Effect of dietary energy substrate and days on feed on apparent total tract digestibility, ruminal short-chain fatty acid absorption, acetate and glucose clearance, and insulin responsiveness in finishing feedlot cattle¹

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ABSTRACT: The objective of this study was to determine the effect of dietary energy substrate and days on feed on apparent total tract digestibility, ruminal fermentation, short-chain fatty acid (SCFA) absorption, plasma glucose and acetate clearance rates, and insulin responsiveness. Eight ruminally cannulated, crossbred growing heifers were randomly allocated to 1 of 2 dietary treatments. The control (CON) diet consisted of 75.2% barley grain, 9.8% canola meal, 9% mineral and vitamin supplement, and 6% barley silage (DM basis). To evaluate the effect of energy source, a high-lipid, high-fiber byproduct pellet (HLHFP) was included in the diet by replacing 55% of the barley grain and 100% of canola meal. The study consisted of 4 consecutive 40-d periods (P1 to P4), with data and sample collection occurring in the last 12 d of each period. Dry matter intake tended ($P = 0.10$) to decrease by period and HLHFP-fed heifers tended to eat less ($P = 0.09$). The ADG of the CON was greater than that of the HLHFP during P1 and P4 (treatment $\times$ period, $P = 0.02$). Heifers fed HLHFP tended to have greater mean ruminal pH (6.10 vs. 5.96; $P = 0.07$) than heifers fed the CON, but pH was not affected by period. The CON heifers had a

greater digestibility for DM, OM, CP, and NDF ($P \leq 0.03$), and the digestibility for DM and OM linearly increased ($P = 0.01$) and for CP, NDF, and starch quadratically increased ($P \leq 0.04$) with advancing period. Total SCFA concentration in the rumen was greater ($P < 0.01$) for the CON than for the HLHFP (141.6 vs. 128.1 mM). The molar proportion of acetate and isobutyrate linearly increased and butyrate and valerate linearly decreased ($P \leq 0.05$) with advancing periods. The rate of valerate absorption tended to increase (linear, $P = 0.06$) and the ruminal liquid passage rate tended to decrease (linear, $P = 0.08$) with advancing period. The arterial clearance rate of acetate tended to quadratically increase ($P = 0.06$) with period, whereas the clearance rate of glucose was not affected by treatment or period. Both fasting plasma insulin and the area under the insulin curve in response to glucose infusion linearly increased ($P = 0.04$) with period. These data suggest that partially replacing barley grain with HLHFP negatively affects total tract digestibility and performance. Moreover, with advancing days on feed, digestibility and insulin resistance increases without changes in ruminal pH and plasma metabolite clearance rates.

Key words: byproduct, cattle, days on feed, digestibility, feedlot, insulin

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INTRODUCTION

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Byproduct feeds can be a cost-effective alternative to cereal grains, and blending byproducts can help overcome limitations associated with inclusion of a single byproduct (Górka et al., 2013; Zenobi et al., 2014). One strategy to increase the energy density of blended byproduct feeds has been to use byproducts from the oilseed industry (Górka et al., 2013). Although the effects of lipid supplementation are

Table 1. Ingredient and chemical composition of a barley-based diet (control [CON]) or a high-lipid, high-fiber byproduct pellet (HLHFP) diet fed to finishing heifers

Variable	Diet	
	CON	HLHFP
Ingredient, % of DM		
Barley silage	6.0	6.0
Rolled barley grain	75.2	34.1
Canola meal	9.8	0.0
High-lipid byproduct pellet ¹	0.0	51.2
Vitamin–mineral pellet ²	8.0	8.0
Limestone	1.0	0.7
Chemical composition, mean (SD)		
No.	8	8
DM, %	85.3 (1.2)	85.0 (1.2)
CP, % of DM	15.5 (0.3)	13.6 (0.3)
Starch, % of DM	46.6 (0.8)	39.5 (0.9)
Ether extract, % of DM	3.8 (0.2)	5.7 (0.3)
NDF, % of DM	20.2 (1.2)	26.4 (1.4)
ADF, % of DM	9.1 (0.3)	14.3 (0.7)
Lignin, % of DM	2.6 (0.1)	3.5 (0.3)
Ash, % of DM	5.4 (0.4)	6.9 (0.2)
Ca, % of DM	0.94 (0.01)	0.88 (0.02)
P, % of DM	0.53 (0.13)	0.43 (0.09)
NEm, ³ Mcal/kg DM	1.87 (0.02)	1.81 (0.02)
NEg, ³ Mcal/kg DM	1.23 (0.02)	1.18 (0.02)

¹Ingredient composition of the high-lipid byproduct pellet: 29.7% wheat, 14.9% off-grade canola, 26.4% wheat screenings, 11.2% oat hulls, and 17.8% pea screenings on a DM basis.

²Contained (DM basis) 2.5% NaCl, 5% Ca, 0.46% P, 2.0% Mg, 1.96% K, 2.0% S, 5.06 mg Co/kg, 161.0 mg Cu/kg, 8.8 mg I/kg, 494.8 mg Fe/kg, 370.6 mg Mn/kg, 2.5 mg Se/kg, 345.2 mg Zn/kg, 44,052.8 IU vitamin A/kg, 16,519.8 IU vitamin D, 330.4 IU vitamin E, 901.4 mg choline/kg, 442.7 mg monensin/kg, and 0.68 mg melengestrol acetate/kg.

