Effects of dietary chromium propionate on growth performance, metabolism, and immune biomarkers in heat-stressed finishing pigs¹

Edith J. Mayorga,[†] Sara K. Kvidera,[†] Jacob T. Seibert,[†] Erin A. Horst,[†] Mohannad Abuajamieh,[†] Mohammad Al-Qaisi,[†] Samantha Lei,[†] Jason W. Ross^{†,‡}, Colin D. Johnson^{†,‡}, Brian Kremer,^{||} Luis Ochoa,^{||} Robert P. Rhoads,^{\$} and Lance H. Baumgard^{†,2}

[†]Department of Animal Science, Iowa State University, Ames, IA 50011; [‡]Iowa Pork Industry Center, Ames, IA 50011; ^{||}Kemin Industries, Des Moines, IA 50317; and ^{\$}Department of Animal and Poultry Sciences, Virginia Tech, Blacksburg, VA 24061

ABSTRACT: Study objectives were to determine the effects of chromium (Cr) propionate (Cr propionate 0.04%; 0.5 g/kg of feed to deliver 200 parts per billion Cr/d; KemTRACE Cr, Kemin Industries, Inc., Des Moines, IA) on growth performance, metabolism, and health biomarkers in heat-stressed and nutrient-restricted pigs. Crossbred barrows ($n = 96$; 105 ± 1 kg BW) were enlisted in an experiment conducted in two replicates, blocked by initial BW, and randomly assigned to one of six dietary-environmental treatments: (i) thermoneutral (TN) and fed ad libitum a control diet (TN_{Ctrl}), (ii) TN and fed ad libitum a Cr supplemented diet (TN_{Cr}), (iii) TN and pair-fed a control diet (PFC_{Ctrl}), (iv) TN and pair-fed a Cr supplemented diet (PFC_{Cr}), (v) heat stress (HS) and ad libitum fed a control diet (HSC_{Ctrl}), or (vi) HS and ad libitum fed a Cr supplemented diet (HSC_{Cr}). The study consisted of three experimental periods (P). During P0 (5 d), all pigs were housed in TN conditions (21.3 ± 0.1 °C, $56.8 \pm 0.3\%$ relative humidity [RH]) and fed the control diet ad libitum. During P1 (5 d), pigs were fed their respective dietary treatments ad libitum and kept in TN conditions. During P2 (35 d), HSC_{Ctrl} and HSC_{Cr}-treated pigs were fed ad libitum and exposed to

progressive cyclical HS conditions (27 to 31 °C, $50 \pm 0.3\%$ RH), while TN_{Ctrl}, TN_{Cr}, PFC_{Ctrl}, and PFC_{Cr} pigs remained in TN conditions and were fed ad libitum or pair-fed to their respective HSC_{Ctrl} and HSC_{Cr} counterparts to eliminate the confounding effects of dissimilar feed intake. Overall, HS pigs had increased ($P < 0.01$) rectal temperature, skin temperature, and respiration rate (0.3 °C, 3.8 °C, and 32 breaths per minute, respectively) relative to TN pigs. Overall, HS decreased ADFI and ADG (20 and 21% , respectively; $P < 0.01$) compared with TN controls. Final BW tended to be increased in HSC_{Cr} (2.7 kg, $P = 0.06$) compared with HSC_{Ctrl} pigs. Similarly, ADG tended to be increased during P2 in HSC_{Cr} relative to HSC_{Ctrl}-treatment (0.77 vs. 0.72 kg/d; $P = 0.10$). There were no effects of Cr on most production parameters, but ADFI tended to be increased in Cr relative to Ctrl-fed pigs (3.19 vs. 3.09 kg/d; $P = 0.08$). No effects of Cr supplementation were detected on circulating glucose, insulin, NEFA, cholesterol, triglycerides, or lipopolysaccharide binding protein. However, blood neutrophils were increased in HSC_{Cr} (37% ; $P < 0.01$) relative to HSC_{Ctrl} pigs. In summary, these results suggest Cr supplementation may benefit growth performance during HS.

Key words: chromium, growth performance, heat stress, pig

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²Corresponding author: baumgard@iastate.edu

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INTRODUCTION

Heat stress (HS) is a common environmental issue in animal agriculture and a major limitation to efficient and profitable pig production.

The estimated economic losses in the U.S. swine industry are nearly \$1 billion annually (Pollmann, 2010). This lost revenue is mainly explained by reduced and inconsistent growth, decreased carcass value, poor reproduction, and inefficient facility utilization (Baumgard and Rhoads, 2013; Ross et al., 2017). Pigs are particularly sensitive to HS due to their reduced capacity to dissipate heat (i.e., dysfunctional sweat glands and thicker subcutaneous fat tissue); consequently, reducing metabolic heat production (HP) is emphasized in an attempt to maintain eutheria (Renaudeau et al., 2012). Voluntarily reducing feed intake is the main strategy pigs employ to decrease HP during HS (Renaudeau et al., 2012). Further, HS markedly alters postabsorptive carbohydrate, lipid, and protein metabolism (independently of reduced feed intake), homeorhetic adaptations mediated in large part by increased circulating insulin (Baumgard and Rhoads, 2013). Hence, identifying nutritional approaches with the potential to ameliorate the detrimental effects of HS on productivity and health is of particular interest.

