The Effect of Live Yeast Supplementation on Beef Cattle Performance: A Systematic Review and Meta-Analysis

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Abstract

This meta-analysis evaluates the effects of yeast supplementation (Saccharomyces cerevisiae) on dry matter intake (DMI) and average daily gain (ADG) in beef cattle. The inclusion criteria were complete and randomized trials and supplementation with yeast S. cerevisiae versus no supplementation to measure DMI or ADG. Data were extracted from relevant papers via pre-defined protocols. A meta-analysis of random effects was conducted for each indicator separately including the mean of the control and treated groups. The results were presented with the pooled mean difference (MD), 95% of confidence interval, and I² (percentage of total variation between studies that is due to heterogeneity rather than chance). A total of 12 publications reporting 22 trials conducted in 1,161 cattle were analysed. The heterogeneity between studies was high and ranged from 92 to 99%. No effects were observed in ADG with the inclusion of yeast in the diet (MD = -2.849 g/day, p = 0.492). However, there was a reduction in the DMI (MD = -0.885 kg/day; p = 0.023) despite the high heterogeneity among studies (I^2 = 92.4%; p < 0.001). The ADG increased when the forage level in the diet was between 30 and 50% (MD = 641.08g/day; p = 0.001) and decreased when the level range from 51 to 75% (MD = -2.90 g/day; p < 0.001). In over 60% of the Neutral Detergent Fibre, the use of yeast in the diet decreased the ADG by 406.94 g/day (p = 0.034). Feedlot animals showed a reduction in the DMI (MD = -0.97 kg/day; p = 0.019) if supplemented with yeast. Supplementation with S. cerevisiae in the diet of beef cattle had no effect on ADG; however, it does improve the feed conversion due to the reduction in DMI.

Keywords: intake, nutrition, performance, Saccharomyces cerevisiae

1. Introduction

The intensification of livestock production has continued. Yields are improved by providing appropriate levels of protein, vitamins, minerals and energy. The use of food additives can also improve animal performance because they can modulate rumen function (Berchielli & Bertipaglia, 2010). However, some countries restrict certain additives including antibiotics in the European Union. This has increased the use of alternative additives in animal nutrition (Morais, Berchielli, & Reis, 2011).

Of these additives, live yeast is one of the most important for cattle nutrition—especially *Saccharomyces cerevisiae* yield. This yeast can stimulate microbial growth—mainly lactic acid-utilizing bacteria—and then reduce the likelihood of acidosis (Lila et al., 2004; Pinloche et al., 2013; Ding et al., 2014). Moreover, *S. cerevisiae* decreases the redox potential of the rumen and promotes a more favorable environment for the development of microorganisms—mainly cellulose consumers—which maximize the fibre degradation rates (McAllister et al., 2011).

The results of the use of yeasts in the diet of beef cattle depend on many factors including the strain, dosage and diet composition (Williams, Tait, Innes, & Newbold, 1991; Newbold, Wallace, Chen, & McIntosh, 1995). The literature has described conflicts about the inclusion of yeast in the diet of beef cattle. The aim of this study was

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to better understand the effects of performance on the inclusion of *S. cerevisiae* in the diet of beef cattle via a systematic review and meta-analysis.

2. Materials and Methods

2.1 Protocols and Research Question

This systematic review was developed to identify the effects of the inclusion of *S. cerevisiae* live yeast in the diet for beef cattle. Outcome metrics included average daily gain (ADG) and dry matter intake (DMI). The review protocol was developed in accordance with the guidelines previously published by Sargeant, Amezcua, Rajić, and Waddell (2005), and Higgins and Green (2011).

The review question was defined in terms of population (P), intervention (I), comparator (C), and outcome (O) as follows: (1) the population studied was beef cattle; (2) the intervention, the inclusion of *S. cerevisiae* live yeast in the diet for beef cattle; (3) the comparator was cattle without yeast supplementation in the diet; and (4) the outcomes of interest were performance indicators (*i.e.*, DMI and ADG).

The protocol used in this systematic review as well as each screening tool was adapted from Mederos et al. (2012) and pre-tested before implementation.

2.2 Search Strategy and Study Selection

The final list of terms and algorithms was summarized by population, intervention and outcome and is depicted in Table 1. To ensure that search terms have not been forgotten, the keywords were reviewed in peer-reviewed publications and in traditional literature reviews.

Table 1. Population, intervention, and outcome search terms strings used in the systematic review

Acronym	Search string
Population	bovine OR "beef cattle" OR cal* OR herd OR heifers OR steers
Intervention	"Saccharomyces cerevisiae" OR yeast culture OR supplementation
Outcome	intake OR gain OR performance

A systematic literature search identified peer-reviewed publications published through January 2015. The server of the Federal University of Rio Grande do Sul (UFRGS, Brazil) was used to perform the search in the ISI Web of Science (Thomson Reuters, 1900-2015), Scopus (Elsevier, 1960-2015), and Science Direct (Elsevier, 1823-2015) databases.