³Net energy calculated based on a summation equation (Weiss, 1998).

variable, Górká et al. (2013) and Joy et al. (2016) demonstrated that high-lipid, high-fiber byproduct pellets can be a viable alternative to barley grain; however, a reduction in G:F has been observed.

In addition to a diet-related cause, the reduction in G:F with advancing days on feed (**DOF**) is attributed to increased energy required per unit gain (Welegedara et al., 2012) as cattle approach a mature BW (NASEM, 2016). That said, it may be possible that other factors are involved. For example, the incidence of digestive-related mortalities is greater in the latter part of the finishing period (Smith, 1998), corresponding to increased prevalence and severity of ruminal acidosis (Castillo-Lopez et al., 2014). Low ruminal pH can reduce fiber digestibility (Russell and Wilson, 1996) and short-chain fatty acid (**SCFA**) absorption (Schwaiger et al., 2013) and may lead to systemic inflammation (Gozho et al., 2005). All of the previously mentioned factors could reduce G:F. However, we are not aware of previous studies that have evaluated changes in di-

gestibility, SCFA absorption, and postabsorptive nutrient metabolism with advancing DOF and whether dietary energy substrate influences the response.

We hypothesized that the inclusion of high-lipid, high-fiber byproduct pellets will alter ruminal fermentation and improve the SCFA absorption and metabolite clearance rates in finishing heifers. It was further hypothesized that benefits arising from the high-lipid, high-fiber supplementation would be most prominent toward the latter part of the finishing period.

MATERIALS AND METHODS

Heifer Management

All procedures involving heifers were preapproved by the University of Saskatchewan Animal Research Ethics Board (protocol number 20100021) and followed the guidelines of the Canadian Council on Animal Care (2009). Eight forage-fed 18-mo-old Hereford heifers with an initial mean BW of 454 kg (SD 15) were fitted with a ruminal cannula (model 9C; Bar Diamond Inc., Parma, ID) prior to the start of the study. Upon arrival, all heifers were treated with Ivermectin pour-on endectoparasiticide (5 mg/mL; Alberta Veterinary Laboratories, Calgary, AB, Canada) by topical application. Throughout the study, heifers were housed at the Livestock Research Building at the University of Saskatchewan (Saskatoon, SK, Canada) in individual pens (9 m²) fitted with rubber mats as bedding. Pens were scraped and washed daily.

Dietary Treatments, Feeding, and Experimental Design

This study was conducted as a generalized randomized complete block design. Heifers were blocked by BW into 2 blocks to facilitate the labor-intensive sampling protocol (blocks started the study with a 2-wk lag between blocks) and, within block, were randomly assigned to treatments. Dietary treatments consisted of a barley grain and canola meal–based finishing diet (control [CON]) or a diet in which 55% of the barley grain and 100% of canola meal were replaced with a high-lipid, high-fiber byproduct pellet (**HLHFP**; Table 1). The HLHFP was formulated using byproducts from the cereal grain and oilseed sectors and was similar to that used by Górká et al. (2013, 2015) and Joy et al. (2016). Canola meal was used in the CON diet to balance the CP concentration between treatments, and limestone was added to adjust the Ca:P ratio. Diets were formulated to be isocaloric and isonitrogenous; however, based on retrospective ingredient analysis, the CP concentration of the CON was 1.9 percentage units greater than the

HLHFP (Table 1). All diets contained melengestrol acetate to deliver 0.4 mg/heifer per day to prevent estrus.

The study was conducted over 160 d, including a 21-d dietary transition. Heifers were initially fed a diet consisting of 92% grass hay and 8% of a vitamin and mineral supplement pellet with barley grain as a carrier. Feed was offered *ad libitum* once daily at 0830 h to allow for feed refusals equating to 5% of the weight offered on an as-fed basis. Heifers had free access to water throughout the study. To evaluate the effect of period, the 160-d study was divided into four 40-d periods (**P1**, **P2**, **P3**, and **P4**). The first period also included the 21-d dietary transition from a forage-based diet to a high-grain diet. The diet transition was accomplished using 7 steps in which the concentrate component gradually increased with each step (35, 45, 54, 62, 70, 76, and 82% of the diet DM) at the expense of barley silage. Each intermediate diet was fed for 3 d. For the HLHFP, the high-lipid, high-fiber pellet replaced 60% of the barley grain and canola meal in each step. This approach was used to simultaneously adapt heifers to the HLHFP and decreasing forage concentration. Performance, ruminal fermentation, and postabsorptive nutrient metabolism data were collected in each of the 4 periods.

Feed Intake and ADG

Heifers were weighed on arrival and at the start and end of P1, P2, P3 and P4 by taking the average BW from 2 consecutive days. The change in weight between the start and end of each 40-d period was used to determine ADG. Feed intake and feed refusals were measured daily with samples of feed (twice weekly composites) and refusals (during sampling days) being analyzed for DM content. The DM offered and DM refused were used to calculate DMI, and the ingredient DM values were used to ensure the formulated diet composition was achieved. Feed and refusal samples were dried in a forced-air oven at 55°C for 72 h and were composited by period (feed) and heifer (refusals). Prior to compositing, samples were ground using a hammer mill with a 1-mm screen (Christy and Norris Ltd., Chelmsford, UK). Ground samples were submitted to Cumberland Valley Analytical Services (Hagerstown, MD) and analyzed for DM, CP, NDF, ADF, lignin, ash, starch, ether extract (acid hydrolysis), Ca, and P as described by Rosser et al. (2013).

