Influence of form of selenium supplementation and tall fescue endophyte toxicity on growth performance, serum parameters, and tissue masses of grazing beef steers

Kelsie L. Webb,1 Ronald J. Trotta,1 Yang Jia,2 Phillip J. Bridges, and James C. Matthews3

Department of Animal and Food Sciences, University of Kentucky, Lexington, KY 40546, USA

1These authors contributed equally to this manuscript as co-first authors.
2Current address: Inner Mongolia Agricultural University, Hohhot, People’s Republic of China.
3Corresponding author: james.matthews@uky.edu

ABSTRACT
To test the hypothesis that average daily gain (ADG) and clinical parameters of steers grazing novel non-toxic (NTE) or toxic KY31 (TE) endophyte-infected tall fescue would be improved by ad libitum intake of vitamin-mineral mixes (V-M) that contain 27 ppm Se as a 1:1 blend of SELPLEX:sodium selenite (MIX) vs. sodium selenite (ISe), 32 fescue-naïve beef steers partially depleted of Se were randomly assigned to ad libitum consumption ISe vs. MIX for 35 days and fed enough of a NTE/alfalfa/grain diet to achieve 0.57 kg BW gain/day. Then, within Se-form treatments, two steers were randomly assigned to each of four NTE (ISe = 316 ± 31 kg BW, MIX = 315 ± 22 kg BW) or TE (ISe = 316 ± 37 kg BW, MIX = 314 ± 39 kg BW) paddocks for 84 days and had ad libitum access to their respective V-M. The MIXED procedure of SAS was used to assess effects of day, Se-form (ISe, MIX) and endophyte (NTE, TE) treatments, and their interactions. Whole blood Se decreased (P < 0.01) 31% from days 0 to 84 and was 0.2% greater (P < 0.01) for MIX steers. Serum prolactin decreased (P < 0.01) 18% for NTE and 48% for TE steers from days 0 to 84 and was 17% greater (P = 0.01) for MIX vs. ISe for TE steers. Serum alkaline phosphatase activity decreased (P < 0.02) 27% from days 0 to 84 and was 15% greater (P < 0.02) for MIX steers. Serum urea nitrogen increased (P < 0.02) 8.2% from days 0 to 84 for TE but not NTE steers. Average daily gain was less (P < 0.01) for steers grazing TE (~0.18 kg/day) compared with NTE (0.09 kg/d). Although there was increased serum alkaline phosphatase activity and increased serum prolactin for TE + MIX steers compared with TE + ISe steers, MIX supplementation was unable to increase serum prolactin concentrations or ADG to the same levels as steers grazing NTE. Longer adaptation to MIX supplementation ad libitum may be necessary for maximal Se assimilation to restore serum prolactin levels in steers grazing TE.

INTRODUCTION
Most tall fescue (Lolium arundinaceum) is infected with an endophyte (Epichloë coenophiala) that is important for imparting tolerance to biotic and abiotic stressors yet, the production of toxic ergot alkaloids can lead to fescue toxicosis when consumed by livestock (Bush et al., 1982; Lyons et al., 1986; Porter et al., 1979; Strickland et al., 2011). Ergot alkaloids have similar structures to biogenic amines such as serotonin, dopamine, epinephrine, and norepinephrine (Berde, 1980), and thus, can interact with their respective receptors to cause numerous effects on animal physiology and metabolic function (Klotz, 2015). Symptoms of fescue toxicosis include decreased feed intake, decreased weight gain, decreased milk production, increased respiration rate, elevated body temperature, vasocostriction, increased time spent in water or shade, decreased serum prolactin, excessive salivation, and lower reproductive performance (Strickland et al., 2011). Non-toxic endophyte-infected tall fescue (NTE) was engineered to contain the endophyte but not produce ergot alkaloids. Thus, NTE could be beneficial for both drought resistance of tall fescue and to prevent fescue toxicosis in cattle (Kallenbach, 2015).
In many areas where tall fescue is consumed, Se intake is insufficient to support optimal growth (Gleed et al., 1983), immune function (Boye and Arthur, 1979), and reproductive function (McClure et al., 1986) of grazing cattle. Beef cattle require 0.1 mg Se per kg of BW per d; however, approximately 50% of all forages and grains available in Kentucky do not contain adequate Se concentrations to meet NASEM (2016) recommendations (Ammerman and Miller, 1975). Soil where forages are grown contain multiple forms of inorganic Se (ISe) including selenate and selenite and forages contain primarily organic forms of Se (OSe) such as selenomethionine and selenocysteine. Inorganic forms of Se are often included in free-choice vitamin–mineral mixes (V-M) to supplement grazing cattle (Ammerman and Miller, 1975). Although ISe forms are most commonly included, the use of OSe in V-M typically results in greater blood and tissue Se concentrations, suggesting greater bioavailability (Gunter et al., 2003; Liao et al., 2011; Nicholson et al., 1991). Interestingly, feeding a 1:1 blend of ISe:OSe (MIX) results in equal amount of Se in whole blood, red blood cells, serum, and liver of heifers as when supplemented with only OSe, both of which are greater than ISe-supplemented heifers (Brennan et al., 2011).

Suppressed prolactin concentration in serum is the primary biomarker for fescue toxicosis in cattle (Schillo et al., 1988). Previous research has demonstrated that supplementation of 3 mg/day of either OSe or MIX increases serum prolactin concentrations compared with ISe supplementation for steers grazing TE (Jia et al., 2018). Moreover, the mechanisms by which OSe and MIX affect serum prolactin concentrations are likely different (Li et al., 2019). Li et al. (2019) concluded that OSe increases prolactin synthesis capacity while MIX increases both prolactin synthesis capacity and release potential in the pituitaries of steers grazing TE. Therefore, supplementation of MIX may be more beneficial for supplementing cattle grazing TE to increase serum prolactin concentrations. The objectives of this experiment were to understand the interactions between supplemental forms of Se and endophyte toxicity on growth, serum parameters, and tissue masses of beef steers.

**MATERIALS AND METHODS**

All animal experimental procedures were approved by the University of Kentucky Institutional Animal Care and Use Committee.

**Animals and Experimental Design**

Thirty-two, predominantly Angus, steers (285 ± 21.8 kg BW) were purchased from a commercial cattle broker and transported to the University of Kentucky Research and Education Center in Princeton, KY. Because steers were purchased from the Northern United States they were presumed to be fescue-naïve. Steers were managed under a four-phase (Se depletion, Se repletion, grazing, slaughter) experimental regimen over 140 days (Figure 1). Steers were housed in a feedlot shed in groups of 4 steers/pen and subjected to a 21-day Se-depletion phase. During the Se-depletion phase, steers were fed a diet composed of NTE, alfalfa hay, and grain mixture that was formulated to increase BW by 0.57 kg/day. The targeted growth rate (0.57 kg/day) for the pre-grazing period was chosen because our previous study found that steers grazing low TE fescue gained 0.57 kg/day (Jackson et al., 2015) and so that the growth rate between phases would be equivalent. Steers had ad libitum access to a basal V-M mix (11.2% Ca, 10.2% Na, 6.3% P, 2.29% Mg, 0.91% S, 0.77% K, 3.68 g Mn/kg, 2.92 g Zn/kg, 1.54 g Cu/kg, 1.29 g Fe/kg, 1.70 mg Mb/kg, 250 kIU vitamin A/kg, and 225 IU vitamin E/kg) that did not contain Se.