A reference search verification was performed by searching the reference lists from seven literature reviews addressing the *S. cerevisiae* supplementation in the diet of cattle (Martin & Nisbest, 1992; Newbold, 1996; Nicodemo, 2001; Denev et al., 2007; Chaucheyras, Walker, & Bach, 2008; França & Rigo, 2011; Calsamiglia, Blanch, Ferret, & Moya, 2012). We also manually searched the electronic search results to identify relevant studies missed in the primary search.

Three reviewers contributed to the different levels and were analysed 30 abstracts in the pre-test level. The citation was considered relevant when: (1) it was primary research; (2) included live yeast supplementation of *S. cerevisiae* in the diet for beef cattle; and (3) measured ADG and/or DMI. The study designs were randomized and non-randomized clinical trials, cohort studies, and case-controls. At this stage, no limits were applied for year and language.

Titles and abstracts (when available) of all records identified by the search strategy were independently evaluated by three investigators. When all reviewers responded "No" to at least one of the above questions, the citation was excluded from this review. Differences in opinion between reviewers were resolved by consensus, by referring back to the original data, or by consulting another reviewer in case of persisting disagreement.

All citations were imported into the reference manager End Note[®] (Thomson Reuters, New York, USA) and duplicate citations were manually removed. A Microsoft Excel[®] (Microsoft Corporation, Redmond, WA, USA) spreadsheet was used to store, organize, and manipulate the systematic review data.

2.3 Methodological Assessment and Data Extraction

Using standardized forms, the first author extracted data on 12 publications. Metrics included the study population, intervention, outcomes, and results. Manuscript-level information included the journal name, the author(s) name(s), the year of publication, and the original language. The methodological assessment and data

extraction of the relevant publications selected through abstract screening was performed using full-texts. The full-texts were evaluated based on language (English, Spanish, or Portuguese), appropriate control groups, and amount of detail. Sufficient details were needed to extract data and conduct a meta-analysis. At this stage, publications were restricted to languages used by the research team.

For each outcome, we sought to extract the mean, standard error or any available measure of dispersion, measurement unit, p-value, and the number of animals in each group. In publications that only reported the coefficient of variation (CV), the standard error of the mean (S_x) for the control and treated groups was derived from the formula described by Higgins and Green (2011):

$$S = \overline{X} \times CV \tag{1}$$

$$Sx = S/\sqrt{n} \tag{2}$$

Where, \overline{X} = mean, S = standard deviation, and n = number of animals in the treatment and control groups.

When the results were described but not actually recorded, we contacted the corresponding author by electronic mail and asked for summary statistics. The study was excluded when we did not receive a response.

2.4 Assessment of Risk of Bias

We used the Cochrane Collaboration Risk of Bias Tool with minor modifications to evaluate the risk of systematic bias in individual studies (Higgins & Green, 2011). The modification consisted of considering ADG and DMI as low risk of bias regardless of whether the blinding outcome assessment were used or not.

2.5 Meta-Analysis

The studies in the quantitative analysis showed enough data to estimate the standardized mean difference (MD) between control and treatment groups with 95% confidence interval. All analyses were conducted using the Stata V 14.0 (Stata Corp., Texas, USA) software.

The random effect meta-analysis and meta-regression were carried out given the *a priori* assumption of heterogeneity between studies. The DerSimonian and Laird (1986) methods were used to estimate the variation between studies.

To compare groups in the meta-analysis, we used a separate meta-analysis with various subsets of data. Each consisted of at least two individual studies that investigated similar treatments and used the same experimental design and evaluated the same outcome. The Q Cochran (chi-square test for heterogeneity) and I^2 (percentage of total variation across studies that is due to heterogeneity rather than chance) were calculated based on the result. The magnitude of I^2 was considered low, moderate or high, with I^2 values of 25, 50 and 75% (Higgins, Thompson, Deeks, & Altman, 2003). Differences were considered significant at p < 0.05 and trends at $0.05 \ge p < 0.1$.

2.6 Publication Bias

The Begg's adjusted rank correlation and Egger's regression asymmetry tests were used in combination with a funnel plots for each outcome (DMI and ADG). Bias was considered to be present if at least one of the statistical methods was significant (p < 0.10). If there was any statistical evidence of publication bias, the "trim-and-fill" method (Duval & Tweedie, 2000) was used to estimate and correct for this publication bias.

2.7 Influential Studies

Studies influencing the summary effect were identified by sensitivity analyses by manually removing and replacing one study at a time and evaluating whether the MD changed by $\pm 30\%$.