Ruminal Fermentation

Ruminal pH was measured in the ventral sac every 5 min from d 29 to 33 of each period using the Lethbridge Research Centre Ruminal pH Measurement

System (Dascor, Inc., Escondido, CA) as described by Penner et al. (2006). The pH systems were standardized before being inserted into and after removal from the rumen using standard pH buffers 7.0 and 4.0 at 39°C. Data were transformed from millivolt recordings to pH using beginning and ending linear regressions while assuming linear drift in measurements over time. A pH threshold of 5.5 was used to define subacute ruminal acidosis and pH below 5.2 for acute ruminal acidosis (Penner et al., 2007; Aschenbach et al., 2011). The mean, minimum, and maximum pH and the area and duration that ruminal pH was <5.5 were also calculated.

On d 36, 37, and 38 of each period, samples of ruminal digesta were collected starting at 0800 h on d 36 with 9-h intervals between sampling points, resulting in 8 samples/heifer. Ruminal digesta was collected from the anterior, ventral, and posterior regions of the rumen (250 mL/region) and placed in a common container. Digesta samples were then strained through 2 layers of cheesecloth, and two 10-mL aliquots of filtrate were transferred into 15-mL tubes. One sample was added to 2 mL of 25% (wt/vol) metaphosphoric acid and kept for the analysis of SCFA using gas chromatography and the other sample was kept as a spare. All samples were sealed and stored at -20°C. Prior to analysis, an equal volume of sample from each collection time point within a period was combined to yield a period composite. Samples were then used to determine SCFA concentration using gas chromatography (Agilent 6890 plus GC system; Agilent Technologies, Santa Clara, CA) as described by Alborno et al. (2013).

Short-Chain Fatty Acid Absorption and Liquid Passage Rate

The fractional rate of SCFA absorption was measured using the Cr-EDTA/*n*-valeric acid technique (Allen et al., 2000; Resende Júnior et al., 2006; Penner et al., 2009) from d 34 to 36 of each experimental period. Briefly, 500 mL of Cr-EDTA/*n*-valeric acid solution (20 mM of valerate adjusted to pH of 6.0 with NaOH solution and 1 g/100 mL of Cr) was pulse-dosed into the rumen, and digesta was manually mixed for 1 min. Representative ruminal fluid samples were collected at 0 (before infusion), 60, 120, 240, 480, 960, 1,440, 2,880, and 4,320 min after infusion. Samples of ruminal fluid were mixed with 25% (wt/vol) metaphosphoric acid (ratio of 5:1 mL rumen fluid:metaphosphoric acid) and immediately frozen at -20°C. The concentration of Cr (by atomic absorption spectrophotometry; model iCE 3300 spectrometer; Thermo Fisher Scientific, Waltham, MA) and valerate (by gas chromatography; Agilent 6890 plus GC system) were determined in the ruminal fluid samples at each time point. The exponential decay of Cr and

n-valeric acid was determined according to Penner et al. (2009). The fractional passage rate (**Kp**) was determined according to the clearance of Cr. The fractional clearance rate (**Kc**) of valerate was assumed to include both passage and absorption. Therefore, the fractional absorption rate (**Ka**) of valerate was determined by difference ($Kc - Kp$) when corrected for baseline concentrations.

Plasma Glucose and Insulin Measurements

An indwelling jugular catheter (14 gauge; MILA International, Inc., Erlanger, KY) was inserted into each heifer 1 d before the initiation of the sampling period (d 35). The catheter was used to collect blood samples that were then used to prepare period composites and to evaluate nutrient clearance (described below). Catheter patency was ensured by infusing 5 mL of heparinized physiological saline (10 IU/mL) twice daily. Blood samples used to prepare period composites, were collected using vacutainers on the same days and at the same time points as used for ruminal digesta samples. Blood samples were processed to separate plasma (148 IU of lithium heparin; Becton, Dickinson and Company, Franklin Lakes, NJ). Whole blood was placed on ice until being centrifuged at $2,500 \times g$ for 15 min at 4°C. All samples were stored at -20°C until analysis. For glucose and insulin measurements, plasma samples collected at 9-h intervals over 3 d were composited by period (equal volume basis) before analyses.

Plasma glucose was determined by enzymatic oxidation of glucose to gluconic acid and the subsequent enzymatic oxidation of *o*-dianisidine in the presence of glucose oxidase and peroxidase enzymes (PGO Enzymes; Sigma-Aldrich Corp., St. Louis, MO) as described by Penner and Oba (2009). Oxidized *o*-dianisidine was detected by absorption at 450 nm (Spectramax Plus384; Molecular Devices Inc., Sunnyvale, CA). Plasma insulin was determined by using a commercial kit (Bovine Insulin ELISA; Mercodia AB, Uppsala, Sweden) with an intra-assay CV of 2.52% and interassay CV of 2.56%.