Dietary chromium (Cr) is thought to increase traditional farm animal productivity parameters via increasing insulin action in insulin-sensitive tissues (i.e., adipose and muscle; Davis and Vincent, 1997). Despite inconsistencies (Kim et al., 2009; Seibert et al., 2018), dietary Cr has been shown to stimulate feed intake (Hayirli et al., 2001; Hung et al., 2014) and improve growth, carcass characteristics, and reproductive performance in a variety of species (Lindemann et al., 1995; Soltan, 2010). Additionally, previous studies indicate improved immune function with Cr supplementation (Burton et al., 1993; Horst et al., 2018), suggesting dietary Cr may play an important role during immunoactivation. We hypothesized that dietary Cr would increase productivity during HS and therefore, study objectives were to evaluate the effects of supplemental Cr on growth performance and metabolic and immunity-related biomarkers during HS in finishing pigs.

MATERIALS AND METHODS

Animals, Diets, and Experimental Design

All procedures were approved by the Iowa State University Institutional Animal Care and Use Committee (#9-14-7853-S). c 12), (ii) TN ad libitum Cr diet (TNCr; $n = 12$), (iii) TN pair-fed control diet (PFCtl; $n = 12$), (iv) TN pair-fed Cr diet (PFCr; $n = 12$), (v) HS ad libitum control

diet (HSCtl; $n = 24$), or (vi) HS ad libitum Cr diet (HSCr; $n = 24$). Pigs were allocated to one of two environmentally controlled rooms. Each room had 24 crates (57×221 cm) where pigs were housed individually. Each crate was equipped with a stainless-steel feeder and a nipple drinker. Water was provided ad libitum during the entire experiment. One pig from the HSCr treatment was removed from the experiment due to health issues and data from it was not included in the analysis.

Two diets were formulated and mixed according to the following specifications: (i) a control (Ctl) diet based on corn–soybean meal and (ii) a Cr diet formulated based on corn–soybean meal and supplemented with Cr (Cr propionate 0.04%, KemTRACE Cr propionate, Kemin Industries, Inc., Des Moines, IA) at the rate of 0.5 g/kg of feed, to deliver 200 parts per billion Cr. Both Ctl and Cr diets were treated with an antioxidant (ENDOX, Kemin Industries, Inc.) at the rate of 0.125 g/kg of feed. Diets were processed in meal form and mixed at the Iowa State University Swine Nutrition Center Mill. Diets were formulated to meet or exceed finishing pig predicted requirements for energy, essential amino acids, protein, minerals, and vitamins (NRC, 2012; Table 1).

The study was divided into three experimental periods (P): P0, P1, and P2. Period 0 (5 d) was an acclimation period where all pigs were housed in individual crates, subjected to TN conditions (21.3 ± 0.1 °C, $56.8 \pm 0.3\%$ relative humidity [RH]; Federation of Animal Science Societies, 2010) with a 12 h:12 h light–dark cycle, and fed the control diet ad libitum (pigs were allotted to treatment prior to P0). During P1 (5 d), pigs were fed their respective dietary treatments ad libitum and kept in TN conditions for collecting baseline body temperature indices and production parameters. During P2 (35 d), HSCtl and HSCr animals were fed ad libitum and exposed to progressive cyclical HS conditions with temperatures ranging from 27 to 31 °C (d 1: 27.1 °C; d 2: 28.5 °C from 0800 to 1800 hours and 26.9 °C from 1800 to 0800 hours; days 3 to 7: 29.6 °C from 0800 to 1800 hours and 27 °C from 1800 to 0800 hours; days 8 to 35: 31.4 °C from 0800 to 1800 hours and 27.3 °C from 1800 to 0800 hours; Figure 1). Both temperature and humidity were monitored and recorded every 5 min by a data logger (Lascar EL-USB-2-LCD, Erie, PA). One data logger was placed in each quadrant of each room (eight data loggers in total) and data were condensed into hourly averages by room. During P2, pigs assigned to the TNCtl and TNCr

Table 1. Ingredient composition and chemical and nutritional composition of experimental diets (as-fed basis)

Item	Control diet	Chromium diet
Ingredient composition		
Corn, %	86.10	86.05
Soybean meal, %	11.43	11.44
L-Lys HCl, %	0.19	0.19
L-Thr, %	0.03	0.03
Monocalcium phosphate, %	0.55	0.55
Limestone, %	0.87	0.87
NaCl, %	0.50	0.50
Vitamin premix ¹ , %	0.16	0.16
Trace mineral premix ² , %	0.15	0.15
Endox ³ , %	0.01	0.01
Chromium propionate ⁴ , %	0	0.05
Diet composition		
Dry matter ⁵ , %	86.74	86.93
NE, kcal/kg	2,547	2,545
ME, kcal/kg	3,309	3,308
NE:ME ratio	0.76	0.76
CP ⁵ , %	12.13	11.82
ADF, %	3.1	3.1
NDF, %	8.8	8.8
Ether extract ⁵ , %	2.55	2.03
SID ⁶ AA, %		
Lys	0.61	0.61
Thr	0.40	0.40
Met + Cys	0.39	0.39
Trp	0.11	0.11
Ca, %	0.48	0.48
Total P, %	0.42	0.42
STTD ⁷ P, %	0.22	0.22

¹Vitamin premix provided the following (per kg diet): 4,900 IU of vitamin A, 560 IU of vitamin D3, 40 IU of vitamin E, 2.4 mg of menadione (to provide vitamin K), 39 µg of vitamin B12, 9 mg of riboflavin, 22 mg of D-pantothenic acid, and 45 mg of niacin.

²Mineral premix provided the following (per kg diet): 165 mg of Fe (ferrous sulfate), 165 mg of Zn (zinc sulfate), 39 mg of Mn (manganese sulfate), 2 mg of Cu (copper sulfate), 0.3 mg of I (calcium iodate), and 0.3 mg of Se (sodium selenite).

³ENDOX (Kemin Industries, Inc.).

⁴Chromium propionate, 0.5 g/kg of feed to deliver 200 parts per billion (KemTRACE Cr propionate 0.04%, Kemin Industries, Inc.).

