

YEAST CELL WALL SUPPLEMENTATION ALTERS THE PERFORMANCE AND  
HEALTH OF NEWLY RECEIVED CROSSBRED HEIFERS

By

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## **ABSTRACT**

Many natural feed additives have been evaluated to determine their effectiveness on improving cattle health and performance. One such feed additive is yeast and yeast by-products. Yeast and yeast cell wall supplementation have been reported to improve immune function of host animals, as well as offer advantages in performance traits such as ADG and DMI. The objective of the first study was to determine the effects of supplementing yeast cell wall (YCW) on heifer performance during a 56-d receiving period, as well as performance following a mild endotoxin, lipopolysaccharide (LPS), challenge along with heat stress. A second study was designed to determine the effect of feeding YCW products on the physiological and acute-phase responses of heifers to a LPS challenge. Finally, a third experiment was held in conjunction with the second experiment to evaluate the effects of YCW on the metabolic response of heifers during an LPS challenge.

Cattle in Experiment 1 were sorted by source on arrival. A source x treatment interaction was detected, and data were interpreted accordingly. Results from Source 1 showed that supplementation of YCW-C improved ADG from d 0 to 28 and d 0 to 42. The DMI was increased in YCW-C heifers from d 0 to 42, as well as d 14 to 28 and d 28 to 42. Within Source 2, a linear effect for YCW-A and -AA was detected for d 14 BW, d 0 to 14 ADG, and d 0 to 14 G:F. Following the LPS challenge, YCW C was superior in terms of ADG as well as feed efficiency within Source 1. These results suggest that supplementation of YCW-C may be advantageous during the receiving period, as well as during times of immune challenges and heat stress. The linear effects of YCW-A and -

AA in Source 2 would suggest the higher dose of 5 g/head·d may be more beneficial during the first 14 d on feed.

In experiment 2, heifers receiving YCW-C maintained lower vaginal temperature post-LPS than control (CON) heifers as well as YCW A heifers. Sickness behavior scores (SBS) increased post-LPS but were not affected by treatment. Cortisol concentrations were greatest in CON heifers post LPS compared with YCW-A and -C. Concentrations of interferon- $\gamma$  (IFN- $\gamma$ ) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) increased post-LPS but were not affected by treatment. Serum interleukin-6 (IL-6) concentrations increased post-LPS and were greater in CON heifers than in YCW-A and -C heifers. Together these data indicated that YCW supplementation can decrease the acute-phase and physiological response of heifers to an endotoxin challenge.

Experiment 3 revealed differences in metabolism of heifers in response to the LPS challenge. Post-LPS, glucose increased and was less in YCW-A than in CON and YCW-C heifers. Post-LPS, insulin also increased and was greater in YCW-A and YCW-C than in CON. Post-LPS, non-esterified fatty acid (NEFA) concentrations were lower in YCW-C heifers compared with CON and YCW-A. Pre-LPS, blood urea nitrogen (BUN) concentrations were greater in YCW-A heifers than in CON, and post-LPS concentrations greater in YCW-A than in CON and YCW-C. These data indicate that YCW products can enhance the metabolic response of heifers during an immune challenge without mobilizing body tissue for energy.



Overall, it is evident that YCW supplementation can alter performance, immune response, and metabolism of stressed cattle. Thus, YCW may be a valuable tool for cattle feeders in today's industry.

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## **CHAPTER I**

### **INTRODUCTION**

The receiving period is one of the most important phases of beef production. This period is a crucial transition time in which proper management can substantially increase efficiency of production and profitability. During the receiving period, cattle experience stress from many different sources such as weaning, transportation, feed and water deprivation, commingling, exposure to new pathogens, etc. As a result of this stress, cattle immunity can be compromised (Blecha et al., 1984), and performance suffers. Bovine respiratory disease (BRD) is the most common cause of cattle morbidity and mortality during the receiving period. Treatment costs during this time can be devastating to costs of gain and greatly affect the overall profitability of an operation. Buhman et al. (2000) reported that most cattle are treated for BRD by d 27 of the receiving period. Treatment for BRD was consistently associated with decreased performance (Schneider et al., 2009; Bateman et al., 1990; and Gardner et al., 1999). Therefore, management strategies must be put in place to ease this transition period, improve and maintain the health status of newly-received cattle, and increase profitability.

Various antibiotics have been given for treatment of sick individuals or groups of at risk cattle for prevention of sickness and improved performance. The use of these antibiotics has contributed to an efficient and profitable feeding industry. Nonetheless, a growing concern over antibiotic resistance has resulted in a movement to limit use of antibiotics in livestock management and nutrition, which creates a market for other natural nutritional supplements.

Probiotics, direct-fed microbials, and other feed additives can offer advantages in terms of overall digestive tract health. The term probiotic has been defined as “a live microbial feed supplement which beneficially affects the host by improving its intestinal microbial balance” (Fuller, 1989). Eicher et al. (2010) reported that dietary supplements can alter the immune system and assist calves during the receiving period when stress is typically high. *Saccharomyces cerevisiae* is a probiotic yeast studied for its beneficial effects on animal growth, host immune function, and inhibition of pathogen adhesion (Jurgens et al., 1997; Perez-Sotelo et al., 2005). Yeast supplementation can be in the form of live yeast, yeast cell wall components, and yeast culture. Live yeast would be a viable yeast cell. Yeast cell wall components include mannan and  $\beta$ -glucan, and yeast culture includes the yeast as well as the medium in which it was grown. The effects of yeast supplementation on animal performance have been researched extensively throughout the last century. Yeast supplementation increased milk production in dairy cows (Bilek and Hynek, 1931), enhanced DMI in dairy cows (Wohlt et al., 1998; Dann et al., 2000), and increased DMI and ADG of stress calves (Phillips and VonTungeln, 1985). Cole et al. (1992) reported greater DMI following an immune challenge and quicker recovery from sickness in calves fed yeast culture. Yeast components, such as yeast cell wall, have also been reported to improve animal immune function and performance. Ghosh et al. (2011) reported improved feed conversion as well as a decrease in *Escherichia coli* in the digesta of broilers. Cell wall components of yeast offer benefits in terms of immune function of the host animal. Bacterial adhesion to intestinal epithelial cell depends on the mucopolysaccharide outer layer of the bacteria

and the similar layer on the intestinal cells (Fuller and Brooker, 1974). Firon et al. (1983) showed that the mannan component of yeast cell wall is capable of binding to receptors of pathogenic bacteria such as *E. coli* and *Salmonella*, thereby preventing adhesion and colonization in the intestine. It has also been reported that  $\beta$ -glucan components have the ability to stimulate the release of cytokines, such as tumor necrosis factor- $\alpha$  (Majtán et al., 2005).

With the available information regarding yeast and yeast cell wall supplementation, it is clear that it could be a valuable tool as a feed additive in today's livestock feeding industry. The receiving period is one such area that could benefit from the use of these supplements, by improving calf immune function and performance during a time of stress and transition.

## **CHAPTER II**

### **LITERATURE REVIEW**

The receiving period into the feedlot is perhaps the most critical time during the feeding period. Calves experience tremendous amounts of stress during this time from weaning, transportation, exposure to new pathogens, etc. The combination of these factors can have a negative effect on calf performance and health. By increasing intake and improving immune system function during the receiving period, performance traits such as gain and feed efficiency can be positively affected throughout the entire feeding period, thereby increasing profitability.

Yeast cell wall supplementation has been proven to have positive effects on cattle performance during the receiving period. Components of the cell wall include mannan oligosaccharides (mannan) and  $\beta$ -glucan components. The mannan component is capable of binding to pathogenic bacteria and ultimately aid in clearance of pathogens from the gastrointestinal tract. The  $\beta$ -glucan component interacts with the immune system to enhance its reaction capabilities. Yeast cell wall supplementation contributes to overall digestive tract health and improved immune system function, which in turn contributes to improved performance of the host animal.

#### **Receiving Cattle**

The receiving phase is a very important time for cattle during the feedlot period. There are many opportunities for improvement in this crucial period. Calves experience stress during this time from weaning, transportation, feed and water deprivation,

commingling, and exposure to new pathogens. Blecha et al. (1984) reported that stress can have negative effects on the immune system during a time when calves may be exposed to new pathogens as a result of commingling. Feed intake by stressed calves is low (Galyean and Hubbert, 1995; Cole, 1996), which can add to the negative effects of stress on immune function. Stressed beef calves seem to have an altered eating pattern compared with their unstressed counterparts (Lofgreen, 1983). Loerch and Fluharty (2000) suggested that when calves are commingled in the feedlot, the social hierarchy is destroyed, and additional stress is imposed. In neonate and in stressed calves, the microbial population is in transition and extremely sensitive, and abrupt changes in diet or the environment can cause alterations in microbial populations in the gastrointestinal tract (Savage, 1977). Stress can alter microorganisms in the rumen and lower gut (Williams and Mahoney, 1984), resulting in decreased performance and increased morbidity and mortality. Results of studies have indicated that modifications of the receiving diet can offer advantages in health, performance, and DMI of stressed calves (Cole, 1982; Hutcheson, 1988; Lofgreen, 1988). Management practices can be implemented to limit stress, develop an adequate immune system, and improve performance of newly received calves. Dietary supplements can alter the immune system and assist calves during transition periods that are associated with frequent managerial stressors, such as processing, diet changes, etc. (Eicher et al., 2010). By improving the health status of calves, profitability can be increased as a result of increasing overall performance and lowering treatment costs. Buhman et al. (2000) reported that most cattle are treated for Bovine Respiratory Disease (BRD) on or before day 27 of the



receiving period. Bovine respiratory disease has been reported to cost the industry \$750 million annually (Griffin, 1997). The incidence of BRD was reported as 14.4% by USDA-APHIS (2001), from a study of feedlots from 12 states in 1999. Treatment for BRD was associated with a decrease of  $0.37 \pm 0.03$  kg in acclimation ADG and  $0.07 \pm 0.01$  in overall ADG (Schneider et al., 2009), results that are similar to those of Bateman et al. (1990) and Gardner et al. (1999). Schneider et al. (2009) reported that greater than 71% of cattle that were never treated graded Choice or better, whereas cattle treated once, twice, and thrice or more graded Choice or greater 57, 55, and 52%, respectively. When untreated cattle are compared with the chronically ill cattle that were treated at least 3 times, the frequency of cattle that fell within the Standard grade was 5 times greater (Schneider et al., 2009). McNeill et al. (1996) reported similar findings. When untreated cattle were compared with BRD treatments 1, 2, and 3+, there was a difference of \$23.23, \$30.15, and \$54.01, respectively, in carcass value (Schneider et al., 2009).

## **Yeast Supplementation**

### **""Performance**

Past research has indicated that supplementation of yeast and yeast components can have positive effects on animal performance. Bilek and Hynek (1931) obtained greater milk production in dairy cows when irradiated yeast was added to the winter ration. Increased DMI has been reported in dairy cows in response to live yeast supplementation (Wohlt et al., 1998; Dann et al., 2000). Phillips and VonTungeln (1985) reported that yeast culture increased DMI and daily gain by stressed calves in 2 trials but

had no effect on performance in 2 other trials. Morbid calves fed yeast culture responded more favorably to antibiotic therapy and spent fewer days in the hospital pen than did control calves. Data from an infectious bovine rhinotracheitis virus (IBRV) challenge indicated that morbid calves fed yeast culture had greater feed intakes than control calves (Cole et al., 1992). Results of experiments using yeast culture in diets of stressed calves are highly variable, as are results using nonstressed animals. Under some circumstances yeast culture seems to have beneficial effects on the health and performance of stressed calves; however, the proper circumstances under which yeast or yeast product supplementation is beneficial remain to be determined (Cole et al., 1992). Gill et al. (1987) suggested that extremely healthy calves and extremely sick calves might be less likely to respond to direct-fed microbials (DFM) treatment. Yeast cell wall (YCW) products improved feed conversion rate of broilers, and the effects were comparable to those obtained with antibiotic growth promoters (Ghosh et al., 2011). Yeast cell wall decreased *E. coli* in the digesta of broilers (Ghosh et al., 2011). Distribution of enteric bacteria in the digesta and on the mucosal surface possibly explains the better feed efficiency of broilers in the yeast and YCW-treated groups (Ghosh et al., 2011). Yeast culture had a quadratic effect on serum urea N concentration on d 7 and 28. Serum urea N concentrations increased as yeast culture concentration increased from 0 to 1.125% of the diet, then decreased at 1.5% of the diet. Yeast culture had a quadratic effect on serum FFA concentrations on d 7, and on d 56 calves fed yeast culture had lower FFA concentrations than did controls (Cole et al., 1992). Lambs fed yeast culture had greater

apparent DM and N digestibility, N retention, and Na absorption than lambs fed the control diet (Cole et al., 1992).

#### **Health**

The host immune system can be classified as either nonspecific (innate) or specific (adaptive) immune responses. Innate immunity includes physical/chemical barriers. Acquired immunity is induced by natural exposure or vaccination (Abbas et al., 1991). Besides its role in digestion and absorption, the digestive tract serves as a defense mechanism for the host animal against pathogens in feed and other ingesta. Immune cells in the gut, such as macrophages, natural killer cells, and neutrophils, can be activated to combat pathogenic organisms. Interleukins 1 and 6, TNF- $\alpha$ , interferons, and other molecules contribute to the acute-phase immune response and can help initiate the development of specific immune responses. One of the methods to decrease intestinal colonization by pathogenic microbes is to use probiotic organisms for competitive exclusion of the former from the gut. Probiotics quickly introduce a commensal micro flora in chicks and decrease the number of the enteric pathogens (Timmerman et al., 2006). *Lactobacilli* and yeasts (*Saccharomyces* spp.) are probably the most widely used probiotic microorganisms in the animal feed industry.

Apart from the live yeast, the yeast cell wall has many possibilities to offer as a growth and immune modulator. The yeast cell wall contains polysaccharides such as mannans and beta-glucans, which can help in establishing a healthy population of microbes in the gastrointestinal tract (Santin et al., 2001). Because of the content of the

active polysaccharides B-D-glucan and alpha-D-mannan, application of yeast cell wall products as feed supplements to pigs led to beneficial results such as enhancing weanling piglets protection from bacterial infections and increased weight gain (Kim et al., 2000; LeMieux et al., 2003; Davis et al., 2002, 2004; Miguel et al., 2004; Rozeboom et al., 2005). Prepared derivatives of (1 $\rightarrow$ 3)-B-D-glucan isolated from the cell walls of baker's yeast *Saccharomyces cerevisiae* have the ability to stimulate release of cytokines, such as TNF- $\alpha$  from macrophages (Majtan et al. 2005). Administration of B-D-glucan led to enhanced T cell interferon-gamma release in swine, which resulted in increased protection against porcine reproductive and respiratory syndrome virus (Xiao et al., 2004) and increased resistance of pigs and newborn piglets against bacterial endotoxin (Eicher et al., 2006; Li et al., 2006). Oyofe et al. (1989) reported that the mannans present in yeast cell wall structurally simulate the gut intestinal receptors containing D-mannose, which may bind with Gram-negative bacteria with fimbriae like *E. coli* and *Salmonella*. Flemming et al. (2004) reported that these bacteria might decrease nutrient absorption by increasing nutrient passage rate and interfere with intestinal tissue turnover. Mannose-specific lectins predominate in many intestinal bacterial pathogens and by binding to the mannose-rich epithelial surface of gut and intestines the mannan component of yeast cell wall can mediate adherence and subsequent colonization and infection (Baumler et al., 1997). Alpha-D-Mannan binds to such mannose-specific lectin-type receptors (Type 1 fimbriae) of enteropathogenic bacteria such as *E. coli* and *Salmonella spp.*, and in this way, it serves as a decoy and prevents adhesion to the mannose-rich surface

blycoproteins of villi and subsequent colonization and dissemination of bacterial pathogens (Firon et al., 1983).

#### **""Heat Stress**

Any beneficial effects of yeast culture may be more pronounce when the animal is subjected to heat stress, either via elevated ambient temperatures or fever (Cole et al., 1992).

It was suggested by Arambel and Ket (1990) that yeast products might be more effective under stress rather than in normal conditions. Feeding a culture of *S. cerevisiae* to mid-lactation dairy cows during summer improved efficiency (Schingoethe et al., 2004), which suggests that yeast culture can benefit cows subjected to heat stress. Results indicate that supplemental yeast culture improved lactation performance of dairy cows exposed to heat stress by increasing milk yields (Bruno et al., 2008). Williams et al. (1987) noted an improvement in performance of heat-stressed lambs when yeast culture was added to the diet.

