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Performance, health and physiological responses of newly weaned feedlot cattle supplemented with feed-grade antibiotics or alternative feed ingredients

K. A. de Souza[1,2], R. F. Cooke[1†], K. M. Schubach[1], A. P. Brandão[1], T. F. Schumaher[1,3], I. N. Prado[2], R. S. Marques[1] and D. W. Bohnert[1]

[1]*Eastern Oregon Agricultural Research Center, Oregon State University, Burns, OR 97720, USA;* [2]*Departamento de Zootecnia, Universidade Estadual de Maringá, Maringá, PR 87020–900, Brazil;* [3]*Faculdade de Medicina Veterinária e Zootecnia, Universidade Estadual Paulista (UNESP), Botucatu, SP 18168-000, Brazil*

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With increased regulations regarding the use of feed-grade antimicrobials in livestock systems, alternative strategies to enhance growth and immunity of feedlot cattle are warranted. Hence, this experiment compared performance, health and physiological responses of cattle supplemented with feed-grade antibiotics or alternative feed ingredients during the initial 60 days in the feedlot. Angus × Hereford calves (63 steers + 42 heifers) originating from two cow–calf ranches were weaned on day −3, obtained from an auction yard on day −2 and road-transported (800 km; 12 h) to the feedlot. Upon arrival on day −1, shrunk BW was recorded. On day 0, calves were ranked by sex, source and shrunk BW, and allocated to one of 21 pens. Pens were assigned to receive (7 pens/treatment) a free-choice total mixed ration containing: (1) lasalocid (360 mg/calf daily of Bovatec; Zoetis, Florham Park, NJ, USA) + chlortetracycline (350 mg/calf of Aureomycin at cycles of 5-day inclusion and 2-day removal from diet; Zoetis) from days 0 to 32, and monensin only (360 mg/calf daily of Rumensin; Elanco Animal Health, Greenfield, IN, USA) from days 33 to 60 (PC), (2) sodium saccharin-based sweetener (Sucram at 0.04 g/kg of diet dry matter; Pancosma SA; Geneva, Switzerland) + plant extracts containing eugenol, cinnamaldehyde and capsicum (800 mg/calf daily of XTRACT Ruminants 7065; Pancosma SA) from days 0 to 32 and XTRACT only (800 mg/calf daily) from days 33 to 60 (EG) or (3) no supplemental ingredients (CON; days 0 to 60). Calves were assessed for bovine respiratory disease (BRD) signs and dry matter intake was recorded from each pen daily. Calves were vaccinated against BRD pathogens on days 0 and 22. Shrunk BW was recorded on day 61, and blood samples collected on days 0, 6, 11, 22, 33, 43 and 60. Calf ADG was greater (P = 0.04) in PC v. *EG and tended (P = 0.09) to be greater in PC* v. *CON. Feed efficiency also tended (P = 0.09) to be greater in PC* v. *CON, although main treatment effect for this response was not significant (P = 0.23). Mean serum titers against* bovine respiratory syncytial virus *were greater in EG* v. *PC (P = 0.04) and CON (tendency; P = 0.08). Collectively, the inclusion of alternative feed ingredients prevented the decrease in feed efficiency when chlortetracycline and ionophores were not added to the initial feedlot diet, and improved antibody response to vaccination against the* bovine respiratory syncytial virus *in newly weaned cattle.*

Keywords: beef cattle, growth, immunity, nutrition

Implications

Supplementing newly weaned cattle with feed-grade antibiotics (chlortetracycline and ionophores) during the initial 60 days in the feedlot tended to improve average daily gain and feed efficiency compared with non-supplemented cattle. Replacing these feed-grade antibiotics with plant extracts (eugenol, cinnamaldehyde and capsicum) and sodium saccharin-based sweetener prevented the decrease in feed efficiency when feed-grade antibiotics were not added to the diet. Cattle supplemented with these alternative ingredients also had improved humoral response to vaccination against the *bovine respiratory syncytial virus*. Hence, plant extracts and sodium saccharin-based sweetener may replace feed-grade antibiotics without substantially impairing feed efficiency of newly weaned feedlot cattle.

Introduction

Feedlot receiving is one of the most critical phases within the beef production cycle, comprising the initial 8 weeks in the feedlot when cattle are exposed to several stress and health challenges that impact their welfare and productivity

† Present address: Department of Animal Science, Texas A&M University, College Station, TX 77845, USA. E-mail: reinaldocooke@tamu.edu

(Duff and Galyean, 2007). These include weaning, road transport, commingling with different animals and exposure to novel diets and environments (Cooke, 2017). Feed intake is often inadequate during the receiving period because of these stressors, which further impairs cattle growth and immunocompetence (Lippolis *et al*., 2017). Accordingly, the incidence of bovine respiratory disease (BRD) is elevated during feedlot receiving, despite vaccination against BRD pathogens and efforts to minimize stress (Snowder *et al*., 2006).