After completion of the Se-depletion phase, steers were randomly assigned (n = 16 steers per treatment) to have ad libitum access to the basal V-M mix that was formulated to contain either 27 ppm Se as sodium selenite (ISe; 307 ± 19.1 kg BW) or a 1:1 blend of ISe and organic Se (SEL-PLEX, Alltech Inc., Nicholasville, KY) forms (MIX; 307 ± 25.1 kg BW) for 35 days. The ISe V-M mix contained 24.2 ± 0.27 ppm Se and the MIX V-M mix contained 29.4 ± 4.8 ppm Se, and did not differ (P = 0.14). During the 35-day Se-repletion phase, all steers were fed the same mixed diet as the Se-depletion phase and were re-sorted into pens by treatment.

After completion of the Se-repletion phase, 2 steers within their Se-form treatments were randomly assigned to graze one of eight paddocks (0.809 ha) containing either NTE (LACEFIELD MAXQ II) or TE (KY-31) for 84-day (May 30, 2019 to August 21, 2019). This resulted in 4 treatments: 1) NTE + ISe, 2) NTE + MIX, 3) TE + ISe, and 4) TE + MIX. Throughout the grazing phase, steers had ad libitum access to their respective Se-form V-M mix through 0.13 m³ mineral feeders and to shade structures (2.4 × 2.4 × 2.4 m). Steers were weighed on days −1, 0, 14, 28, 56, 83, and 84 of the experimental phase. On days 0 and 84 of the grazing period, steers were denied access to water and feed for 14 h to determine shrunk BW for calculation of ADG throughout the grazing period.

Steers were slaughtered over a 23-day period from days 90 to 113 (August 27, 2019 to September 19, 2019) of the study. Specifically, two steers from one TE and NTE paddock were killed per slaughter day, with two steers (one paddock) from each of the four treatment groups killed/week. All steers had ad libitum access to water, and their respective mineral treatments throughout the study (except during the 14-h shrink period on the day before, and after, the grazing phase).

**Forage Sampling and Analysis**

Forage samples were collected from each of the 16 paddocks (6 sites per paddock) on days −1, 28, 56, and 83 of the 84-day grazing period as described by Brown et al. (2009). Samples were stored on ice during transportation to the laboratory and then frozen and stored at −20 °C. Within a paddock,
samples were pooled across sampling days. For proximate and mineral analyses, forage samples were dried at 60 °C in a forced-air oven (NFTA 2.2.2.5.) and then ground to pass a 1-mm screen using a Wiley mill. Dry matter content was determined by oven-drying for 3-h at 105 °C. Nitrogen content was analyzed by combustion (AOAC, 2006; method 990.03) using a CN628 Carbon/Nitrogen Determinator (Leco Corporation, St. Joseph, MI). Crude protein was calculated by multiplying N concentration × 6.25. Acid detergent fiber and neutral detergent fiber concentrations were determined using the filter bag technique (ANKOM Technology Methods 14 and 15, respectively). Total digestible nutrients and dietary NE₃ were calculated using equations from NASEM (2016). Samples were prepared for mineral analyses by pre-digesting samples first with HNO₃ and HCl and then with 30% H₂O₂, followed by two-stage digestion, and analysis using inductively coupled plasma spectroscopy. Selenium concentrations were determined by the Michigan State University Veterinary Diagnostic Laboratory using inductively coupled plasma mass spectrometry (Wahlen et al., 2005). For ergot alkaloid forage analysis, samples were freeze-dried and then ground to pass a 1-mm screen using a Wiley mill. Ergot alkaloid concentrations (ergovaline, ergovalanine, ergotamine, and ergotamine) were measured by the laboratory of Huihua Ji (University of Kentucky) using ultra-performance liquid chromatography/tandem mass spectrometry (Acquity UPLC-Ji (University of Kentucky) using ultra-performance liquid ergotaminine) were measured by the laboratory of Huihua concentrations (ergovaline, ergovalanine, ergotamine, and

Statistical Analysis

Only data collected during phase III (grazing period) and phase IV (post-slaughter) of the experiment were analyzed. All variables were checked for normality using the Shapiro-Wilk test of the UNIVARIATE procedure of SAS (version 9.4, SAS Inst. Inc., Cary, NC). Because serum prolactin concentrations were not normally distributed, a log₁₀ transformation of the data was performed to conform to a normal distribution. Paddock was the experimental unit for all analyses. Nutrient and ergot alkaloid concentrations of the forages were analyzed using the GLM procedure of SAS for fixed effects of treatment.

Body weight and serum analytes were analyzed using the repeated measures statement of the MIXED procedure of SAS. Antedependence 1, autoregressive 1, compound symmetry, simple, and unstructured variance–covariance structures for the repeated measures statement were assessed for fit using Bayesian information criterion. The model included fixed effects of day, endophyte treatment, form of Se supplementation, and their interactions. Paddock was used as a random effect. The initial measurement of a parameter (initial BW, initial concentration on day 0) was used as a covariate in repeated measures analysis for that parameter. If two- or three-way interactions including day were not significant, then polynomial contrasts (linear, quadratic, cubic, quartic) were used to describe the effect of day.

Average daily gain, carcass characteristics, and tissue mass were analyzed using the GLM procedure of SAS as a completely randomized design with a 2 × 2 factorial arrangement of treatments. The model included fixed effects of endophyte treatment, form of Se supplementation, and the endophyte treatment × form of Se supplementation interaction. Partial correlations among serum variables were assessed using the manova/printe statement of the GLM procedure of SAS with day and the endophyte treatment × form of Se supplementation interaction included in the model statement. The Kenward–Roger adjustment was used to calculate the denominator degrees of freedom (Kenward and Roger, 1997). Least square means and their standard errors were generated for each fixed effect included in the models. Pairwise differences of least square means were separated using the Tukey–Kramer adjustment, protected by a significant F-test. Results were considered significant if P ≤ 0.05. Tendencies were declared when 0.05 < P ≤ 0.10.