#### **""Mode of Action**

The intestine contains a complex and dynamic microflora including more than 2000 micro-organism species coexisting in a complex equilibrium with the host. This microflora has various effects including metabolic activities, trophic effects on the intestinal epithelium, interactions with the host immune system (Guarner and Malagelada, 2003) and acts as a barrier to prevent colonization by opportunistic and

pathogenic microorganisms (Vollaard and Clasener, 1994). Epithelial cells protect the intestine through different mechanisms such as barrier function, mucus secretion, antibacterial peptide synthesis, and the secretion of cytokines and chemokines (Oswald, 2006). Intestinal epithelial cells are involved in innate immunity as well as in the induction of adaptive immunity at the mucosal surface. Jones and Rutter (1972) suggested that attachment to the intestinal wall was important for enterotoxin-producing strains of *E. coli* to induce diarrhea. Adhesion is thought to be mediated either nonspecifically by physicochemical factors, or specifically by adhesive bacterial surface molecules and epithelial receptor molecules (Holzapfel et al., 1998). The ability of bacteria to adhere to epithelial cells may depend on the interaction between an acidic mucopolysaccharide forming the outer layer of the bacterial cell wall and the similar mucopolysaccharide layer on the intestinal cells (Fuller and Brooker, 1974). Fibrils are often found on adhering bacteria and might reinforce attachment (Fuller and Brooker, 1980).

The term probiotic has been defined as “a live microbial feed supplement which beneficially affects the host by improving its intestinal microbial balance” (Fuller, 1989). Holzapfel et al. (1998) outlined several criteria as keys for DFM: nonpathogenicity, survival through regions of the gut, specificity to the host, and genetic stability. Bacterial DFM have been reported to modify the balance of intestinal microorganisms, adhere to intestinal mucosa and prevent pathogen adherence or activation, influence gut permeability, and modulate immune function (Salimen et al., 1996; Holzapfel et al., 1998). *Saccharomyces cerevisiae* is a probiotic yeast studied for its beneficial effects on

animal growth, host immune function, and inhibition of pathogen adhesion (Jurgens et al., 1997; Perez-Sotelo et al., 2005). *Saccharomyces cerevisiae* has been shown to exert in vitro antagonist effects against *E. coli* (Etienne-Mesmin et al., 2010). *Saccharomyces boulardii*, which is closely related to *S. cerevisiae*, protected hosts through multiple mechanisms such as inhibition of pathogen adhesion (Wu et al., 2008), neutralization of bacterial virulence factors (Castagliuolo et al., 1999), maintenance of epithelial barrier integrity (Czerucka et al., 2000), decreased pathogen-associated inflammation (Mumy et al., 2007), and stimulation of the immune system (Rodrigues et al., 2000).

Administration of the yeast *S. boulardii* has been shown to protect pigs in decreasing enterotoxigenic *E. coli* translocation (Lessard et al., 2009). In vitro studies showed that *S. boulardii* secretes soluble factors that decrease the expression of pro-inflammatory cytokines induced by enteric pathogens (Zanello et al., 2009). Interleukin-6 and IL-8 mRNA levels were up-regulated in presence of killed *S. cerevisiae*, probably as a result of yeast cell wall structures such as  $\beta$ -glucans (Sonck et al., 2010). Experimental studies indicated that *S. boulardii* induces a protection against enteric pathogens (Czerucka and Rampal, 2002; Mumy et al., 2007); modulates the host immune response (Ozkan et al., 2007; Rodrigues et al., 2000); decreases inflammation (Lee et al., 2005; Sougioultzis et al., 2006); inhibits bacterial toxins (Castagliuolo et al., 1999; Tasteyre et al., 2002); and enhances trophic factors such as brush border membrane enzymes and nutrient transporters (Buts et al., 1986; Buts et al., 1994). *Saccharomyces boulardii* acts on the epithelial barrier by improving tight-junction structure and restoring membrane

permeability disrupted by infectious pathogens (Czerucka et al., 2000; Dahan et al., 2003; Mumy et al., 2007).

## **Conclusion**

Numerous research trials have been conducted over the past century on the effectiveness of yeast and yeast cell wall supplementation on cattle performance and health. Results with yeast supplementation have been highly variable; nonetheless, yeast supplementation seems to have beneficial effects on the health and performance of stressed calves on many occasions. Dietary supplements, such as yeast cell wall, can alter the immune system and assist calves during transition periods with frequent managerial stressors (Eicher et al., 2010). There are numerous reports indicating a positive effect on performance of yeast-supplemented cattle during various production phases (Phillips and von Tungeln, 1985; Cole et al., 1992; Wohlt et al., 1998). Yeast cell wall supplementation may be a viable nutritional supplement to producers in today's industry.

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### CHAPTER III

#### YEAST CELL WALL SUPPLEMENTATION ALTERS THE PERFORMANCE AND HEALTH OF BEEF HEIFERS DURING THE RECEIVING PERIOD

##### Abstract

A study was designed to determine the effect of feeding yeast cell wall (YCW) products on feedlot performance of newly received crossbred heifers. Heifers ( $n = 140$ ;  $225 \pm 9.4$  kg) were obtained from commercial sale barns and transported to the Texas Tech University Beef Center in New Deal, TX. Heifers were sorted by source ( $n = 2$ ) on arrival and arranged in a completely randomized block design (35 pens; 7 pens/treatment; 4 heifers/pen). Heifers were separated into treatment groups receiving a Control Diet (CON), YCW A ( $2.5 \text{ g} \cdot \text{hd}^{-1} \cdot \text{d}^{-1}$ ), YCW AA ( $5.0 \text{ g} \cdot \text{hd}^{-1} \cdot \text{d}^{-1}$ ), YCW B ( $2.5 \text{ g} \cdot \text{hd}^{-1} \cdot \text{d}^{-1}$ ), or YCW C ( $2.5 \text{ g} \cdot \text{hd}^{-1} \cdot \text{d}^{-1}$ ) and were fed for 56 d. Daily DMI was recorded and individual BW was collected every 14 d. On d 56, cattle in treatments CON, YCW A, and YCW C were fitted with vaginal temperature (VT) probes. Cattle were re-weighed and challenged with a subcutaneous dose ( $0.5 \text{ } \mu\text{g/kg BW}$ ) of lipopolysaccharide (LPS). A final BW was measured and vaginal probes removed 14 d post-challenge. A significant source  $\times$  treatment interaction was detected, and data were separated accordingly. In Source 1, at d 28, YCW-A ( $278 \pm 8.1$  kg) and YCW C ( $285 \pm 8.1$  kg) showed a greater increase in BW compared to CON ( $272 \pm 8.1$  kg;  $P = 0.03$ ). The YCW-C treatment exhibited a greater BW at d 42 compared with all other treatments ( $P = 0.02$ ). From d 0 to 28, YCW-A ( $1.87 \pm 0.102$  kg) and YCW-C ( $2.10 \pm 0.102$  kg) had greater ADG compared with CON ( $1.65 \pm 0.102$  kg;  $P = 0.03$ ). The YCW-C treatment showed improved ADG from d 0 to 42

compared with all other treatments ( $P < 0.01$ ). Dry matter intake was increased for YCW-AA ( $7.27 \pm 0.233$  kg) and YCW-C ( $7.92 \pm 0.233$  kg) compared with CON ( $6.75 \pm 0.233$  kg;  $P = 0.04$ ) for d 0 to 42. The YCW-C treatment had greater DMI vs. CON from d 14 to 28 and d 28 to 42 ( $P = 0.05$  and  $0.02$ , respectively). Cumulative G:F was lower for YCW-B compared with all other treatments ( $P = 0.03$ ). In Source 2, a linear effect for YCW-A was detected from d 0 to 14 in BW, ADG, and G:F ( $P = 0.01$ ,  $0.02$ , and  $0.03$ , respectively). Following the subcutaneous LPS challenge, in Source 1, YCW-C exhibited greater ADG ( $P < 0.01$ ) and G:F ( $P = 0.01$ ) compared with CON. There was an increase in VT in all treatments post-LPS ( $P < 0.01$ ), with YCW-C ( $39.1 \pm 0.01^\circ\text{C}$ ) maintaining greater VT post-LPS than CON ( $38.9 \pm 0.01^\circ\text{C}$ ) and YCW-A ( $38.9 \pm 0.01^\circ\text{C}$ ;  $P < 0.05$ ). In Source 2, no significant differences in performance were observed. There was an increase in VT in all treatments post-LPS ( $P < 0.01$ ), with YCW-C ( $38.9 \pm 0.02^\circ\text{C}$ ) maintaining greater VT post-LPS than CON ( $38.8 \pm 0.02^\circ\text{C}$ ) and YCW-A ( $38.8 \pm 0.02^\circ\text{C}$ ;  $P < 0.05$ ). Ambient temperature was extremely high during this study (greater than  $45^\circ\text{C}$  at certain times), indicating a period of high heat stress. Collectively these data suggest that YCW supplementation can offer advantages in BW gain and feed intake during the receiving period as well as affect the physiological response to a mild endotoxin challenge during high heat stress.

## **Introduction**

The receiving period into the feedlot is perhaps the most critical time during the feeding period. Calves may experience stress during this time from weaning,

transportation, exposure to new pathogens, etc. Blecha et al. (1984) reported that stress can have negative effects on the immune system during a time when calves may be exposed to new pathogens as a result of commingling. Buhman et al. (2000) reported that most cattle are treated for BRD by d 27 of the feeding period. Treatment for BRD is consistently associated with decreased performance (Schneider et al., 2009; Bateman et al., 1990; and Gardner et al., 1999). By improving immune system function and increasing intake during the receiving period, performance traits such as gain and feed efficiency can be positively affected throughout the entire feeding period, thereby increasing profitability.

Eicher et al. (2010) reported that dietary supplements can alter the immune system and assist calves during the receiving period when stress is usually high. *Saccharomyces cerevisiae* is a live yeast studied for its beneficial effects on animal growth, immune function, and inhibition of pathogen adhesion (Jurgens et al., 1997; Perez-Sotelo et al., 2005). Yeast cell wall supplementation has proved to have positive effects on cattle performance during the receiving period. Phillips and von Tungen (1985) reported that yeast culture increased DMI and ADG of stressed calves in two trials. Firon et al. (1983) showed that the mannan component of yeast cell wall is capable of binding to receptors of pathogenic bacteria such as *E. coli* and *Salomonella*, thereby preventing adhesion and colonization in the intestine. It has also been reported that  $\beta$ -glucan components have the ability to stimulate the release of cytokines, such as tumor necrosis factor- $\alpha$  (Majtán et al., 2005).

The objectives of this study were to: 1) examine the effects of 3 YCW products on animal performance and health during a 56-d receiving period; and 2) determine the effects of these products on animal performance and response to a mild endotoxin challenge.

## **Materials and Methods**

All procedures involving live animals were approved (#10085-11) by the Texas Tech University Animal Care and Use Committee.

### ***""Cattle***

One hundred sixty-two crossbred beef heifers, purchased from auction barns in San Saba and Fredericksburg, TX, arrived in 2 loads (received April 15 and April 21, 2011) at the Texas Tech University Beef Center at New Deal, Texas. Off truck weights were  $225.6 \pm 8.33$  kg and  $224.4 \pm 9.62$  kg, for loads 1 and 2 respectively. The cattle were housed in dirt pens with ad libitum access to sudangrass hay on arrival and processed the following morning. Initial processing of both groups (on the mornings of April 16 and April 22) included: 1) measurement of BW [Pearson squeeze chute, Thedford, NE; set on 4 electronic load cells (Gallagher Smart Scale Systems, North Kansas City, MO; readability of  $\pm 0.91$  kg); scales were calibrated with 454 kg of certified weights (Texas Department of Agriculture) before use]; 2) individual identification by ear tag; 3) vaccination with an IBR-BVD-PI<sub>3</sub>-BRSV vaccine (Vista 5, Intervet/Schering-Plough Animal Health); 4) vaccination with a clostridial bacterin toxoid (Vision 7, with SPUR,

Intervet/Schering-Plough Animal Health); 5) treatment for internal and external parasites with ivermectin pour-on (Durvet, Inc.); and 6) antibiotic treatment with Micotil (Elanco Animal Health, Greenfield, IN). Heifers were allowed ad libitum access to sudangrass hay until the beginning of the trial, and implanted with Ralgro (36 mg of zeranol, Intervet/Schering-Plough Animal Health) on d 0.

#### ***""Experimental Design, Treatment, and Pen Assignment***

Load 1 was re-weighed on d 0 (April 20, 2011); Load 2 was re-weighed on d 0 (April 22). Heifers were blocked by BW within their respective load (4 blocks in load 1 and 3 blocks in load 2). Within a block, 5 treatments were assigned to pens using a randomized block design (35 pens; 7 pens/treatment; 4 heifers/pen). Treatments were as follows: Control Diet (**CON**), YCW A ( $2.5 \text{ g} \cdot \text{hd}^{-1} \cdot \text{d}^{-1}$ ), YCW AA ( $5.0 \text{ g} \cdot \text{hd}^{-1} \cdot \text{d}^{-1}$ ), YCW B ( $2.5 \text{ g} \cdot \text{hd}^{-1} \cdot \text{d}^{-1}$ ), and YCW C ( $2.5 \text{ g} \cdot \text{hd}^{-1} \cdot \text{d}^{-1}$ ). All yeast cell wall products were derived from *Saccharomyces cerevisiae*. On d 0, initial BW was recorded, and cattle were sorted into their home pen (3 m x 9.1 m pipe feedlot pens; with a dirt floor and concrete aprons around water troughs and feed bunks).

#### ***""Management***

Cattle were fed once daily in the morning (0700 to 0800 h) and adjustments in feed delivery for each pen were made to ensure ad libitum access to feed, wasting as little feed as possible. The feeding order throughout the trial was in numerical pen order. Feed was mixed and delivered daily in a drag type Rotomix feed wagon (Dodge City, KS).



Treatments were top-dressed in feed bunks daily at a rate of 91 g per heifer. Cattle were fed a 65% concentrate diet initially (19 d for Load 1; 21 d for Load 2) and a 75% concentrate diet for the next 14 d. Concentrate was increased to 85% and fed for the remainder of the trial (23 d for Load 1; 21 d for Load 2). Feed was offered at 95% of the previous day's delivery on each transition day. Diets were formulated to meet or exceed NRC (1996) recommendations for nutrients (Table 1).

All premixes were made at the Texas Tech University Burnett Center Feed Mill in a paddle type mixer (Marion Mixers Inc.). The supplement premix included standard trace minerals, vitamins, and monensin (Rumensin 90, Elanco Animal Health). Ingredients for the yeast cell wall premix included ground corn, corn oil, and yeast cell wall (excluded in the control premix). Yeast cell wall was measured out into an individual clean bowl on a Mettler (Novatech UK Limited, United Kingdom) electronic balance (accuracy  $\pm 4.5$  g). Corn oil was measured in a similar fashion. Ground corn was measured on an Ohaus (Pine Brook, NJ) electronic balance (accuracy  $\pm 0.1$  g). Ground corn was added first, followed by corn oil, and finally the appropriate quantity and type of yeast cell wall. All ingredients were mixed for 5 minutes. Once mixing was finished, premixes were divided evenly into 5 labeled barrels (per treatment). Samples were taken at the beginning, middle, and end of allocation to barrels. The mixer was swept and blown out with pressurized air between each premix to help decrease contamination. Yeast cell wall premixes were weighed out for each pen daily into plastic containers with corresponding numbered lids. The yeast cell wall premixes were top dressed at a rate of 91 g/heifer daily. Diet samples were taken weekly and stored frozen

until sent to Servi-Tech (Amarillo, TX) for analysis of chemical composition or dried in a forced-air oven at 100°C for approximately 24 h to determine DM content. Weights for DM determination were taken on an Ohaus (Pine Brook, NJ) electronic balance (accuracy  $\pm 0.1$ g).

At approximately 0600 h on the morning of each weigh day (d 14, 28, 42, and 56) feed refusals were collected and weighed, and a sample of remaining feed was dried as described above to determine the DM content. The DMI by each pen was calculated by subtracting the quantity of dry feed unconsumed at the end of every 14 d from the total dietary DM delivered to each pen during that period.