⁵Assayed values.

⁶Standardized ileal digestibility.

⁷Standardized total tract digestibility.

treatments remained in TN conditions and were fed ad libitum. Pigs in PFCtl and PFCr treatments also remained in TN conditions but were pair-fed to their HS counterparts to directly evaluate HS by eliminating the confounding effect of dissimilar nutrient intake. ADFI in P1 was averaged for each pig and used as a baseline. During P2, the decrease in ADFI in HS pigs was calculated everyday as a percentage of ADFI reduction relative to P1. The

percentage of ADFI reduction was averaged for all pigs in HS treatments per day of heat exposure and applied individually to the baseline of each pig in the PF treatments. The daily amount of feed provided to pigs in the PF treatments was divided into two equal portions during P2 (delivered at ~0800 and 1800 hours) to minimize large metabolic changes associated with gorging. To accomplish the pair-feeding, pigs assigned to the PF treatments remained 2 calendar days behind the TN and HS treatments throughout the experiment. This technique of pair-feeding has been extensively utilized by our research program (Pearce et al., 2013a; Sanz Fernandez et al., 2015).

Body Temperature Measurements

During both P1 and P2, body temperature indices (rectal temperature [T_R], skin temperature [T_S] and respiration rate [RR]) were obtained twice daily (~0700 and 1800 hours). Rectal temperatures were measured using a calibrated electronic thermometer (SureTemp Plus 690, accuracy: ± 0.1 °C; Welch Allyn, Skaneateles Falls, NY). Skin temperature was measured at the rump using a calibrated infrared thermometer (IRT207: The Heat Seeker 8:1 Mid-Range Infrared Thermometer, accuracy: ± 2 °C; General Tools, New York, NY), and RR were determined by counting flank movements for 15 s and multiplied by 4 to obtain breaths per minute (bpm). All indices recorded were condensed into weekly AM and PM averages.

Production Parameters

Feed intake was measured daily (~0700 hours) during P1 and P2 as feed disappearance. BWs were obtained at the beginning of P0 and P1, at the end of P1, and on days 7, 14, 21, 28, and 35 of P2. In addition, 10th-rib back fat thickness and loin eye area were measured via ultrasound scan (Cai et al., 2008) on day 1 of P0 and day 35 of P2.

Blood Sampling and Analysis

Blood samples were obtained by jugular venipuncture (plasma and serum; K₂EDTA and BD Vacutainers, Franklin Lakes, NJ) on days 1 and 5 of P1, and days 7 and 35 of P2. Serum and plasma samples were stored at 4 °C before submission to the Iowa State Department of Veterinary Pathology for blood chemistry and hematology analysis. A second set of plasma samples were harvested by centrifugation at 4 °C and 1,500 × g, aliquoted, and stored

Figure 1. Ambient temperature (°C) in the thermoneutral (TN; 21.3 ± 0.1 °C, $56.8 \pm 0.3\%$ relative humidity) and the heat stress (HS; 27 to 31 °C, $50 \pm 0.3\%$ relative humidity) rooms during period 1 (days -5 to -1) and period 2 (days 1 to 35).

at -20 °C until analysis. Plasma NEFA (Wako Pure Chemical Industries, Ltd., Osaka, Japan), insulin (Mercodia Porcine Insulin ELISA; Mercodia AB; Uppsala, Sweden), and lipopolysaccharide (LPS) binding protein (LBP; Hycult Biotech, Uden, the Netherlands) were measured following the manufacturers' instructions. The intra- and inter-assay coefficients of variation for NEFA, insulin, and LBP were 6.1% and 8.8%, 8.1% and 1.6%, and 6.5% and 14.3%, respectively.

Statistical Analysis

All data from P2 were statistically analyzed using SAS version 9.4 (SAS Institute, Inc., Cary, NC). Daily measurements were condensed into weekly means. Body temperature indices, blood metabolites, and production parameters were analyzed using PROC MIXED of SAS with an autoregressive covariance structure and week of experiment as the repeated measure. The model included treatment, week, treatment by week interaction, block, and replicate as fixed effects and pig as the random effect. Period 1 values for each variable were used as a covariate. Final BW, back fat thickness, and loin eye area were analyzed using PROC MIXED with a diagonal covariance structure and P1 value of the parameter of interest used as a covariate. Pre-planned contrasts were assessed to evaluate dietary (i.e., Ctl vs. Cr) and environmental (i.e., TN vs. PF, TN vs. HS, or PF vs. HS) effects. Results are reported as least square means and considered significant if $P \leq 0.05$ and a tendency if $0.05 < P \leq 0.10$.

RESULTS

Body Temperature Indices

During P2, all pigs exposed to HS had an overall increase in T_R relative to TN and PF treatments (0.40 °C; $P < 0.01$; Table 2). Skin temperature was also increased during P2 (13%; 4.6 °C; $P < 0.01$; Table 2) in the HS environment when compared with TN and PF treatments. Respiration rates were increased in HS relative to TN and PF pigs (71%, 33 bpm; $P < 0.01$; Table 2). Both T_R and T_S were decreased (0.16 and 1.69 °C, respectively; $P < 0.01$; Table 2) in PF treatments relative to TN controls. There were no differences in T_S or RR between HSCtl and HSCr treatments, but T_R at 1800 hours was increased in the HSCr (0.11 °C; $P = 0.01$; Table 2; Figure 2) relative to HSCtl pigs. Overall, irrespective of environment, there were no differences in any body temperature indices when comparing Ctl vs. Cr-fed treatments ($P > 0.10$; Table 2).