Postabsorptive Nutrient Clearance

Clearance rates of acetate and glucose were used as an indicator for postabsorptive nutrient utilization (Benschop and Cant, 2009). Prior to measurements, heifers were fasted overnight for 12 h but had ad libitum access to water. On d 39 of each period, the clearance rate of acetate and glucose were determined. The clearance rate of acetate was measured prior to the glucose clearance rate with a 1-h interval between the final sample used for acetate clearance and the initial sample used for the assessment of the glucose clearance rate. Glucose

and acetate were chosen due to the reliance on glucose as an energy source during growth for intramuscular fat accretion, with acetate and glucose both contributing to lipogenesis during the late finishing stage (Smith and Crouse, 1984). The acetate solution for infusion was prepared from sodium acetate (Sigma-Aldrich Corp.; 3 M, 5.2 pH), adjusted to pH 7.4 using NaOH, sterilely filtered (0.22- μ m filter), and infused at a dose rate of 2.18 mmol/kg BW^{0.75}. The infusion was accomplished over a 1-min time period with a constant flow rate. Blood samples were collected at -10, 0 (immediately after completion of the infusion), 2, 4, 6, 8, 10, 15, 20, 25, and 30 min after infusion into a vacutainer containing 148 IU lithium heparin (Becton, Dickinson and Company). Blood samples were placed on ice and then centrifuged at $2,500 \times g$ for 15 min at 4°C for separation of plasma. The plasma was frozen until being analyzed for acetate concentration using a commercial kit (K-ACETRM 07/12; Megazyme International Ireland, Bray, Ireland).

To evaluate the arterial glucose clearance rate, a 2.78 M solution of glucose was used for infusion. Glucose was infused at a dose rate of 7.57 mmol/kg BW^{0.75}. The solution was infused over a 2-min period, and blood was collected at -10, 0, 5, 10, 15, 20, 25, 30, 45, 60, 90, 120, and 180 min after infusion. The blood collected in the vacutainer was immediately placed on ice and centrifuged as described above, and the plasma was frozen until glucose and insulin were measured. Urine was collected for 24 h after glucose infusion using an indwelling urinary catheter (Bardex Foley Catheter; C.R. Bard, Inc., Covington, GA), and urinary glucose concentration was analyzed as described above for plasma.

Apparent Total Tract Digestibility

Total tract digestibility was determined based on measurements of total fecal DM mass excreted and the amount of feed DM offered and feed refused. Collection of feed and feed refusals was previously described. Feces were collected off the pen floor and placed in clean plastic containers every 4 h starting from 0800 h on d 36 and finishing on d 38 of each period. The weight of the feces was recorded, and a representative sample equal to 5% of the wet weight was collected and composited across the 72-h measurement. The composite fecal sample was stored at -20°C until being used to determine DM content and for chemical analysis. Twenty-four hours prior to the start of total collection, urinary catheters were inserted and urine was collected to avoid urinary contamination of feces. Representative samples of feed refusals were also collected during the 3 d of total collection and were composited by period for each heifer. Refusals and feces were sent to Cumberland Valley Analytical Services for chemical analysis as described above.

Table 2. Performance and apparent digestibility coefficients for beef heifers fed a barley-based diet (control [CON]) or a high-lipid, high-fiber byproduct pellet (HLHFP) diet during advancing periods of a finishing feedlot phase

Item	Treatment			Period ¹					P-value			
	CON	HLHFP	SEM ²	P1	P2	P3	P4	SEM ²	Treatment	Period		Treatment × period
										Linear	Quadratic	
BW												
Initial ³	452.2	455.7	8.0	454.0	480.0	555.8	616.9	8.1				
Final ³	694.0	618.0	13.8	480.0	555.8	616.9	656.0	8.9				
ADG, kg/d	1.46	0.99	0.08	0.65	1.90	1.53	0.83	0.15	<0.01	0.79	<0.01	0.02
DMI, kg/d	10.57	8.51	0.78	10.22	9.84	9.47	8.61	0.68	0.09	0.10	0.73	0.70
G:F	0.138	0.119	0.005	0.059	0.200	0.164	0.091	0.016	0.05	0.41	<0.01	0.26
Apparent digestibility, %												
DM	78.18	72.77	1.07	71.98	75.00	78.26	76.41	1.40	0.01	0.02	0.10	0.53
OM	80.18	74.99	1.04	74.28	77.18	80.07	78.82	1.34	0.01	0.01	0.13	0.23
CP	77.16	74.42	0.62	72.74	75.47	78.57	76.44	1.03	0.01	<0.01	0.03	0.29
NDF	45.44	36.45	2.35	36.94	41.82	46.37	39.16	2.77	0.03	0.37	0.04	0.51
ADF	27.64	27.65	4.31	25.22	25.28	31.32	25.82	2.67	0.99	0.51	0.31	0.12
Starch	97.27	97.64	0.18	94.57	97.67	98.64	98.93	0.29	0.52	<0.01	<0.01	0.72
Ether extract	77.39	76.37	2.91	76.27	79.06	76.27	77.62	1.89	0.69	0.88	0.71	0.03

¹P1 = d 1 to 40; P2 = d 41 to 80; P3 = d 81 to 120; P4 = d 121 to 160.

²n = 4/treatment.

³Data are based on BW measured on 2 consecutive days.

Statistical Analysis

All data were tested for normality using graphical representation and the Shapiro–Wilk test. All data except apparent total tract starch digestibility and time to peak insulin concentration following the glucose infusion were normally distributed. Data that were not normally distributed were transformed using the Box–Cox method. The *P*-values arising from the transformed data analysis were reported. All variables were analyzed considering a repeated measure structure of data using the mixed procedure of SAS (SAS version 9.2; SAS Inst. Inc., Cary, NC) as described by Wang and Goonewardene (2004), with period as the repeated statement. Block was removed from the model wherever it was not significant. The best covariance structure was chosen based on the structure that yielded the lowest Akaike and Bayesian information criteria. The model used was as follows:

$$y_{ijk} = \mu + D_i + P_k + DP_{ik} + E_{ikl},$$

in which μ is the overall mean, D_i is the fixed effect of diet (CON vs. HLHFP), P_k is the fixed effect of period (P1, P2, P3, and P4), DP_{ik} is the fixed effect of the diet × time interaction, and E_{ikl} is the random error.