Unshrunk BW measurements were taken every 14 d for 56 d before the daily feeding between 0630 and 0800 h. On d 14, cattle were revaccinated (Vista 5, Intervet/Schering-Plough Animal Health). Cattle health was evaluated daily between 0700 and 0800 for signs of illness or injury. Cattle diagnosed for respiratory disease were treated with Resflor GOLD (florfenicol and flunixin meglumine, Intervet Schering-Plough Animal Health) at a rate of 6 mL per 45.4 kg, subcutaneously. Cattle requiring a second treatment were treated with Draxxin (Pfizer Animal Health) at a rate of 1 mL/40 kg, subcutaneously. Lamé cattle were treated with Noromycin 300 LA (oxytetracycline, Norbrooke Labs, Lenexa, KS) at a rate of 6 mL per 45.4 kg, subcutaneously, and Banamine (flunixin meglumine, Intervet Schering-Plough Animal Health) at a rate of 1 mL per 45.4 kg, intramuscularly. All cattle were immediately returned to their home pen after treatment.

On d 56, cattle in treatments CON, YCW-A, and YCW-C were fitted with vaginal temperature (VT) probes. Cattle were re-weighed and challenged with a subcutaneous dose (0.5µg/kg BW) of lipopolysaccharide on d 63 (Load 1) and d 65 (Load 2). A final BW was measured and vaginal probes removed on d 77 and d 79.

### ***Statistical Analyses***

All BW used for analysis were unshrunk weights. All performance data were analyzed as a completely randomized block design using the MIXED procedure of SAS (SAS Inst., Inc., Cary, NC). Treatment was included as a fixed effect, and block nested with source was included as a random effect. A  $P$ -value of  $\leq 0.05$  was considered significant.

## **Results**

### ***Performance***

A significant source x treatment interaction was detected, and data were separated accordingly. In Source 1, at d 28, YCW-A and YCW-C resulted in greater BW compared with CON ( $P = 0.03$ ). The cattle in YCW-C treatment exhibited a greater BW at d 42 compared with all other treatments ( $P = 0.02$ ). From d 0 to 28, YCW-A and YCW-C had higher ADG compared with CON ( $P = 0.03$ ). The YCW-C cattle had greater ADG from d 0 to 42 than cattle in all other treatments ( $P < 0.01$ ), and DMI was greater for YCW-AA and YCW-C than for CON ( $P = 0.04$ ) from d 0 to 42. The YCW-C treatment resulted in greater DMI vs. CON from d 14 to 28 and d 28 to 42 ( $P = 0.05$  and  $0.02$ , respectively).

Cumulative G:F was lower for YCW B compared to all other treatments ( $P = 0.03$ ). In Source 2, a linear effect for YCW A was detected from d 0 to 14 in BW, ADG, and G:F ( $P = 0.01, 0.02$ , and  $0.03$ , respectively).

### ***Subcutaneous LPS Challenge***

In Source 1, supplementing YCW-C resulted in greater ADG ( $P < 0.01$ ) and G:F ( $P = 0.01$ ) post-LPS compared with CON. There was an increase in VT in all treatments post-LPS ( $P < 0.01$ ), with YCW-C ( $39.1 \pm 0.01^{\circ}\text{C}$ ) maintaining greater VT post-LPS than CON ( $38.9 \pm 0.01^{\circ}\text{C}$ ) and YCW-A ( $38.9 \pm 0.01^{\circ}\text{C}$ ;  $P < 0.05$ ). In Source 2, no significant differences in performance were observed post-LPS. There was an increase in VT in all treatments post-LPS ( $P < 0.01$ ), with YCW-C ( $38.9 \pm 0.02^{\circ}\text{C}$ ) maintaining greater VT post-LPS than CON ( $38.8 \pm 0.02^{\circ}\text{C}$ ) and YCW-A ( $38.8 \pm 0.02^{\circ}\text{C}$ ;  $P < 0.05$ ). Ambient temperature was extremely high during this study (greater than  $45^{\circ}\text{C}$  at certain times), indicating a period of high heat stress.

### **Discussion**

The receiving period is a transition phase often associated with managerial stressors. Blecha et al. (1984) reported that stress can have a negative effect on the immune system. By supplementing stressed calves with growth and immune modulators, such as YCW, we can positively affect performance traits such as DMI, ADG, and G:F. Cattle used in this trial came from 2 sources, and noticeable differences in relative condition were detected on arrival. Cattle in Source 1 seemed to be in worse condition in

terms of flesh than cattle in Source 2. More cattle were diagnosed with BRD in Source 1 as well. The difference in condition on arrival and morbidity rates may have reflected differences in background and might help explain the variation in response to YCW supplementation. It has been reported that any beneficial effects of yeast product supplementation may be more pronounced under stress vs. normal conditions (Cole et al., 1992; Arambel and Ket, 1990). Gill et al. (1987) reported that sick calves may be less likely to respond to direct fed microbial supplementation, which may further explain the source x treatment interaction detected in the present trial. Results of Source 1 in this study suggest that YCW supplementation can improve performance of beef heifers during the receiving period. Heifers receiving YCW-A and YCW-C showed the greatest performance advantages over control, specifically during the first 28 d on feed. Buhman et al. (2000) reported that most cattle are treated for BRD by d 27 of the feeding period, and treatment for BRD is consistently associated with decreased performance (Schneider et al., 2009; Bateman et al., 1990; and Gardner et al., 1999). The improved performance of cattle supplemented with YCW-A and YCW-C would suggest that these heifers were able to adapt more quickly to the feedlot setting.

Heifers receiving YCW-C also displayed superior performance following a LPS challenge. Cole et al. (1992) reported that morbid calves fed yeast culture responded better to antibiotic therapy and had greater intakes than control calves following an infectious bovine rhinotracheitis virus challenge. During the present study, calves were also subjected to heat stress immediately following the LPS challenge, with ambient temperatures exceeding 45°C. Cole et al. (1992) suggested that yeast supplementation

may offer advantages during times of heat stress, either via elevated ambient temperatures or fever. The VT response to LPS would be similar to results obtained from other studies (Carroll et al., 2010). Heifers supplemented with YCW-C maintained greater VT post-LPS than control cattle. This increase in VT may be a results of a more active metabolism. These heifers were more efficient during the 2 wk period post-LPS, and a more active metabolism may have had an effect on core body temperature.

Supplementation of YCW might improve the immune response of cattle, which could lead to improved performance and more favorable costs of gain associated with lowered treatment costs. Given the significant source x treatment interaction, it is clear that more studies need to be completed to gain a better understanding. Yeast cell wall supplementation might result in advantages in performance and health and be a valuable tool to today's producers.

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**Table 3.1.** Diet composition

Ingredients, % <sup>1</sup>	% concentrate in diet <sup>1</sup>		
	65 %	75 %	85 %
Corn Grain, Steam Flaked	45.75	57.15	67.90
Cottonseed, Hulls	25.00	15.00	5.00
Alfalfa Hay, Mid Bloom	10.00	10.00	10.00
Cottonseed, Meal - Sol-41%CP	10.50	9.00	7.00
Molasses, Cane	4.00	4.00	4.00
Tallow	1.00	1.00	2.00
Urea	0.55	0.65	0.80
Limestone	0.80	0.80	0.90
MIN-AD	0.40	0.40	0.40
Receiving Supplement <sup>2</sup>	2.00	2.00	2.00

<sup>1</sup>Dry Matter Basis

<sup>2</sup>Supplement for the diet contained (DM basis): 66.383% cottonseed meal; 0.500% Endox® (Kemin Industries, Inc., Des Moines, IA); 0.648% dicalcium phosphate; 10% potassium chloride; 4.167% ammonium sulfate; 15.000% salt; 0.002% cobalt carbonate; 0.196% copper sulfate; 0.083% iron sulfate; 0.003% ethylenediamine dihydroiodide; 0.333% manganese oxide; 0.125% selenium premix (0.2% Se); 0.986% zinc sulfate; 0.010% vitamin A (1,000,000 IU/g); 0.157% vitamin E (500 IU/g); 0.844% Rumensin (176.4 mg/kg; Elanco Animal Health, Indianapolis, IN); and 0.563% Tylan (88.2 mg/kg; Elanco Animal Health). Concentrations in parentheses are expressed on a 90% DM basis.

**Table 3.2.**Source 1-Heifer performance during the receiving period

Item	Control	YCW A	YCW AA	YCW B	YCW C	SEM <sup>1</sup>	<i>P</i> -value
		2.5 g/(heifer·d)	5.0 g/(heifer·d)	2.5 g/(heifer·d)	2.5 g/(heifer·d)		Trt
BW, kg							
Day 0	226	226	226	225	226	8.5	0.60
Day 14	245	248	247	245	251	9.4	0.76
Day 28	272 <sup>a</sup>	278 <sup>b</sup>	273 <sup>ab</sup>	272 <sup>ab</sup>	285 <sup>c</sup>	8.1	0.03
Day 42	300 <sup>a</sup>	305 <sup>a</sup>	306 <sup>a</sup>	300 <sup>a</sup>	317 <sup>b</sup>	8.5	0.02
Day 56	326	336	334	325	340	10.8	0.09
ADG, kg							
0-14	1.40	1.59	1.53	1.47	1.77	0.215	0.79
0-28	1.65 <sup>a</sup>	1.87 <sup>b</sup>	1.70 <sup>ab</sup>	1.66 <sup>ab</sup>	2.10 <sup>c</sup>	0.102	0.03
0-42	1.77 <sup>a</sup>	1.89 <sup>a</sup>	1.90 <sup>a</sup>	1.77 <sup>a</sup>	2.15 <sup>b</sup>	0.063	0.01
0-56	1.79	1.96	1.93	1.79	2.04	0.083	0.12
14-28	1.90	2.14	1.87	1.95	2.30	0.207	0.44
28-42	2.03	1.94	2.30	1.98	2.28	0.160	0.30
42-56	1.85	2.16	2.02	1.74	2.18	0.241	0.51
DMI, kg							
0-14	5.40	5.79	5.88	5.88	5.82	0.285	0.67
0-28	6.24	6.73	6.77	6.75	7.39	0.289	0.09
0-42	6.75 <sup>a</sup>	7.14 <sup>ab</sup>	7.27 <sup>b</sup>	7.16 <sup>ab</sup>	7.92 <sup>c</sup>	0.233	0.04
0-56	7.15	7.48	7.69	7.57	7.73	0.283	0.54
14-28	7.03 <sup>a</sup>	7.61 <sup>a</sup>	7.63 <sup>a</sup>	7.74 <sup>a</sup>	8.55 <sup>b</sup>	0.329	0.05
28-42	7.78 <sup>a</sup>	7.97 <sup>a</sup>	8.25 <sup>a</sup>	7.91 <sup>a</sup>	8.95 <sup>b</sup>	0.230	0.02
42-56	8.36	8.52	8.96	8.42	9.01	0.270	0.19
G:F							
0-14	0.255	0.271	0.260	0.250	0.304	0.0310	0.75
0-28	0.264	0.279	0.252	0.247	0.286	0.0134	0.07
0-42	0.263	0.265	0.262	0.248	0.273	0.0098	0.45
0-56	0.251 <sup>a</sup>	0.262 <sup>a</sup>	0.251 <sup>a</sup>	0.236 <sup>b</sup>	0.264 <sup>a</sup>	0.0061	0.03
14-28	0.271	0.285	0.248	0.254	0.270	0.0320	0.85
28-42	0.261	0.243	0.280	0.249	0.255	0.0191	0.61
42-56	0.222	0.252	0.224	0.208	0.240	0.0242	0.63

<sup>1</sup>Standard error of the difference between the treatment means<sup>a,b</sup>Means with in a row differ ( $P < 0.05$ )

**Table 3.3.** Source 1-YCW A Contrasts

Item	CON	YCW A	YCW AA	SEM <sup>1</sup>	Contrast <i>P</i> -value		
		2.5 g/(heifer·d)	5.0 g/(heifer·d)		0vsY	Linear	Quad.
BW, kg							
Day 0	226	226	226	8.5	0.83	0.95	0.74
Day 14	245	248	247	9.4	0.56	0.69	0.63
Day 28	272	278	273	8.0	0.19	0.65	0.08
Day 42	300	305	306	8.3	0.12	0.16	0.43
Day 56	326	336	334	10.8	0.11	0.20	0.27
ADG, kg							
0-14	1.40	1.59	1.53	0.215	0.56	0.68	0.65
0-28	1.65	1.87	1.70	0.090	0.20	0.65	0.08
0-42	1.77	1.89	1.90	0.055	0.09	0.13	0.43
0-56	1.79	1.96	1.93	0.083	0.11	0.20	0.29
14-28	1.90	2.14	1.87	0.181	0.59	0.93	0.23
28-42	2.03	1.94	2.30	0.139	0.57	0.18	0.22
42-56	1.85	2.16	2.02	0.213	0.32	0.54	0.36
DMI, kg							
0-14	5.40	5.79	5.88	0.285	0.20	0.22	0.63
0-28	6.24	6.73	6.77	0.254	0.09	0.12	0.44
0-42	6.75	7.14	7.27	0.202	0.09	0.09	0.60
0-56	7.15	7.48	7.69	0.283	0.19	0.16	0.85
14-28	7.03	7.61	7.63	0.288	0.10	0.14	0.40
28-42	7.78	7.97	8.25	0.199	0.20	0.12	0.84
42-56	8.36	8.52	8.96	0.237	0.17	0.07	0.59
G:F							
0-14	0.2550	0.2713	0.2596	0.0310	0.79	0.92	0.72
0-28	0.2637	0.2785	0.2524	0.0122	0.87	0.37	0.08
0-42	0.2631	0.2652	0.2623	0.0085	0.95	0.94	0.79
0-56	0.2512	0.2617	0.2512	0.0061	0.45	1.00	0.15
14-28	0.2709	0.2852	0.2477	0.0281	0.89	0.53	0.42
28-42	0.2610	0.2429	0.2795	0.0165	0.99	0.44	0.20
42-56	0.2222	0.2524	0.2244	0.0211	0.52	0.94	0.26

<sup>1</sup>Standard error of the difference between the treatment means

**Table 3.4.**Source 2-Heifer performance during the receiving period

Item	CON	YCW A	YCW AA	YCW B	YCW C	SEM <sup>1</sup>	<i>P</i> -value Trt
		2.5 g/(heifer·d)	5.0 g/(heifer·d)	2.5 g/(heifer·d)	2.5 g/(heifer·d)		
BW, kg							
Day 0	224	224	224	225	224	9.4	0.97
Day 14	239	243	249	246	245	8.1	0.11
Day 28	262	268	271	263	263	10.5	0.87
Day 42	291	293	300	287	287	9.1	0.61
Day 56	321	324	326	320	311	7.5	0.29
ADG, kg							
0-14	1.03	1.30	1.75	1.53	1.46	0.245	0.16
0-28	1.36	1.54	1.65	1.39	1.28	0.256	0.76
0-42	1.59	1.63	1.79	1.48	1.42	0.182	0.52
0-56	1.73	1.78	1.81	1.70	1.54	0.098	0.32
14-28	1.68	1.78	1.56	1.74	1.33	0.346	0.85
28-42	2.05	1.80	2.07	1.66	1.66	0.461	0.89
42-56	2.16	2.22	1.87	2.36	1.85	0.251	0.43
DMI, kg							
0-14	4.56	4.68	4.87	4.40	4.69	0.231	0.40
0-28	5.67	5.75	6.00	5.53	5.62	0.302	0.68
0-42	6.29	6.22	6.45	6.11	6.04	0.326	0.84
0-56	6.84	6.66	6.78	6.59	6.27	0.238	0.51
14-28	7.10	6.92	7.22	6.92	6.54	0.405	0.76
28-42	7.55	7.16	7.34	7.27	6.85	0.520	0.86
42-56	8.26	7.99	7.79	8.02	7.28	0.384	0.43
G:F							
0-14	0.226	0.276	0.360	0.342	0.314	0.0515	0.15
0-28	0.239	0.267	0.273	0.249	0.227	0.0376	0.84
0-42	0.252	0.259	0.278	0.242	0.232	0.0204	0.47
0-56	0.253	0.266	0.266	0.258	0.246	0.0092	0.39
14-28	0.234	0.259	0.211	0.251	0.204	0.0415	0.77
28-42	0.271	0.245	0.281	0.227	0.239	0.0540	0.90
42-56	0.263	0.280	0.239	0.295	0.256	0.0360	0.71