Growth Performance

ADFI decreased during P2 (20%, 0.70 kg/d; $P < 0.01$; Figure 3A) in HS pigs relative to TN controls. Similarly, ADG was decreased in HS pigs compared with TN controls (21%, 0.20 kg/d; $P < 0.01$; Table 3). Final BW was decreased in HS (6.5 kg, $P < 0.01$; Figure 3B) relative to TN treatments. During P2, G:F did not differ between HS and TN environments ($P = 0.34$; Table 3). By experimental design, PFCtl and PFCr pigs had a similar pattern and extent in ADFI reduction and their BW

Table 2. Effects of chromium propionate supplementation on body temperature indices

Parameter	Treatment ¹						SEM	P			Contrasts ⁵				
	TNCtl	TNCr	PFctl	PFcr	HSCtl	HSCr		Trt ²	Wk ³	Trt × Wk ⁴	TN vs. PF	TN vs. HS	PF vs. HS	HSCtl vs. HSCr	Ctl vs. Cr
T_R^6 , °C															
0700 hours	38.81 ^b	38.78 ^b	38.64 ^c	38.62 ^c	38.98 ^a	38.99 ^a	0.04	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	0.76	0.71
1800 hours	39.19 ^c	39.15 ^c	39.00 ^d	39.02 ^d	39.57 ^b	39.68 ^a	0.04	<0.01	<0.01	0.21	<0.01	<0.01	<0.01	0.01	0.36
T_S^7 , °C															
0700 hours	35.11 ^b	35.30 ^b	33.64 ^c	33.05 ^d	38.57 ^a	38.72 ^a	0.16	<0.01	<0.01	0.02	<0.01	<0.01	<0.01	0.38	0.49
1800 hours	36.96 ^b	36.92 ^b	35.37 ^c	35.46 ^c	41.11 ^a	41.19 ^a	0.15	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	0.58	0.69
RR ⁸ , bpm															
0700 hours	44.5 ^b	45.9 ^b	42.6 ^b	41.6 ^b	64.5 ^a	65.3 ^a	1.6	<0.01	<0.01	<0.01	0.05	<0.01	<0.01	0.62	0.73
1800 hours	48.1 ^b	53.2 ^b	48.8 ^b	47.8 ^b	92.9 ^a	96.1 ^a	2.3	<0.01	<0.01	0.02	0.31	<0.01	<0.01	0.18	0.16

^{a-c}Means within a row with different superscripts differ ($P \leq 0.05$).

¹TNCtl = thermoneutral control; TNCr = thermoneutral chromium; PFctl = pair-fed control; PFcr = pair-fed chromium; HSCtl = heat-stress control; HSCr = heat-stress chromium.

²Treatment.

³Week.

⁴Treatment by week interactions.

⁵TN = TNCtl and TNCr; PF = PFctl and PFcr; HS = HSCtl and HSCr; Ctl = TNCtl, PFctl, and HSCtl; Cr = TNCr, PFcr, and HSCr.

⁶Rectal temperature.

⁷Skin temperature.

⁸Respiration rate.

Figure 2. Effects of chromium propionate supplementation on rectal temperature (T_R) at 1800 hours. Treatments: TNCtl = thermoneutral control diet, TNCr = thermoneutral chromium diet, PFctl = pair-fed control diet, PFcr = pair-fed chromium diet, HSCtl = heat-stress control diet, and HSCr = heat-stress chromium diet.

and ADG variables were similar to the HS pigs ($P > 0.05$; Table 3). Additionally, G:F was decreased in pigs from the PF treatments when compared with TN (8%, $P = 0.02$) and HS pigs (9%, $P < 0.01$; Table 3). There were no differences in ADFI between HSCtl and HSCr (2.80 vs. 2.92 kg/d, respectively; $P = 0.12$; Figure 3A). Final BW tended to be increased in HSCr (2.7 kg; $P = 0.06$; Figure 3B) compared with HSCtl pigs. Similarly, a tendency for increased ADG during P2 was observed in the HSCr pigs ($P = 0.10$; Table 3) relative to

Figure 3. Effects of chromium propionate supplementation on (A) ADFI and (B) final BW during period 2. Treatments: TNCtl = thermoneutral control diet, TNCr = thermoneutral chromium diet, PFctl = pair-fed control diet, PFcr = pair-fed chromium diet, HSCtl = heat-stress control diet, and HSCr = heat-stress chromium diet. ^{a-c}Values with differing superscripts denote differences ($P \leq 0.05$).

Table 3. Effects of chromium propionate supplementation on growth performance and carcass characteristics

Parameter	Treatment ¹							<i>P</i>			Contrasts ⁵				
	TNCtl	TNCr	PFCtl	PFCr	HSCtl	HSCr	SEM	Trt ²	Wk ³	Trt × Wk ⁴	TN vs. PF	TN vs. HS	PF vs. HS	HSCtl vs. HSCr	Ctl vs. Cr
ADFI, kg	3.52 ^a	3.61 ^a	2.95 ^{bc}	3.04 ^b	2.80 ^c	2.92 ^{bc}	0.08	<0.01	<0.01	<0.01	<0.01	<0.01	0.07	0.12	0.08
ADG, kg	0.92 ^a	0.97 ^a	0.72 ^b	0.70 ^b	0.72 ^b	0.77 ^b	0.03	<0.01	<0.01	<0.01	<0.01	<0.01	0.24	0.10	0.19
IBW ⁶ , kg	104.0	104.1	104.6	103.8	104.4	103.9	0.7	0.95	—	—	0.82	0.91	0.91	0.46	0.45
FBW ⁷ , kg	144.2 ^a	146.5 ^a	138.4 ^{bc}	136.6 ^c	137.5 ^{bc}	140.2 ^b	1.4	<0.01	—	—	<0.01	<0.01	0.34	0.06	0.32
G:F	0.25 ^{bc}	0.27 ^{ab}	0.24 ^c	0.24 ^c	0.26 ^{ab}	0.27 ^{ab}	0.01	0.02	<0.01	<0.01	0.02	0.34	<0.01	0.61	0.39
BF ⁸ , cm	2.04 ^x	2.12 ^x	1.90 ^{xy}	1.77 ^y	1.97 ^{xy}	1.97 ^{xy}	0.08	0.08	—	—	<0.01	0.18	0.11	0.95	0.82
LEA ⁹ , cm ²	53.6 ^{xy}	55.1 ^x	52.2 ^y	51.8 ^y	52.8 ^y	52.3 ^y	0.9	0.09	—	—	<0.01	0.04	0.53	0.59	0.76