2.8 Cumulative Meta-Analysis

The cumulative meta-analysis analysed the pooled estimate of the treatment each time the result of a new study was published. If we sort by sample size, then we can display the potential impact of the publication bias. By sorting the studies chronologically retrospectively, we were able to identify when the treatment effect first reached conventional levels of statistical significance (Egger, Smith, & Altman, 2001; Borenstein, Hedges, Higgins, & Rothstein, 2009).

2.9 Meta-Regression

A method-of-moments estimator under a random-effect model was performed to detect the sources of heterogeneity between studies that might affected the outcomes (Borenstein et al., 2009). The impact of publication year, continent (North America, Central America, South America, Europe or Asia), cattle group (Bos taurus, Bos indicus or crossbred), intervention follow-up period, type of S. cerevisiae strain, production system

(pasture or feedlot), and the amount of total digestible nutrients (TDN) and neutral detergent fibre (NDF) in the total diet were explored using meta-regression.

3. Results

3.1 Search Results and Characteristics

Figure 1 shows the flow of records throughout the systematic review process. The initial screening comprised 104 records, in which 58 studies were excluded in the first step. Among the full-text publications that were assessed for eligibility and methodological soundness, 28 were excluded. Out of the remaining, six publications did not have enough data to conduct the quantitative analysis (Appendix A). Thus, 12 publications were included in this systematic review meta-analysis about live yeast supplementation (Table 2). The total number of cattle included in this meta-analysis was 536 and 626 for DMI and ADG, respectively. After the final assessment, 12 publications reporting 22 trials were included. The characteristics of the publications are presented in Table 3.

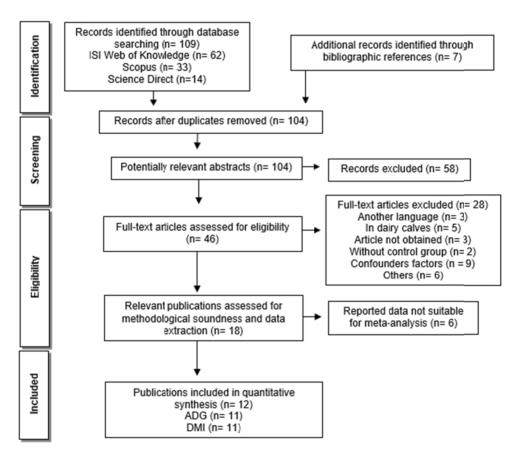


Figure 1. Flow diagram through the systematic review indicating the number of abstracts and publications included and excluded in each level

Note. ADG: average daily gain; DMI: dry matter intake.

3.2 Risk of Bias

We could not accurately evaluate the bias because several publications failed to provide sufficient details (Appendix B).

For the performance bias, none of the publications provided sufficient information about the blindness of the people involved in each study. Thus, the bias risk was considered unclear. The risk of detection bias was not relevant for DMI and ADG despite the lack of blindness because these were performed with an equipment (weighing scale for ADG and DMI).

Table 2. A descriptive summary of relevant publications included in the systematic review and used in the meta-analysis and meta-regression

Reference	Country	Language	Number of animals/group	Outcome measure	Follow-up period (days)
Z. Mir and P. S. Mir (1994)	Canada	English	9	ADG/DMI	84/70/64/24
P. S. Mir and Z. Mir (1994)	Canada	English	9	ADG/DMI	84/60/42
Singh et al. (1998)	India	English	10	ADG/DMI	122
Hinman et al. (1998)	USA	English	36	ADG/DMI	115
Cabrera et al. (2000)	Mexico	English	7	ADG/DMI	90
Kamra et al. (2001)	India	English	9	ADG/DMI	159
Gattas et al. (2008)	Brazil	Portuguese	40/5	ADG	60
Gomes et al. (2011)	Brazil	Portuguese	18	ADG/DMI	84
Rodrigues et al. (2013)	Brazil	English	19	ADG/DMI	112
Prohmann et al. (2013)	Brazil	Portuguese	8	ADG	112
Vyas et al. (2014)	Canada	English	6	DMI	63
Swyers, et al. (2014)	USA	English	63	ADG/DMI	125

Note. Numbers separated by "/" represent observations from different experiments in the same study; ADG = Average daily gain; DMI = Dry matter intake.

3.3 Meta-Analysis for DMI

Combining data from 11 publications (n = 20 trials), we obtained a MD of -0.88 kg (95% confidence interval: -1.650, -0.120; p = 0.023) with high heterogeneity ($I^2 = 92.4\%$, p < 0.001; Figure 2).