<sup>1</sup>Standard error of the difference between the treatment means

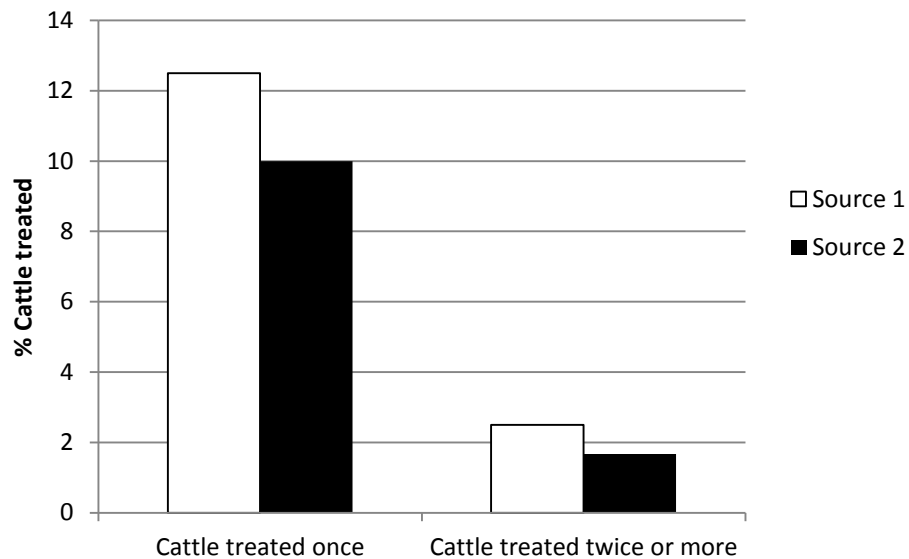
**Table 3.5.** Source 2-YCW A Contrasts

Item	YCW A		YCW AA		Contrast <i>P</i> -value		
	CON	2.5	5.0	SEM <sup>1</sup>	0vsY	Linear	Quad.
		g/(heifer·d)	g/(heifer·d)				
BW, kg							
Day 0	224	224	224	9.4	0.95	1.00	0.90
Day 14	239	243	249	7.9	0.03	0.01	0.69
Day 28	262	268	271	9.3	0.41	0.39	0.89
Day 42	291	293	300	7.9	0.50	0.34	0.73
Day 56	321	324	326	7.5	0.57	0.53	0.96
ADG, kg							
0-14	1.03	1.30	1.75	0.204	0.06	0.02	0.70
0-28	1.36	1.54	1.65	0.209	0.37	0.34	0.89
0-42	1.59	1.63	1.79	0.149	0.52	0.35	0.73
0-56	1.73	1.78	1.81	0.098	0.58	0.54	0.97
14-28	1.68	1.78	1.56	0.282	0.96	0.75	0.65
28-42	2.05	1.80	2.07	0.376	0.80	0.98	0.58
42-56	2.16	2.22	1.87	0.205	0.66	0.34	0.43
DMI, kg							
0-14	4.56	4.68	4.87	0.202	0.26	0.17	0.84
0-28	5.67	5.75	6.00	0.249	0.48	0.34	0.79
0-42	6.29	6.22	6.45	0.267	0.90	0.68	0.65
0-56	6.84	6.66	6.78	0.238	0.69	0.86	0.62
14-28	7.10	6.92	7.22	0.331	0.95	0.76	0.57
28-42	7.55	7.16	7.34	0.426	0.57	0.73	0.59
42-56	8.26	7.99	7.79	0.314	0.36	0.32	0.92
G:F							
0-14	0.226	0.276	0.360	0.0444	0.06	0.03	0.69
0-28	0.239	0.267	0.273	0.0307	0.43	0.45	0.77
0-42	0.252	0.259	0.278	0.0166	0.43	0.30	0.80
0-56	0.253	0.266	0.266	0.0092	0.21	0.26	0.53
14-28	0.234	0.259	0.211	0.0339	0.99	0.64	0.41
28-42	0.271	0.245	0.281	0.0441	0.89	0.87	0.58
42-56	0.263	0.280	0.239	0.0294	0.93	0.57	0.43

<sup>1</sup>Standard error of the difference between the treatment means

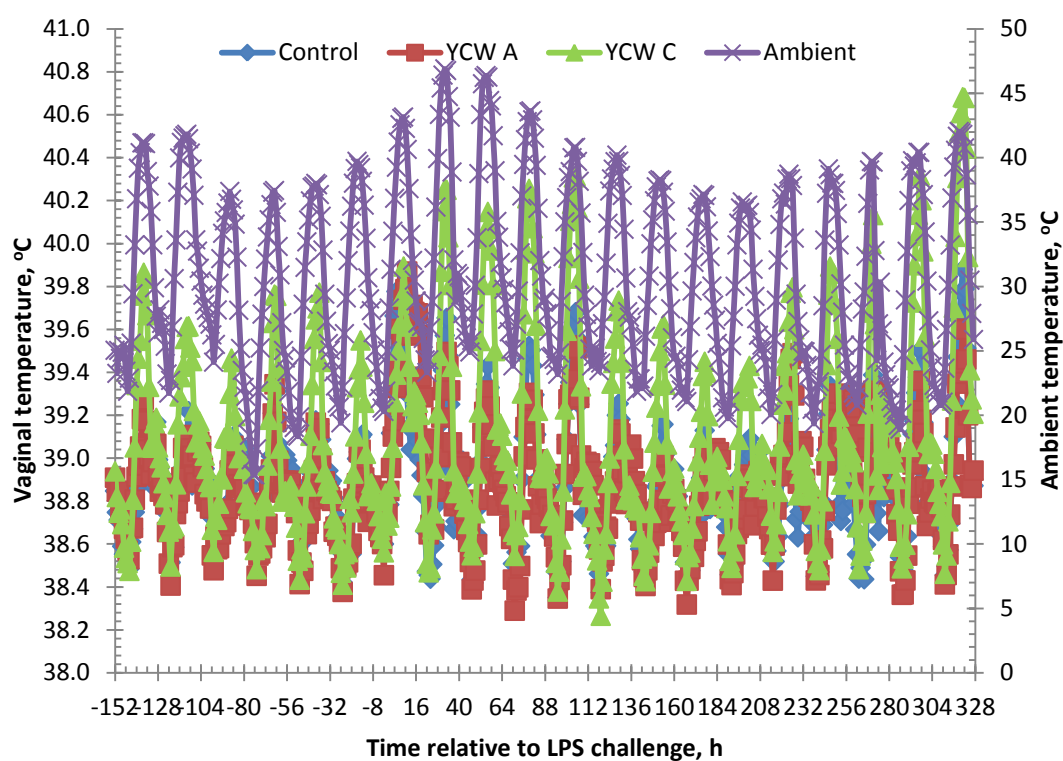
**Table 3.6.** Effects of yeast supplementation on respiratory morbidity during the receiving period

Item	Control	YCW A	YCW AA	YCW B	YCW C
		2.5 g/(heifer·d)	5.0 g/(heifer·d)	2.5 g/(heifer·d)	2.5 g/(heifer·d)
Source 1					
Cattle treated at least once, %	18.75	6.25	12.50	6.25	18.75
Cattle treated at least twice, %	0.00	0.00	0.00	6.25	6.25
Source 2					
Cattle treated at least once, %	12.50	0.00	6.25	12.50	6.25
Cattle treated at least twice, %	0.00	0.00	0.00	0.00	6.25

**Figure 3.1.** Effect of source on morbidity

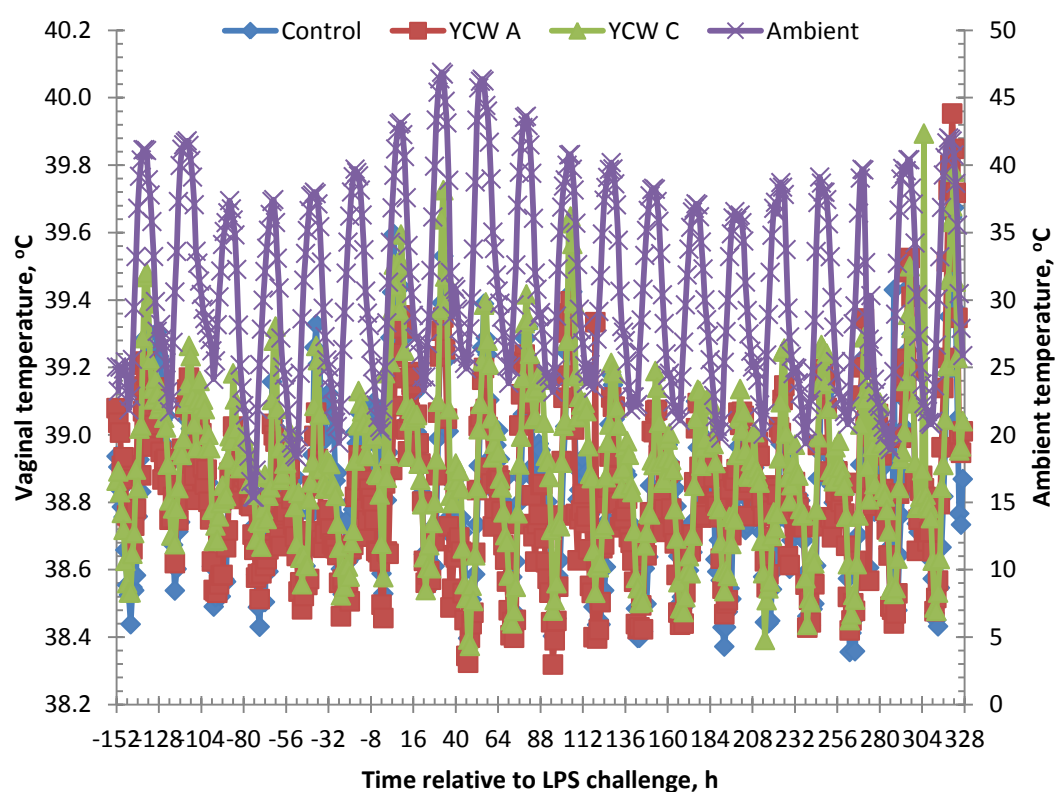
**Table 3.7.** Source 1-Heifer performance following an immune challenge

Item	Control	YCW A	YCW C	SEM <sup>1</sup>	<i>P</i> -value
		2.5 g/(heifer·d)	2.5 g/(heifer·d)		
ADG, kg	1.72 <sup>a</sup>	1.73 <sup>a</sup>	2.25 <sup>b</sup>	0.075	<0.01
DMI, kg	8.82	8.88	9.22	0.273	0.10
G:F	0.196 <sup>a</sup>	0.196 <sup>a</sup>	0.244 <sup>b</sup>	0.0093	0.01

<sup>1</sup>Standard error of the difference between the treatment means<sup>a,b</sup>Means with in a row differ ( $P < 0.05$ )**Figure 3.2.** Source 1 vaginal temperature during an LPS challenge

**Table 3.8.** Source 2-Heifer performance following an immune challenge

Item	Control	YCW A	YCW C	SEM <sup>1</sup>	<i>P</i> -value
		2.5 g/(heifer·d)	2.5 g/(heifer·d)		
ADG, kg	1.44	1.59	1.63	0.224	0.82
DMI, kg	7.25	8.02	7.60	0.536	0.62
G:F	0.198	0.199	0.215	0.0243	0.86

<sup>1</sup>Standard error of the difference between the treatment means<sup>a,b</sup>Means with in a row differ ( $P < 0.05$ )**Figure 3.3.** Source 2 vaginal temperature during an LPS challenge



## CHAPTER IV

# YEAST CELL WALL SUPPLEMENTATION ALTERS THE PHYSIOLOGICAL AND ACUTE-PHASE RESPONSES OF CROSSBRED HEIFERS TO AN ENDOTOXIN CHALLENGE

### Abstract

A study was conducted to determine the effect of feeding yeast cell wall (YCW) products on the physiological and acute-phase responses of crossbred newly received heifers to endotoxin (lipopolysaccharide; **LPS**) challenge. Heifers ( $n = 24$ ;  $219 \pm 2.4$  kg) were obtained from commercial sale barns and transported to the Texas Tech University Beef Center in New Deal, Texas. Heifers were separated into treatment groups receiving a Control diet (**C**;  $n = 8$ ), YCW-A ( $2.5 \text{ g} \cdot \text{heifer}^{-1} \cdot \text{d}^{-1}$ ;  $n = 8$ ) or YCW-C ( $2.5 \text{ g} \cdot \text{heifer}^{-1} \cdot \text{d}^{-1}$ ;  $n = 8$ ) and were fed for 52 d. On d 36, heifers were fitted with indwelling vaginal temperature (**VT**) recording devices and jugular catheters and moved into a barn with individual stalls. On d 37 heifers were challenged i.v. with LPS ( $0.5 \mu\text{g/kg BW}$ ) and blood samples were collected every 0.5 h from -2 to 8 h and again at 24 h relative to LPS challenge (0 h). Sickness behavior scores (**SBS**) were also assigned following collection of each blood sample. Serum was isolated and stored at  $-80^{\circ}\text{C}$  until analysis for cortisol, interleukin-6 (**IL-6**), interferon- $\gamma$  (**IFN- $\gamma$** ), and tumor necrosis factor- $\alpha$  (**TNF- $\alpha$** ) concentrations. There was an increase in VT in all treatments post-LPS ( $P < 0.001$ ), with YCW-C ( $38.90 \pm 0.03^{\circ}\text{C}$ ) maintaining lower VT post-LPS than C ( $39.00 \pm 0.3^{\circ}\text{C}$ ) and YCW-A treatments ( $38.99 \pm 0.03^{\circ}\text{C}$ ;  $P < 0.01$ ). Although low, SBS increased post-LPS but were not affected by treatment ( $P = 0.54$ ). Cortisol concentrations were greatest in C

( $39.7 \pm 1.5$  ng/mL) heifers post-LPS than YCW-A ( $31.3 \pm 1.7$  ng/mL) or YCW-C treatments ( $32.0 \pm 1.7$  ng/mL;  $P < 0.001$ ). Concentrations of IFN- $\gamma$  and TNF- $\alpha$  increased post-LPS ( $P < 0.001$ ) but were not affected by treatment ( $P = 0.50$  and  $0.35$ , respectively). Serum IL-6 concentrations increased post-LPS ( $P < 0.0001$ ) and were greater in C ( $351.5 \pm 36.0$  pg/mL) heifers than YCW-A ( $85.8 \pm 42.9$  pg/mL) and YCW-C ( $136.2 \pm 36.0$  pg/mL;  $P < 0.001$ ) heifers. These data indicate that YCW supplementation can decrease the physiological and acute-phase responses of newly received heifers to endotoxin challenge.

## **Introduction**

As researchers and producers continue to make progress in maximizing productivity in the livestock industry, one area that can be improved is animal health. In addition to changing management strategies to decrease stressors known to inhibit immunity, there is potential to alter immune function through feed supplementation. Studies on the use of feed supplements to enhance animal health are in increasing demand as a result of the movement to decrease and potentially eliminate the use of sub-therapeutic doses of antibiotics in feedstuffs. Because of the assumption that feeding sub-therapeutic antibiotics in feed may lead to the development of antibiotic-resistant bacteria, the European Union has banned the use of direct-fed antibiotics (Muirhead, 1998). Therefore, it is essential that more research be conducted to look at viable alternatives to feed-grade antibiotics.

The receiving period at a feedlot is very stressful, as cattle are exposed to various stressors including the handling associated with transportation and processing and comingling with unfamiliar cattle. These stressors alone can increase the incidence of disease; yet, the transfer of pathogens between unfamiliar cattle further heightens this risk. Indeed, there is a high rate of morbidity in receiving cattle, mainly attributed to bovine respiratory disease (Duff and Galyean, 2007). Therefore, methodologies that enhance the health of receiving cattle have the potential to decrease costs associated with medication and the loss of gain associated with illness, and are consequently in high demand.

Yeast and yeast cell wall products have been demonstrated to improve the productivity during several period of cattle production, and have the potential to be a viable non-antibiotic alternative feed supplement. Yeast supplementation has been demonstrated to improve DMI and ADG, while decreasing morbidity (Phillips and VonTungeln, 1985; Keyser et al., 2007; Magalhães et al., 2008). In addition, a previous study using live yeast or yeast cell wall (**YCW**) products demonstrated lower rectal temperature and cytokine concentrations in response to endotoxin (lipopolysaccharide, **LPS**) in steers, suggesting yeast products can improve cattle health (Carroll et al., 2010). Therefore, the present study was designed to determine the effect of supplementing 2 different yeast cell wall products on the physiological and acute-phase responses of newly received heifers to an LPS challenge.