Prophylactic medication with feed-grade antimicrobials, including ionophores and chlortetracycline, is often effective in mitigating the incidence of BRD and other health syndromes during feedlot receiving (Duff and Galyean, 2007; Wilson *et al*., 2017). With increased regulations regarding the use of feed-grade antimicrobials in livestock systems (US Food and Drug Administration, 2015), alternative dietary strategies that enhance immunity of receiving cattle are warranted. These include the use of sodium saccharin-based sweetener in feedlot receiving diets to increase cattle dry matter intake (DMI) (Ponce *et al*., 2014). Another strategy is supplementing plant extracts containing organic compounds known to enhance rumen function and immunity in cattle, such as cinnamaldehyde, eugenol and capsicum oleoresin (Yang *et al*., 2010a and 2010b; Ayrle *et al*., 2016). Based on this information, we hypothesized that plant extracts and sodium saccharin-based sweetener are alternatives to feed-grade antimicrobials in enhancing cattle immunocompetence and productivity during feedlot receiving. Hence, this experiment compared performance, health and physiological responses of newly weaned cattle supplemented with feed-grade antibiotics, the aforementioned alternative ingredients, or without such supplements during a 60-day feedlot receiving period.

Material and methods

This experiment was conducted at the Oregon State University – Eastern Oregon Agricultural Research Center (Burns, OR, USA) from April to June 2017. During the experiment, the environmental temperature ranged from 35°C to −5°C, with an average of 12°C and 54% humidity, and 16 mm of total precipitation as rain. For all management procedures that required cattle to be restrained, a Silencer Chute (Moly Manufacturing, Lorraine, KS, USA) mounted on Avery Weigh-Tronix load cells (Fairmount, MN, USA; readability 0.45 kg) was utilized.

Animals and treatments

One hundred and five Angus × Hereford calves (63 steers and 42 heifers) were purchased from a commercial auction yard (Producers Livestock Marketing Association, Vale, OR, USA) and utilized in this experiment (days −2 to 61). Calves originated from two cow–calf operations (eastern Oregon and western Idaho, USA) and weaned on day −3, loaded into a double-deck commercial livestock trailer (Legend 50′ cattle liner; Barrett LLC., Purcell, OK, USA) at the auction yard (day −2; 1800 h), and transported for 800 km. During transport, the driver stopped once after 6 h of driving to rest for 60 min, whereas total transport time was 12 h. Calves remained in the truck throughout the 12-h transportation period. Minimum, maximum and average environmental temperatures during transport were −3°C, 8°C and 3°C, respectively, whereas average humidity was 70% and no precipitation was observed. Transportation length and distance were selected to simulate the stress of a long-haul that beef cattle originated from western or southeastern US cow–calf operations experience when transferred to feedlots in the midwestern US (Cooke *et al*., 2013).

On day −1, calves were unloaded (0600 h) at the Eastern Oregon Agricultural Research Center, immediately weighed (initial shrunk BW = 197 ± 3 kg), and maintained in a single paddock (160 × 100 m) with *ad libitum* access to alfalfa-grass hay, water and a commercial mineral mix (described in Table 1) for 24 h. On day 0, calves were ranked according to sex, source and shrunk BW, and allocated to 1 of 21 drylot pens (7 × 15 m; three steers and two heifers per pen) in a manner that pens had equivalent initial shrunk BW and calves from both sources to stimulate the stress of commingling (Step *et al*., 2008). Pens were assigned to receive one of three treatments: (1) lasalocid (360 mg/calf daily of Bovatec; Zoetis, Florham Park, NJ, USA) + chlortetracycline (350 mg/calf of Aureomycin at cycles of 5-day inclusion and 2-day removal from diet; Zoetis) from days 0 to 32, and monensin only (360 mg/calf daily of Rumensin; Elanco Animal Health, Greenfield, IN, USA) from days 33 to 60 (PC; $n = 7$), (2) sodium saccharin-based sweetener (Sucram at 0.04 g/kg of diet dry matter (DM); Pancosma SA; Geneva, Switzerland) + plant extracts containing eugenol, cinnamaldehyde and capsicum (800 mg/calf daily of XTRACT Ruminants 7065; Pancosma SA) from days 0 to 32 and XTRACT only (800 mg/calf daily) from days 33 to 60 (EG; $n = 7$) or (3) no supplemental ingredients (CON; $n = 7$). The inclusion and

Table 1 *Ingredient composition and nutrient profile of total mixed ration offered during the experiment (days 0 to 60)*[1]

Items	A	B	C	D
Ingredient (% DM basis)				
Grass hay	74.5	58.2	37.0	33.7
Cracked corn	17.5	35.0	54.6	58.2
Soybean meal	7.2	6.0	7.7	7.4
Mineral mix[2]	0.80	0.80	0.70	0.70
Nutrient profile (DM basis)				
Net energy for maintenance (Mcal/kg)	1.38	1.55	1.76	1.80
Net energy for growth (Mcal/kg)	0.80	0.95	1.14	1.17
NDF (%)	46.8	39.3	29.5	27.9
ADF (%)	30.9	24.9	17.2	16.0
CP (%)	13.7	13.1	13.6	13.5