The data analysis for “time to peak” insulin after glucose infusion was conducted using PROC GLIMMIX of SAS using the model described above. When interactions were significant, mean separation was completed using Tukey’s test. Polynomial contrasts were used to compare the period effect. Significance was declared when $P \leq 0.05$, and tendencies were reported when $0.05 < P \leq 0.10$.

RESULTS

Diet Composition

No statistical analysis were conducted on the diets (Table 1), and therefore, the results are presented as the mean ± SD. Both the dietary treatments were formulated to be isoenergetic and isonitrogenous; however, the CP content of the CON diet was greater (15.5%) than that of the HLHFP diet (13.6%). Nevertheless, both treatments met the minimum requirements for all nutrients according to the National Academies of Sciences, Engineering, and Medicine (2016). Owing to the greater inclusion rate of barley grain, the starch content of the CON diet (46.6%) was greater than that of the HLHFP diet (39.5%). The HLHFP was formulated to be greater in ether extract content than the CON diet (5.7 vs. 3.8%). The byproducts incorporated in the pellets such as grain screenings and oat hulls resulted in a greater NDF and ADF concentration in the HLHFP diet relative to the CON diet (26.4 vs. 20.2% and 14.3 vs. 9.1%, respectively). Overall, the diet formulation succeeded in providing 2 diets differing in the energy substrates.

Dry Matter Intake and ADG

There was a treatment × period interaction ($P = 0.02$; Table 2) for ADG, with the CON heifers gaining more than the HLHFP heifers during P1 and P4 (Fig. 1). Despite having a transition protocol similar to that of the CON diet, heifers fed the HLHFP diet

Figure 1. Interaction between treatment (diet) and days on feed (period) for ADG for heifers fed either a barley-based diet (control [CON]) or a high-lipid, high-fiber byproduct pellet (HLHFP)-based diet (gray columns) during a finishing feedlot phase. The *P*-values for the treatment, period, and treatment $\times$ period interaction are <0.01 , <0.01 , and 0.02 , respectively. ^{a-d}Within period, columns with different letters differ ($P < 0.05$).

had a tendency ($P = 0.09$; Table 2) for less DMI and consequently less ADG in P1. The daily DMI tended to linearly decrease ($P = 0.10$) with advancing periods. The G:F was less ($P = 0.05$) for heifers fed the HLHFP diet than those fed the CON diet, and it quadratically decreased ($P < 0.01$) with period.

Total Tract Digestibility

The apparent total tract digestibility of DM, OM, CP, and NDF for the HLHFP was less ($P \leq 0.03$; Table 2) compared with the CON, whereas ADF and starch digestibility were not different ($P \geq 0.52$) between dietary treatments. There was a treatment $\times$ period interaction ($P = 0.03$) for ether extract digestibility; however, the Tukey's post hoc mean separation test did not detect means that differed within each period (data not shown). Total tract digestibility of CP, NDF, and starch showed a quadratic increases ($P < 0.04$) with advancing periods whereas that of DM and OM showed a linear increase ($P < 0.02$).

Ruminal Fermentation and Short-Chain Fatty Acid Absorption

Mean ruminal pH tended ($P = 0.07$) to be greater for heifers fed HLHFP than for heifers fed the CON diet, but minimum and maximum pH and the duration and area that ruminal pH was <5.5 were not affected ($P > 0.18$; Table 3) by treatment or period. The total SCFA concentration for heifers fed the HLHFP diet was 9.5% less ($P < 0.01$) than for those fed the CON diet. Dietary treatment had no effect ($P > 0.37$) on the molar proportions of individual SCFA except

for butyrate, where a treatment $\times$ period interaction ($P = 0.05$; data not shown) was observed. Although the interaction was significant for butyrate, the Tukey's post hoc separation did not indicate individual means that differed within period. Total SCFA concentration tended to linearly decrease ($P = 0.05$) from P1 to P4. The proportion of acetate tended to quadratically increase ($P = 0.09$) whereas isobutyrate tended to linearly increase ($P = 0.05$) with advancing period. The molar proportion of valerate linearly decreased ($P = 0.03$) with advancing period.

The ruminal K_a , K_c , and K_p did not differ ($P \geq 0.73$; Table 3) between treatments. A tendency for a linear increase ($P = 0.06$) in K_a and a linear decrease ($P = 0.08$) in K_p were observed with advancing periods.

Plasma Glucose and Acetate Clearance

The fasted plasma glucose concentration (Table 4) did not differ between treatments ($P = 0.70$) but was quadratically affected by periods ($P = 0.05$). Fasting insulin concentration was not affected ($P = 0.40$) by diet but linearly increased ($P = 0.04$) from P1 to P4. The composite plasma insulin did not differ ($P > 0.14$) between treatments or periods. The insulinogenic ratio in fasting and composite plasma, a measure of insulin sensitivity, did not differ ($P > 0.20$) between treatments. However, the fasting insulinogenic ratio linearly increased with period ($P = 0.05$) and tended to increase for the composite sample ($P = 0.10$), indicating a decreased insulin sensitivity. The area under the insulin curve in response to glucose infusion did not differ ($P = 0.69$) between treatments but linearly increased ($P = 0.04$) with advancing periods. Peak insulin concentration in plasma following glucose infusion and the time required for plasma insulin concentration to peak following the glucose challenge did not differ ($P > 0.13$) between the CON and HLHFP treatments nor with period.