^{a-c}Means within a row with different superscripts differ ($P \leq 0.05$).

^{xy}Means within a row with different superscripts tended to differ ($P \leq 0.10$).

¹TNCtl = thermoneutral control; TNCr = thermoneutral chromium; PFCtl = pair-fed control; PFCr = pair-fed chromium; HSCtl = heat-stress control; HSCr = heat-stress chromium.

²Treatment.

³Week.

⁴Treatment by week interactions.

⁵TN = TNCtl and TNCr; PF = PFCtl and PFCr; HS = HSCtl and HSCr; Ctl = TNCtl, PFCtl, and HSCtl; Cr = TNCr, PFCr, and HSCr.

⁶Initial BW.

⁷Final BW.

⁸Back fat.

⁹Loin eye area.

their HSCtl counterparts, but there was no difference in G:F between HSCtl and HSCr treatments ($P = 0.61$; Table 3). Overall, when comparing Ctl vs. Cr-fed pigs, no differences were detected for final BW, ADG, or G:F; however, ADFI tended to be increased (3.19 vs. 3.09 kg/d; $P = 0.08$; Figure 3A) in Cr relative to Ctl-fed pigs.

There were no differences in back fat between HS and TN treatments ($P = 0.18$; Table 3), or between HS and PF pigs ($P = 0.11$; Table 3); but back fat was decreased in the PF pigs (12%; $P < 0.01$; Table 3) when compared with their TN counterparts. There was no treatment effect on back fat when comparing HSCtl and HSCr treatments ($P = 0.95$; Table 3). Overall, no differences in back fat were detected when comparing Ctl vs. Cr-fed pigs ($P = 0.82$; Table 3). Compared with TN treatments, loin eye area was decreased in HS and PF treatments (3% and 4%, respectively; $P < 0.05$; Table 3). However, no differences were observed in loin eye area between HSCtl and HSCr treatments ($P = 0.59$; Table 3) or due to Cr supplementation ($P = 0.76$; Table 3).

Metabolism and Hematology

No treatment differences were observed for circulating insulin during P2 ($P = 0.17$; Figure 4A). However, PF pigs had increased insulin relative to HS pigs (0.24 vs. 0.15 $\mu\text{g/L}$; $P = 0.03$). There was no treatment effect on circulating insulin between

HSCtl and HSCr-fed pigs ($P = 0.52$). Overall, no treatment differences were observed in circulating insulin when comparing Ctl vs. Cr-fed animals ($P = 0.35$). Blood glucose content did not differ between treatments ($P = 0.69$; Figure 4B). Similarly, no treatment effects were observed for plasma NEFA levels ($P = 0.92$; Figure 4C).

Compared with TN treatments, pigs in the HS treatments tended to have increased LBP levels (36%; $P = 0.07$; Figure 5A). Similarly, LBP was increased in HS pigs relative to PF pigs (42%; $P = 0.05$). However, no differences in LBP levels were observed between HSCtl and HSCr pigs ($P = 0.11$) or between Ctl and Cr-fed pigs ($P = 0.15$). Compared with TN and PF controls, pigs in the HS treatments had decreased ($P < 0.01$; 18%) circulating alkaline phosphatase (Supplementary Table 1).

Blood neutrophils were increased in HSCr relative to HSCtl pigs (37%; $P < 0.01$; Figure 5B). There were no overall dietary treatment effects on circulating lymphocytes ($P = 0.20$; Table 4). However, a tendency for decreased lymphocytes was observed in HS relative to TN treatments (7%; $P = 0.08$; Table 4). In addition, PF pigs had increased circulating lymphocytes when compared with their HS counterparts (9%; $P = 0.03$; Table 4). Monocytes were increased in HSCr pigs when compared with HSCtl pigs (16%; $P = 0.05$; Table 4). However, no dietary treatment effects were detected on other white blood cells including eosinophils

Figure 4. Effects of chromium propionate supplementation on circulating (A) insulin, (B) glucose, and (C) NEFA. Treatments: TNCtl = thermoneutral control diet, TNCr = thermoneutral chromium diet, PFCtl = pair-fed control diet, PFCr = pair-fed chromium diet, HSCtl = heat-stress control diet, and HSCr = heat-stress chromium diet.

and basophils ($P > 0.10$; Table 4). A tendency for increased red blood cells was observed in the PF treatments when compared with TN controls (3%; $P = 0.07$; Table 4). Additionally, red blood cells tended to be reduced in Cr relative to Ctl-fed pigs ($P = 0.10$). However, no differences were observed in red blood cells between HSCtl and HSCr treatments ($P = 0.75$). Plasma hemoglobin tended to be increased in PF animals (3%; $P = 0.06$; Table 4) relative to TN animals. No differences in hemoglobin were detected between HSCtl and HSCr treatments

Figure 5. Effects of chromium propionate supplementation on circulating (A) lipopolysaccharide binding protein (LBP) and (B) neutrophils. Treatments: TNCtl = thermoneutral control diet, TNCr = thermoneutral chromium diet, PFCtl = pair-fed control diet, PFCr = pair-fed chromium diet, HSCtl = heat-stress control diet, and HSCr = heat-stress chromium diet. ^{a-c}Values with differing superscripts denote differences ($P \leq 0.05$). ^{xy}Values with differing superscripts denote tendencies ($P \leq 0.10$).