DM = dry matter.
[1]A = days 0 to 7; B = days 8 to 18; C = days 19 to 32; and D = days 33 to 60. Calves had free-choice access to the total mixed ration and water throughout the experimental period.
[2]Cattleman's Choice (Performix Nutrition Systems, Nampa, ID, USA) containing 14% Ca, 10% P, 16% NaCl, 1.5% Mg, 3 200 mg/kg of Cu, 65 mg/kg of I, 900 mg/kg of Mn, 140 mg/kg of Se, 6000 mg/kg of Zn, 136 000 IU/kg of vitamin A, 13 000 IU/kg of vitamin D_3 and 50 IU/kg of vitamin E.

administration rate of the PC and EG ingredients were according to manufacturer's recommendations for growing cattle. Ionophores and chlortetracycline were chosen based on traditional US feedlot practices (Samuelson *et al*., 2016). Chlortetracycline was supplemented from days 0 to 32 when elevated BRD incidence was expected (Snowder *et al*., 2006; Lippolis *et al*., 2017), whereas lasalocid was used during this period because it is approved for use in combination with chlortetracycline (US Food and Drug Administration, 2017). In turn, monensin was supplemented from days 33 to 60 when chlortetracycline supplementation ended, given that monensin is the primary ionophore used by US commercial feedlots (Samuelson *et al*., 2016). Sucram was supplemented from days 0 to 32 to stimulate DMI upon feedlot arrival (McMeniman *et al*., 2006), whereas XTRACT was supplemented throughout the receiving period as an immunostimulant and dietary alternative to ionophores (Yang *et al*., 2010a and 2010b).

From days 0 to 60, calves had free-choice access to water and total mixed ration (TMR; Table 1), which was offered twice daily (0800 and 1300 h). Sucram was mixed daily in 4 l of water, whereas 2 l were mixed with the morning and 2 l with the afternoon TMR allocation of each EG pen (days 0 to 32). The PC and CON pens received the same amount of water without the addition of Sucram (days 0 to 32). Lasalocid, chlortetracycline, monensin and XTRACT were mixed with soybean meal and top-dressed daily into the morning TMR feeding of respective PC or EG pens during the supplementation period (0.25 kg of mixture/calf daily). Moreover, chlortetracycline was supplemented to PC calves on days 0 to 4, days 7 to 11, days 14 to 18, days 21 to 25 and days 28 to 32. Soybean meal was also top-dressed into the morning TMR feeding of CON pens (0.25 kg/calf daily) from days 0 to 61, without the addition of the experimental ingredients. Based on daily visual observations, all pens consumed the top-dress within 5 min after feeding.

On day 0, calves were vaccinated against *Clostridium* and *Mannheimia haemolytica* (One Shot Ultra 7; Zoetis), *bovine respiratory syncytial virus* (BRSV), *bovine herpesvirus-1* (BHV-1), *bovine viral diarrhea virus* (BVD) 1 and 2 and *parainfluenza-3 virus* (PI3; Bovi-Shield Gold 5; Zoetis), and were administered an anthelmintic (Dectomax; Zoetis). On day 22, calves were re-vaccinated against *Clostridium* (Ultrabac 8; Zoetis), BRSV, BHV-1, BVD-1 and 2 and PI3 (Bovi-Shield Gold 5), following the manufacturer's recommendation for revaccination against these pathogens (Zoetis).

Sampling

Samples of TMR ingredients were collected weekly, pooled across all weeks and analyzed for nutrient content by a commercial laboratory (Dairy One Forage Laboratory, Ithaca, NY, USA). All samples were analyzed by wet chemistry procedures for concentrations of CP, ADF and NDF as described by Lippolis *et al*. (2017). Calculations for net energy for maintenance and gain were calculated with the equations proposed by the National Research Council (2000). Nutrient profile of TMR is described in Table 1.

Full BW was recorded on days 0, 5, 11, 22, 33, 43 and 60 of the experiment at 0700 h, before the first TMR feeding of the day. Shrunk BW was recorded on day 61, after 16 h of water and feed withdrawal. Shrunk BW values from days −1 and 61 were used to calculate calf ADG during the experiment. Intake of TMR (DM basis) was evaluated daily from days 0 to 60 from each pen by collecting and weighing offered and non-consumed TMR. All samples were dried for 96 h at 50°C in forced-air ovens for DM calculation. Total TMR intake of each pen was divided by the number of calves within each pen and expressed as kg per calf/day. Total BW gain and TMR intake of each pen were used for feed efficiency calculation. Calves were observed daily for BRD signs according to the DART system (Zoetis) and received antimicrobial treatment as in Lippolis *et al*. (2017).