## Materials and Methods

### *Experimental design*

All experimental procedures were in compliance with the *Guide for the Care and Use of Agricultural Animals in Research and Teaching* and approved by the Institutional Animal Care and Use Committee at Texas Tech University (Approval Number: 10079-11).

Twenty-four newly-received crossbred heifers ( $218.9 \pm 2.4$  kg BW) were obtained from commercial sale barns and transported to the Texas Tech University Beef Center in New Deal, Texas. Heifers were blocked by BW and assigned to one of 3 treatments: 1) negative control; no yeast additive, 2) yeast cell wall product A (YCW-A;  $2.5 \text{ g} \cdot \text{heifer}^{-1} \cdot \text{d}^{-1}$ ; Lesaffre Feed Additives, Milwaukee, WI); and 3) yeast cell wall product C (YCW-C;  $2.5 \text{ g} \cdot \text{heifer}^{-1} \cdot \text{d}^{-1}$ ; Lesaffre Feed Additives). All yeast cell wall products were derived from *Saccharomyces cerevisiae*. Cattle were fed a 65% concentrate diet initially; concentrate level was increased at d 14 and d 28 (to 75 and 85% concentrate diets, respectively). The 85% concentrate diet was fed for the remainder of the trial (d 28 to 52). Feed was offered at 95% of the previous day's delivery on each transition day. Diets were formulated to meet or exceed NRC (1996) recommendations for nutrients (Table 1).

On d 36, heifers were fitted with jugular vein catheters and indwelling vaginal temperature recording devices (Burdick et al., 2011) that measured vaginal temperature continuously at 1-min intervals in the absence of a human operator. For the jugular cannulation procedure, a small 2 to 3 cm incision was made in the skin in to more easily

access the jugular vein. Temporary indwelling jugular catheters, consisting of approximately 30.48 cm of sterile Tygon® tubing (AAQ04133; US Plastics; 1.27 mm i.d. and 2.286 mm o.d.), were inserted into the jugular vein using a 14-gauge by 5.08-cm thin-walled stainless steel biomedical needle (o.d. = 3 mm). The catheter was held in place using tag cement and a 2.08-cm wide porous surgical tape around the incision site, and then the entire neck region of the heifers were wrapped with vet wrap to ensure stability of the catheterization site. The remaining tubing not inserted into the heifer served as the catheter extension for collection of blood samples. During these procedures cattle were restrained in a working chute for approximately 10 to 15 min.

Following these procedures, heifers were moved to a facility that contained individual stalls (2.13-m long x 0.76-m wide) that housed the heifers through the duration of the study. Heifers were placed so that treatments were alternated by stall. During the challenge, the heifers had ad libitum access to feed and water. The extension tubing of the catheter was extended above the stall to allow researchers to collect blood throughout the study without disturbing the heifer, whether the heifers were standing or lying down.

On d 55, whole blood samples were collected into blood tubes containing no additive every 0.5 h beginning 2 h before and continuing 8 h after administration of LPS (0.5 µg/kg BW; *Escherichia coli* O111:B4; Sigma-Aldrich, St. Louis MO, USA) and again at 24 h. Whole blood was allowed to clot for 30 min and serum was collected after centrifugation at 1,250 x g for 20 min at 4°C. Serum was stored at -80°C until analyzed for cortisol and cytokine concentrations. Before administration of LPS, catheters became

dislodged from 1 YCW-A heifer; therefore, data presented represents 23 heifers (Control, n = 8; YCW-A, n = 7; YCW-C, n = 8).

### ***Sickness Behavior***

A trained observer assessed and recorded each heifer's sickness behavior score by visual observation following the collection of each blood sample. Heifers were scored on a scale of 1 (active or agitated) showing the least amount of sickness behavior, to 5 (lying on side with labored breathing) showing the greatest amount of sickness behavior (Table 2; Burdick et al., 2011). Heifers were assigned sickness behavior scores by the same observer throughout the experiment.

### ***Assays for Cortisol and Cytokines***

All serum samples were analyzed in duplicate. Serum cortisol concentrations were determined using a commercially available enzyme immunoassay kit according to the manufacturer's directions (Arbor Assays, Ann Arbor, MI) by comparison of unknowns to standard curves generated with known concentrations of cortisol. The minimum detectable cortisol concentration was 45.4 pg/mL, and the intra- and inter-assay coefficients of variation were 7% and 20%, respectively. Data are presented as ng/mL.

Serum cytokine concentrations (TNF- $\alpha$ , IFN- $\gamma$ , and IL-6) were determined by a custom bovine 4-plex sandwich-based chemiluminescence ELISA kit (Searchlight-Aushon BioSystems, Inc., Billerica, MA). The minimum detectable concentrations were 0.5, 0.1, and 3.3 pg/mL for TNF- $\alpha$ , IFN- $\gamma$ , and IL-6, respectively. All intra-assay

coefficients of variation were less than 9% and all inter-assay coefficients of variation were less than 21% for all assays.

### ***Statistical Analyses***

Before analysis, vaginal temperature data were averaged into 60-min intervals. Data for vaginal temperature, sickness behavior scores, cortisol, and cytokines were analyzed using the MIXED procedure of SAS (SAS, Inc., Cary, N.C.) for repeated measures with treatment, time, and time x treatment interaction included as fixed effects. Specific pre-planned treatment comparisons were made using Fisher's Protected LSD with  $P < 0.05$  considered significant. Data are presented as the least squares means  $\pm$  the standard error of the mean.

## **Results**

### ***Vaginal temperature***

There was no difference in vaginal temperature in the 12-h period before administration of LPS (treatment:  $P = 0.251$ ; Figure 1), although vaginal temperature decreased over time ( $P < 0.001$ ). In response to LPS administration at time 0 h, vaginal temperature increased ( $P = 0.010$ ), reaching peak values within 2 h before decreasing. Post-LPS vaginal temperatures were greater in Control ( $39.00 \pm 0.03^{\circ}\text{C}$ ) and YCW-A heifers ( $38.99 \pm 0.03^{\circ}\text{C}$ ) than YCW-C heifers ( $38.90 \pm 0.03^{\circ}\text{C}$ ;  $P < 0.001$ ).

### ***Sickness behavior scores***

Before administration of LPS, there was no difference in observed sickness behavior scores as a result of treatment (Figure 2;  $P = 0.381$ ). Although sickness behavior scores increased ( $P < 0.001$ ) following administration of LPS at time 0 h, the heifers showed very limited sickness behaviors, as indicated by the low peak score between 1.3 and 1.5 (on a scale of 1 to 5). There was no effect of YCW supplementation on sickness behavior scores post-LPS ( $P = 0.539$ ).

### ***Serum cortisol concentration***

There was no effect of YCW treatment on pre-LPS serum cortisol concentrations (Figure 3;  $P = 0.773$ ). In response to administration of LPS at time 0 h, cortisol concentrations increased within 0.5 h ( $P < 0.001$ ). Post-LPS cortisol concentrations were greater in Control ( $39.7 \pm 1.5$  ng/mL) than in YCW-A ( $31.3 \pm 1.7$  ng/mL) and YCW-C heifers ( $32.0 \pm 1.8$  ng/mL;  $P < 0.001$ ).

### ***Serum cytokine concentrations***

Serum concentration of IFN- $\gamma$  (Figure 4A) was not affected by YCW treatment pre- ( $P = 0.612$ ) or post-LPS administration ( $P = 0.497$ ); however, concentrations changed over time both pre- ( $P = 0.028$ ) and post-LPS ( $P < 0.001$ ). Similarly, serum concentration of TNF- $\alpha$  (Figure 4B) was not affected by YCW treatment pre- ( $P = 0.991$ ) or post-LPS administration ( $P = 0.349$ ). Pre-LPS TNF- $\alpha$  concentrations were not



affected by time ( $P = 0.775$ ), yet post-LPS TNF- $\alpha$  concentrations were increased 1 h post-LPS ( $P < 0.001$ ).

There was no effect of YCW treatment ( $P = 0.683$ ) or time ( $P = 0.672$ ) on serum IL-6 concentration prior to LPS administration (Figure 4C). Serum concentration of IL-6 increased within 1.5 h post-LPS ( $P < 0.001$ ). Moreover, post-LPS IL-6 concentration was greater in Control heifers ( $351.5 \pm 36.0$  pg/mL) than in YCW-A ( $85.8 \pm 42.9$  pg/mL) and YCW-C heifers ( $136.2 \pm 36.0$  pg/mL;  $P < 0.001$ ).

## **Discussion**

The use of yeast supplements in cattle is a growing area of research; however, at the present time there is limited information regarding the use of yeast product supplements on the health of beef cattle. A study in young dairy calves demonstrated that feeding a yeast culture during the first 70 d of age improved survival rate of calves (Magalhães et al., 2008), which demonstrates that yeast supplementation can modulate the health of cattle. An enhancement of the health of beef cattle during the receiving period is essential for the industry, as the stress endured during this period as a result of increased handling and commingling with unfamiliar cattle increases the susceptibility to immune challenges (Galyean et al., 1999). Results have indicated nutritional supplementation can have direct influences on the immune system (Galyean et al., 1999; Duff and Galyean, 2007; Carroll and Forsberg, 2007). The present study aimed to examine the effect of YCW supplementation on the physiological and acute-phase responses of newly received heifers to an endotoxin challenge. The data from this study

demonstrated that YCW supplementation can decrease both physiological and acute-phase responses elicited following an LPS challenge, as indicated by changes in vaginal temperature, cortisol, and cytokine concentrations.

Vaginal temperature is one of the most common and useful measurements to evaluate the health status of cattle (Burdick et al., 2011). As acute stress has been demonstrated to increase core body temperature (Olivier et al., 2005), it is not unusual to see a slight rise in vaginal temperature during the initial hours of sampling before the administration of LPS as humans will be entering the facility where the cattle were housed for the first time. Therefore, the slight increase in vaginal temperature likely represents a minor stress response to the increased activity in the animal facility.

The vaginal temperature response to LPS is similar to that observed in other studies in which LPS was administered to cattle (Carroll et al., 2010; Burdick et al., 2011). The lower vaginal temperatures observed following administration of LPS in YCW-supplemented cattle is similar to that which was observed in steers supplemented with live yeast and YCW (Carroll et al., 2010). An increase in core body temperature is a necessary response to a pathogen, as greater body temperatures contribute to pathogen clearance. The lower vaginal temperature response observed in YCW-supplemented heifers may infer that these heifers were healthier, and did not need as great of a vaginal temperature response to dispatch the infectious agent. This is supported by the lower IL-6 concentrations observed in YCW-supplemented heifers following administration of LPS. The secretion of IL-6, as well as TNF- $\alpha$  and IL-1 $\beta$ , have been reported to increase

core body temperature (Dinareello, 1996; Steiger et al., 1999; Black, 2002); however, there were no differences in the secretion of TNF- $\alpha$  in the current study.

There were very limited behavioral signs of sickness exhibited by the heifers in the present study in response to LPS administration. Perhaps the heifers were healthy prior to the LPS challenge, as stated above, which decreased the visible behavioral signs of sickness. The low cytokine concentrations observed in the current study further support this claim. The sickness scores observed in the current study are less than what has been previously observed in Brahman bulls (Burdick et al., 2011); however, *Bos indicus*-influenced cattle are more sensitive to LPS than *Bos taurus*-influenced cattle, as demonstrated in the necessity to administer a lower dose of LPS to Brahman-influenced cattle than *Bos taurus* cattle in order to prevent mortality. In addition, studies have demonstrated differences in sickness behavior between heifers and bulls (Carroll et al., 2009), which may further contribute to the limited sickness behaviors observed in the current study.

Cortisol is well known for its negative role in regulation of the immune system; however, in response to a pathogen, cortisol is necessary to prevent a hyper-inflammatory state caused by increased concentrations of pro-inflammatory cytokines. Serum cortisol concentrations were greater in Control than YCW-supplemented heifers. This finding corresponds to lower concentrations of IL-6 observed in YCW-supplemented heifers and lower vaginal temperatures following administration of LPS. Therefore, a muted cortisol response may be a result of a lesser cytokine response. Collier et al. (2011) reported lower cortisol concentrations in live yeast-supplemented pigs 1 h after administration of

LPS. In cattle, however, Carroll et al. (2010) reported a lower cortisol response in steers supplemented with a combination of live yeast and YCW, which is similar to results of the current study. It should be noted, however, that cortisol concentrations in the aforementioned study peaked at concentrations twice as high as observed in the current study. The differences observed between studies may be a result of the source of cattle, as greater morbidity was observed in the aforementioned study.

As mentioned earlier, cytokine concentrations produced following LPS administration were relatively low compared with other published studies in which LPS was administered to cattle (Sartin et al., 2003; Reuter et al., 2008; Carroll et al., 2009; Carroll et al., 2011; Kahl et al., 2011). Nonetheless, not all of the previous studies used the same dose of LPS, which may have contributed to greater cytokine concentrations post-LPS administration. A previous study in cattle reported a tendency for greater IFN- $\gamma$  concentrations prior to administration of LPS (Carroll et al., 2010). Because of the variability observed in pre-LPS IFN- $\gamma$  concentrations in the current study, no differences were observed. In addition, no differences in IFN- $\gamma$  concentrations were observed post-LPS administration in the current study. The current study also indicated no effect of treatment on TNF- $\alpha$  concentration, which is in contrast to a study by Collier et al. (2011), who reported that administration of live yeast to young pigs accelerated and increased the TNF- $\alpha$  response to LPS. The difference observed between the current study and the study by Collier et al. (2011), which used pigs, may demonstrate differences between species or differences between a live yeast product and a yeast cell wall product.

In contrast to IFN- $\gamma$  and TNF- $\alpha$ , differences in IL-6 concentrations were apparent following LPS administration in the current study. The supplementation of YCW products decreased serum IL-6 concentrations, which is consistent with the lower vaginal temperature and cortisol responses observed. The lower concentrations of IL-6 observed in YCW-supplemented heifers also agrees with the lower expression of IL-6 that has been observed in a porcine small epithelial cell line stimulated with live yeast (Zanello et al., 2011). The reason for observed differences in IL-6 but not IFN- $\gamma$  and TNF- $\alpha$  in the current study is not clear, but it might be related to the actions of IL-6 to stimulate release of acute-phase proteins and stimulate the adaptive immune response, aspects which require further study.