RESULTS

Nutrient and Ergot Alkaloid Profiles of Forages

The composited means of proximate, mineral, and alkaloid analysis of pasture samples are presented in Table 1. Dry matter, total digestible nutrients, crude protein, acid detergent fiber, and NE₃ did not differ (P ≥ 0.06) between pastures. The Ca concentration was greater (P = 0.03) for TE + MIX pastures compared with NTE + MIX. Concentrations of P, Mg, K, Na, Fe, Zn, Cu, Mn, Mb, and Se did not differ (P ≥ 0.19).
between pastures. Ergovaline and ergovalinine concentrations were greater \((P < 0.01)\) in TE pastures compared with NTE pastures. Ergotamine and ergotaminine concentrations did not differ \((P \geq 0.26)\) between TE and NTE pastures.

### Body Weight and Average Daily Gain

There were no two- or three-way interactions among day, form of Se supplementation, or endophyte treatment for body weights (Figure 2A). Body weights were not affected \((P = 0.26)\) by form of Se supplementation. Body weights were greater \((P < 0.01)\) for NTE steers than TE steers. Body weights responded in a cubic \((P < 0.01)\) manner, increasing from days 0 to 28, then decreasing from days 28 to 56, then increasing from days 56 to 84. Average daily gain was not affected \((P = 0.42)\) by form of Se supplementation (Figure 2B). Average daily gain was greater \((P = 0.04)\) for NTE steers than TE steers.

### Serum Parameters

There were no three-way interactions among day, form of Se supplementation, or endophyte treatment for any serum variables measured (data not shown). There were endophyte \(\times\) form of Se supplementation \((P < 0.01)\) and day \(\times\) endophyte treatment interactions \((P = 0.01)\) for prolactin concentrations in serum (Figure 3). Serum prolactin concentrations were greater \((P < 0.01)\) for NTE steers compared to TE steers on days 14 and 28; however, serum prolactin concentrations in TE + MIX steers increased \((P < 0.01)\) and were intermediate of the NTE and TE + ISe treatments on days 56 and 84. Serum prolactin concentrations did not differ among treatments on day 0 but, then decreased \((P = 0.01)\) on day 14 in TE steers and remained lesser throughout the 84-day grazing period.

There was a day \(\times\) endophyte treatment interaction \((P \leq 0.01)\) for serum urea nitrogen concentrations (data not shown). There was a divergent response where serum urea-N concentrations increased for TE steers and decreased for NTE from days 0 to 14, TE remained greater than NTE from days 14 to 56, and then converged on day 84. There was a day \(\times\) endophyte treatment interaction \((P = 0.05)\) for serum \(\gamma\)-glutamyltransferase activity because it was greater on day 56 for TE steers (data not shown). There was a day \(\times\) endophyte treatment \((P = 0.04)\) interactions for serum globulin concentration (data not shown). The concentration of globulin for TE steers on days 0 and 28 were greater \((P \leq 0.05)\) but, were greater for NTE steers on day 84. There was a day \(\times\) form of Se supplementation interaction \((P = 0.01)\) for serum aspartate aminotransferase activity because

### Table 1

| Analyte                          | Treatment | SEM   | \(P\)-value* |
|----------------------------------|-----------|-------|--------------|
|                                  | TE + ISe  | TE + MIX | NTE + ISe  | NTE + MIX |
| **Proximate analysis**           |           |        |              |           |
| DM, %                            | 0.72      | 0.20   | 0.66         | 0.56      |
| Total digestible nutrients, %    | 0.11      | 0.06   | 0.56         | 0.56      |
| Crude protein, % of DM           | 0.26      | 0.24   | 2.44 \(\times 10^3\) | 0.25      |
| Acid detergent fibre, % of DM    | 0.37      | 0.85   | 0.54         | 0.54      |
| Neutral detergent fibre, % of DM | 0.66      | 0.66   | 0.09         | 0.09      |
| Net energy for gain, Mcal/kg     | 2.97 \(\times 10^{-3}\) | 0.79   | 0.07         | 0.07      |
| **Mineral analysis**             |           |        |              |           |
| Ca, %                            | 0.49\(a\) | 0.50\(a\) | 0.47\(ab\) | 0.45\(b\) |
| P, %                             | 0.39      | 0.39   | 0.36         | 0.36      |
| Mg, %                            | 0.26      | 0.26   | 0.24         | 0.24      |
| K, %                             | 2.23      | 2.29   | 2.47         | 2.47      |
| Na, %                            | 0.02      | 0.02   | 0.01         | 0.01      |
| Fe, ppm                          | 360       | 451    | 312          | 452       |
| Zn, ppm                          | 18.6      | 20.9   | 21.6         | 21.1      |
| Cu, ppm                          | 6.88      | 7.31   | 7.63         | 7.38      |
| Mn, ppm                          | 52.4      | 53.2   | 56.94        | 53.00     |
| Mb, ppm                          | 1.71      | 1.87   | 1.51         | 1.39      |
| Se, ppm                          | 0.04      | 0.03   | 0.03         | 0.04      |
| **Ergoalkaloid analysis**        |           |        |              |           |
| Ergovaline, µg/g                  | 0.272\(a\) | 0.280\(a\) | 0.006\(a\) | 0.009\(b\) |
| Ergovalinine, µg/g                | 0.158\(a\) | 0.149\(a\) | 0.009\(b\) | 0.005\(b\) |
| Ergotamine, µg/g                  | 0.006     | 0.007  | 0.003        | 0.009     |
| Ergotaminine, µg/g                | 0.003     | 0.004  | 0.003        | 0.004     |
| Total ergot alkaloids, µg/g       | 0.439\(a\) | 0.440\(a\) | 0.021\(b\) | 0.027\(b\) |

---

1Values are the least square means \((n = 4)\) of pooled \((days −1, 28, 56, and 83)\) forage sample from ISe and MIX paddocks. Samples were obtained systematically from 6 sites \(\cdot\) paddock\(−1\) \(\cdot\) sample day\(−1\).

2Sum of ergovaline, ergovalinine, ergotamine, and ergotaminine concentrations.
Endophyte toxicity interactions with Se form

whereas, steers consuming MIX had greater \((P = 0.01)\) aspartate aminotransferase activity on day 56.

Supplementation of MIX increased \((P < 0.01)\) whole blood Se concentrations compared to supplementation of ISe (Table 2). Serum alkaline phosphatase activity and the albumin:globulin were increased \((P < 0.05)\) with MIX supplementation. Serum aspartate aminotransferase activity tended to be greater \((P = 0.06)\) in steers consuming NTE + ISe compared to other treatments. For NTE + ISe steers, serum \(\gamma\)-glutamyltransferase activity tended to be lesser \((P = 0.09)\) compared with other treatments. Creatinine concentration in serum tended to increase \((P = 0.09)\) with MIX supplementation. Total bilirubin concentrations were greater \((P = 0.05)\) in steers supplemented with ISe. Urea-N:creatinine and albumin:globulin ratios in serum were increased \((P < 0.04)\) for steers grazing TE. There were form of Se supplementation × endophyte treatment interactions \((P < 0.04)\) for serum globulin and total protein concentrations. Serum globulin concentrations were greater for NTE + ISe steers than NTE + MIX steers but were not different from TE + ISe or TE + MIX steers. Serum albumin, glucose, and creatine kinase activity were not influenced by form of Se supplementation or endophyte treatment. Serum mineral concentrations of Na, K, Cl, Ca, P, and Mg were not influenced by form of Se supplementation or endophyte treatment.