Blood samples were collected from all calves, concurrently with full BW evaluation into commercial blood collection tubes (Vacutainer, 10 ml; Becton Dickinson, Franklin Lakes, NJ, USA) containing no additive or containing freeze-dried sodium heparin for serum and plasma collection, respectively. During each sampling day, ~16 ml of blood was collected from each calf, being 8 ml in each collection tube. After collection, all blood samples were placed immediately on ice, centrifuged ($2500 \times \mathbf{g}$ for 30 min; 4°C) for plasma or serum harvest, and stored at −80°C on the same day of collection.

Laboratorial analyses

Plasma samples collected from days 0 to 33 were analyzed for cortisol (Immulite 1000; Siemens Medical Solutions Diagnostics, Los Angeles, CA, USA) and haptoglobin concentrations (Cooke and Arthington, 2013), given that adrenocortical and acute-phase protein responses return to baseline levels in receiving cattle within 4 weeks after feedlot entry (Cooke, 2017). Plasma samples collected on days 0, 33 and 60 were analyzed for IGF-I concentrations (Immulite 1000) to metabolically assess calf nutritional status throughout the experimental period (Lippolis *et al*., 2017). The intra- and inter-assay CV for haptoglobin were, respectively, 2.4% and 10.8%. Plasma IGF-I and cortisol were analyzed within single assays, and the intra-assay CV were, respectively, 7.4% and 1.9%.

Serum samples collected from 2 calves/pen not observed with BRD signs during the experiment were selected for analysis of antibody titers against BRD pathogens, to ensure that this response was associated with vaccine efficacy rather than pathogenic infection (Callan, 2001). More specifically, samples collected on days 0, 5, 11, 22, 33 and 43 were analyzed for antibody titers against BRSV, BHV-1, BVD-1 and PI3 using virus neutralization tests, and for antibodies against *M. haemolytica* via a quantitative agglutination test (Texas A&M Veterinary Medical Diagnostic Laboratory, Amarillo, TX, USA). It is not certain if selected calves were indeed healthy or just asymptomatic to BRD, although none of them exhibited BRD signs and clinical symptoms throughout the experimental period as mentioned previously.

Statistical analysis

Pen was considered the experimental unit for all analyses. Quantitative data were analyzed using the MIXED procedure of SAS (SAS Institute Inc., Cary, NC, USA), whereas binary data were analyzed using the GLIMMIX procedure of SAS (SAS Institute Inc.) with a binomial distribution and logit link function. All data were analyzed using Satterthwaite approximation to determine the denominator df for tests of fixed effects, with pen(treatment) and calf(pen) as random variables, but for DMI and feed efficiency that used pen(treatment) as a random variable. Model statements for initial and final BW, ADG, feed efficiency and morbidity-related results contained the effects of treatment and calf sex as an independent covariate. Model statements for DMI, cumulative BRD incidence, full BW change and blood variables contained the effects of treatment, day, the resultant interaction and calf sex as an independent covariate. Blood variables were analyzed using results from day 0 as an independent covariate, whereas calf source was also included as an independent covariate for antibody titers against BRD pathogens. The specified term for all repeated statements was day, with pen (treatment) as a subject for DMI and calf(pen) as a subject for all other analyses. The covariance structure used was first-order autoregressive, which provided the smallest Akaike information criterion and hence the best fit for all variables analyzed. All results are reported as covariately adjusted least square means. Significance was set at $P \leqslant 0.05$ and tendencies were determined if $P > 0.05$ and $\leqslant 0.10$. Repeated measures are reported according to main treatment effect if the treatment × day interaction was $P > 0.10$.

Results

A tendency for a treatment effect was detected ($P = 0.10$) for ADG, which was greater ($P = 0.04$) in PC *v.* EG calves, and tended ($P = 0.09$) to be greater in PC *v.* CON calves (Table 2). However, no main treatment effects were detected ($P \geqslant 0.55$) for final shrunk BW (day 61; Table 2) or full BW during the 60-day receiving period (Figure 1). No treatment effects were detected for DMI ($P = 0.52$; Table 2 and Figure 2) and feed efficiency ($P = 0.23$; Table 2). Despite the lack of main treatment effect for feed efficiency, it should be noted that this response tended to be greater ($P = 0.09$) in PC *v.* CON calves, and did not differ ($P \geqslant 0.38$) in EG *v.* PC and CON calves.

