs 17 improved the animal performance (higher ADG, 18 final live weight, and carcass weight). WALIA et al. 19 (2016) evaluated finishing pigs and found that the use 20 of sodium butyrate at a dose of 3,000 ppm for 24 and 21 28 days before slaughter resulted in improved ADG 22 (respectively, +2.6 and +7.0%) and feed conversion 23 (FC) (respectively, between -4.3 and -8.5%) compared 24 to animals that did not receive supplementation. 25 The better ADG could be attributed to increased 26 digestibility of dietary nutrients and the bioavailability 27 of amino acids, effects specific of the segment of 28 the gastrointestinal tract in which the molecule acts 29 (MOQUET et al., 2017). In addition, in the protected 30 condition, butyrate release is greater in the lower 31 portion of the gastrointestinal tract (BEDFORD & 32 GONG, 2018), influencing intestinal quality.

33 Regarding the phytogenic treatment 34 (AX), no significant improvement in ADG was observed with respect to the NC or PC treatments. 35 Significant increases in ADG have been obtained 36 37 with the supplementation of pig diets with 38 phytogenic agents during lactation (7–35 days of age) 39 (HANCZAKOWSKA & ŚWIĄTKIEWICZ, 2012), 40 growth (YAN et al., 2011), and finishing phases 41 (CHO et al., 2012). Although, in the finishing phase, 42 the improvement in ADG (on average 5.8% higher) 43 is not always significant (HANCZAKOWSKA et al., 44 2015). Nonetheless, in this study, live weight (LW) 45 at 120 days of age was significantly higher for AX supplemented animals, besides the final LW being 46 47 approximately 2.5 kg higher than in the NC and PC 48 treatments. The composition of phytogenic used in 49 our study mainly included garlic oil but also cinnamic 50 aldehyde, thymol, carvacrol, and eugenol. It has been 51 suggested that these components have many beneficial effects, such as antimicrobial activity (medium 52 for carvacrol and thymol and strong for eugenol,

cinnamaldehyde, and garlic-allicin) (ADAMS, 1999) and anti-inflammatory action (FRANKIČ et al., 2009). The reasons that different results are obtained between studies include differences in the quality of herbal components, inclusion of particular herbs, and forms of their administration (WINDISCH et al., 2008). The FC of the animals of the AX and PC+AX treatments were significantly better in relation to the PC treatment when considering the total period of the study. Treatments with phytogenic 10 agents compared to NC treatments have generated 11 considerable numerical improvements over the FC 12 (-5.9% on average) (HANCZAKOWSKA et al., 13 2015) and some statistically significant improvements 14 (HANCZAKOWSKA & ŚWIĄTKIEWICZ, 15 2012). However, there are studies that demonstrate 16 variation in results of feed efficiency and dry matter, 17 nitrogen, and energy digestibility with the use of 18 this class of phytogenics (YAN et al., 2011; CHO 19 et al., 2012), whose reasons may include variations 20 in the housing conditions of the animals and in the 21 22 species of plants used to compose the phytogenic agent (HANCZAKOWSKA et al., 2015), as well 23 as differences in composition and nutritional 24 contribution of the basal diets (CHO et al., 2012). 25

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In this study, although not significant, 26 the inclusion of phytogenics in the diets caused a 27 2.1% increase in the final LW compared to the PC 28 29 treatment, which can be attributed to the significant 30 improvement in FC in the total test period for the AX compared to the PC treatment. Such an effect may 31 be due to the phytogenic benefits described above, 32 since the product used has many components that are 33 digestive stimulants (e.g. cinnamaldehyde, eugenol, 34 thymol, and carvacrol) (FRANKIČ et al., 2009). 35

As for the association between AGP and 36 their substitutes, the use of PC+AD in the diets, 37 compared with the AD treatment, did not favor the 38 performance of the animals. The use of PC+AX also 39 40 provided similar results to those obtained with the exclusive use of AX. For PC+AX treatment, ADG 41 improved during finishing phase II in relation to the PC 42 treatment, and the final LW improved in comparison to 43 the NC and PC treatments, which was not observed for 44 the animals treated exclusively with AX. 45

The bactericidal, bacteriostatic, and 46 modulatory action in the intestinal microbiota of 47 48 acids and phytogenics is primary and therefore has positive effects on the animal (PARTANEN & 49 MROZ, 1999; DAVIDSON & TAYLOR, 2007). 50 When these additives were associated with tylosin, as 51 previously noted, results were not potentialized. This 52 condition may have been limited by the impairment 53

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1 of the intestinal microbiota due to the action of 2 tylosin, which, under low doses, has a bacteriostatic 3 action against Gram-positive bacteria (BARCELLOS 4 et al., 2014). In addition, according to GAVIOLI et 5 al. (2013), when tylosin is used in the diet of pigs in 6 the growing and finishing phase, it results in higher 7 shedding of the intestinal epithelium compared with 8 diets containing pre- and probiotics, with worsening 9 of the villous-to-crypt ratio.

10 According LI et al. (2018), organic 11 acids are more effective than antibiotics as growth 12 promoters on the cecum microbiota modulation, 13 improving the production of short chain fatty acids, 14 which represents an important energy source for 15 enterocyte renewal (WILLIAMS et al., 2001).