**Partial Correlation of Whole Blood Se and Prolactin Concentrations with Serum Parameters**

Across treatments, weak positive correlations \((0.33 > r > 0.26)\) were observed between whole blood Se and serum urea nitrogen \((P = 0.02)\), total protein \((P = 0.01)\), and globulin \((P = 0.05)\) (Table 3). In contrast, whole blood Se was weakly and negatively correlated with potassium \((r = -0.23, P ≤ 0.01)\). Across treatments, a moderate positive correlation was found between whole blood Se and creatinine \((r = 0.43, P ≤ 0.01)\) and negative correlation was found between whole blood Se and glucose \((r = -0.44, P ≤ 0.01)\). There was a tendency for a positive correlation between whole blood Se and albumin \((r = 0.25, P = 0.06)\). There were no correlations \((P ≥ 0.10)\) between whole blood Se and log\(_{10}\) prolactin, creatinine kinase, alkaline phosphatase, aspartate aminotransferase, \(\gamma\)-glutamyltransferase, total bilirubin, Na, Cl, Ca, P, and Mg.

Across treatments, positive correlations were found between log\(_{10}\) prolactin and total protein \((r = 0.30, P = 0.02)\) and globulin \((r = 0.31, P = 0.02)\). There was a positive correlation tendency between log\(_{10}\) prolactin and aspartate aminotransferase \((r = 0.25, P = 0.06)\). There were no correlations \((P ≥ 0.10)\) between log\(_{10}\) prolactin and whole blood Se, urea nitrogen, creatinine, creatinine kinase, glucose, alkaline phosphatase, \(\gamma\)-glutamyltransferase, albumin, total bilirubin, Na, K, Cl, Ca, P, and Mg.

**Tissue Masses**

There were no endophyte treatment × form of Se supplementation interactions for actual and BW-relative pituitary, kidney, and liver weights (Table 4). Pituitary mass \((g \text{ and } g/100 \text{ kg BW})\) was greater \((P = 0.02)\) for MIX steers than ISe steers, but there was no \((P ≥ 0.30)\) endophyte effect. Kidney mass \((g \text{ and } g/100 \text{ kg BW})\) was not affected \((P ≥ 0.21)\) by endophyte treatment or form of Se supplementation. Liver mass

![Figure 2](image2.png)

**Figure 2.** Body weight (A) and average daily gain (B) of steers during grazing of toxic endophyte-infected (TE) tall fescue or non-toxic endophyte-infected (NTE) tall fescue and consuming ad libitum vitamin-mineral mix containing 27 ppm Se in inorganic (ISe) or a 1:1 blend of ISe and organic Se (MIX) for 84 days. Data are least square means ± SE for the day × endophyte × Se form interaction. (A) Day \((P < 0.01)\), endophyte \((P < 0.01)\), Se form \((P = 0.26)\), and Se form × endophyte interaction \((P = 0.32)\). Note that the \(y\)-axis does not begin at 0. (B) Endophyte \((P = 0.04)\), Se form \((P = 0.42)\), and Se form × endophyte \((P = 0.60)\).

![Figure 3](image3.png)

**Figure 3.** Serum prolactin \((\log_{10})\) concentrations in steers grazing toxic endophyte-infected (TE) tall fescue or non-toxic endophyte-infected (NTE) tall fescue and consuming ad libitum vitamin-mineral mix containing 27 ppm Se in inorganic (ISe) or a 1:1 blend of ISe and organic Se (MIX) for 84 days. Data are least square means ± SE for the day × endophyte × Se form interaction. Form of Se supplementation \((P = 0.53)\), endophyte \((P < 0.01)\), day \((P < 0.01)\), endophyte × day interaction \((P < 0.01)\), and endophyte × Se form interaction \((P = 0.01)\). Note that the serum prolactin data is \(\log_{10}\) transformed.
Webb et al. (g) was greater (\(P = 0.01\)) for NTE steers than TE steers but did not differ among endophyte treatments as a proportion of BW. Liver mass (g and g/100 kg BW) was not affected (\(P \geq 0.64\)) by form of Se supplementation.

**DISCUSSION**

**Experimental Model**

The current study uses concepts developed in prior experiments (Brown et al., 2009; Jackson et al., 2015; Jia et al., 2018, 2019; Li et al., 2019) to expand our understanding of how ergot alkaloid consumption and form of Se supplementation interact to affect growth performance and physiology of cattle. The current and previous experiments were comprised of a summer-long grazing period. Steers used for prior studies were raised (Jia et al., 2018, 2019; Li et al., 2019) or purchased (Brown et al., 2009; Jackson et al., 2015) in Kentucky and, presumably, adapted to both TE and environmental conditions in Kentucky. The current experiment used steers that purchased in the Northern United States and shipped south to Kentucky. Because of their prior origin, it is presumed that steers used in the current study did not graze tall fescue before the start of experimentation and that steers were not adapted to environmental conditions that could lead to heat stress.

Previous studies from our laboratory have evaluated effects of fescue toxicosis or effects of Se supplementation form on growth and serum metabolites of steers. These studies have similarities and differences in ergot alkaloid concentrations and Se concentrations that should be noted. The steers from Brown et al. (2009) grazed TE with an ergot alkaloid concentration of either 0.017 µg ergovaline + ergovalinine/g (low) or 0.52 µg ergovaline + ergovalinine/g (high) and had ad libitum access to 35 ppm ISe. Similarly, steers grazed TE with an ergot alkaloid concentration of either 0.022 µg ergovaline + ergovalinine/g (low) or 0.43 µg ergovaline + ergovalinine/g (high) (Jackson et al., 2015). Jia et al. (2018) and Jia et al. (2019) used pastures that were comprised of mostly TE (0.51 μg ergovaline + ergovalinine/g) but, did not have a NTE treatment. In the current study, steers grazed pastures that contained either TE (0.43 µg ergovaline + ergovalinine/g) or NTE (0.015 µg ergovaline + ergovalinine/g) tall fescue. Concentrations of ergovaline + ergovalinine in TE pastures were similar to those of prior studies and NTE was similar to the low-endophyte treatment used by Brown et al. (2009) and Jackson et al. (2015).