Table 3. Descriptive characteristics of 12 publications included in the systematic review and meta-analysis

Variable	Description	Categories	Number of publications
Data published	Year of study publication	1990-2000	5
		2001-2015	7
Language	Language of study publication	English	9
		Portuguese	3
Continent		North America	5
		South America	4
		Central America	1
		Asia	2
Cattle groups	Cattle group in which interventions	Bos taurus	3
	were evaluated	Bos indicus	2
		Crossbred	7
Production systems	Production systems in which studies	Pasture	2
Troud vier systems	were evaluated	Feedlot	10
Forage (%)	Amount of forage in the total diet	< 30	3
101	Thirduit of foruge in the total diet	30-50	7
		51-75	2
		> 75	4
Total detergent nutrients (%)	Amount of TDN in the total diet	< 65	3
Total detergent nutrients (70)	7 mount of 1514 in the total diet	65-75	7
		> 75	4
Neutral detergent fibre (%)	Amount of NDF in the total diet	< 40	6
redutal detergent fibre (70)	Amount of NDF in the total diet	40-60	5
		> 60	3
Saccharomyces cerevisiae strain	Type of strain ^a	1	2
Saccharomyces cerevisiae strain	Type of strain		3
		2 3	2
		_	2
		4	
		5	1
		6	1
		7	1
Colony-forming unit (CFU)	Number of colony forming units	10 ⁰⁶	3
	tested in the studies	10 ⁰⁷	1
		10^{08}	2
		10 ⁰⁹	5
		10 ¹⁰	1
Dosage of yeast in the diet (g)	Amount of yeast in the diet	< 6	4
		10	6
		28	2

Note. a 1 = Diamond; 2 = 1026 Beef Sacc; 3 = Alltech Biotechnology; 4 = ITCCF 2094; 5 = Levucell; 6 = Procreatin 7; 7 = AB Vista.

The effect of *S. cerevisiae* supplementation on DMI are depicted in Table 4. Cattle reared in feedlot systems including the supplemented group showed lower DMI (p = 0.019). In publications with a follow-up period less than 90 days, the DMI tended to be higher ($p \le 0.10$) in the control group. The *Bos indicus* cattle provided with yeast supplementation had their DMI increased. In *Bos taurus*, this same feeding strategy decreased the outcome.

The animals provided with yeast supplementation and that received forage percentages between 51 and 75% (p = 0.082) and above 75% (p = 0.051) tended to show a lower DMI. When the amount of TDN ranged from 65 to 75%, the DMI of control group increased. The DMI decreased when animals were supplemented with yeast at

 10^9 CFU/g. For strains 3 and 4, the supplementation decreased the DMI. When the yeast dose was equal to 10 g, the DMI was lower (p \leq 0.001) for the group that received yeast supplementation.

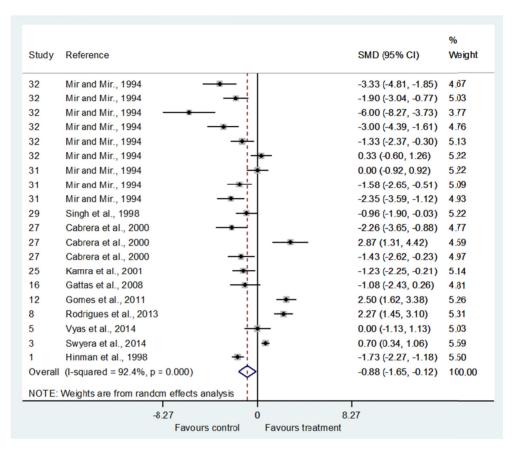


Figure 2. Forest plot of 11 publications that tested yeast supplementation in beef cattle expressed as dry matter intake (kg/day). The effect size is the mean difference between control and treated groups

Note. The centre of the square represents the point estimate for that study and the area of the square is proportional to the weight assigned to that study. The dashed line is the average effect of treatment obtained by the analysis, whereas the solid vertical line marks the value at which the treatment would have no effect. The diamond (◆) at the bottom of the dashed line shows the 95% of the confidence interval for the overall effect obtained from the DerSimonian and Laird (1986) methods.

3.4 Publication Bias and Influential Studies for DMI

A visual inspection of the funnel plot (Figure 3) suggested that a publication bias might be present. Furthermore, the Egger's and Begg's test was significant (p = 0.050 and 0.004, respectively). However, the random-effect "trim-and-fill" method did not result in any change in the effect of treatment; no missing studies were imputed. The sensitivity analysis showed that removing only one study (Z. Mir & P. S. Mir, 1994) changed the pooled estimate from -0.085 to -0.298 kg/day.

3.5 Meta-Analysis for ADG

The overall mean difference reported in the 11 publications (n = 21 trials) indicated no significant effect (MD = -2.85 g/day; 95% CI: -10.977, 5.279; p = 0.492) of yeast supplementation in ADG, and a high heterogeneity between studies ($f^2 = 98.1\%$, p < 0.001).