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**Table 4.1.** Diet composition

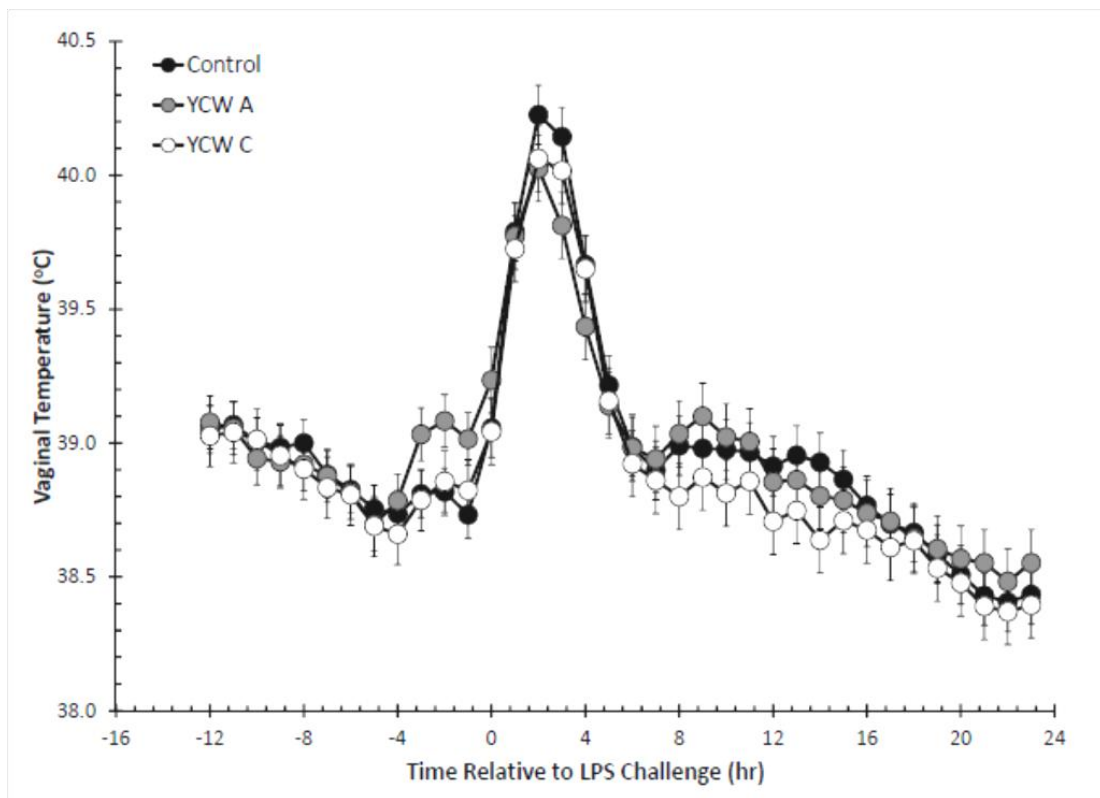
Ingredients, % <sup>1</sup>	% concentrate in diet <sup>1</sup>		
	65 %	75 %	85 %
Corn Grain, Steam Flaked	45.75	57.15	67.90
Cottonseed, Hulls	25.00	15.00	5.00
Alfalfa Hay, Mid Bloom	10.00	10.00	10.00
Cottonseed, Meal - Sol-41%CP	10.50	9.00	7.00
Molasses, Cane	4.00	4.00	4.00
Tallow	1.00	1.00	2.00
Urea	0.55	0.65	0.80
Limestone	0.80	0.80	0.90
MIN-AD	0.40	0.40	0.40
Receiving Supplement <sup>2</sup>	2.00	2.00	2.00

<sup>1</sup>Dry Matter Basis

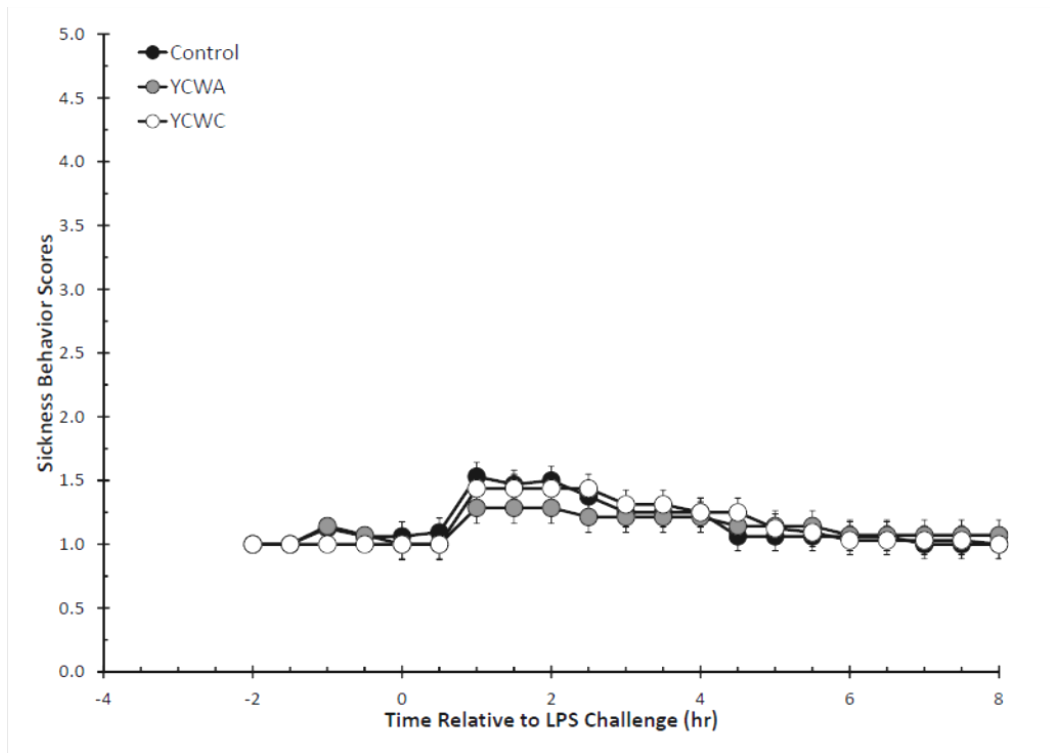
<sup>2</sup>Supplement for the diet contained (DM basis): 66.383% cottonseed meal; 0.500% Endox® (Kemin Industries, Inc., Des Moines, IA); 0.648% dicalcium phosphate; 10% potassium chloride; 4.167% ammonium sulfate; 15.000% salt; 0.002% cobalt carbonate; 0.196% copper sulfate; 0.083% iron sulfate; 0.003% ethylenediamine dihydroiodide; 0.333% manganese oxide; 0.125% selenium premix (0.2% Se); 0.986% zinc sulfate; 0.010% vitamin A (1,000,000 IU/g); 0.157% vitamin E (500 IU/g); 0.844% Rumensin (176.4 mg/kg; Elanco Animal Health, Indianapolis, IN); and 0.563% Tylan (88.2 mg/kg; Elanco Animal Health). Concentrations in parenthesis are expressed on a 90% DM basis.

**Table 4.2.** Sickness score definitions of visual signs of sickness.

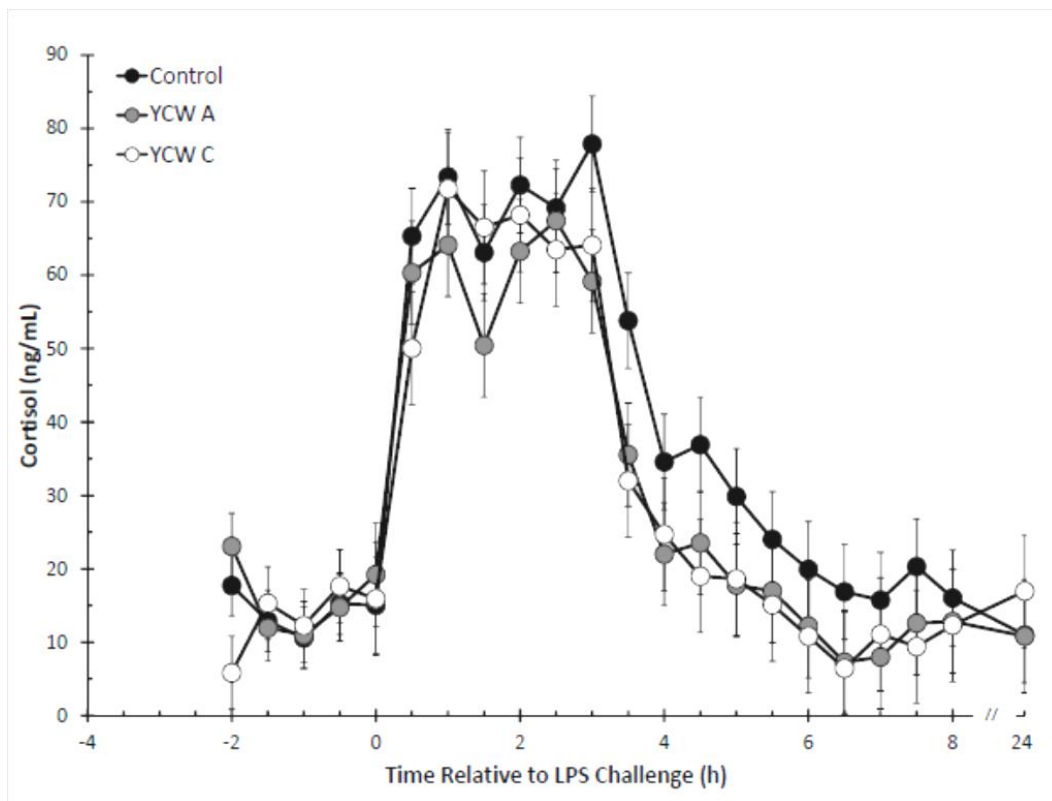
Score	Description
1	Normal, alert, ears erect; head level or high, eyes open, standing, locomotor activity, responsive, performing maintenance behaviors
2	Calm but less alert, less activity, less responsive, standing or lying ventral, semi-lateral.
3	Lying, calm, head distended or tucked, less alert, signs of some mild respiratory problems (coughing, wheezing)
4	Clinical signs of sickness, respiratory problems, not responsive, head distended, lethargic.
5	All/most respiratory problems, mucus/foam. Head distended, not responsive- medical intervention required.



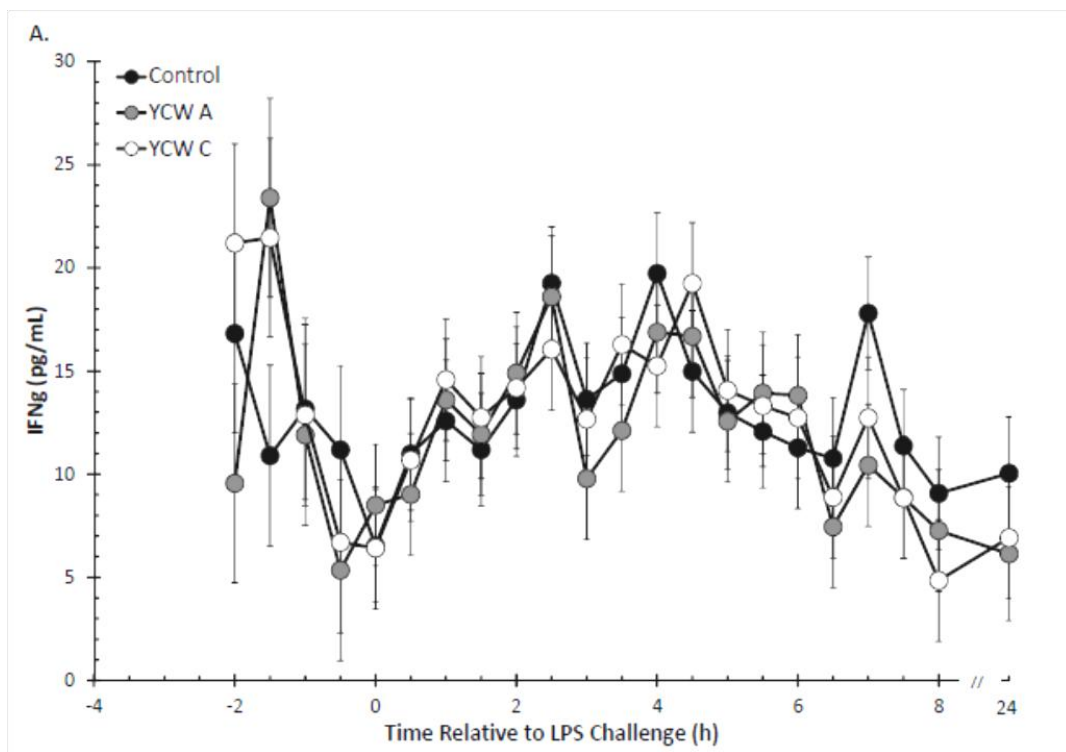
**Figure 4.1.** Vaginal temperature response to a LPS challenge.



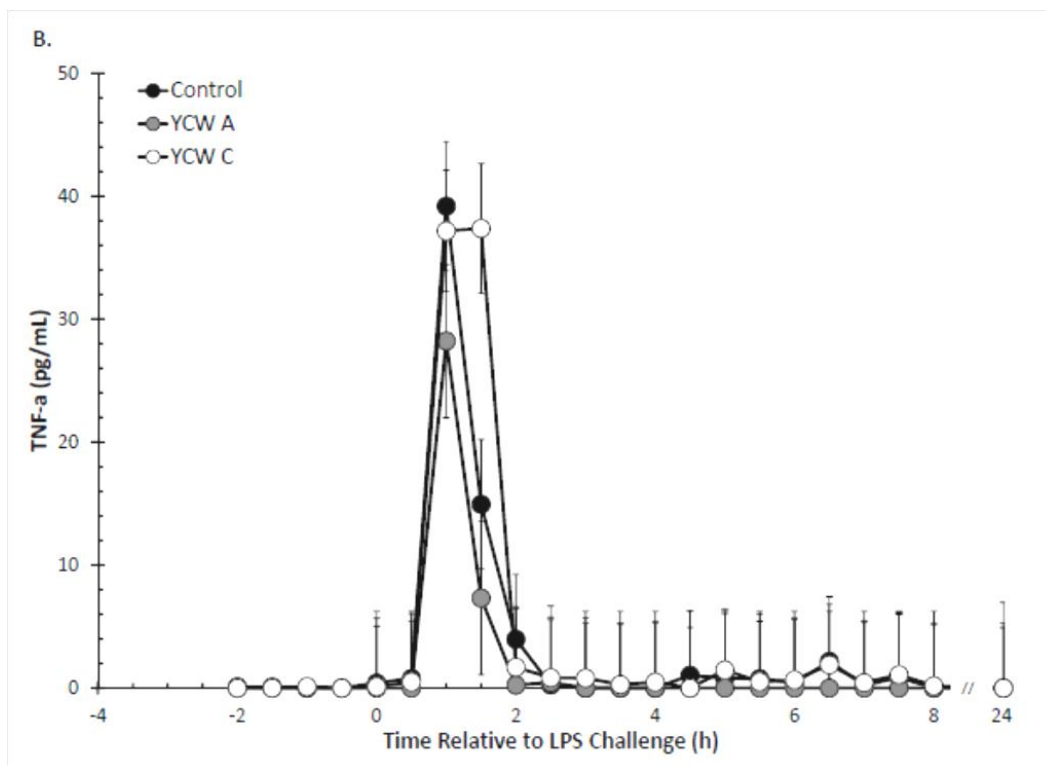
**Figure 4.2.** Sickness behavior scores during a LPS challenge.



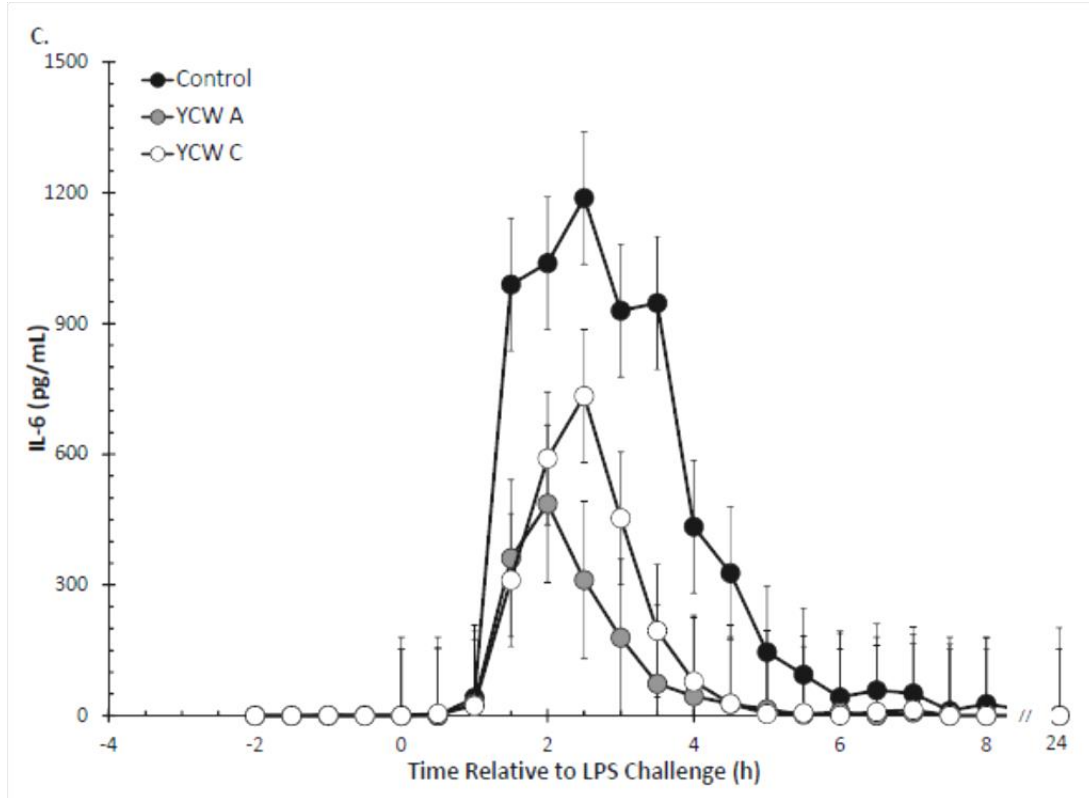
**Figure 4.3.** Cortisol concentrations during a LPS challenge.