Brennan et al. (2011) demonstrated that supplemental selenium (ISe, OSe, or MIX) increased concentrations of Se in whole blood, red blood cells, serum, and liver of heifers compared with no supplementation of Se. However, MIX and OSe resulted in greater concentrations of Se in these tissues compared with ISe, indicating that form of Se supplementation is important for maintaining or maximizing Se assimilation (Brennan et al., 2011). Jia et al. (2018) demonstrated that controlled supplementation of Se (3 mg/day) as OSe or MIX increased whole blood Se concentrations compared with ISe supplementation. In the current study,

### Table 2. Whole blood Se and serum parameters of steers grazing toxic endophyte-infected (TE) tall fescue and non-toxic endophyte-infected (NTE) tall fescue and consuming ad libitum vitamin-mineral mix containing 27 ppm Se in inorganic (ISe) or a blend of ISe and organic Se (MIX) for 84 days

| Parameter                          | Treatment¹ | SEM⁴ | P-value³ |
|------------------------------------|------------|------|----------|
|                                    | ISe        |       |          |
|                                    | NTE TE     |      |          |
| Whole blood Se, ng/mL              | 201 193    | 212 207 | 4.68     | 0.71 <0.01 0.77 |
| Alkaline phosphatase, U/L          | 76.3 72.6  | 80.8 90.1 | 10.9    | 0.69 0.02 0.23 |
| Aspartate aminotransferase, U/L    | 68.0 60.6  | 63.5 61.4 | 0.89 <0.01 0.24 0.06 |
| y-Glutamyltransferase, U/L         | 9.25 11.2  | 10.3 11.2 | 0.36 0.08 0.12 0.09 |
| Creatine kinase, U/L               | 221 239    | 217 210 | 9.21 0.75 0.35 0.48 |
| Urea nitrogen, mg/dL               | 8.50 10.5  | 7.97 10.4 | 0.93 <0.01 0.25 0.37 |
| Creatinein, mg/dL                  | 1.55 1.42  | 1.51 1.37 | 0.01 0.20 0.09 0.97 |
| Urea nitrogen: creatinine          | 7.13 8.32  | 6.66 8.10 | 0.12 0.04 0.13 0.55 |
| Glucose, mg/dL                     | 131 119    | 121 118 | 5.45 0.29 0.58 0.52 |
| Albumin, g/dL                      | 6.71 6.74  | 6.51 6.85 | 0.28 0.25 0.53 0.04 |
| Globulin, g/dL                     | 2.73 2.83  | 2.75 2.94 | 0.03 0.14 0.13 0.69 |
| Albumin: globulin                  | 0.69 0.73  | 0.72 0.75 | 0.03 <0.01 0.05 0.05 |
| Total bilirubin, mg/dL             | 0.244 0.257 | 0.226 0.239 | 0.005 0.15 0.05 0.98 |
| Na, mmol/L                         | 134 134    | 134 137 | 0.57 0.70 0.50 0.12 |
| Cl, mmol/L                         | 97.9 98.5  | 97.0 98.8 | 0.42 0.68 0.75 0.51 |
| Ca, mg/dL                          | 9.26 9.46  | 9.30 9.59 | 0.06 0.40 0.38 0.66 |
| P, mg/dL                           | 7.58 8.00  | 8.07 8.15 | 0.12 0.66 0.08 0.36 |
| K, mmol/L                          | 5.59 5.75  | 5.61 5.84 | 0.07 0.10 0.65 0.81 |
| Mg, mg/dL                          | 2.08 2.08  | 2.12 2.17 | 0.03 0.32 0.16 0.61 |

¹Data are least square means (\(n = 4\)).
²Means within a row that lack a common letter differ (\(P < 0.05\)).
³P-values are associated with the \(F\)-statistics.
⁴SEM values are the most conservative standard error of the means.

and Se concentrations (\(P = 0.01\)) for NTE steers than TE steers but did not differ among endophyte treatments as a proportion of BW. Liver mass (g and g/100 kg BW) was not affected (\(P \geq 0.64\)) by form of Se supplementation.
Table 3. Partial correlation analysis of whole blood Se and serum prolactin (log$_{10}$ transformed) concentrations with clinical analytes of steers grazing toxic endophyte-infected (TE) tall fescue or non-toxic endophyte-infected (NTE) tall fescue and consuming ad libitum vitamin-mineral mix containing 27 ppm Se in inorganic (ISe) or a blend of ISe and organic Se (MIX) for 84 days.

| Item                      | Whole blood Se | Serum parameters |
|---------------------------|----------------|------------------|
|                           | Coefficient    | P-value          | Coefficient | P-value |
| Whole blood Se            | 1              | —                | 0.22        | 0.10    |
| log$_{10}$Prolactin       | 0.22           | 0.10             | 1           | —       |
| Urea nitrogen             | 0.31           | 0.02             | -0.20       | 0.13    |
| Creatinine                | 0.43           | <0.01            | -0.05       | 0.68    |
| Creatinine kinase         | -0.40          | 0.75             | -0.70       | 0.59    |
| Glucose                   | -0.44          | <0.01            | -0.16       | 0.24    |
| Alkaline phosphatase      | -0.13          | 0.33             | -0.90       | 0.50    |
| Aspartate aminotransferase| -0.22          | 0.10             | 0.25        | 0.06    |
| γ-Glutamyltransferase     | 0.21           | 0.12             | -0.05       | 0.70    |
| Total protein             | 0.33           | 0.01             | 0.30        | 0.02    |
| Albumin                   | 0.25           | 0.06             | 0.09        | 0.51    |
| Globulin                  | 0.26           | 0.05             | 0.31        | 0.02    |
| Total bilirubin           | -0.13          | 0.34             | -0.07       | 0.61    |
| Na                        | 0.01           | 0.95             | 0.03        | 0.81    |
| K                         | -0.23          | <0.01            | -0.18       | 0.18    |
| Cl                        | -0.07          | 0.63             | -0.12       | 0.37    |
| Ca                        | -0.01          | 0.96             | -0.03       | 0.80    |
| P                         | 0.01           | 0.91             | 0.002       | 0.99    |
| Mg                        | -0.11          | 0.39             | -0.16       | 0.24    |

1Whole blood Se vs. serum analytes.
2log$_{10}$Prolactin vs. serum analytes.

our Se concentration in the V-M mix (27 ppm) was similar to those of prior studies by Brennan et al. (2011) (35 ppm) and Jia et al. (2018) (35 ppm). However, in the current study, intake of Se was not controlled to 3 mg/day like in the prior studies.

A limitation of the current study is that feed intake was not measured. Therefore, it is unknown how consumption of tall fescue compares with previous studies and if TE resulted in decreased DM intake compared with NTE. Moreover, access to V-M mix containing ISe or MIX were offered ad libitum and it is unknown if Se intake differed between treatments and how comparable Se intakes are to previous studies that measured similar parameters. With that being addressed, changes in biomarker concentrations for fescue toxicosis and Se supplementation indicate that the animal model was successful. Decreased prolactin concentration in serum is a classic marker of fescue toxicosis (Schillo et al., 1988). In the current study, consumption of TE decreased serum prolactin concentrations by 48% compared with NTE, indicating that the grazing model for fescue toxicosis was successful. Brennan et al. (2011) demonstrated that the effects of supplemental forms of Se can be evaluated from multiple samples to determine Se status. In the current study, supplementation of MIX increased whole blood Se concentrations by 6.2% compared with ISe supplementation. This indicates that ad libitum consumption of MIX was effective at increasing Se concentrations compared with ISe, which is similar to results found with controlled intakes of Se (Brennan et al., 2011; Jia et al., 2018).

