



Effects of autolyzed yeast on leukocyte oxidative metabolism and pneumonia occurrence in feedlot steers¹

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ABSTRACT.- Garbossa G., Delarezi D., Rossi P.S., Thomaz G.R., Flores G.B., Horner W., Neumann M., Peres J.A. & Bertagnon H.G. 2023. **Effect of autolyzed yeast on leukocyte oxidative metabolism and pneumonia occurrence in feedlot steers.** *Pesquisa Veterinária Brasileira* 43:e07066, 2023. Departamento de Medicina Veterinária, Universidade Estadual do Centro-Oeste, Alameda Élio Antonio Dalla Vecchia 838, Bairro Vila Carli, Guarapuava, PR 85040-167, Brazil. E-mail: hbertagnon@hotmail.com

Although yeast supplementation has shown an immunostimulant effect in feedlot cattle, the question remains whether it influences the occurrence of the bovine respiratory disease complex (BRD) in feedlot cattle. Therefore, our objective was to evaluate whether dietary supplementation with autolyzed yeast affects the efficiency of blood phagocytes, reducing inflammation and the occurrence of BRD in feedlot cattle. A randomized experimental trial was conducted with whole steers with half Angus blood for 106 days: control (n=10): diet without yeast; Y4 (n=12): yeast diet (4g per animal per day); and Y7 (n=7): yeast diet (7g per animal per day). On Days 0, 14, 42, 70, and 105, blood count, leukocyte oxidative metabolism, serum haptoglobin, frequency of nasal secretion and orbital temperature were evaluated. On slaughter day, a lung evaluation was performed. On Days 42 and 70 of feedlot finishing, the treated animals showed increased leukocyte oxidative metabolism (D42 $P=0.04$; D70 $P=0.02$) compared to the control group. These animals had a lower frequency of mucopurulent nasal secretion, lower orbital temperature and reduced pneumonia occurrence than the treated groups ($P=0.05$) with less lung lesion severity ($P=0.01$), allowing us to infer that the autolyzed yeast improves blood phagocytic function and decreases the inflammation and BRD of feedlot steers, especially at a dose of 4g.

INDEX TERMS: autolyzed yeast, bovine respiratory disease, feedlot, oxidative burst, *Saccharomyces cerevisiae*.

RESUMO.- [Efeito da levedura autolisada no metabolismo oxidativo leucocitário e na ocorrência de pneumonia em novilhos terminados em confinamento.] Embora a suplementação com leveduras tenha demonstrado efeito imunoestimulante em bovinos, permanece-se a dúvida se ela influencia na ocorrência do complexo doença respiratória bovina (CDRB) em bovinos confinados. Portanto, objetivou-se avaliar se a suplementação dietética com levedura autolisada influencia a eficiência de fagócitos sanguíneos, reduzindo inflamações e a ocorrência de CDRB em bovinos confinados. Realizou-se um ensaio experimental randomizado com 36 novilhos inteiros 1/2 sangue Angus por 106 dias: controle

(n=10): dieta sem levedura; Y4 (n=12): dieta com levedura (4g por animal por dia); e Y7 (n=7): dieta com levedura (7g por animal por dia). Nos dias 0, 14, 42, 70 e 105, hemograma, metabolismo oxidativo de leucócitos, haptoglobina sérica, frequência de secreção nasal e temperatura orbital foram avaliados. No dia do abate, foi realizada avaliação pulmonar. Nos dias 42, e 70 de terminação em confinamento, os animais tratados apresentaram aumento do metabolismo oxidativo dos leucócitos (D42 $P=0,04$; D70 $P=0,02$) em relação ao grupo controle. Esses animais apresentaram menor frequência de secreção nasal mucopurulenta, menor temperatura orbital, menor ocorrência de pneumonias ($P=0,05$) com menor gravidade das lesões pulmonares ($P=0,01$), permitindo inferir que a levedura autolisada na dieta melhorou a eficiência dos fagócitos sanguíneos, reduzindo inflamações e a ocorrência de CDRB, especialmente na dosagem de 4g.

TERMOS DE INDEXAÇÃO: confinamento, doença respiratória bovina, levedura autolisada, metabolismo oxidativo, *Saccharomyces cerevisiae*.