The plasma clearance rate of glucose was not affected by treatment or period ($P > 0.21$; Table 4), with a mean clearance rate of 0.67 mmol/min. The urinary excretion of glucose following a mean pulse dose of 78 ± 8.9 g of glucose averaged 1.4 ± 1.0 g and was not different ($P > 0.10$) between treatments or periods (data not shown). Therefore, renal excretion of glucose accounted for less than 2% of the total glucose dose. There was a tendency for a greater basal plasma acetate concentration in CON heifers compared with HLHFP heifers (390.1 vs. 295.8 μ M; $P = 0.10$) but no differences ($P \geq 0.57$; Table 4) were observed among periods. The arterial clearance rate of acetate did not differ with treatment ($P \geq 0.83$) but tended to quadratically increase ($P = 0.06$) with period.

Table 3. Ruminal fermentation parameters for beef heifers fed a barley-based diet (control [CON]) or a high-lipid, high-fiber byproduct pellet (HLHFP) diet during advancing periods of a finishing feedlot phase

Item	Treatment			Period ¹					P-value			
	CON	HLHFP	SEM ²	P1	P2	P3	P4	SEM ²	Treatment	Period	Period	Treatment × period
										Linear	Quadratic	
Ruminal pH												
Mean	5.96	6.1	0.05	6.02	5.94	6.03	6.12	0.08	0.07	0.28	0.28	0.37
Minimum	5.24	5.32	0.08	5.34	5.20	5.24	5.33	0.08	0.50	0.99	0.19	0.56
Maximum	6.83	6.93	0.05	6.86	6.82	6.89	6.95	0.06	0.18	0.19	0.34	0.11
Duration pH < 5.5, min/d	306	235	82	230	336	289	193	85	0.56	0.67	0.25	0.27
Area pH < 5.5, pH × min/d	44.7	49.7	29.2	38.0	81.65	61.9	32.0	24.5	0.91	0.73	0.15	0.20
Total ruminal SCFA, ³ mM	141.6	128.1	3.1	139.9	137.6	136.8	124.9	4.9	< 0.01	0.05	0.34	0.62
Acetate, mol/100 mol	47.94	46.62	2.08	41.01	50.41	47.59	50.12	1.93	0.67	<0.01	0.09	0.74
Propionate, mol/100 mol	32.07	29.91	3.15	33.00	28.58	32.95	29.41	2.87	0.64	0.62	0.88	0.72
Butyrate, mol/100 mol	12.72	13.18	2.27	17.15	12.32	10.80	11.53	1.86	0.89	0.04	0.15	0.05
Isobutyrate, mol/100 mol	0.89	0.91	0.12	0.8	0.83	0.92	1.06	0.10	0.92	0.05	0.59	0.27
Isovalerate, mol/100 mol	1.48	1.70	0.31	1.55	1.45	1.55	1.81	0.26	0.63	0.45	0.49	0.11
Valerate, mol/100 mol	2.15	1.85	0.22	2.38	2.18	1.97	1.46	0.28	0.37	0.03	0.59	0.76
Ruminal clearance rates, ⁴ %/h												
Valerate absorption, Ka	36.71	38.00	6.52	29.28	33.67	40.74	45.81	6.39	0.89	0.06	0.96	0.98
Valerate clearance, Kc	53.18	48.81	8.40	44.65	52.55	51.54	55.25	6.82	0.73	0.32	0.76	0.72
Chromium passage, Kp	11.93	10.82	2.92	15.46	14.89	10.8	9.45	2.72	0.80	0.08	0.89	0.20

¹P1 = d 1 to 40; P2 = d 41 to 80; P3 = d 81 to 120; P4 = d 121 to 160.

²n = 4/treatment

³SCFA = short-chain fatty acid.

⁴Ka = fractional absorption rate; Kc = fractional clearance rate; Kp = fractional passage rate.

DISCUSSION

In this study, the effects of diet (treatment), period, and their interaction were evaluated. Because no major interactions were observed, the effects of treatment and period are discussed separately.

Effect of Dietary Treatment

One of the reasons for the observed decrease in G:F in the late finishing stages of feedlot cattle (Joy et al., 2016; NASEM, 2016) may be in part due to ruminal acidosis (Castillo-Lopez et al., 2014). Despite the tendency for improved ruminal pH observed in the current study and that of Górka et al. (2015) when using HLHFP as a partial substitute for barley grain, we observed that HLHFP reduced G:F. Therefore, reducing fermentable carbohydrates by increasing lipids and fiber from byproducts as a strategy to reduce risk for ruminal acidosis is not likely to improve G:F. Diet digestibility contributes toward efficient feed conversion, and the current study supports past research demonstrating that the use of HLHFP results in a marked decrease in apparent total tract OM digestibility compared with barley-fed cattle (Górka et al., 2015). The reasons for decreased digestibility with the HLHFP diet are not known, but it is likely that the use of oat hulls within the pellet (Thompson et al., 2000), greater ether extract content (Jenkins, 1993;

Hess et al., 2008), and small particle size of ingredients (Abouheif et al., 2012) in the HLHFP or a combination of any of these factors (Joy et al., 2016) can be implicated.