**Figure 4.4.** Interferon- $\gamma$  concentrations during a LPS challenge.



**Figure 4.5.** Tumor necrosis factor- $\alpha$  concentrations during a LPS challenge.



**Figure 4.6.** Interleukin-6 concentrations during a LPS challenge.



## CHAPTER V

### YEAST CELL WALL SUPPLEMENTATION ALTERS THE METABOLIC RESPONSES OF CROSSBRED HEIFERS TO AN ENDOTOXIN CHALLENGE

#### Abstract

This study examined the effect of feeding yeast cell wall (YCW) products on the metabolic responses of newly-received heifers to endotoxin (lipopolysaccharide; **LPS**) challenge. Heifers ( $n = 24$ ;  $219 \pm 2.4$  kg) were obtained from commercial sale barns and transported to the Texas Tech University Beef Center. Heifers were separated into treatment groups receiving a Control Diet (**C**;  $n = 8$ ), YCW-A ( $2.5 \text{ g} \cdot \text{heifer}^{-1} \cdot \text{d}^{-1}$ ;  $n = 8$ ) or YCW-C ( $2.5 \text{ g} \cdot \text{heifer}^{-1} \cdot \text{d}^{-1}$ ;  $n = 8$ ) and were fed for 52 d. Heifers were weighed on d 0, 14, 36, 38, and 52. On d 36, heifers were fitted with indwelling jugular catheters and moved into a barn with individual stalls. On d 37 heifers were challenged iv with LPS ( $0.5 \text{ } \mu\text{g/kg BW}$ ), and blood samples were collected every 0.5 h from -2 to 8 h and again at 24 h relative to LPS challenge (0 h). Serum was isolated and stored at  $-80^{\circ}\text{C}$  until analysis for glucose, insulin, non-esterified fatty acid (**NEFA**), and blood urea nitrogen (**BUN**) concentrations. Heifer BW increased from d 0 to 36 and from d 38 to 52, but was not affected by treatment ( $P > 0.32$ ). Post-LPS, YCW-A heifers ( $-6.0 \pm 0.9$  kg) lost more weight (from d 36 to 38) than C ( $-2.4 \pm 0.9$  kg) and YCW-C heifers ( $-4.2 \pm 0.9$  kg;  $P = 0.04$ ). Post-LPS, glucose increased ( $P < 0.001$ ) and was less in YCW-A ( $98.5 \pm 2.5$  mg/dL) than C ( $105.6 \pm 2.4$  mg/dL) and YCW-C heifers ( $109.5 \pm 2.4$  mg/dL;  $P < 0.01$ ). Pre-LPS, insulin was greater in YCW-A ( $0.80 \pm 0.06$  ng/mL) and YCW-C ( $0.087 \pm 0.06$  ng/mL) than C heifers ( $0.44 \pm 0.06$  ng/mL;  $P < 0.01$ ). Post-LPS, insulin increased ( $P <$

0.01) with YCW-C ( $0.95 \pm 0.04$  ng/mL) and YCW-A ( $0.71 \pm 0.05$  ng/mL) having greater insulin than C heifers ( $0.59 \pm 0.04$  ng/mL;  $P < 0.001$ ). Pre-LPS, NEFA tended ( $P = 0.07$ ) to be less in YCW-C ( $0.14 \pm 0.01$  mmol/L) than C ( $0.18 \pm 0.01$  mmol/L) and YCW-A ( $0.17 \pm 0.01$  mmol/L). The difference in NEFA was significant post-LPS ( $0.18 \pm 0.01$ ,  $0.21 \pm 0.01$ , and  $0.21 \pm 0.01$  mmol/L respectively for YCW-C, C, and YCW-A). Pre-LPS, BUN was greater in YCW-A ( $8.2 \pm 0.3$  mg/dL) than C ( $6.9 \pm 0.3$  mg/dL;  $P = 0.03$ ). Post-LPS, BUN was greater in YCW-A ( $8.9 \pm 0.2$  mg/dL) than C ( $8.2 \pm 0.2$  g/dL) and YCW-C ( $8.1 \pm 0.2$  mg/dL;  $P < 0.01$ ). These data indicate that certain YCW products can enhance the energy metabolism during an immune challenge without causing lipolysis or muscle catabolism.

## **Introduction**

The successful clearance of pathogens from the body involves components of the immune system, the stress response, and metabolism. The activation and maintenance of the immune system response to an invading pathogen is a very energy-costly process. An increase in core body temperature alone increases an animal's metabolic rate by 10 to 13% for a 1°C increase in body temperature (Carroll and Forsberg, 2007). This does not account for the energy required for the production of inflammatory mediators, acute-phase proteins, and immunoglobulins. Therefore, a major driver of the immune system is the energy available to the animal.

As researchers and cattle producers continue to adjust management practices in order to maximize productivity and decrease morbidity, feed supplements that can

demonstrate benefits in these 2 areas are of increasing demand. A previous study utilizing a chromium propionate feed supplement found differences in metabolites that helped to explain enhancement of the immune response to an endotoxin challenge (Burdick et al., 2011a). Live yeast and yeast cell wall (YCW) products have been shown to enhance the health of cattle (Phillips and VonTungeln, 1985; Keyser et al., 2007; Magalhães et al., 2008). Following observed differences in the physiological (vaginal temperature) and acute-phase responses (cortisol, interleukin-6) in heifers supplemented with 2 different YCW products, the hypothesis that the differences could be a results of differences in metabolism was developed. Therefore, this study was designed to determine the effect of supplementing two different yeast cell wall products on the metabolic response of newly received heifers to an LPS challenge.

## **Materials and Methods**

### ***Experimental design***

All experimental procedures were in compliance with the *Guide for the Care and Use of Agricultural Animals in Research and Teaching* and approved by the Institutional Animal Care and Use Committees of Texas Tech University (approval number 10079-11).

### ***Experimental Design***

Twenty-four newly received crossbred heifers ( $218.9 \pm 2.4$  kg BW) were obtained from commercial sale barns and transported to the Texas Tech University Beef Center in

New Deal, TX. Heifers were blocked by BW and assigned to one of 3 treatments: 1) negative control (C); no yeast additive, 2) yeast cell wall product A (YCW-A; 2.5 g•heifer<sup>-1</sup>•d<sup>-1</sup>); and 3) yeast cell wall product C (YCW-C; 2.5 g•heifer<sup>-1</sup>•d<sup>-1</sup>). All yeast cell wall products were derived from *Saccharomyces cerevisiae*. Cattle were fed a 65% concentrate diet initially; concentrate level was increased at d 14 and d 28 (to 75 and 85% concentrate diets, respectively). The 85% concentrate diet was fed for the remainder of the trial (d 28 to 52). Feed was offered at 95% of the previous day's delivery on each transition day. Diets were formulated to meet or exceed NRC (1996) recommendations for nutrients (Table 1). Individual heifer BW were collected on d 0, 14, 36, 38, and 52 for calculation ADG.

On d 36, heifers were fitted with indwelling jugular vein catheters. For the jugular cannulation procedure a small 2 to 3 cm incision was made in the skin to more easily access the jugular vein. Temporary indwelling jugular catheters, consisting of approximately 30.48 cm of sterile Tygon® tubing (AAQ04133; US Plastics; 1.27 mm i.d. and 2.286 mm o.d.), were inserted into the jugular vein using a 14-gauge by 5.08-cm thin-walled stainless steel biomedical needle (o.d. = 3 mm). The catheter was maintained in place using tag cement and a 2.08-cm wide porous surgical tape around the incision site, and then the entire neck region of the heifers were wrapped with Vet Wrap to ensure stability of the catheterization site. The remaining tubing not inserted into the heifer served as the catheter extension for collection of blood samples. During these procedures cattle were restrained in a working chute for approximately 10 to 15 min. Following these procedures heifers were moved to a facility that contained individual stalls (2.13-m

long x 0.76-m wide) that housed the heifers through the duration of the study. Heifers were placed so that treatments were alternated by stall. During the challenge the heifers had ad libitum access to feed and water. The extension tubing of the catheter was extended above the stall to allow researchers to collect blood throughout the study without disturbing the heifer, whether the heifers were standing or lying down. On d 55, whole blood samples were collected into blood tubes containing no additive every 0.5 h beginning 2 h prior to and continuing 8 hr after administration of LPS (0.5 µg/kg BW; *Escherichia coli* O111:B4; Sigma-Aldrich, St. Louis MO, USA) and again at 24 h. Whole blood was allowed to clot for 30 min and serum was collected after centrifugation at 1250 x g for 20 min at 4°C. Serum was stored at -80°C until analyzed for glucose, insulin, non-esterified fatty acids (**NEFA**), and blood urea nitrogen (**BUN**) concentrations. Prior to administration of LPS, catheters became dislodged from 1 YCW A heifer; therefore, data presented represents 22 heifers (Control, n = 8; YCW-A, n = 7; YCW-C, n = 8).

### ***Serum Analyses***

All serum samples were analyzed in duplicate. Serum glucose concentrations were determined by modification of the enzymatic Autokit Glucose (Wako Diagnostics, Richmond, VA) to fit a 96-well format. Briefly, 300 µL of prepared working solution was added to 2 µL of serum or prepared standards in a 96-well plate. Plates were incubated at 37°C for 5 min and then read using a plate reader at 505 nm. Concentration of glucose was determined by comparing unknown samples to a standard curve of known

glucose concentrations. The minimum detectable concentration was 3.8 mg/dL and the intra- and inter-assay coefficients of variation were 8.0% and 7.6%, respectively. Data are presented as the concentration in mg/dL.

Insulin concentrations were determined by a bovine-specific insulin ELISA according to the manufacturer's instructions (Cat # 80-INSBO-E01; Alpco Diagnostics, Salem, NH). The minimum detectable concentration was 0.1 ng/mL and the intra- and inter-assay coefficients of variation were 3.6% and 8.8%, respectively. Data are presented as the concentration in ng/mL.

Concentrations of NEFA were determined by modification of the enzymatic HR Series NEFA-HR (2) assay (Wako Diagnostics, Richmond, VA) to fit a 96-well format. Briefly, 200  $\mu$ L of the prepared Color Reagent A were added to 5  $\mu$ L of serum or prepared standards in a 96-well plate. Plates were incubated at 37°C for 5 min and then absorbance read using a spectrophotometer at 550 nm. Next, 100  $\mu$ L of prepared Color Reagent B was added to all wells on the 96-well plate. Plates were incubated for an additional 5 min and read for a second time using a plate reader at 550 nm.

Concentrations of NEFA were determined by comparing unknown samples to a standard curve of known NEFA concentrations. The minimum detectable concentration was 0.0014 mEq/L and the intra- and inter-assay coefficients of variation were 9.0% and 14.3%, respectively. Data are presented as the concentration in mEq/L.

Serum concentrations of BUN were determined by a colorimetric assay according to the manufacturer's directions (K024-H1; Arbor Assays, Ann Arbor, MI) by comparison of unknowns to standard curves generated with known concentrations of urea

nitrogen. The minimum detectable BUN concentration was 0.065 mg/dL and the intra- and inter-coefficients of variation were 4.0% and 15.7%, respectively. Data are presented as the concentration in mg/dL.

### ***Statistical Analyses***

Data for glucose, insulin, NEFA, and BUN were analyzed using the MIXED procedure of SAS (SAS, Inc., Cary, N.C.) specific for repeated measures with treatment, time, and time x treatment interaction included as fixed effects. Specific pre-planned treatment comparisons were made using Fisher's Protected LSD. Data for BW and ADG were analyzed using the MIXED procedure of SAS with treatment included as a fixed effect. For all data,  $P < 0.05$  was considered significant. Data are presented as the least squares means  $\pm$  the standard error of the mean.

## **Results**

### ***Performance***

Heifer BW increased from d 0 through d 52 ( $P < 0.001$ ), but was not affected by treatment (Table 2;  $P > 0.440$ ). For ADG, there was a trend ( $P = 0.130$ ) for YCW A and YCW C-supplemented heifers to have greater ADG from d 0 to 36 compared to control. During the LPS challenge period from d 36 to 38 (with LPS challenge on d 37), control heifers had greater ADG than YCW-A and YCW-C heifers ( $P = 0.040$ ), which was a result of YCW-A and YCW-C heifers losing numerically more BW from d 36 to 38.

Following the LPS challenge, there was a trend ( $P = 0.140$ ) for YCW-C-supplemented heifers to have greater ADG than Control and YCW A heifers from d 38 to 52.

### ***Glucose***

There was no effect of treatment ( $P = 0.776$ ) or time ( $P = 0.289$ ) on serum glucose concentrations prior to administration of LPS (Figure 1). Post-LPS glucose concentrations initially increased before decreasing below baseline concentrations (time:  $P < 0.001$ ). Serum glucose concentrations post-LPS were greater in Control ( $105.6 \pm 2.4$  mg/dL) and YCW-C heifers ( $109.5 \pm 2.4$  mg/dL) compared to YCW-A heifers ( $98.5 \pm 2.5$  mg/dL).

### ***Insulin***

Prior to administration of LPS, serum insulin concentrations were greater in YCW-A ( $0.80 \pm 0.06$  ng/mL) and YCW-C heifers ( $0.87 \pm 0.06$  ng/mL) than in Control heifers ( $0.44 \pm 0.06$  ng/mL;  $P < 0.001$ ; Figure 2). Following administration of LPS, insulin concentration increased within 2 h ( $P < 0.001$ ). Post-LPS, insulin concentration was greater in YCW-C ( $0.95 \pm 0.04$  ng/mL) than in YCW-A ( $0.71 \pm 0.05$  ng/mL) and Control heifers ( $0.59 \pm 0.04$  ng/mL;  $P < 0.001$ ).

### ***NEFA***

There was a tendency ( $P = 0.073$ ) for an effect of YCW treatment on serum NEFA concentrations prior to LPS administration, with greater NEFA concentrations in



Control ( $0.179 \pm 0.012$  mmol/L) than YCW-C ( $0.142 \pm 0.014$  mmol/L) with YCW-A being intermediate to Control and YCW-C ( $0.171 \pm 0.014$  mmol/L; Figure 3). There was an increase in NEFA concentration post-LPS ( $P < 0.001$ ). In addition, NEFA concentrations were greater in Control ( $0.211 \pm 0.007$  mmol/L) and YCW-A ( $0.206 \pm 0.008$  mmol/L) compared to YCW-C ( $0.176 \pm 0.006$  mmol/L) following LPS administration.

### ***BUN***

Serum concentrations of BUN were affected by YCW treatment prior to administration of LPS (Figure 4). Specifically, BUN concentration was greater in YCW-A ( $8.2 \pm 0.3$  mg/dL) than Control heifers ( $6.9 \pm 0.3$  mg/dL), with YCW-C being intermediate ( $7.5 \pm 0.4$  mg/dL;  $P = 0.025$ ). In response to administration of LPS, BUN concentrations increased ( $P < 0.001$ ), with YCW-A-supplemented heifers ( $8.9 \pm 0.2$  mg/dL) maintaining greater BUN concentrations than Control ( $8.2 \pm 0.2$  mg/dL) and YCW-C heifers ( $8.1 \pm 0.2$  mg/dL;  $P < 0.001$ ).

### **Discussion**

This study evaluated differences in metabolites following an LPS challenge in control or YCW-supplemented newly received heifers. Specifically, YCW supplementation altered insulin, NEFA, and BUN concentrations prior to, and altered glucose, insulin, NEFA, and BUN concentrations following administration of LPS.

Although there was trend for YCW-supplemented heifers to have greater ADG prior to the LPS challenge, these heifers still lost more BW during the challenge period compared to control heifers. Nonetheless, YCW-C heifers seemed to have recovered more quickly following the LPS challenge, as reflected by a trend for a greater ADG in the post challenge period.

Glucose concentrations following LPS administration were greater in control heifers compared to YCW-supplemented heifers. It is possible that a greater amount of glucose was being utilized by tissues in YCW-supplemented heifers, leading to lower post-LPS concentrations. Lower glucose concentrations in YCW-supplemented heifers are supported by greater pre- and post-LPS insulin concentrations in these heifers. This finding suggests that YCW-supplementation might prevent or decrease LPS-induced insulin resistance, a condition which has been observed in rats when LPS, interleukin-1 (**IL-1**), or tumor necrosis factor (**TNF**) was administered (Lang et al., 1992 Ling et al., 1994; Spurlock, 1997).