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INTRODUCTION

The feedlot system has several advantages for intensifying meat production; however, situations commonly experienced under feedlot conditions can result in the appearance of diseases, especially infectious diseases such as bovine respiratory disease (BRD), which is the result of an immune deficiency and causes substantial economic losses (Baptista et al. 2017). The use of additives in the diet of feedlot steers is considered attractive to mitigate these effects because it may improve performance and immunity (Shurson 2018).

The main yeast used is *Saccharomyces cerevisiae*, as either live yeast or products derived from its cell wall. This approach has attracted attention in the scientific community because yeast exerts immunomodulatory effects (Adili et al. 2020, Kim et al. 2020) and does not leave a residue in the animal carcass or induce bacterial resistance (Kogan & Kocher 2007).

These additives contain mannan oligosaccharides, which can activate the immune response without inducing excessive inflammation, possibly by inducing regulatory cytokines and stimulating the migration of immune cells to specific sites. Additionally, these additives contain β -glucans, which increase the functionality of macrophages and neutrophils (Williams et al. 1996, Oliveira et al. 2010, Ollé et al. 2017).

Despite the potential of these components to improve the health of feedlot steers, there are few studies in beef cattle concerning the benefits of these additives for the immune system and respiratory diseases. Keyser et al. (2007) and Finck et al. (2014) noted that supplementation with yeast additives reduced morbidity, mortality, and the number of treatments for this disease. Nevertheless, the authors did not study any immunological mechanism.

Because autolyzed yeast supplementation in the diet of feedlot steers may improve animal immunity, we believe that this supplementation can also minimize the occurrence of diseases such as BRD, which frequently occurs in beef cattle subjected to intensive management. This work aimed to evaluate whether daily supplementation with autolyzed yeast interferes with innate immunity and reduces the incidence of respiratory disorders in finished feedlot steers.

MATERIALS AND METHODS

Animals, experimental design and treatments. The experimental design was completely randomized and developed as a blind model

study in relation to the treatment for immune and histopathological evaluations. Thirty-six crossbred $\frac{1}{2}$ Angus-Nelore steers (BW 355 ± 10 kg, 11 ± 0.5 months), previously dewormed, without vaccines against BRD, were used. These animals were from a property near the experimental unit. They were housed in a feedlot at the “Núcleo de Produção Animal” (NUPRAN) at the “Universidade Estadual do Centro-Oeste” (Unicentro), located in Guarapuava, Paraná, Brazil.

The climate of the Guarapuava region is humid mesothermal subtropical (Cfb), without a dry season, with fresh summer and mild winter according to the classification of Köppen. Guarapuava lies at an altitude of approximately 1,100m, with an average annual rainfall of 1,944mm, an average annual minimum temperature of 12.7°C , and an average annual maximum temperature of 23.5°C with a relative humidity of 77.9%.

The animals were homogeneously distributed among the three treatments, with 12 replicates each of control: diet without yeast; Y4: yeast diet (4g per animal day-1 of the product RumenYeast®, São Paulo, ICC Brazil); and Y7: yeast diet (7g per animal day-1 of the product RumenYeast®, São Paulo, ICC Brazil).

The product RumenYeast® is composed of 100% autolyzed yeast based on *Saccharomyces cerevisiae* from the fermentation of sugar cane, with approximately 21% β -glucans and 12% mannan oligosaccharides.

Food management and facilities. The food was provided twice daily, at 6:00 a.m. and 5:30 p.m., as a total mixed ration (TMR). The original and experimental diets were the same, consisting of 5% ryegrass haylage, 35% corn silage, and 60% commercial concentrate on a dry matter basis. The following foods were used to manufacture the concentrate: soybean meal, soybean husk, barley root, ground corn grains, calcite limestone, dicalcium phosphate, common salt, livestock urea, and vitamin-mineral premix (Table 1).

Leftover food was weighed daily in the trough to adjust the volumes of feed provided, and the food was adjusted so that 5% of the dry matter was left.

The experimental facilities consisted of 20 feedlot stalls, with an area of 15m^2 each ($2.5\text{m} \times 6.0\text{m}$). Each stall had a concrete feeder measuring 2.30m long, 0.60m wide and 0.35m high and an automatic metallic waterer.