The effect of *S. cerevisiae* supplementation on ADG are shown in Table 5. Crossbred cattle had higher ADG (p = 0.02) when supplemented with yeast. When the percentage of forage in the diet was between 30 and 50, the animals provided with yeast supplementation showed higher ADG (p ≤ 0.001). However, when the forage represented 51 to 75% of the total diet, the non-supplemented group had a higher ADG. The amount of NDF above 60% decreased (p = 0.034) the ADG in supplemented cattle. This same group tended (p = 0.088) to show

higher ADG when the TDN concentration was below 65%. Animals that received yeast supplementation with strain 2 or with yeast dosage lower than 6 g showed an increase (p = 0.002) in the ADG.

Table 4. Meta-analysis results of comparison groups to dry matter intake.

Variable	Publications	Estimate	95% CI	P-value	<i>I</i> ² (p-value)	
Production systems						
Pasture	3	-0.303	-3.18, 2.58	0.837	92.5 (< 0.001)	
Feedlot	17	-0.975	-1,79, -0.16	0.019	92.8 (< 0.001)	
Follow-up period (days)						
< 60	4	-1.134	-2.34, 0.07	0.066	78.0 (0.003)	
61-90	11	-1.179	-2.49, 0.14	0.080	92.3 (< 0.001)	
91-120	2	0.260	-3.66, 4.18	0.896	98.4 (< 0.001)	
> 120	3	0.700	-1.83, 0.96	0.539	90.2 (< 0.001)	
Cattle group						
Bos taurus	11	-1.681	-2.78, -0,58	< 0.001	92.1 (< 0.001)	
Bos indicus	2	2.379	1.78, 2.98	< 0.001	0.0 (0.712)	
Crossbred	7	-0.808	-1.66, 0.04	0.063	81.0 (< 0.001)	
Forage (%)						
< 30	4	-0.837	-1.93, 0.76	0.214	94.4 (< 0.001)	
30-50	6	0.278	-1.18, 1.73	0.708	92.2 (< 0.001)	
51-75	3	-1.679	-3.57, 0.21	0.082	87.4 (< 0.001)	
> 75	7	-1.817	-3.06, -0.47	0.051	90.2 (< 0.001)	
TDN (%)						
< 65	6	-0.740	-1.89, 0.41	0.209	81.9 (< 0.001)	
65-75	10	-1.410	-2.71, -0.10	0.034	92.2 (< 0.001)	
> 75	4	-0.017	-1.68, 1.65	0.984	96.6 (< 0.001)	
NDF (%)						
< 40	10	-1.727	-1.85, 0.17	0.106	93.5 (< 0.001)	
40-60	5	-1.381	-3.79, 1.02	0.261	94.4 (< 0.001)	
> 60	5	-0.663	-2.05, 0.72	0.348	85.4 (< 0.001)	
CFU						
10^{06}	3	-0.678	-2.54, 1.18	0.474	96.4 (< 0.001)	
10^{07}	1	-	-	-	-	
10^{08}	3	-0.303	-3.18, 2.58	0.837	92.5 (< 0.001)	
10^{09}	12	-1.456	-2.49, -0.42	0.006	90.6 (< 0.001)	
10^{10}	1					
Strain ^a						
1	2	-0.505	-2.88, 1.87	0.677	98.1 (< 0.001)	
2	3	1.307	-0.55, 3.17	0.169	90.6 (< 0.001)	
3	9	-1.944	-2.96, -0.93	< 0.001	84.8 (< 0.001)	
4	2	-1.085	-1.77, -0.39	0.02	0.0 (0.706)	
5	3	-0.303	-3.18, 2.58	0.837	92.5 (< 0.001)	
7	1					
Dosage (g)						
< 6	4	0.988	-0.60, 2.57	0.222	89.7 (< 0.001)	
10	14	-1.479	-2.27, -0.68	< 0.001	84.3 (< 0.001)	
28	2	-0.505	-2.88. 1.87	0.677	98.1 (< 0.001)	

Note. Estimate = standard mean difference of the effect size; CI = confidence interval; I^2 = between-study heterogeneity; TDN = total digestible nutrients; NDF = neutral detergent fibre; CFU = colony-forming unit; a 1 = Diamond; 2 = 1026 Beef Sacc; 3 = Alltech Biotechnology; 4 = ITCCF 2094; 5 = Levucell; 6 = Procreatin 7; 7 = AB Vista.

3.6 Publication Bias and Influential Studies for ADG

The fairly symmetrical funnel plot and the non-significant effect in the Egger's and Begg's tests suggested that publication bias was likely not present.

The sensitivity analysis showed that by removing four publications one at a time (Z. Mir & P. S. Mir, 1994; Singh, Chowdhary, Kamra, & Pathak, 1998; Kamra, Chaudhary, Agarwau, Singh, & Pathak, 2002; Gomes, Antunes, Silva, & Leme, 2011) from the analysis decreased and increased the effect from -2.85 to -4.73, -1.89, 1.66 and 35.41 g/day, respectively.