($P = 0.55$; Table 4). However, plasma hemoglobin tended to be reduced in Cr compared with Ctl-fed pigs (2%; $P = 0.09$). Hematocrit did not differ between HS and TN treatments ($P = 0.88$; Table 4), but PF treatments tended to have increased hematocrit levels compared with TN controls (3%; $P = 0.07$). Similarly, hematocrit was increased in PF in comparison to HS pigs (3%; $P = 0.05$; Table 4). Overall, hematocrit was reduced in Cr compared with Ctl-fed pigs (2.5%; $P = 0.04$; Table 4). No treatment differences were detected on circulating platelets ($P = 0.57$; Table 4).

Blood Chemistry

There were marginal dietary and environmental effects on most blood chemistry variables (Supplementary Table 1). The primary environmental effects were characterized by decreased HCO_3^- and cholesterol and increased creatinine in HS pigs vs. TN and PF controls ($P < 0.05$; Supplementary Table 1).

Table 4. Effects of chromium propionate supplementation on complete blood cell count

Parameter	Treatment ¹						<i>P</i>			Contrasts ⁵					
	TNCtl	TNCr	PFCtl	PFCr	HSCtl	HSCr	SEM	Trt ²	Wk ³	Trt × Wk ⁴	TN vs. PF	TN vs. HS	PF vs. HS	HSCtl vs. HSCr	Ctl vs. Cr
WBC ⁶ , × 10 ³ /μL	21.7	21.4	20.6	21.1	19.4	21.3	0.9	0.32	<0.01	0.05	0.46	0.16	0.53	0.06	0.36
Lymph. ⁷ , × 10 ³ /μL	13.3	13.4	13.1	14.1	12.4	12.4	0.5	0.20	<0.01	0.01	0.71	0.08	0.03	0.97	0.39
Mono. ⁸ , × 10 ³ /μL	1.25	1.19	1.17	1.23	1.20	1.39	0.09	0.34	0.55	0.51	0.81	0.37	0.24	0.05	0.37
Eosin. ⁹ , × 10 ³ /μL	0.56	0.53	0.58	0.68	0.57	0.64	0.07	0.74	0.79	0.15	0.27	0.39	0.71	0.48	0.46
Basop. ¹⁰ , × 10 ³ /μL	0.12	0.12	0.11	0.09	0.11	0.10	0.01	0.85	0.22	0.81	0.34	0.50	0.66	0.68	0.54
RBC ¹¹ , × 10 ⁶ /μL	7.59 ^{xy}	7.47 ^y	7.91 ^x	7.57 ^y	7.60 ^y	7.64 ^y	0.10	0.10	<0.01	0.29	0.07	0.41	0.21	0.75	0.10
Hb. ¹² , gm/dL	13.6 ^b	13.4 ^b	14.2 ^a	13.5 ^b	13.5 ^b	13.7 ^b	0.2	0.05	<0.01	0.27	0.06	0.59	0.11	0.55	0.09
Hct. ¹³ , %	43.3 ^{ab}	42.2 ^b	45.1 ^a	42.9 ^b	42.8 ^b	42.9 ^b	0.6	0.04	<0.01	0.28	0.07	0.88	0.05	0.88	0.04
Platelets × 10 ³ /μL	301	620	303	349	287	319	25	0.57	0.14	0.49	0.58	0.74	0.34	0.27	0.12

^{a-c}Means within a row with different superscripts differ ($P \leq 0.05$).

^{x-y}Means within a row with different superscripts tended to differ ($P \leq 0.10$).

¹TNCtl = thermoneutral control; TNCr = thermoneutral chromium; PFCtl = pair-fed control; PFCr = pair-fed chromium; HSCtl = heat-stress control; HSCr = heat-stress chromium.

²Treatment.

³Week.

⁴Treatment by week interactions.

⁵TN = TNCtl and TNCr; PF = PFCtl and PFCr; HS = HSCtl and HSCr; Ctl = TNCtl, PFCtl, and HSCtl; Cr = TNCr, PFCr, and HSCr.

⁶White blood cells.

⁷Lymphocytes.

⁸Monocytes.

⁹Eosinophils.

¹⁰Basophils.

¹¹Red blood cells.

¹²Hemoglobin.

¹³Hematocrit.

DISCUSSION

When pigs are exposed to environmental conditions that exceed their TN zone, reduced metabolic HP is necessary to maintain euthermia (Collin et al., 2001). The main strategy to reduce HP is by decreasing voluntary ADFI, a conserved response to HS across species (Quiniou et al., 2000). Furthermore, HS alters carbohydrate, lipid, and protein metabolism independently of nutrient intake. This homeorhetic process involves changes in fuel supply and use by different tissues, an energetic approach mediated in large part by increased basal and stimulated circulating insulin (Baumgard and Rhoads, 2013). Consequently, physiological and metabolic adjustments to a thermal load result in decreased farm animal performance, which negatively impacts agriculture economics and global food security. In the pig industry, financial losses caused by HS are mainly explained by decreased and inconsistent growth, decreased carcass quality, increased health care costs, reduced fecundity, increased mortality, and reduced facility efficiency (Baumgard and Rhoads, 2013; Ross et al., 2015, 2017). Thus, developing protocols to mitigate the

negative consequences of HS is critical. Nutritional interventions represent a practical, flexible, and economical opportunity to maximize productivity during the warm summer months. Dietary Cr is thought to potentiate insulin action by facilitating the binding of insulin to its extracellular receptor (NRC, 1997; Vincent, 2000), consequently enhancing cellular glucose uptake (Chen et al., 2006). Additionally, previous studies indicate that Cr supplementation improves ADFI, growth performance, reproductive parameters, and the immune response in multiple species (Burton et al., 1993; Lindemann et al., 1995; Hayirli et al., 2001; Sadri et al., 2009; Sales and Jancik, 2011; Hung et al., 2014; Yasui et al., 2014). We hypothesized supplementing Cr may enhance animal productivity and health during HS. Herein, we evaluated potential effects of Cr supplementation in heat-stressed and nutrient-restricted pigs.