Table 2 *Performance parameters from beef calves supplemented or not (no supplemental ingredients (CON);* n = *7) with feed-grade antibiotics (lasalocid + chlortetracycline from days 0 to 32, and monensin from days 33 to 60 (PC);* n = *7) or alternative feed ingredients (sodium saccharin-based sweetener + plant extracts from days 0 to 32, and plant extracts only from days 33 to 60 (EG);* n = *7) during a 60-day feedlot receiving*

Items	CON	PC	EG	SEM	*P*-value
Initial BW (day −1; kg)	199	198	195	7	0.90
Final BW (day 61; kg)	291	297	287	6	0.58
ADG (kg/day)	1.50[b]	1.59[a]	1.47[b]	0.04	0.10
DMI (kg/day)	8.36	8.45	8.05	0.19	0.52
Feed efficiency (g/kg)	0.181	0.191	0.186	0.003	0.23

[a,b]Within rows, values with different superscripts differ ($P \leqslant 0.05$).

No treatment differences were detected ($P = 0.94$) for BRD incidence (Table 3), which were only observed during the initial 15 days of feedlot receiving (Figure 2; day effect, $P < 0.01$). No treatment differences were detected ($P \geqslant 0.39$; Table 3) for other morbidity reasons (physical injury), number of antimicrobial treatments required upon BRD diagnosis, and percentage of cattle that required ⩾1 antimicrobial treatment upon BRD diagnosis. No incidence of mortality was observed during the experiment.

No treatment effects were detected ($P \geqslant 0.56$) for plasma concentrations of cortisol, haptoglobin and IGF-I (Table 4), whereas day effects were detected ($P \leqslant 0.01$) for these variables (Table 5). No treatment effects were detected ($P \geqslant 0.35$) for serum titers against *M. haemolytica*, PI3, BVD-1 and BHV-1 (Table 4). A tendency for a treatment effect was detected ($P = 0.09$) for serum titers against BRSV, which was greater ($P = 0.04$) in EG *v.* PC and tended to be greater ($P = 0.08$) in EG *v.* CON calves, and were similar ($P = 0.80$) between CON and PC calves. Moreover, day effects were also detected ($P \leqslant 0.01$) for all serum titers against BRD pathogens (Table 5).

Discussion

Calves utilized in this experiment were considered high-risk, given that their prior management and health history were not fully known (Wilson *et al.*, 2017). Moreover, cattle experienced the stress of weaning, auction, transportation, commingling, vaccination and feedlot entry within a 72-h period, whereas the combination of these stressors impacts cattle immunocompetence and performance (Cooke, 2017). Hence, the experimental model adopted herein represented the stress and health challenges that commercial feeder cattle typically experience during feedlot receiving in the USA (Duff and Galyean, 2007).

The inclusion of chlortetracycline and ionophores in the receiving diet tended to improve cattle ADG as previously reported by others (Perry *et al.*, 1986; Duffield *et al.*, 2012), although such difference was not sufficient to impact final BW on day 61 (Table 2; Figure 1). This outcome should be primarily attributed to the tendency for improved feed efficiency in PC *v.* CON cattle (Perry *et al.*, 1986; Birkelo, 2003), given that DMI, BRD incidence, as well as physiological responses were similar among all treatment groups (Tables 2–4). Accordingly, ionophores and chlortetracycline have been shown to increase feed efficiency in cattle by, respectively, improving rumen fermentation efficiency (Russell and Strobel, 1989; Callaway *et al.*, 2003), and increasing nutrient supply due to reduced intestinal mass and energy loss as methane (Visek, 1978; Zinn, 1993; Baldwin *et al.*, 2000). It also should be noted that DMI in the present experiment was not depressed by ionophore inclusion (Table 2; Figure 1), either lasalocid or monensin according to the experimental schedule, despite previous research