Concentrations of NEFA remained lower in YCW-C-supplemented heifers than YCW-A-supplemented and control heifers both pre- and post-LPS. This finding indicated that YCW-C heifers did not have to break down as much adipose tissue to provide energy for the immune defenses. These results are also supported by lower BUN concentrations in control and YCW-C-supplemented heifers compared to YCW-A-supplemented heifers. Studies have indicated that increases in cytokine concentrations can increase protein catabolism in rats and pigs (Flores et al., 1989; Webel et al., 1997). Specifically, Webel et al. (1997) concluded that an increase in concentrations of  $\text{TNF-}\alpha$

and IL-6 following administration of 5 µg/kg BW to pigs resulting in a peak in plasma urea nitrogen 12 h after injection. Nonetheless, BUN concentrations were greater in YCW-A heifers than control and YCW-C heifers, even though YCW-supplemented heifers had lower IL-6 concentrations. Therefore, other factors might contribute to the differences observed in BUN concentrations in control and YCW-treated heifers; however, in the current study, a 12-h sample was not collected.

The measurement of other metabolic hormones, including growth hormone (**GH**) and insulin-like growth factor-1 (**IGF-I**) may be necessary to further understand the complex paradigm associated with nutritional supplementation, growth and metabolism, and immune function. Studies in cattle have demonstrated that both GH and IGF-I concentrations decrease in response to an immune challenge (Elsasser et al., 1987; and Elsasser et al., 1988).

Cytokines have been found to modulate the metabolic response to infection (Spurlock, 1997; Webel et al., 1997). Results of a study in pigs indicated that administration of LPS increased concentrations of TNF- $\alpha$ , IL-6, cortisol, and plasma urea N but did not affect glucose, triglyceride, or NEFA concentrations (Webel et al., 1997). In a companion study to the present one (Chapter IV), concentrations of interleukin-6 (**IL-6**), but not tumor necrosis factor- $\alpha$  (**TNF- $\alpha$** ) or interferon- $\gamma$  (**IFN- $\gamma$** ) were less in YCW-supplemented heifers, which may have influenced the differences observed in the metabolic responses in the current study (Burdick et al., 2012).

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**Table 5.1.** Diet composition.

Ingredients, % <sup>1</sup>	% concentrate in diet <sup>1</sup>		
	65 %	75 %	85 %
Corn Grain, Steam Flaked	45.75	57.15	67.90
Cottonseed, Hulls	25.00	15.00	5.00
Alfalfa Hay, Mid Bloom	10.00	10.00	10.00
Cottonseed, Meal - Sol-41%CP	10.50	9.00	7.00
Molasses, Cane	4.00	4.00	4.00
Tallow	1.00	1.00	2.00
Urea	0.55	0.65	0.80
Limestone	0.80	0.80	0.90
MIN-AD	0.40	0.40	0.40
Receiving Supplement <sup>2</sup>	2.00	2.00	2.00

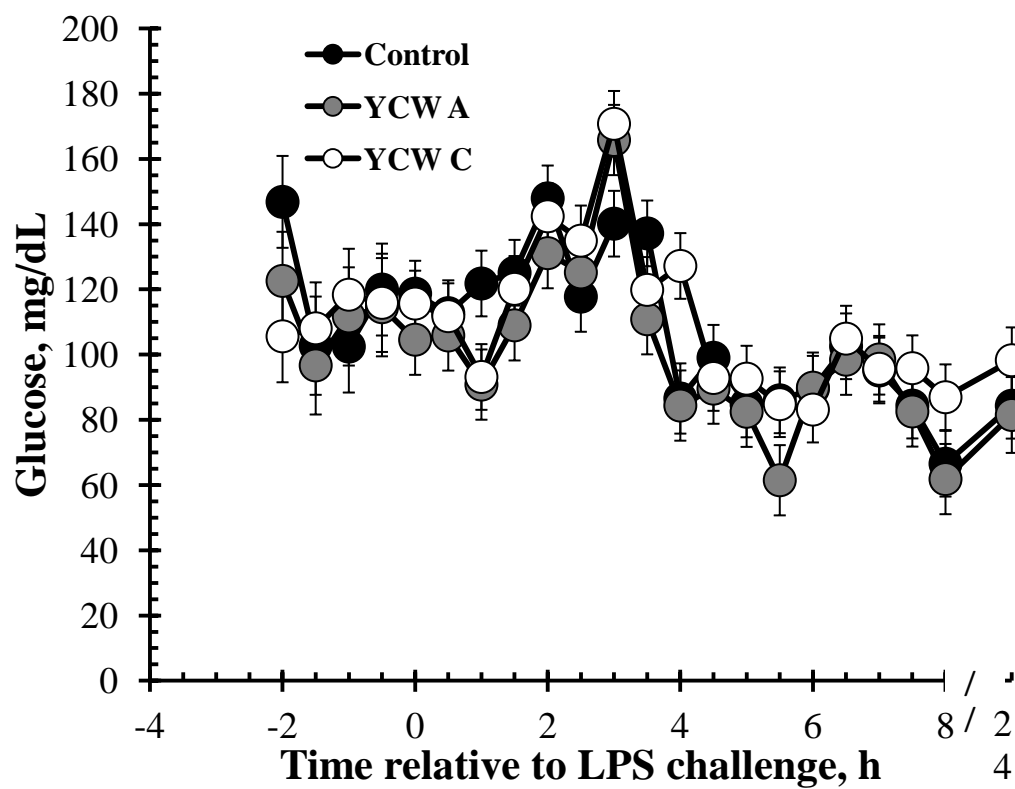
<sup>1</sup>Dry Matter Basis

<sup>2</sup>Supplement for the diet contained (DM basis): 66.383% cottonseed meal; 0.500% Endox® (Kemin Industries, Inc., Des Moines, IA); 0.648% dicalcium phosphate; 10% potassium chloride; 4.167% ammonium sulfate; 15.000% salt; 0.002% cobalt carbonate; 0.196% copper sulfate; 0.083% iron sulfate; 0.003% ethylenediamine dihydroiodide; 0.333% manganese oxide; 0.125% selenium premix (0.2% Se); 0.986% zinc sulfate; 0.010% vitamin A (1,000,000 IU/g); 0.157% vitamin E (500 IU/g); 0.844% Rumensin (176.4 mg/kg; Elanco Animal Health, Indianapolis, IN); and 0.563% Tylan (88.2 mg/kg; Elanco Animal Health). Concentrations in parenthesis are expressed on a 90% DM basis.

**Table 5.2.** Heifer performance before, during, and after an endotoxin (lipopolysaccharide, LPS) challenge.

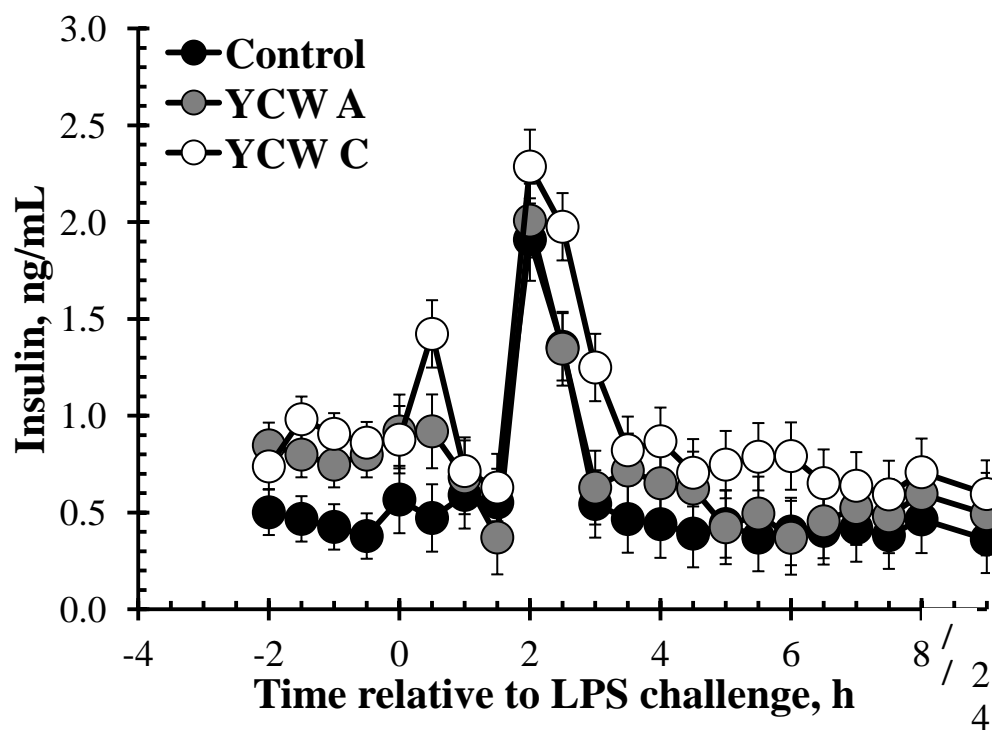
Item	Control	YCW A	YCW C	SEM <sup>1</sup>	TRT <i>P</i> -value
<i>BW, kg</i>					
d 0	219	219	219	4.8	1.00
d 14	236	246	242	6.6	0.51
d36	274	285	283	7.0	0.45
d 38	269	273	275	6.3	0.77
d 52	302	307	313	6.4	0.44
<i>ADG, kg</i>					
d 0-14	1.22	1.96	1.63	0.282	0.18
d 0-36	1.52	1.83	1.78	0.117	0.13
d 0-38	1.31	1.42	1.47	0.103	0.51
d 0-52	1.59	1.68	1.80	0.082	0.16
d14-36	1.70	1.74	1.88	0.163	0.69
d 36-38	-2.41	-5.96	-4.23	0.939	0.04
d 38-52	2.34	2.40	2.71	0.144	0.14

<sup>1</sup>Standard error of the difference between the treatment means

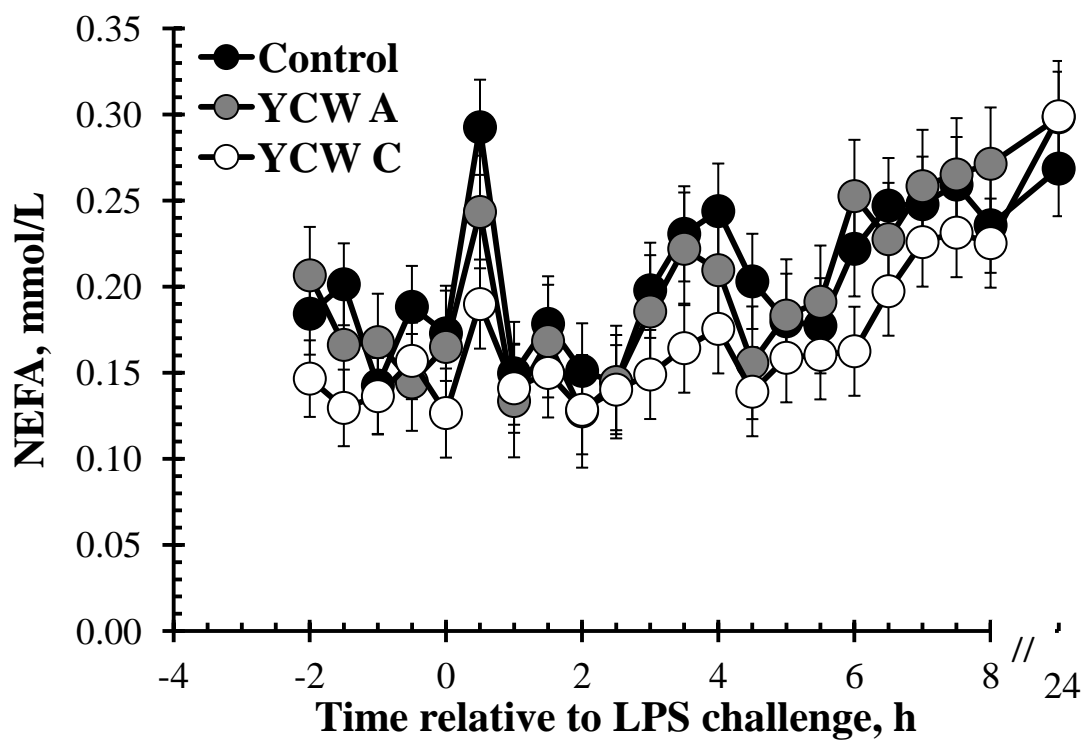


**Figure 5.1.** Glucose concentrations during a LPS challenge.

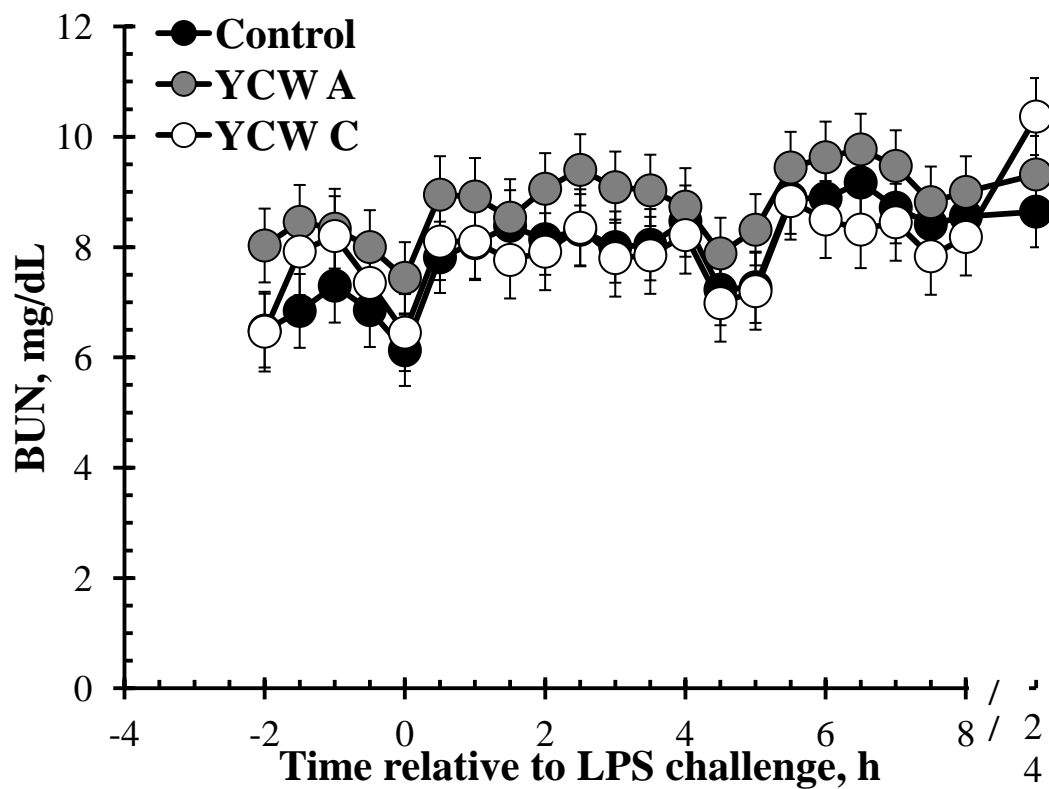




**Figure 5.2.** Insulin concentrations during a LPS challenge.



**Figure 5.3.** Non-esterified fatty acid (NEFA) concentration during a LPS challenge.



**Figure 5.4.** Blood urea nitrogen (BUN) concentration during a LPS challenge.

## **CHAPTER VI**

### **CONCLUSION**

Numerous research trials have been conducted over the past century on the effectiveness of yeast and yeast cell wall supplementation on cattle performance and health. Unlike antibiotic growth promoters and treatments, results with yeast supplementation have been highly variable. Under some circumstances, yeast supplementation seems to have beneficial effects on the health and performance of stressed calves. Dietary supplements, such as yeast cell wall, can alter the immune system and assist calves during transition periods with frequent managerial stressors. There are numerous reports indicating a positive effect on performance of yeast-supplemented cattle during various production phases. The present studies yielded positive results regarding yeast cell wall supplementation. Performance traits such as DMI and ADG can be positively affected, and the immune response and metabolism altered to improve the overall health status of supplemented cattle. Yeast cell wall supplementation could be a viable nutritional supplement to producers in today's industry.