16 It should also be considered that the 17 evaluation was conducted under conditions of few 18 health and environmental challenges, since the main requirements of the animals were preserved 19 20 for the phases to which they were submitted. Such a 21 situation fits under the considerations of BORATTO 22 et al. (2004), who consider that the beneficial action 23 of the AGPs is inversely related to animal health and 24 environmental conditions of the farm. Under ideal 25 hygienic-sanitary conditions, the effect of antibiotics 26 is minimal.

27 The results of the treatments on hot carcass 28 weight (CW) were similar to the one observed on final 29 LW, with advantages observed for the animals of the 30 AD treatment, which had higher CW in comparison to treatments NC and PC, and of the PC+AX 31 32 treatment, with higher CW than the pigs in the NC 33 treatment. Although advantages have been found for 34 phytogenic agents over the control and antibiotic 35 groups, ROSSI et al. (2013) observed that the CW of animals fed from weaning to finishing with the 36 37 inclusion of these products were not different from 38 the NC carcass weights without supplementation. 39 The same was also observed in pigs fed 125 ppm 40 and 500 ppm of a plant extract mixture containing 41 thymol, carvacrol capsaicin, cinnamon aldehyde, eugenol, flavonoids, and essential oils (composition 42 43 similar to the phytogenic of this study) from 20 to 100 44 kg LW (KORNIEWICZ et al., 2007).

45 In the same sense, treatments AD and 46 PC+AX yielded higher amounts of lean meat in the carcass (represented in kg) compared to the 47 48 carcasses of the NC animals, once again attributed 49 to the higher final LW and CW of animals from 50 both treatments with additives compared to NC. 51 In relation to the percentage of lean meat in the carcass, no significant differences were seen among 52 the treatments. While some studies have observed 53

the absence of differences between treatments with and without phytogenic agents for carcass lean meat (KORNIEWICZ et al., 2007; HANCZAKOWSKA et al., 2015) and percentage of intramuscular fat (KOŁODZIEJ-SKALSKA et al., 2011), others have demonstrated advantages for the *Longissimus dorsi* muscle area (indirect indicator of the proportion of lean meat in the carcass) when pigs are supplemented with phytogenic compounds (KORNIEWICZ et al., 2007; YAN et al., 2010; CHO et al., 2012), a situation mostly attributed to the higher protein retention due to the improved digestibility provided by these additives (YAN et al., 2010).

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No differences were observed in backfat thickness (BT) among the treatments, corroborating with HANCZAKOWSKA et al. (2014), who made use of sodium butyrate, and ROSSI et al. (2013) and KORNIEWICZ et al. (2007), who supplemented the diets of pigs with plant extracts. Heavier animals, influenced by the positive effects of treatments with sodium butyrate and a phytogenic, should have higher BT values; however, the large variation of this measure is inherent to this parameter, resulting in high coefficients of variation, which hinders the observation of differences among the treatments.

No differences in the occurrence of diseases 26 and deaths were observed among the treatments. 27 This may indicate that the use of the additives in 28 the diets influenced the results (LIU et al., 2018). 29 From a health point of view, butyrate is an important 30 source of energy for epithelial cells of the large 31 intestine (BEDFORD & GONG, 2018), maintaining 32 high efficiency in epithelial development (GALFI & 33 BOKORI, 1990). CHIOFALO et al. (2014) observed 34 that piglets treated with two types of sodium butyrate, 35 one in free form and the other encapsulated, during 45 36 days after weaning, presented occasional diarrhea and 37 no deaths. In addition, for essential oil treatments, the 38 benefits in intestinal mucosal integrity preservation, 39 immune system stimulation, and antibacterial action 40 (BRENES & ROURA, 2010) may justify the health 41 status observed in this study, which would justify the 42 best performance and carcass indexes obtained for 43 this treatment. 44

The use of butyrate and phytogenic, 45 without association with tylosin, showed an 46 improvement in performance, carcass weight, and 47 lean meat. According to Huyghebaert et al. (2011), 48 alternative additives to AGPs should at least act 49 in a similar manner to that of the antibiotic in use. 50 Nevertheless, the results may vary in intensity given 51 the dependence of some factors such as diet type and 52 herd status (LIU et al., 2018). 53

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CONCLUSION

The inclusion of encapsulated sodium butyrate (AD treatment) was effective in increasing ADG, final live weight, and carcass weight compared to supplementation with tylosin (PC treatment). The inclusion of phytogenic (AX treatment) improved FC compared to the PC. Supplementation of AD+PC and AX+PC had no positive effect on growth performance and carcass traits compared to inclusion AD or AX only. 

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# 20 BIOETHICS AND BIOSSECURITY 21 COMMITTEE APPROVAL

All procedures were previously approved by the Akei Animal Research Ethics Committee (protocol no. 04/2016).

# DECLARATION OF CONFLICTS OF INTERESTS

The authors declare no conflict of interest. The founding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, and in the decision to publish the results.

The authors David Vanni Jacob, Alessandra Luckmann Voorsluys, Alexandre José Ulbrich, and Tim Goossens report their affiliation and involvement in Adisseo, an organization with interest in the subject matter and materials discussed in this manuscript.

#### **AUTHORS' CONTRIBUTIONS**

All authors contributed equally to the design and writing of the manuscript. All authors critically reviewed the manuscript and approved the final version.

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