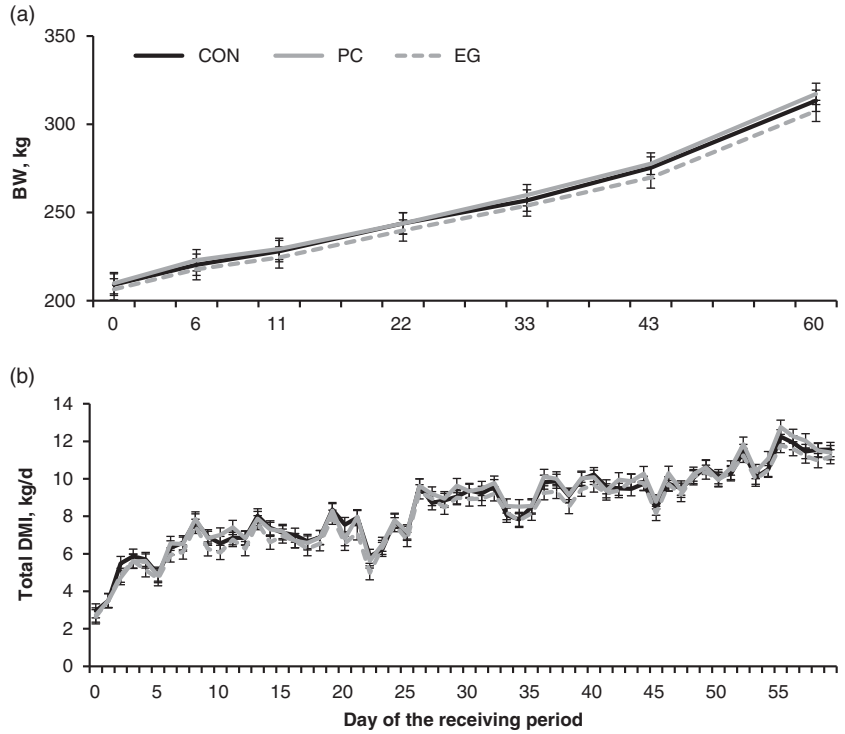

Figure 1 BW (a) and dry matter intake (DMI) (total mixed ration; b) during a 60-day feedlot receiving from beef cattle assigned to lasalocid + chlortetracycline from days 0 to 32, and monensin from days 33 to 60 (PC); sodium saccharin-based sweetener + plant extracts from days 0 to 32, and plant extracts only from days 33 to 60 (EG); and no supplemental ingredients (CON). Values reported are least square means ± SEM. No treatment effect was detected ($P \geqslant 0.52$).

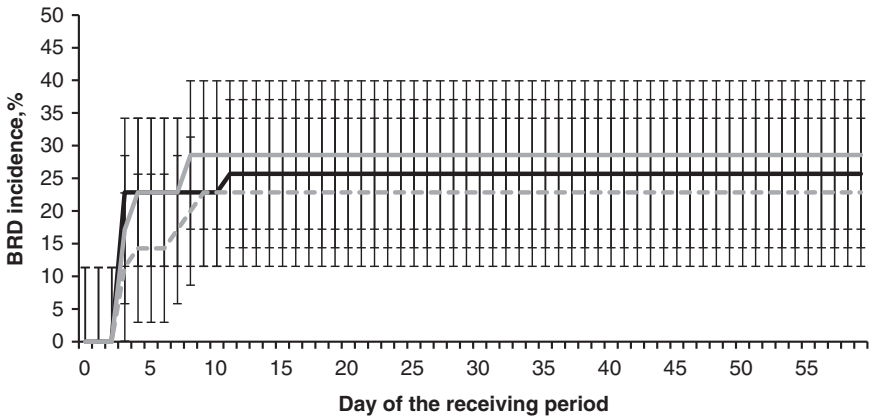

Figure 2 Cumulative incidence of bovine respiratory disease (BRD) signs during a 60-day feedlot receiving in beef cattle assigned to lasalocid + chlortetracycline from days 0 to 32, and monensin from days 33 to 60; sodium saccharin-based sweetener + plant extracts from days 0 to 32, and plant extracts only from days 33 to 60; and no supplemental ingredients. Values reported are least square means ± SEM. No treatment effect or treatment × day interaction were detected ($P \geqslant 0.94$).

Table 3 *Morbidity and mortality parameters in beef calves supplemented or not (no supplemental ingredients (CON); n = 7) with feed-grade antibiotics (lasalocid + chlortetracycline from days 0 to 32, and monensin from days 33 to 60 (PC); n = 7) or alternative feed ingredients (sodium saccharin-based sweetener + plant extracts from days 0 to 32, and plant extracts only from days 33 to 60 (EG);* n = *7) during a 60-day feedlot receiving*

Items	CON	PC	EF	SEM	*P*-value
Incidence of bovine respiratory disease signs (%)	25.7	28.6	22.9	11.8	0.94
Number of antimicrobial treatments required	1.22	1.20	1.00	0.12	0.39
Calves that required ⩾ 1 antimicrobial treatment (%)	22.2	20.0	0.0	12.1	0.39
Other morbidity reasons[1] (%)	2.86	2.86	0.00	2.33	0.61
Mortality (%)	0.0	0.0	0.0	–	–

[1]All non-BRD-related morbidity was due to physical injury.

Table 4 *Physiological and humoral responses from beef calves supplemented or not (no supplemental ingredients (CON);* n = *7) with feed-grade antibiotics (lasalocid + chlortetracycline from days 0 to 32, and monensin from days 33 to 60 (PC);* n = *7) or alternative feed ingredients (sodium saccharin-based sweetener + plant extracts from days 0 to 32, and plant extracts only from days 33 to 60 (EG);* n = *7) during a 60-day feedlot receiving*

Items	CON	PC	EF	SEM	*P*-value
Physiological variables					
Plasma cortisol (ng/ml)	54.5	52.5	54.9	3.1	0.84
Plasma haptoglobin (mg/ml)	0.283	0.292	0.318	0.037	0.78
Plasma IGF-I (ng/ml)	223	235	232	8	0.56
Serum antibody variables (titer log 2)					
Mannheimia haemolytica	9.34	9.53	9.42	0.19	0.79
Parainfluenza-3 virus	6.60	5.89	6.05	0.35	0.35
Bovine respiratory syncytial virus	2.82^{y}	2.62^{b}	3.82^{ax}	0.42	0.09
Bovine viral diarrhea virus-1	2.62	2.87	3.42	0.43	0.39
Bovine herpesvirus-1	1.07	1.37	1.58	0.30	0.51

a,b;x,yWithin rows, values with different superscripts differ at $P = 0.04$ or $P = 0.08$, respectively.