Measurements, sampling, and analysis. The experiment lasted 106 days, with 105 days to finish the animals in the feedlot and slaughter on Day 106. The animals were acclimated to the experimental facilities for one week. Then, the first blood collection occurred (Day 0): at this time point, yeast supplementation started, according to the treatment groups. The prebiotic was distributed longitudinally in the feeding

Table 1. Chemical composition of the feed used for animal feeding and average values of the experimental ration, based on total dry matter (DM)

Parameter	Ryegrass haylage	Corn silage	Concentrate	Experimental diet*
Dry matter, % NM	57.35	40.63	90.40	71.33
Mineral matter, % DM	5.59	2.51	6.36	4.97
Crude protein, % DM	12.43	8.44	20.20	15.70
Ethereal extract, % DM	3.28	2.65	2.05	2.32
Neutral detergent fibre, % DM	48.89	46.14	31.47	37.48
Acid detergent fibre, % DM	37.89	25.98	13.08	18.84
Lignin, % DM	6.90	3.43	4.73	4.38
Total digestible nutrients, % DM	54.74	68.66	78.68	73.98
Ca, % DM	0.58	0.14	1.67	1.08
P, % DM	0.26	0.22	0.58	0.44

* Premix guaranteed level per kg of concentrate: vit. A = 16000IU, vit D3 = 2000IU, vit. E = 25 IU, S = 0.36g, Mg = 0.74g, Na = 3.6g, Co = 0.52mg, Cu = 22.01mg, F = 18.00mg, I = 1.07mg, Mn = 72.80mg, Se = 0.64mg, Zn = 95.20mg; NM = natural matter.

through during the diet administration. Then, at the beginning of the feedlot time (Day 14), in the middle (Days 42 and 70) and at the end of the feedlot time (Day 105), additional samples were taken. The animals that presented clinical signs compatible with BRD at the beginning of the feedlot time, such as an increase in rectal temperature, pulmonary auscultation consistent with pneumonia, changes in the color of mucous membranes compatible with parasitic sadness, and reduced consumption, were removed from the experiment. Within those criteria, two animals in the control group (2/12) and five in the 7g yeast group (5/12) were removed from the experiment because they showed signs of BRD between Days 0 and 14 of the feedlot time. They were treated and recovered clinically from the disease 7 to 14 days later but stayed out of the experiment.

Hematological analysis. The animals' innate immunity was evaluated using the complete blood count, leukocyte oxidative metabolism (ROS-reactive oxygen species), and serum haptoglobin measurement.

Therefore, at the sampling time points, blood samples (8mL) were collected by venipuncture of the external jugular into vacuum flasks containing heparin, ethylenediaminetetraacetic acid (EDTA), or no anticoagulants. The blood count in blood samples containing EDTA was performed in an automatic cell counter (SDH-3 VET, Labtest, São Paulo, Brazil). Leukocyte cell populations were classified according to the morphological characteristics of the blood smear and observed under optical microscopy at 1,000× magnification.

In the blood samples with heparin, the leukocyte oxidative metabolism test was performed using the 5% NBT (tetrazolium nitroblue) quantitative technique (Sigma®, São Paulo, Brazil) according to Flores et al. (2019).

In blood samples without anticoagulants, serum haptoglobin was measured. The serum was immediately separated from the whole blood by centrifugation at 3,500rpm (rotations per minute) x 15 min at room temperature. Subsequently, the serum was frozen at -20°C until the end of blood collection. Haptoglobin was measured by a commercial kit using the ELISA technique (Bovine Haptoglobin EB0011 Fine Test®, WU, China) according to the manufacturer's instructions. The assay's intra- and inter-coefficients of variation were 6.6% and 7.8%, respectively.

Identification of respiratory disorders. Bovine nasal secretions detected by direct inspection and orbital temperature measured with an infrared thermometer (AKSO, AK30 New, China) at a distance of one meter from the animal's eye, with the observer outside the animals' pens, were evaluated at the same time of day on each of five consecutive days between each experimental time point (Days 0, 14, 42, 70 and 105). The presence (score 2) or absence (score 1) of nasal secretions for each sample time point was calculated. From these medians, the frequency of animals with the mucopurulent nasal discharge was identified. The means of orbital temperature for each sample time point were calculated.