HS was successfully implemented as indicated by increased T_R and T_S (0.3 and 3.8 °C, respectively) and RR (32 bpm) in HS relative to TN pigs. Interestingly, HSCr pigs had a slightly increased T_R (0.1 °C) at 1800 hours relative to HSCtl pigs. Presumably, increased ADG and numerically

increased ADFI in HSCr fed pigs (discussed below) relative to their HSCtl counterparts contributed to enhanced metabolic HP and thus increased body temperature indices. Conversely, decreased T_R and T_S (0.2 and 1.7 °C, respectively) were observed in the PF treatments when compared with their TN counterparts, suggesting decreased basal HP associated with reduced thermic effect of feeding as previously reported by our group (Pearce et al., 2013a; Seibert et al., 2018).

As expected, thermal stress considerably decreased ADFI, ADG, and final BW (~20%, 21%, and 4%, respectively) relative to TN pigs. The pattern and magnitude of reduced ADFI is comparable to that observed in our previous experiments (Johnson et al., 2015a,b), and by experimental design, pigs in the PF treatments followed the same pattern and extent of decreased ADFI. Decreased ADFI during HS reduces the energy available for tissue synthesis and partially explains the decrease in growth performance (Le Bellego et al., 2002; Kerr et al., 2003; Johnson et al., 2015a,b). Interestingly, regardless of environment, pigs fed Cr had a tendency for increased ADFI (~3%) compared with Ctl-fed pigs. Despite inconsistencies (Kegley et al., 2000; Mathews et al., 2001; Uyanik et al., 2002), Cr supplementation has been shown to increase ADFI in a variety of species (Hayirli et al., 2001; Sahin et al., 2003; Hung et al., 2014). Additionally, pigs fed Cr during HS tended to have increased ADG and final BW. Results reported herein also agree with previous studies where Cr supplementation enhanced growth performance during HS. For instance, increased production variables have been demonstrated in heat-stressed laying quail and broilers supplemented with Cr (Lien et al., 1999; Sahin et al., 2002; Sahin et al., 2005; Toghyani et al., 2012). In heat-stressed lactating dairy cows, dietary Cr improved dry matter intake, milk production, and reproductive performance (Soltan et al., 2010; Mirzaei et al., 2011). Nevertheless, studies on Cr supplementation during HS in swine are scarce and its effects have been equivocal. Accordingly, Kim et al. (2009) and Seibert et al. (2018) did not observe differences in growth performance of heat-stressed pigs supplemented with Cr. In contrast, increased ADFI and improved ADG and lactating performance were observed in pigs supplemented with Cr during the summer (Hung et al., 2014; Liu et al., 2017). Variations of the phenotypic responses to Cr supplementation during HS might be due to dissimilar experimental models, species, Cr source, supplementation doses, and type of HS insult. Regardless, in the current study, Cr

supplementation improved some key economically important phenotypes during HS.

Intriguingly, feed efficiency in HS pigs was not different when compared with the TN pigs, but was increased in HS pigs relative to their PF counterparts (0.27 vs. 0.24 kg gain/kg feed, respectively). Traditionally, the dogma is that G:F is compromised during HS because of the presumed increase in maintenance costs. Increased energy expenditure during HS is attributed to the energy costs for heat dissipation (i.e., panting, sweating) as previously reported in pigs (Campos et al., 2014), poultry (Yahav, 2007), cattle (McDowell et al., 1969; Beede and Collier, 1986), and rodents (Collins et al., 1980) and increased chemical reaction rates as predicted by the Van't Hoff Law (Kleiber, 1961; Fuquay, 1981). However, the effects of thermal load on G:F are inconsistent as some studies have reported HS decreases (Kerr et al., 2003; Renaudeau et al., 2008; Pearce et al., 2013a; Johnson et al., 2015b), increases (Lefaucheur et al., 1991), or has no effect (Collin et al., 2001; Johnson et al., 2015a) on feed efficiency. Furthermore, HS markedly reduces circulating thyroid hormones in multiple species (Prunier et al., 1997; Garriga et al., 2006; Johnson et al., 2015c; Kahl et al., 2015; Sanz Fernandez et al., 2015) and thus, metabolic rate is also presumably decreased during HS (Johnson et al., 2015a,b). The likely decrease in maintenance costs (Baumgard and Rhoads, 2013) explain why severely heat-stressed pigs actually grow while pair-fed thermal neutral controls lose BW (Pearce et al., 2013a). Additionally, as further discussed below, large differences in body composition may partially explain why a simple ratio of gross BW to ADFI is a poor metric of feed conversion during HS.