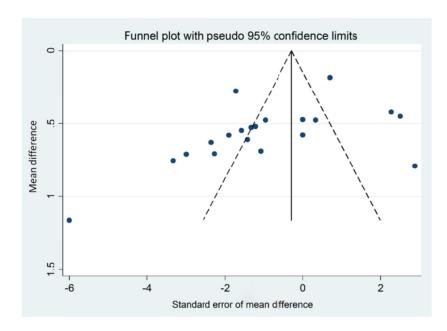


Figure 3. Funnel plot of the point estimates of the effect of the yeast supplementation on the dry matter intake (kg/day) in beef cattle

3.7 Cumulative Meta-Analysis

There was no evidence for a time effect for DMI or ADG.

3.8 Meta-Regression

Eleven publications reporting 20 and 21 trials were included in the meta-regression analyses for DMI and ADG, respectively.

The meta-regression results for DMI showed that publication year was associated (p = 0.005) with the outcome and explained 41.2% of the total variance. An increase in one unit in the publication year resulted in an increase in the predicted DMI by a factor 0.159 kg (95% CI: 0.056, 0.263). Univariable meta-regression indicated that the studies conducted in Central America had a predicted mean difference in DMI 2.84 kg greater than studies performed in North America (p = 0.032). The analysis also suggested that *Bos indicus* cattle had a greater predicted value (MD = 4.128 kg/day; p = 0.003) compared with *Bos taurus*.

Meta-regression results for ADG showed that sample size explained 15.75% of the total variance and was associated (p = 0.047) with the outcome. When the study size was increased by one unit, the predicted ADG increased by a factor of 58.57 g/day (95% CI: 0.864, 116.275). Studies conducted in Central America reported higher ADG (MD = 414.1 g/day; p = 0.052) versus those in North America.

4. Discussion

The inclusion of *S. cerevisiae* yeast in the diet for beef cattle had no effect on ADG, but reduced the DMI and improved feed conversion. The available literature is inconclusive and suggests that best performance of yeast supplementation occurs with an increase in feed intake (França & Rigo, 2011). Although the comparison between control and supplemented groups showed no changes in DMI when the animals were reared on pastures, the DMI was reduced in cattle that received live yeast and were reared in a feedlot.

The mechanisms underlying feed ingestion remain unclear. Acetate and propionate appear to exert some effect on the control of meal size because propionate infusion in the steers' mesenteric vein reduced feed intake, but acetate did not. Thus, the propionate evokes a greater decrease in feed ingestion than acetate and butyrate (Allen, 2000).

Table 5. Meta-analysis results of comparison groups to average daily gain

Variable	Publications	Estimate	95% CI	P-value	<i>I</i> ² (P-value)	
Production systems					· · · · · · · · · · · · · · · · · · ·	
Pasture	5	-205.170	-485.63, 75.29	0.152	96.9 (< 0.001)	
Feedlot	16	2.940	-10.74, 4.86	0.460	98.4 (< 0.001)	
Follow-up period (days)						
< 60	4	-0.708	-9,61, 8.20	0.876	98.4 (< 0.001)	
61-90	10	2.940	-7.52, 13.40	0.582	96.6 (< 0.001)	
91-120	4	-295.165	-824.80, 234.47	0.275	98.9 (< 0.001)	
> 120	3	887.491	-484.07, 2259,05	0.492	99.3 (< 0.001)	
Cattle group						
Bos taurus	10	-0.518	-5.32, 5.37	0.824	97.0 (< 0.001)	
Bos indicus	2	1624.897	-535.05, 3784.84	0.149	97.7 (< 0.001)	
Crossbred	9	-325.130	-649.46, -109.33	0.029	98.6 (< 0.001)	
Forage (%)						
< 30	5	0.612	-6.80, 8.02	0.871	99.0 (< 0.001)	
30-50	6	641.081	261.76, 1020.38	0.001	98.6 (< 0.001)	
51-75	3	-2941.180	-3535.38, -2346.97	< 0.001	0.0 (0.390)	
> 75	7	-125. 368	-328.62, 77.88	0.227	98.1 (< 0.001)	
TDN (%)						
< 65	5	609.980	-90.93, 1310.88	0.088	98.3 (< 0.001)	
65-75	12	0.176	-6.38, 6.73	0.958	96.6 (< 0.001)	
> 75	4	332.680	-2174.18, 2839.54	0.795	99.3 (< 0.001)	
NDF (%)						
< 40	6	-725.826	-2706.57, 1254.92	0.473	99.0 (< 0.001)	
40-60	10	1.348	-5.780, 8.48	0.711	97.6 (< 0.001)	
> 60	5	-406.939	-784.07, -29.81	0.034	96.0 (< 0.001)	
CFU						
10^{06}	3	4400.815	-3149.88, 11951.51	0.253	99.5 (< 0.001)	
10^{07}	1	-	-	-	-	
10^{08}	3	-501.474	-1424.73, 421.78	0.257	97.2 (< 0.001)	
10^{09}	12	-2.849	-6.64, 2.40	0.357	96.3 (< 0.001)	
10^{10}	2	-6.400	-320.05, 307.25	0.968	98.2 (< 0.001)	
Strain ^a						
1	2	-742. 401	-9072.24, 7587.43	0.861	99.7 (< 0.001)	
2	3	569.183	2135.93, 9262.42	0.002	98.9 (< 0.001)	
3	9	-0.193	-3.51, 3.13	0.909	95.0 (< 0.001)	
4	2	-371.771	-928.61, 185.06	0.191	96.1 (< 0.001)	
5	3	-501.474	-1424.73, 421.78	0.287	97.2 (< 0.001)	
6	2	-6.400	-320.05, 307.25	0.968	98.2 (< 0.001)	
Dosage (g)						
< 6	3	2750.00	2135.93, 9262.42	0.002	98.9 (< 0.001)	
10	16	-2.494	-7.35, 2.36	0.314	95.8 (< 0.001)	
28	2	-2.849	-9072.24, 7587.43	0.861	99.7 (< 0.001)	