Table 5 *Concentrations of plasma cortisol (ng/ml), haptoglobin (mg/ml), IGF-I (ng/ml) and serum titers against* Mannheimia haemolytica *(MH),* parainfluenza-3 virus *(PI3),* bovine respiratory syncytial virus *(BRSV),* bovine viral diarrhea virus-*1 (BVD-1) and* bovine herpesvirus-1 *(BHV) in beef cattle during an 60-day feedlot receiving*

	Plasma variables			Serum antibody titers				
Days	Cortisol	Haptoglobin	IGF-I	MH	PI3	BRSV	BVD	BHV
0	41.5^{d}	0.151^{d}	88^{c}	6.05^{e}	4.86^{d}	0.63^{d}	0.76^{d}	0.19^{d}
5	40.4^{d}	0.383^{a}	–	7.34^{d}	5.31^{cd}	3.11^{b}	0.63^{d}	0.52^{cd}
11	54.0^{c}	0.278^{bc}	–	9.61^{c}	5.94^{b}	3.07^{b}	0.81^{d}	0.79^{bc}
22	57.6^{b}	0.312^{b}	–	10.63^{a}	5.88^{bc}	1.41^{c}	2.38^{c}	1.08^{b}
33	64.7^{a}	0.228^{c}	221^{b}	10.02^{b}	6.83^{a}	4.09^{a}	4.83^{b}	2.14^{a}
43	–	–	–	9.32^{c}	6.43^{ab}	3.68^{ab}	6.52^{a}	1.99^{a}
60	–	–	234^{a}	–	–	–	–	–
SEM	1.6	0.030	5	0.18	0.32	0.33	0.33	0.22
P-value	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01

^{a,b,c,d}Within columns, values with different superscripts differ ($P \leqslant 0.05$).

reporting such outcome in feedlot cattle (Zinn, 1987; Duff *et al*., 1995; Duff and Galyean, 2007).

Cattle DMI and ADG were not improved by the inclusion of sodium saccharin-based sweetener and plant extracts (Table 2; Figure 1). Contrary to our findings, Ponce *et al*. (2014) reported that supplementing the same sweetener utilized herein increased DMI by 17% during feedlot receiving, although this effect was observed when sweetener was included at 200 g/ton of diet DM. McMeniman *et al*. (2006) also included sodium saccharin-based sweetener into a feedlot receiving diet at 200 g/ton of diet DM and reported a trend in increased DMI from days 29 to 56 after feedlot arrival. Yet, both authors also reported that ADG and feed efficiency were not impacted by inclusion of sodium saccharin-based sweetener. Perhaps DMI was not improved in EG cattle herein because the sweetener was included at a different dose than Ponce *et al*. (2014) and McMeniman *et al*. (2006), and was only fed from days 0 to 32 when receiving DMI is inconsistent and often inadequate (Duff and Galyean, 2007). Others have also reported that supplementing plant extracts also failed to improve ADG in ruminants consuming concentrate-based diets (Yang *et al*., 2010a; Geraci *et al*., 2012). It should be noted that the EG treatment prevented the decrease in feed efficiency when chlortetracycline and ionophores were not included into the diet, based on similar feed efficiency between EG *v*. PC and tendency for greater feed efficiency in PC *v*. CON calves (Table 2). Plant-derived organic compounds such as eugenol, cinnamaldehyde and capsicum appear to enhance rumen fermentation in cattle consuming high-concentrate diets (Cardozo *et al*., 2005 and 2006) and may be used as alternatives to ionophores such as monensin (Fandiño *et al*., 2008). Accordingly, Geraci *et al*. (2012) reported similar feed efficiency in feedlot cattle supplemented with monensin or a mixture of eugenol, cinnamaldehyde and capsicum during an 84-day feeding period. In contrast, no research has compared the effects of plant extracts and/or sodium saccharin-based sweetener with chlortetracycline in feedlot receiving diets to debate further the performance results reported herein.