Increased particle passage rate may be beneficial for HLHFP when considering the high ether extract content and the potential negative effect of lipids on ruminal fermentation. That said, there is a debate whether lipid sources positively or negatively affect performance of cattle fed finishing diets (Górka et al., 2013; Lima et al., 2016). Some studies have indicated a negative consequence of lipids on fiber digestion (Jenkins, 1993; Hess et al., 2008) whereas others have shown no effect (Kucuk et al., 2004), particularly when dietary ether extract content is less than 6% (Hess et al., 2008). The potential negative effect of lipids on fiber digestion may be an important factor for HLHFP because byproduct pellets have a greater concentration of NDF relative to barley grain. On the other hand, given the low level of forage inclusion in finishing diets for feedlot cattle and reduced NDF digestibility for the HLHFP diet, it is unlikely that the ether extract content in the HLHFP diet, although greater, fully compensated for the reduced starch relative to the CON diet.

In the current study, the ruminal SCFA concentration decreased with HLHFP feeding compared with the CON diet. However, the rate of SCFA absorption from the rumen did not differ between treatments. The response for less ruminal SCFA concentration with

Table 4. Plasma metabolite clearance and insulin parameters for beef heifers fed a barley-based diet (control [CON]) or a high-lipid byproduct-based diet (HLP) during advancing periods of a finishing feedlot phase

Item	Treatment			Period ¹					P-value			
	CON	HLP	SEM ²	P1	P2	P3	P4	SEM ²	Treatment	Period	Period	Treatment
										Linear	Quadratic	× period
Infused plasma metabolites												
Basal acetate, μM	390.1	295.8	34.4	347	342.6	364.5	317.6	36.8	0.10	0.69	0.57	0.14
Acetate clearance, μmol/min	308.8	328.9	43.8	276	357.5	323.1	318.5	32.8	0.83	0.71	0.06	0.95
Basal glucose, mM	4.19	4.15	0.08	4.10	4.23	4.30	4.05	0.10	0.70	0.89	0.05	0.36
Glucose clearance, mmol/min	0.67	0.67	0.001	0.67	0.67	0.67	0.67	0.002	0.60	0.21	0.55	0.52
Fasting plasma insulin, μg/L	1.65	1.37	0.21	1.17	1.39	1.81	1.58	0.17	0.40	0.04	0.21	0.12
Composite plasma insulin, μg/L	4.57	2.78	0.86	2.72	3.28	4.82	3.88	0.74	0.19	0.14	0.32	0.14
Insulinogenic ratio												
Fasting insulin:glucose	0.39	0.33	0.05	0.28	0.35	0.42	0.39	0.04	0.39	0.05	0.25	0.10
Composite insulin:glucose	1.19	0.8	0.22	0.75	0.89	1.09	1.13	0.17	0.25	0.10	0.78	0.19
Insulin response to glucose infusion												
Area of insulin curve, μg × min	220.1	236.5	27.6	188	214.8	262.8	247.7	23.3	0.69	0.04	0.40	0.30
Peak concentration, μg/L	8.5	9.8	0.9	8.4	7.6	11.3	9.0	0.9	0.37	0.17	0.43	0.48
Time to peak, min	11.9	11.3	0.8	10.6	11.9	10.0	13.8	1.1	0.60	0.13	0.25	0.27

¹P1 = d 1 to 40; P2 = d 41 to 80; P3 = d 81 to 120; P4 = d 121 to 160.

²n = 4/treatment.

HLHFP compared with the CON was expected because the diet contained less starch but greater NDF and ether extract concentrations along with a tendency for lower DMI. These dietary shifts were designed to reduce the quantity of substrate available for rapid fermentation (Aschenbach et al., 2011) as an approach to help stabilize ruminal pH. Given that liquid passage rate and SCFA absorption were not affected, the primary cause for the tendency for stabilization of ruminal pH was likely due to reduced ruminal digestibility. Supporting the previous suggestion, Górka et al. (2015) observed increased OM flow from the reticulorumen with increasing inclusion rates of HLHFP in the diet. Collectively, this suggests that the cause for improved ruminal pH and reduced SCFA concentration are likely due to reduced ruminal digestibility and, particularly, fiber digestibility.

Effect of Days on Feed

Although it is accepted that a general decline in G:F with advancing DOF for finishing cattle is due to increased BW and a shift in composition of accreted tissue (NASEM, 2016), the effect of the latter is completely confounded with DOF. Therefore, current models may underemphasize the importance of changes in energetic losses prior to the contribution of feed toward retained energy. A partial objective of the present study was to evaluate whether factors related to digestion, absorption, and postabsorptive utilization of nutrients may also change with period. In the current study, we observed an increase in OM digestibility with advancing periods, and this is in agreement with the findings

of Krehbiel et al. (2000) and Hersom (2005), where older and heavier beef cattle had greater OM digestibility compared with their younger and lighter counterparts. Part of the response for improved digestibility with advancing period in the present study may also be related to the tendency for less DMI with advancing periods and hence reduced ruminal passage rate.