On the day of slaughter, the lungs of all animals were examined macroscopically and by histopathological evaluation by a veterinary pathologist. The severity of pneumonia was based on the extent of pulmonary consolidation, according to Ceribasi et al. (2014), with modifications: a score of 1 for the absence of injury; a score of 2 for injury in up to 50% of the cranioventral lobe; a score of 3 for injury in between 50% and 75% of the cranioventral lobe; and a score of 4 for injuries in more than 75% of the cranioventral lobe (right and left) based on visual inspection and palpation. Then, fragments of the cranioventral lobe were collected in the transition area between normal tissue and consolidation areas of approximately 2 cm². If there was another lobe with the lesion, it was also collected. The tissues were fixed in 10% formaldehyde for 48 hours and embedded

in paraffin. Then, they were sectioned to generate histopathological slides with 5-micrometer (µm) sections of lung tissue, stained with hematoxylin and eosin (HE), and finally observed under an optical microscope. The fragments were classified according to the level of inflammatory cells in the bronchiolar epithelium: score 1, absence of inflammatory cells; score 2, up to 40% of inflammatory cells; score 3, 50% to 70% of the cranioventral lobe injured; and score 4, more than 80% injured.

Statistical analysis. Data analysis with the Kolmogorov-Smirnov test revealed that all immune variable data except leukocytes and their populations were normally distributed. Parametric repeated measures for repeated samples were used to analyze the variance, and Tukey's multiple comparison tests were conducted for the time effect evaluation. The parametric T-test was conducted to measure the treatment effect, with Tukey as a post-test. The results related to leukogram and nasal secretion were analyzed by Kruskal-Wallis and Dunn as a posttest. The other scores (macroscopic lung score and histopathology) were analyzed using the chi-square test and expressed as the frequency of animals with each score. A commercial statistical software program (SAS, version 9.3, SAS Institute Inc., Cary, North Carolina, USA) was used for analyses. Differences were considered significant at $P \leq 0.05$.

RESULTS

The animals that presented clinical signs compatible with BRD or babesiosis and anaplasmosis during the acclimation period (increase in rectal temperature, abnormal pulmonary auscultation sounds, anemia or icteric mucous membranes and reduced consumption) were removed from the experiment. According to those criteria, two animals in the control group (2/12) and five in the 7g yeast group (5/12) were removed from the experiment. They were treated and recovered clinically from the disease 7 to 14 days later but stayed out of the experiment.

Leukocyte oxidative metabolism

Compared to the initial time points in the time course, the control group exhibited a reduction in leukocyte oxidative metabolism ($P=0.0001$; D0 and D14 differed from D42, D70 and D105). For the treatment comparison, the treated groups had higher leukocyte oxidative metabolism than the control on D42 and D70 ($P=0.04$, $P=0.02$, respectively) (Fig.1).

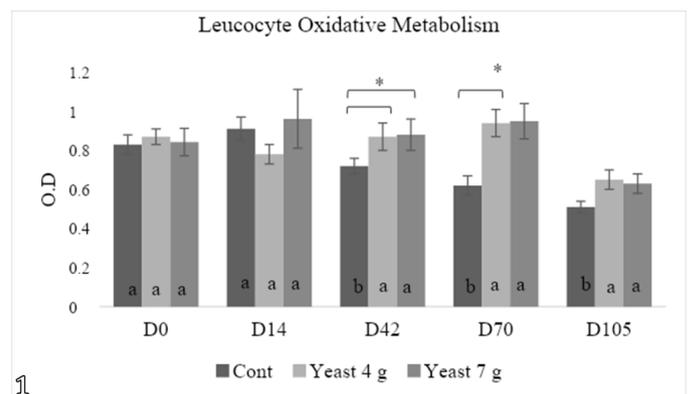


Fig.1. Leukocyte oxidative metabolism of feedlot steers supplemented with autolyzed yeast. O.D. = optical density. Time effect: comparison of the same group at different time points (a, b) ($P \leq 0.05$). Treatment effect: Comparison of different groups at the same time point (asterisk) ($P \leq 0.05$), Tukey's test.

Blood count

Most animals had leukocytosis due to neutrophilia throughout the experiment. This variable had no time or treatment effect.

Serum haptoglobin

There was no time effect. On D70, the control group animals had higher serum haptoglobin than the other groups ($P=0.05$, Fig.2).

Identification of respiratory disorders

The control group had a lower orbital temperature than the Y4 group at D0 ($P=0.003$). However, the Y4 group had a lower orbital temperature than the control at D105 ($P=0.04$) (Fig.3). As this variable is influenced by the environmental temperature, a statistical analysis of the time effect was not performed.