**Body Weight and Average Daily Gain**

In the current study, steers grazing NTE had greater ADG and BW than steers grazing TE, which supports the findings of previous studies with similar pasture ergot alkaloid concentrations (Brown et al., 2009; Jackson et al., 2015). The cubic response of BW, resulting from a decrease in BW from days 28 to 56 across all treatments, is interesting. These data may indicate that steers in the current study had experienced heat stress to some degree between days 28 and 56 in the summer grazing period. However, it appears that steers consuming TE were more affected, indicated by a greater decrease in BW from days 28 to 56, which supports the concept that steers consuming TE may be more susceptible to heat stress. Partitioning the effects (consumption of ergot alkaloids, heat stress, decreased intake) which result in the phenotype of fescue toxicosis is difficult and deserves further attention.

At restricted intakes, previous studies have shown that the form of Se supplementation did not influence BW or ADG of beef cattle (Brennan et al., 2011; Jia et al., 2018). Our study demonstrated that ad libitum consumption of MIX does not influence ADG or BW of beef steers. Previous research has shown that Se supplementation as OSe or ISe at supranutritional levels (~23 mg/day) does not influence DM intake, ADG, or gain:feed of finishing beef steers (Lawler et al., 2004). These data indicate that adaptations in physiological parameters with changes in the form and/or level of Se supplementation do not result in improved growth performance of grazing beef steers.

**Serum Parameters**

Previous research has demonstrated that controlled OSe and MIX supplementation (3 mg/day) increases serum prolactin concentrations in steers grazing TE (Jia et al., 2018) but, apparently by different mechanisms (Li et al., 2019). Organic Se supplementation influences mRNA expression of genes involved in pituitary prolactin synthesis while, MIX supplementation influences both prolactin synthesis and release potential (Li et al., 2019). In the current study, serum prolactin concentrations were greater for steers grazing TE + MIX compared with TE + ISe on days 56 and 84. However, supplementation of MIX to steers grazing TE pastures was unable to restore prolactin concentrations to that of steers grazing NTE. Brennan et al. (2011) concluded that the time required to observe maximal Se assimilation is dependent on the tissue of interest. Those authors suggested that at least 224 days would be required to assess changes in maximal Se assimilation in whole blood or red blood cells (Brennan et al., 2011). Although MIX supplementation did increase serum prolactin concentrations for steers grazing TE, more research is needed to determine if longer supplementation of MIX could restore serum prolactin levels of TE steers to the level of steers grazing NTE.

Decreased serum alkaline phosphatase activity has been widely associated with the onset of fescue toxicosis in beef cattle (Boling et al., 1989; Brown et al., 2009; Jia et al., 2019; Schultz et al., 1999). Brown et al. (2009) reported that steers consuming TE had decreased serum alkaline phosphatase activity compared with steers consuming low endophyte-infected
Table 4. Actual and body weight (BW)-relative pituitary, liver, and kidney masses of steers grazing toxic endophyte-infected (TE) tall fescue or non-toxic endophyte-infected (NTE) tall fescue and consuming ad libitum vitamin-mineral mix containing 27 ppm Se in inorganic (ISe) or a blend of ISe and organic Se (MIX) for 84 days.

| Parameter         | Treatment | ISe     | MIX     | SEM<sup>4</sup> | P-value<sup>1</sup> |
|-------------------|-----------|---------|---------|-----------------|--------------------|
|                   | NTE       | TE      | NTE     | TE              | Endophyte | Se form | Endophyte × Se form |
| Weight (wet)      |           |         |         |                 |         |
| Pituitary, g      | 1.70      | 1.62    | 1.95    | 1.84            | 0.09     | 0.30    | 0.02 | 0.89                    |
| Kidney, g         | 361.4     | 340.0   | 369.3   | 353.1           | 14.0     | 0.21    | 0.47 | 0.86                    |
| Liver, g          | 4,048     | 3,331   | 3,878   | 3,650           | 154.4    | 0.01    | 0.64 | 0.14                    |

<sup>1</sup>Cattle grazed paddocks for 89 to 109 days before slaughter. Values are least square means (n = 4). Body weights are reported in Figure 1.

<sup>2</sup>P-value associated with the F-statistic.

<sup>3</sup>Most conservative error of the mean.

<sup>4</sup>Based on body weight at time of slaughter.

Tissue Masses

Previous research has shown that feeding TE seed to rats decreased liver mass compared with rats fed endophyte-free tall fescue seed (Chestnut et al., 1992; Settivari et al., 2006). Liver mass has been reported to decrease by 10% for steers grazing high TE compared with low TE (Brown et al., 2009). Similarly, we found that steers the grazed TE had liver weights that were 11.9% less at slaughter compared with steers that grazed NTE. It is well established that visceral organ mass, including the liver, responds to the level of dietary intake for both cattle and sheep (Burrin et al., 1990; Johnson et al., 1990; McLeod and Baldwin, 2000). It is possible that reductions in feed intake with TE consumption could have occurred in the current study and contributed to decreased mass of the liver. Several hepatic functions are altered with TE consumption such as gluconeogenesis (Brown et al., 2009), some aspects of hepatic N metabolism (Jackson et al., 2015), and ATP synthesis and oxidative phosphorylation (Liao et al., 2015). In the current study, serum urea nitrogen was greater for steers consuming TE, which could suggest that steers consuming TE were in a protein catabolic state. Although form of supplemental Se did not influence liver mass, previous research has shown that the form of Se supplementation influences liver Se content (Brennan et al., 2011; Liao et al., 2011) and the composition of the hepatic transcriptome (Matthews et al., 2014).

Whole Blood Se and Serum Prolactin Correlates

Whole blood Se concentrations are well correlated with Se intake in cattle (Patterson et al., 2013) and prolactin affects many physiological processes besides lactation (Freeman et al., 2000). The potential relationships between whole blood Se and serum prolactin with measured blood analytes were evaluated by partial correlation analysis. Significant correlations were found between whole blood Se and serum urea nitrogen, creatinine, glucose, total protein and potassium, even though Se treatment per se did not affect their concentrations. In contrast, serum globulin concentrations was affected by an endophyte type × Se form interaction. Although the reasons and physiological consequences of these correlations await determination, the significant correlations between whole blood Se and these analytes indicate that the changes of these parameters were associated with the alterations of whole blood Se. For prolactin, that only globulin and total protein concentrations were correlated (weakly) with serum prolactin concentrations would have been unexpected except that Jackson et al. (2015) also found little evidence for serum prolactin being associated with clinical analyte concentrations of growing steers grazing TE and NTE pastures. Expected or not, the lack of evidence of circulating prolactin is surprising given that prolactin is a multifunctional hormone and tissue expression of prolactin receptors is ubiquitous (Ben-Jonathan et al., 2006).
result in increased serum prolactin concentrations for steers grazing TE.