Note. Estimate = standard mean difference of the effect size; CI = confidence interval; I^2 = between-study heterogeneity; TDN = total digestible nutrients; NDF = neutral detergent fibre; CFU = colony-forming units; ^a 1 = Diamond; 2 = 1026 Beef Sacc; 3 = Alltech Biotechnology; 4 = ITCCF 2094; 5 = Levucell; 6 = Procreatin 7; 7 = AB Vista.

In this sense, Chung, Walker, McGinn and Beauchemin (2011) showed that inclusion of yeast increases propionate concentration in ruminal fluid. This may be due to an increase in lactate-utilizing bacteria, *Selenomonas ruminantium* and *Megasphaera elsdenii*. These bacteria convert lactate to propionate (Lettat, Martin, Berger, & Nozière, 2012; Silberberg et al., 2013) and have their growth stimulated by the supplementation of yeast (Pinloche et al., 2013).

The follow-up period is variable and influences the results, but it is difficult to understand. Rodrigues et al. (2013) observed a reduction in the consumption of cattle supplemented with yeast during the first 84 days without an effect of time period. These authors claimed that this reduction is a consequence of the stimulation caused by yeast on the number of the ruminal bacteria and reflects a continuous use of energy and NDF with less amount of dry matter.

Similarly, Hinman, Sorensen and Momont (1998) reported no differences within the first 86 days, however between day 87 and 115, there was a DMI increase in cattle supplemented with yeast. The authors explained that these results were because of the best efficiency of the microbial growth as the dilution rate of the ruminal fluid increases. However, the question is "why does this change?"

Bos taurus and Bos indicus cattle showed different responses to DMI. The yeast supplementation for Bos taurus group decreased the DMI, while Bos indicus increased. Even though both cattle groups have similar anatomical and physiological characteristics of digestive system, they are adapted to specific local conditions, that is, Bos taurus to temperate climate and Bos indicus to tropical climate (Food and Agriculture Organization [FAO], 2007). The question is not about adaptability, but about the environmental conditions. This mainly concerns the forages in those regions that developed defence mechanisms for each environment. Therefore, the results about intake may not have been affected by cattle group, but it is likely for the experimental conditions. Gaughan, Mader, Holt, Hahn and Young (2002) reported that animals in thermal stress reduced the DMI as a way to regulate their body temperature. Nevertheless, using yeast in the cattle diet reduces the ruminal and rectal temperature (Cho et al., 2014), and increases the DMI. Our results highlighted that crossbred animals supplemented with yeast showed a greater ADG than the control group. These experiments were performed in regions with a tropical climate (Cabrera et al., 2000; Gattas et al., 2008; Prohmann et al., 2013). Thus, the results can be explained by the direct effects of yeast and the characteristics of the animals' diet.

Moreover, at high temperatures, there is an increase in the respiratory rate that facilitates heat loss. This can trigger a respiratory alkalosis state. The consequences are a reduction of the CO₂ pressure and an increase in the HCO₃ excretion by the kidneys. This can affect the HCO₃ salivary concentration (Schneider, Beede, Wilcox, & Collier, 1984). Consequently, the pH and the function of the rumen will drop (Mishra et al., 1970). Salvati et al. (2015) observed that cows supplemented with yeast had a reduced heart rate and an increase in plasma niacin. The stimulus to dilatation of arterial blood vessels (Benyó, Gille, Bennett, Clausen, & Offermanns, 2006) acts with prostaglandin vascular receptors (Cheng et al., 2006) and increases the peripheral heat loss in dairy cattle (Zimbelman, Baumgard, & Collier, 2010). This might be the cause of this effect.