The frequency of animals with mucopurulent nasal secretion decreased for the treated groups on D42 and D70 and Y4 on D105 (time effect $P=0.05$). The frequency of animals with mucopurulent nasal secretion was lower in the treated groups on D70 than in the C group ($P=0.05$) (Fig.4).

The macroscopic pulmonary lesions were used for classifying the severity of pneumonia and were characterized by

reddish-purple consolidation and focal lobes with atelectasis. There was no change in the pleura or adhesions between the pulmonary lobes. No animal had a lesion score of 4 for pneumonia severity. The Y4 group included more animals without pneumonia (score 1) than the control group ($P=0.01$). The Y7 group had the same animal frequency as the Y4 and C groups ($P=0.27$) (Fig.5).

The microscopic lung lesions revealed the presence of inflammatory cells, including, mainly, lymphocytes and fibroblasts, and alterations related to it, such as interalveolar septum thickening, edema, and tissue exudates were mainly of small magnitude, not promoting macroscopically visible modifications in the tissue (C=60%, Y4 25%, and Y7 29% prevalence of animals with inflammatory infiltrate in the lung without macroscopic lesions). The treated groups showed less inflammatory infiltration in the lung than the control group ($P<0.05$) (Fig.5).

DISCUSSION

Supplementation with 4g autolyzed yeast promoted higher cellular immune efficiency, and this improvement reduced the inflammation and respiratory diseases in feedlot steers, mainly when used at the dosage of 4g. At the dose of 7g, the effect was intermediate, as the two treated groups showed greater immune efficiency and reduced indicators of respiratory disease in D42 and D70 in relation to C. This situation continued in Y4 in D105 but not in Y7. It is possible that the loss of five animals from Y7 influenced the statistical analyses. However, as the experiment was carried out in an experimental unit, to which the animals were transported and allocated on the same date, it was not possible to replace the lost animals, as this measure would pose the challenge of different timepoints and the animals would not be exposed to the same conditions.

Although all groups presented leukocytosis due to neutrophilia and lymphocytosis at all times, it is understood that higher leukocyte oxidative metabolism in treated groups after the 42nd and 70th days of the experiment indicates greater efficiency of innate immunity.

Virmond et al. (2020) and Reck (2017) also reported leukocytosis due to neutrophilia and lymphocytosis in Angus

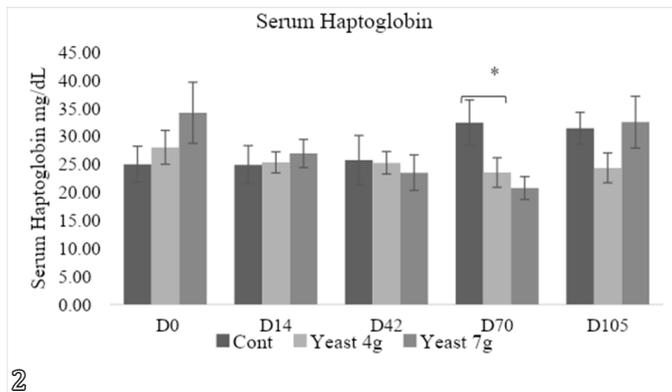


Fig.2. Serum haptoglobin (mg/dL) of feedlot steers supplemented with autolyzed yeast. Time effect: comparison of the same group at different time points (a, b) ($P\leq 0.05$). Treatment effect: comparison of different groups at the same time point (asterisk) ($P\leq 0.05$), Tukey's test.

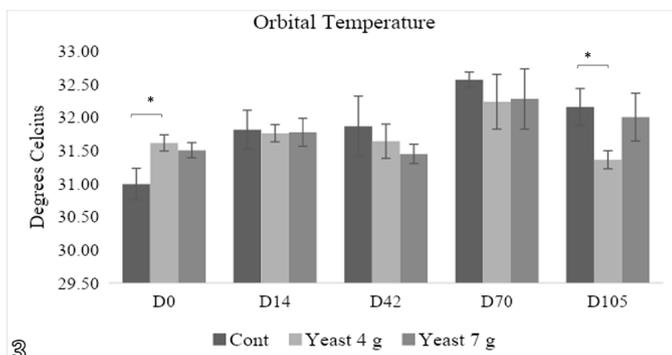


Fig.3. Orbital temperature of feedlot steers supplemented with autolyzed yeast. Treatment effect: comparison of different groups at the same time point (asterisk) ($P\leq 0.05$).