CONCLUSIONS

Grazing TE resulted in decreased ADG, decreased BW, liver mass, and hot carcass weight, and decreased serum prolactin concentrations compared to steers grazing NTE. Replacing ISe with a 1:1 blend of ISe and OSe (MIX) resulted in increased whole blood Se concentrations, increased mass of the pituitary, and increased serum alkaline phosphatase activity. Supplementation of MIX increased serum prolactin concentrations for steers grazing TE. However, MIX treatment did not restore serum prolactin concentrations to that of steers grazing NTE. Despite positive effects of MIX supplementation on serum prolactin and alkaline phosphatase activity, ADG was not improved. More research is needed to determine if a longer adaptation to MIX supplementation could further increase prolactin concentrations in steers grazing TE and if this could correspond to improvements in ADG and/or reduce symptoms of fescue toxicosis.

Acknowledgements

This work is supported by a United States Department of Agriculture-Agricultural Research Service Non-Assisted Cooperative Agreement (J.C.M., P.J.B.) and by the National Institute of Food and Agriculture, U.S. Department of Agriculture, Hatch project No. 1010352.

Conflict of Interest Statement

The authors declare no conflict of interest.

LITERATURE CITED

Ammerman, C. B., and S. M. Miller. 1975. Selenium in ruminant nutrition: a review. J. Dairy Sci. 58:1361–1377. doi:10.3168/jds.S0022-0302(75)84752-7.

Ben-Jonathan, N., E. R. Hugo, T. D. Brandebourg, and C. R. LaPensee. 2006. Focus on prolactin as a metabolic hormone. Trends Endocrinol. Metabolism 17:110–6. doi:10.1016/j.tem.2006.02.005.

Berde, B. 1980. Ergot compounds: a synopsis. Adv. Biochem. Psychopharmacol. 23:2–23.

Boling, J. A., L. D. Bunting, G. M. Davenport, J. L. Van der Veen, K. R. reduce symptoms of fescue toxicosis. This could correspond to improvements in ADG and/or reduction of prolactin and alkaline phosphatase activity, serum prolactin concentrations in steers grazing TE and if adaptation to MIX supplementation could further increase serum prolactin concentrations in steers grazing TE. However, MIX treatment did not restore serum prolactin concentrations to that of steers grazing NTE. Despite positive effects of MIX supplementation on serum prolactin and alkaline phosphatase activity, ADG was not improved. More research is needed to determine if a longer adaptation to MIX supplementation could further increase serum prolactin concentrations in steers grazing TE and if this could correspond to improvements in ADG and/or reduce symptoms of fescue toxicosis.

Acknowledgements

This work is supported by a United States Department of Agriculture-Agricultural Research Service Non-Assisted Cooperative Agreement (J.C.M., P.J.B.) and by the National Institute of Food and Agriculture, U.S. Department of Agriculture, Hatch project No. 1010352.

Conflict of Interest Statement

The authors declare no conflict of interest.

LITERATURE CITED

Ammerman, C. B., and S. M. Miller. 1975. Selenium in ruminant nutrition: a review. J. Dairy Sci. 58:1361–1377. doi:10.3168/jds.S0022-0302(75)84752-7.

Ben-Jonathan, N., E. R. Hugo, T. D. Brandebourg, and C. R. LaPensee. 2006. Focus on prolactin as a metabolic hormone. Trends Endocrinol. Metabolism 17:110–6. doi:10.1016/j.tem.2006.02.005.

Berde, B. 1980. Ergot compounds: a synopsis. Adv. Biochem. Psychopharmacol. 23:2–23.

Boling, J. A., L. D. Bunting, G. M. Davenport, J. L. Van der Veen, K. M. Meekeins, N. W. Bradley, and R. E. Kohls. 1989. Physiological responses of cattle consuming tall fescue to environmental temperature and supplemental phenothiazine. J. Anim. Sci. 67:2377–2385. doi:10.2527/ajas1989.6792377x.

Boyne, R., and J. R. Arthur. 1979. Alterations of neutrophil function in selenium-deficient cattle. J. Comp. Pathol. 89:151–158. doi:10.1016/0021-9975(79)90018-5.

Brennan, K. M., W. R. Burris, J. A. Boling, and J. C. Matthews. 2011. Selenium content in blood fractions and liver of beef heifers is greater with a mix of inorganic/organic or organic versus inorganic supplemental selenium but the time required for maximal assimilation with a mix of inorganic/organic or organic versus inorganic supplemental selenium in blood fractions and liver of beef heifers is greater. J. Anim. Sci. 90:1603–1609. doi:10.2527/jas.2011-4513.

Bush, L. P., P. L. Cornelius, M. A. Cochran, H. A. Fribourg, and J. D. Gwinn. 1992. Effects of hydrated sodium calcium alumino-silicate on fescue toxicosis and mineral absorption. J. Anim. Sci. 70:2838–2846. doi:10.2527/1992.702838x.

Gleed, P. T., W. M. Allen, C. B. Mallinson, G. J. Rowlands, B. F. Sansom, M. J. Vagg, and R. D. Caswell. 1983. Effects of selenium and copper supplementation on the growth of beef steers. Vet. Rec. 113:388–392. doi:10.1136/vr.i113.17.388.

Gunter, S. A., P. A. Beck, and J. M. Phillips. 2003. Effects of supplemental selenium source on the performance and blood measurements in beef cows and their calves. J. Anim. Sci. 81:856–864. doi:10.2527/2003.814856x.

Jackson, J. J., M. D. Lindemann, J. A. Boling, and J. C. Matthews. 2015. Summer-long grazing of high vs. low endophyte (Neotyphodium coenophialum)-infected tall fescue by growing beef steers results in distinct temporal blood analyte response patterns, with poor correlation to serum prolactin levels. Front. Vet. Sci 2:77. doi:10.3389/fvets.2015.00077.

Jia, Y., Q. Li, W. R. Burris, G. E. Aiken, P. J. Bridges, and J. C. Matthews. 2018. Forms of selenium in vitamin-mineral mixes differentially affect serum prolactin concentration and hepatic glutamine synthetase activity of steers grazing endophyte-infected tall fescue. J. Anim. Sci. 96:715–727. doi:10.1093/jas/skx068.

Jia, Y., K. Son, W. R. Burris, P. J. Bridges, and J. C. Matthews. 2019. Forms of selenium in vitamin-mineral mixes differentially affect serum alkaline phosphatase activity, and serum albumin and blood urea nitrogen concentrations, of steers grazing endophyte-infected tall fescue. J. Anim. Sci. 97:2369–2382. doi:10.1093/jas/skz109.