Animals exposed to HS accumulate more adipose tissue and less skeletal muscle than their nutrient intake predicts (as reviewed by Baumgard and Rhoads, 2013; Ross et al., 2015). This phenomenon is biologically interesting as feed-restricted pigs reared in TN conditions prioritize lean tissue deposition at the expense of fat (van Milgen and Noblet, 2003; Oresanya et al., 2008), and this suggests that HS has direct effects on the hierarchy of nutrient partitioning independent of reduced ADFI. Similar results were observed in the current study as subcutaneous fat deposition (as measured by back fat thickness) did not differ between HS and TN treatments (despite a 20% reduction in ADFI of HS pigs). Furthermore, as expected, back fat was decreased in the PF treatments when compared with their TN counterparts. This corroborates previous reports that fat deposition during HS is maintained

despite reduced ADFI, and these observations are likely due to differences in lipid metabolism and the inability to mobilize adipose tissue as demonstrated in a variety of species (as reviewed by [Baumgard and Rhoads, 2013](#)). In contrast to adipose tissue, loin eye area (a rough proxy of muscle accretion) was reduced in both HS and PF pigs (~3% and 4%, respectively) relative to their TN counterparts and thus it appears that this can be explained by decreased ADFI. Consequently, our observations corroborate the idea that HS altered body composition by limiting lean tissue accretion and accentuating lipid deposition ([Le Bellego et al., 2002](#); [Boddicker et al., 2014](#); [Johnson et al., 2015a,b](#)).

Despite striking differences in nutrient intake and growth patterns, no treatment differences were observed on blood energetic markers (i.e., insulin, glucose, and NEFA). This is surprising as normally HS increases circulating and stimulated insulin levels (reported in multiple species and across physiological states), especially compared with PF controls ([Baumgard and Rhoads, 2013](#)). Additionally, HS reduces basal and stimulated NEFA concentrations, and this has been attributed to insulin's antilipolytic effect ([Baumgard and Rhoads, 2013](#)). The effects of HS on circulating glucose levels are minor and inconsistent and largely dependent upon the severity of the heat load. Reasons why there were no observable difference in blood bioenergetics in this study are not clear, but the current HS protocol was substantially longer (35 d) and implemented a much less intense heat load than our previous reports ([Pearce et al., 2013a](#); [Sanz Fernandez et al., 2014, 2015](#)), and maybe metabolic adaption to the thermal load occurred with time.

HS-induced intestinal hyperpermeability is commonly observed in multiple species including pigs ([Lambert et al., 2002](#); [Pearce et al., 2013b](#); [Sanz Fernandez et al., 2014](#)), a scenario that results in intestinal-derived antigens infiltrating into the splanchnic and potentially systemic circulation. The subsequent inflammatory response often includes increased circulating LBP, an acute phase protein produced in response to LPS, an immunogenic bacterial component ([Lu et al., 2008](#)). In the current study, LBP concentrations in HS pigs tended to be or were increased relative to TN and PF pigs, respectively. Increased LBP (ostensibly originating from leaky gut) in HS pigs suggest an increased acute phase protein and inflammatory response. However, the increase in LBP does not agree with our previous reports that indicated LBP decreased within hours of acute HS exposure ([Pearce et al., 2014, 2015](#)). The most likely explanation for this

inconsistency relates to the chronic vs. acute study designs.

Based on the aforementioned immunoactivation, we evaluated how Cr influenced WBC dynamics. Circulating neutrophils and monocytes were increased (37 and 16%, respectively) in HSCr pigs relative to their HSCtl counterparts. This is consistent with previous reports indicating that supplemental Cr has immunomodulatory effects. For instance, [Chang and Mowat \(1992\)](#) and [Moonsie-Shageer and Mowat \(1993\)](#) observed increased immunoglobulin and antibody concentrations in transportation-stressed calves fed Cr. Additionally, [Burton et al. \(1993\)](#) reported increased cell-mediated immune response in periparturient and early lactating dairy cows supplemented with Cr. Furthermore, we and others have observed improved neutrophil counts and activity with Cr supplementation ([Lien et al., 2005](#); [Kafilzadeh et al., 2012](#); [Yasui et al., 2014](#); [Horst et al., 2018](#)). Mechanisms responsible for the immunomodulatory effects of Cr are not well-defined; however, increased circulating leukocytes may be attributed to Cr's role in decreasing circulating cortisol ([Chang and Mowat, 1992](#); [Soltan, 2010](#); [Kafilzadeh et al., 2012](#)), a well-known immunosuppressant ([Coutinho and Chapman, 2011](#)). Likewise, increased neutrophil and monocyte levels suggest Cr supplementation during HS may support the energetic requirements of proliferating innate leukocytes. Upon activation, immune cells become insulin sensitive ([Maratou et al., 2007](#)), and the insulin-sensitizing properties of Cr may improve immune function by enhancing leukocyte glucose uptake and utilization as we have recently discussed ([Horst et al., 2018](#)). Moreover, since no dietary differences in neutrophil counts were observed in TN or PF treatments, Cr's beneficial role at improving leukocyte proliferation may be more pronounced during stress-induced immunoactivation.

In conclusion, chronic cyclical HS increased all body temperature indices, markedly reduced ADFI, and decreased productive parameters including ADG, BW, and carcass traits. Herein we demonstrate Cr supplementation tended to improve final BW and ADG in pigs during chronic HS. In addition, ADFI tended to be increased in Cr relative to Ctl-fed pigs, regardless of environment. Interestingly, dietary Cr supplementation increased circulating neutrophils and monocytes in pigs exposed to HS. No other dietary differences were observed in regards to carcass characteristics, body temperature indices, or blood metabolites. Altogether, Cr supplementation might be a valuable dietary strategy to ameliorate the negative consequences of HS on

growth performance. However, additional research is warranted to better understand the biology and mode of action of dietary Cr in pigs under these circumstances.

SUPPLEMENTARY DATA

Supplementary data are available at *Animal Frontiers* online.

Conflict of interest statement. None declared.

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