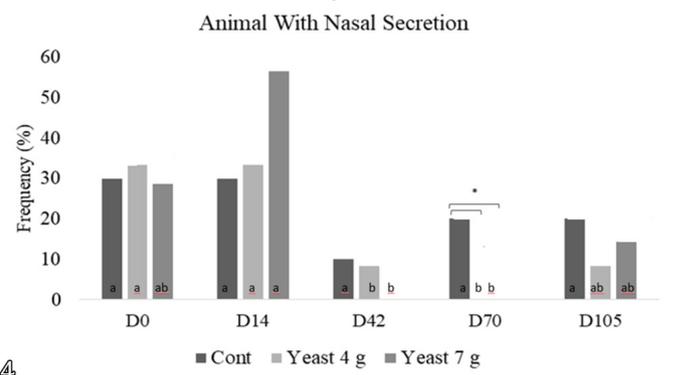


Fig.4. Frequency of mucopurulent nasal secretion of feedlot steers supplemented with autolyzed yeast. Time effect: comparison of the same group at different time points (a, b) ($P\leq 0.05$). Treatment effect: comparison of different groups at the same time point (asterisk) ($P\leq 0.05$), Chi-square test.

The parameters of orbital temperature and mucopurulent nasal secretion were used as indicators of BRD because they can serve as early markers of BRD without manipulating the animals, which would avoid stress and false-positive examination results. For that evaluation, these measurements must be made near the animal before feeding, thus preventing them from licking the nostril and removing the accumulated secretions. The orbital temperature should not be compared with the temperature of other animals because it can be influenced by ambient temperature (Schaefer et al. 2007). However, these indicators do not differentiate changes in the upper respiratory tract from more severe cases, such as those in the lower respiratory tract (Schaefer et al. 2007, McGill & Sacco 2020).

As the C group presented a higher frequency of lung lesions than the Y4 and Y7 groups and a higher frequency of inflammatory infiltrates in the lungs, we assumed that the respiratory indicators were associated with lower respiratory tract disease. The difference between the lung lesions on macroscopic analysis and the inflammatory infiltrate in the lung can be explained by the anatomical components of the respiratory system of ruminants. Unlike in other species, they allow inflammatory infiltration to occur in the lung without visible changes on macroscopic examination. The more developed interlobular septation, composed of dense connective tissue, serves as a mechanical barrier limiting the distribution of the inflammatory infiltrate. The presence of lymphoglandular nodules drains the inflammatory compounds, so macroscopic changes only occur when there is more expressive and lasting inflammation (Samuelson 2007).

It is possible to affirm that Y4 exhibited better pulmonary efficiency in eliminating pathogens and therefore presented a lower frequency of animals with lung lesions both macroscopically and microscopically than the C group. In Y7, despite the lower frequency of animals with inflammatory infiltrate than C, there was no significant difference in the frequency of the animals with macroscopic changes in the lung, possibly due to the low number of animals in this group.

As already mentioned, the cellular wall components of autolyzed *S. cerevisiae* modulate and alter the production of proinflammatory cytokines, activating the functionality of macrophages, the main resident cell in the bronchoalveolar compartment, which decreases the susceptibility to DRB of treated animals (Broadway et al. 2015, McGill & Sacco 2020).

Similarly, Mahmoud et al. (2020) found that calves supplemented with *S. cerevisiae* in culture showed increased oxidative metabolism of blood neutrophils, less neutrophilic infiltration in the lungs, and a lesser extent of lung lesions in calves challenged with bovine respiratory syncytial virus. This finding indicates that *S. cerevisiae*, either in autolyzed form or in culture, promotes immunostimulation and reduces the occurrence of BRD.

Some animals had BRD, babesiosis, and anaplasmosis at the beginning of the feedlot time before *S. cerevisiae* started to take effect (Virmond et al. 2020). Because of these diseases, they were excluded from the experiment. More research is needed to understand whether the supplementation of steers before their entrance into the feedlot could prevent BRD, especially in this first phase, when the incidence of these diseases is higher in the feedlot.

CONCLUSION

Supplementation with autolyzed yeast in the diet has been shown to improve blood phagocytic function and decrease inflammation and bovine respiratory disease (BRD) in feedlot steers, especially at a dose of 4g.

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Conflict of interest statement.- To our knowledge, there are no conflicts of interest among authors, institutions, or organizations.

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