Johnson, D. E., K. A. Johnson, and R. L. Baldwin. 1990. Changes in liver and gastrointestinal tract energy demands in response to physiological workload in ruminants. J. Nutr. 120:649–655. doi:10.1093/jn/120.6.649.

Kallenbach, R. L. 2015. BILL E. KUNKLE INTERDISCIPLINARY BEEF SYMPOSIUM: Coping with tall fescue toxicosis: Solutions and realities. J. Anim. Sci. 93:5487–5495. doi:10.2527/jas.2015-9229.

Kenward, M. G., and J. H. Roger. 1997. Small sample inference for fixed effects from restricted maximum likelihood. Biometrics 53:983–997.

Klotz, J. L. 2015. Activities and effects of ergot alkaloids on livestock physiology and production. Toxins 7:2801–2821. doi:10.3390/toxins7082801.

Lawler, T. L., J. B. Taylor, J. W. Finley, and J. S. Caton. 2004. Effect of supranutritional and organically bound selenium on performance, carcass characteristics, and selenium distribution in finishing beef steers. J. Anim. Sci. 82:1488–1493. doi:10.2527/2004.8251488x.

Li, Q., Y. Jia, W. R. Burris, P. J. Bridges, and J. C. Matthews. 2019. Forms of selenium in vitamin–mineral mixes differentially affect the expression of genes responsible for prolactin, ACTH, and α-MSH synthesis and mitochondrial dysfunction in pituitaries of
steers grazing endophyte-infected tall fescue. *J. Anim. Sci.* 97:631–643. doi:10.1093/jas/sky438.

Liao, S. F., J. A. Boling, and J. C. Matthews. 2015. Gene expression profiling indicates an increased capacity for proline, serine, and ATP synthesis and mitochondrial mass by the liver of steers grazing high vs. low endophyte-infected tall fescue. *J. Anim. Sci.* 93:5659–5671. doi:10.2527/jas.2013-9193.

Liao, S. F., K. R. Brown, A. J. Stromberg, W. R. Burris, J. A. Boling, and J. C. Matthews. 2011. Dietary supplementation of selenium in inorganic and organic forms differentially and commonly alters blood and liver selenium concentrations and liver gene expression profiles of growing beef heifers. *Biol. Trace Elem. Res.* 140:151–169. doi:10.1007/s12011-010-8685-2.

Lyons, P. C., R. D. Plattner, and C. W. Bacon. 1986. Occurrence of peptide and clavine ergot alkaloids in tall fescue grass. *Science* 232:487–489. doi:10.1126/science.3008328.

Matthews, J. C., Z. Zhang, J. D. Patterson, P. J. Bridges, A. J. Stromberg, and J. A. Boling. 2014. Hepatic transcriptome profiles differ among maturing beef heifers supplemented with inorganic, organic, or mixed (50% inorganic: 50% organic) forms of dietary selenium. *Biol. Trace Elem. Res.* 160:321–339. doi:10.1007/s12011-014-0050-4.

McClure, T. J., G. J. Eamens, and P. J. Healy. 1986. Improved fertility in dairy cows after treatment with selenium pellets. *Aust. Vet. J.* 63:144–146. doi:10.1111/j.1751-0813.1986.tb02952.x.

McLeod, K. R., and R. L. Baldwin. 2000. Effects of diet forage: concentrate ratio and metabolizable energy intake on visceral organ growth and in vitro oxidative capacity of gut tissues in sheep. *J. Anim. Sci.* 78:760–770. doi:10.2527/2000.783760x.

NASEM. 2016. *Nutrient requirements of beef cattle. Eighth revised edition.* Washington, DC: The National Academies Press.

Nicholson, J. W. G., R. E. McQueen, and R. S. Bush. 1991. Response of growing cattle to supplementation with organically bound or inorganic sources of selenium or yeast cultures. *Can. J. Anim. Sci.* 71:803–811. doi:10.4141/cjas91-095.

Patterson, J. D., W. R. Burris, J. A. Boling, and J. C. Matthews. 2013. Individual intake of free-choice mineral mix by grazing beef cows may be less than typical formulation assumptions and form of selenium in mineral mix affects blood Se concentrations of cows and their suckling calves. *Biol. Trace Elem. Res.* 155:38–48. doi:10.1007/s12011-013-9768-7.

Porter, J. K., C. W. Bacon, and J. D. Robbins. 1979. Ergosine, ergosinine, and chanoclavine I from *Epichloë typhina*. *J. Agric. Food Chem.* 27:595–598. doi:10.1021/jf60223a045.

Rice, R. L., G. G. Schurig, and D. J. Blodgett. 1988. Evaluation of physiologic indices in mice vaccinated with protein-ergotamine conjugates and fed an endophyte-infected fescue diet. *Am. J. Vet. Res.* 59:1258–1262.

Schillo, K. K., L. S. Leshin, J. A. Boling, and N. Gay. 1988. Effects of endophyte-infected fescue on concentrations of prolactin in blood sera and the anterior pituitary and concentrations of dopamine and dopamine metabolites in brains of steers. *J. Anim. Sci.* 66:713–718. doi:10.2527/jas1988.663713x.

Schuennemann, G. M., J. L. Edwards, F. M. Hopkins, N. R. Rohrbach, H. S. Adair, F. N. Scenna, J. C. Waller, J. W. Oliver, A. M. Saxton, and F. N. Schrick. 2005. Fertility aspects in yearling beef bulls grazing endophyte-infected tall fescue pastures. *Reprod. Fertil. Dev.* 17:479–486. doi:10.1071/rd05005.

Schultze, A. E., B. W. Rohrbach, H. A. Fribourg, J. C. Waller, and J. W. Oliver. 1999. Alterations in bovine serum biochemistry profiles associated with prolonged consumption of endophyte-infected tall fescue. *Vet. Hum. Toxicol.* 41:133–139.

Settivari, R. S., S. Bhussari, T. Evans, P. A. Eichen, L. B. Hearne, E. Antoniou, and D. E. Spiers. 2006. Genomic analysis of the impact of fescue toxicosis on hepatic function. *J. Anim. Sci.* 84:1279–1294. doi:10.2527/2006.8451279x.

Solovyev, N. D. 2015. Importance of selenium and selenoprotein for brain function: from antioxidant protection to neuronal signalling. *J. Inorg. Biochem.* 153:1–12. doi:10.1016/j.inorgbio.2015.09.003.

Strickland, J. R., M. L. Looper, J. C. Matthews, C. F. Rosenkrans, Jr, M. D. Flythe, and K. R. Brown. 2011. Board-invited review: St. Anthony’s Fire in livestock: causes, mechanisms, and potential solutions. *J. Anim. Sci.* 89:1603–1626. doi:10.2527/jas.2010-3478.

Wahlen, R., L. Evans, J. Turner, and R. Hearn. 2005. The use of collision/reaction cell ICP-MS for the determination of elements in blood and serum samples. *Spectroscopy* 20:84–89.