On the other hand, others have found that the proportion of starch digested in the rumen was less for heavy-weight steers compared with light-weight steers when they were fed a fat-supplemented diet (Plascencia et al., 2003). A shift in site of digestion could be beneficial from an efficiency standpoint, if the starch is digested in the intestine, because intestinal starch digestion has been observed to be 42% more efficient than ruminal starch fermentation (Owens et al., 1986). However, given the quadratic increase in NDF digestibility that corresponded to the quadratic increase for apparent total tract starch digestion, it is also possible that digestion in the large intestine was increased. The quadratic increases in apparent total tract starch and NDF digestibility and quadratic decrease in ruminal SCFA concentration with period observed in our study also support the suggestion of a shift in the site of feed digestion from the rumen to the intestine. That said, reduced DMI could also explain the reduction in SCFA concentration.

In ruminants, acetate and glucose are major energy substrates for muscle and adipose tissue (Rhoades et al., 2007). We observed that although basal arterial acetate concentration did not differ with periods, the clearance rate of acetate after infusion tended to be greater with advancing DOF compared with P1.

Depending on the growth phase, beef cattle on finishing diets should accrue a greater proportion of lean tissue during the initial portion of the finishing period, with increasing proportions of fat deposition with advancing periods. The increased subcutaneous fat accretion increasingly relies on acetate rather than glucose as an energy source (Rhoades et al., 2007).

Although past studies have shown that different dietary energy substrates affect glucose supply and tissue utilization of glucose in response to insulin (Rhoades et al., 2007), different energy contents of similar diets do not change insulin sensitivity (Vasconcelos et al., 2009). Although insulin has an important role in maintaining glucose homeostasis, tissue responsiveness to insulin stimulation is lower in ruminants than in other species (Hocquette et al., 1995; Sasaki, 2002). In dairy cattle, insulin resistance has been reported during early lactation to facilitate increased arterial glucose flow to mammary tissue to cope with increased demand (Bell and Bauman, 1997). In the current study, beef heifers elicited insulin resistance with advancing periods. Insulin resistance can be due to decreased insulin sensitivity or decreased insulin responsiveness (in response to a glucose challenge) or a combination of the 2 factors (Kahn, 1978; Muniyappa et al., 2008). The decreased sensitivity of insulin with advancing periods in the current study, evident from the fasting and composite plasma insulin levels, is often linked to increased deposition of adipose tissue. Hocquette et al. (1999) reported a positive relationship between plasma insulin concentration and carcass fat weight. Later, Lawrence et al. (2012) and Fitzsimons et al. (2014) reported that cattle differing in their residual feed intake rank, despite having similar back fat thickness, have similar insulin concentrations, suggesting that decreased insulin sensitivity with advancing periods in the current study might be associated with changing tissue composition as more adipose tissue is deposited. Gregory et al. (1982) indicated that insulin concentration increased with age in both 12- and 30-mo-old Hereford and Holstein steers. As such, a cause-effect relationship between insulin concentration and tissue adiposity is difficult to establish, because the underlying molecular mechanisms in ruminants are still to be elucidated. The increasing area under the insulin curve following the glucose infusion with advancing periods suggests decreasing insulin responsiveness. Hence, the insulin resistance observed in finishing beef cattle toward the late finishing stages could be a sequela of a combination of decreasing insulin sensitivity and insulin responsiveness. Future research is needed to evaluate whether the onset of reduced insulin sensitivity and responsiveness can be mitigated and whether such a strategy may alter adipose tissue deposition.

Development of insulin resistance in the current study interpolates with the decrease in feed efficiency. Multiple factors contributing to insulin resistance might collectively have a negative effect on energetic efficiency. Leptin, synthesized from adipose tissue, is stimulated by increased plasma insulin concentration (Saladin et al., 1995) and has been shown to decrease insulin-stimulated glucose uptake by adipocytes (Müller et al., 1997). Studies evaluating molecular mechanisms of hyperinsulinemia in humans have shown that insulin-induced *GLUT4* translocation to the plasma membrane is reduced in large adipocytes compared with small adipocytes (Franck et al., 2007). Meanwhile, Fitzsimons et al. (2014) has observed an increased expression of *GLUT4* in longissimus muscle of steers at d 92 compared with d 50 of the finishing phase, indicating different regulatory actions of insulin in different tissues at different growth stages. In muscle tissue, insulin normally increases the energy consumption by increasing AA uptake and protein synthesis and reducing proteolysis (Hocquette et al., 1998; Richardson et al., 2004). Keomanivong et al. (2017) has reported increased serum insulin in overfed ewes compared with underfed and control ewes, whereas no difference was observed in pancreatic insulin-containing cell clusters. Because of the pancreatic exhaustion due to continuous stimulation to produce excess insulin and its effects on target tissues for anabolic responses, insulin resistance may be considered one of the major contributing factors to the decreased feed efficiency associated with late finishing stages. The effect of insulin resistance may also drive changes in tissue accretion, because chronic excessive energy consumption results in increased intramyocellular lipid deposition and decreased oxidation of fatty acids in monogastric species (Corcoran et al., 2007). It is also possible that triglyceride accumulation in hepatocytes and pancreatic β cells (Frayn, 2001) may be related to the decrease in feed efficiency with advancing DOF or, alternatively, overconditioned cattle. Future research is needed to determine the role of insulin resistance on tissue accretion and feed efficiency in finishing cattle.

In conclusion, the decrease in the feed efficiency with advancing DOF for finishing beef cattle was not influenced by the dietary energy source. However, use of HLHFP can be expected to decrease the G:F compared with barley grain, due to lower nutrient digestibility. Considering plausible reasons for increased apparent total tract digestibility and no change in plasma acetate and glucose clearance with period, increasing insulin resistance with advancing DOF may be an important factor contributing to decreased feed efficiency in finishing cattle.

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