Morbidity and BRD-related responses were similar among treatments (Table 3; Figure 2), which does not support our experimental hypothesis and the use of chlortetracycline supplementation to reduce morbidity during feedlot receiving (Duff *et al*., 2000; Edwards, 2010; Samuelson *et al*., 2016). Others have also reported that dietary inclusion of sodium saccharin-based sweetener failed to mitigate BRD incidence in receiving cattle (McMeniman *et al*., 2006; Ponce *et al*., 2014), whereas research investigating the effects of plant extracts on BRD is lacking. It should be noted, however, that BRD incidence observed herein were not as elevated compared with previous research from our group (Lippolis *et al*., 2017), as well as research conducted at commercial receiving yards reporting up to 43% of BRD incidence (Snowder *et al*., 2006). In fact, Lippolis *et al*. (2017) commingled cattle obtained from seven cow–calf operations, which is typical of US commercial feedyards, and reported BRD incidence at 66% during an 80-day receiving period. In this experiment, cattle were obtained from two different sources due to market availability, which likely reduced commingling-elicited stress (Step *et al*., 2008) and resulted less BRD incidence compared with previous research (Snowder *et al*., 2006; Lippolis *et al*., 2017). Hence, the reduced prevalence of BRD in the present experiment may have hindered proper assessment of feedlot receiving morbidity, and contributed to the lack of treatment effects on BRD-related responses.

Supplementing sodium saccharin-based sweetener and plant extracts improved acquired humoral immunity against BRSV during the 60-day receiving period (Table 4). Serum antibody titers against all other BRD pathogens were not impacted by treatments but increased during the experiment (Table 5), denoting that cattle effectively acquired humoral immunity against these pathogens upon vaccination (Richeson *et al*., 2008). It should be noted that calves were not re-vaccinated against *M. haemolytica* based on recommendations by the manufacturer (Zoetis), explaining why concentrations of serum titers against this pathogen did not increase beyond day 22. The exact mechanisms by which the EG treatment improved efficacy to BRSV vaccination (Callan, 2001) warrants investigation, and could be attributed to potential immunomodulatory effects of plant extracts (Ayrle *et al*., 2016). Yet, such outcome was also not sufficient to alter BRD incidence in the present experiment, which corroborates with the lack of treatment differences on acquired humoral immunity against *M. haemolytica*, PI3, BHV-1, BVD-1 and PI3.

Similar concentrations of plasma cortisol, haptoglobin and IGF-I among PC, CON and EG cattle (Table 4) indicate that none of the experimental treatments modulated the physiological and acute-phase responses typically associated with feedlot receiving (Cooke, 2017). In turn, the specific impact of ingredients evaluated herein on these plasma variables is either variable or mostly undetermined. As examples, monensin has either increased or failed to change circulating IGF-I concentrations in growing beef cattle (Vendramini *et al*., 2015 and 2016). Supplementing cinnamaldehyde to feedlot steers did not impact serum haptoglobin concentrations, but reduced concentrations of the acute-phase protein serum amyloid A (Yang *et al*., 2010a). Nonetheless, day effects reported for plasma variables (Table 5) corroborate that cattle were exposed to the stress and nutritional changes associated with feedlot entry. Plasma haptoglobin concentrations transiently increased across all treatments upon feedlot arrival, corroborating that calves experienced an acute-phase protein response elicited by weaning, transport, vaccination and feedlot entry (Cooke, 2017). Plasma IGF-I concentrations increased across all treatments during feedlot receiving, mainly due to increased nutrient intake (Table 1) and growth (Table 2) during the experimental period (Lippolis *et al*., 2017). Plasma cortisol concentration also increased across all treatments as the experiment progressed; the exact reason for this outcome is unknown but may be associated with increasing concentrate inclusion in the TMR (Enemark, 2008). Hence, the tendencies for improved ADG and feed efficiency in PC calves were not associated with altered cortisol, IGF-I and acute-phase responses elicited by transport and feedlot entry, although these responses influence nutrient utilization and growth in beef cattle (Cooke, 2017). Collectively, plasma variables evaluated herein failed to elucidate biological mechanisms by which chlortetracycline and ionophore supplementation benefited performance of receiving cattle; perhaps these occurred without substantial impacts on systemic inflammatory and metabolic responses.

Conclusions

Beef cattle supplemented with feed-grade antibiotics (lasalocid, chlortetracycline and monensin) during feedlot receiving tended to have improved ADG and feed efficiency compared with non-supplemented cohorts. Replacing feed-grade antibiotics with plant extracts and sodium saccharin-based sweetener prevented the decrease in feed efficiency when feed-grade antibiotics were not included in the receiving diet. Moreover, cattle supplemented with these alternative feed ingredients had greater serum antibody response to BRSV, suggesting an improved humoral response to immunization against this pathogen compared with all other treatments. Yet, supplementing feed-grade antibiotics or plant extracts and sodium saccharin-based sweetener did not reduce BRD incidence, which was not as prevalent as typically observed in commercial feedlot systems. Nonetheless, results from this experiment suggest that plant extracts and sodium saccharin-based sweetener may replace feed-grade antibiotics in feedlot receiving diets without substantially impairing feed efficiency.

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Declaration of interest
No conflict of interest to report.

Ethics statement
All animals were cared for in accordance with acceptable practices and experimental protocols reviewed and approved by the Oregon State University, Institutional Animal Care and Use Committee (no. 4937).

Software and data repository resources
No software, data or models were deposited in official repositories.

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