Furthermore, some protozoa groups have fibrolytic activity and play a key role in the early colonization of the fibre (Newbold, Fuente, Belanche, Morales, & McEwan, 2015). Their defaunation also decreases the fibrolytic microorganism concentration in the rumen (Newbold et al., 2015). Hence, the effects of diet on the microorganisms may affect the DMI.

In high-concentrate diets, the protozoa population is reduced because it is very sensitive to the fluctuations and decreases in ruminal pH (Granja-Salcedo et al., 2016). Thus, the benefits of yeast are not observed (*i.e.*, protozoa population growth; Arakaki, Stahringer, Garrett, & Dehority, 2010) because of the changes in the starch and lactate intakes by protozoa (Kozloski, 2011). Thus, when a concentrated diet does not decrease pH levels, the population of protozoa can be increased by the presence of yeasts and contribute to the production of short chain fatty acids and NH3 through the fermentation of sugars, amino acids and lactic acid (Kozloski, 2011). However, the presence protozoa in the rumen can also mean bacterial predation (Belanche, Fuente, Moorby, & Newbold, 2012) and detrimental protein for utilization by the host (Newbold et al., 2015).

According to yeasts action mode, as well as their availability for ruminal microorganisms, we expected that higher ADG would be observed at higher dosages. However, the highest ADG levels were observed in cattle supplemented with yeast below 6 g/day. On the other hand, the DMI reduced when the dosage was 10 g/day. Thus, since the yeast effect in the rumen is given by their metabolic activity (Denev et al., 2007), doses above 6 g did not increase the performance effects and might even depress those indicators. There were no differences in other dosages.

The strains had different effects on ADG and DMI. Newbold, Wallace, Chen, and McIntosh (1995), and Robinson and Erasmus (2009) reported that strain affects performance. We found that ADG was higher for cattle supplemented with strain 2, and DMI was reduced in those supplemented with strains 3 and 4. In addition, because there were no differences on ADG, we can assume that the animals had better feed conversion. In general, studies have demonstrated that not all yeast strains can stimulate the ruminal bacteria (Dawson & Hopkins, 1991; Newbold et al., 1995; Newbold, Wallace, & McIntosh, 1996). Dawson and Hopkins (1991) found differences between strains with pure or mixed bacterial culture, and only seven strains had the ability to stimulate the growth of fibrolytic bacteria.

The analysis of yeast regarding their viability, measured as CFU/g, showed no effect on ADG and a reduction in DMI in cattle receiving yeast at 10⁹ CFU/g. Therefore, the yeast effects are not affected by their capacity for multiplication, but rather by their metabolic activity (respiration; Denev et al., 2007).

Animals receiving a total diet containing 30 to 50% of forage and were supplemented with yeast had the greatest ADG suggesting that this range of forage and concentrate favoured the yeast action in the ruminal environment. Furthermore, as highlighted by Ding et al. (2014), the forage to concentrate ratio is responsible for the highest ruminal bacteria concentration, although there is an interaction of forage-to-concentrate ratio with the inclusion of yeast on microbial population in the rumen, *i.e.* (an increase in the total number of bacteria, fungi, protozoa and lactate utilizing bacteria). However, when the percentage of the forage ranged between 51 and 75, the control group showed higher ADG. This result may be related with the increased DMI in non-supplemented animals. Ding et al. (2014) stated that the forage to concentrate ratio has significant impacts on microbial population and on fibre degradation. According to these authors, the highest rumen bacterial concentration (×10¹⁰ copies/mL) are given in the 30:50 ratio with the lowest between 70:30 and 90:10. They still reported an interaction of forage to concentrate ratio with the inclusion of yeast. Treated animals had an increase in the total number of bacteria, fungi, protozoa, lactate-utilizing bacteria and fibre degradation rate.

In this sense, animals provided with diets containing yeast with NDF levels above 60% had lesser ADG than non-supplemented cattle. Contrarily, several studies showed that yeast supplementation increases the activity and amount of ruminal bacteria that degrade the fibre (Michalet-Doreau, Morand, & Martin, 1997; McAllister et al., 2011; Ding et al., 2014). However, Miltko, Kowalik, Majewska, Bełżecki, and Skomiał (2015) showed a reduction in the xylan-degrading enzymes, suggesting that microbial additives can inhibit the digestibility of hemicelluloses in the rumen and explain this lower ADG.

Supplementation with *S. cerevisiae* had positive effects on performance indicators in beef cattle and consequently improves feed conversion. However, the included studies of this meta-analysis produced heterogeneous results and inconsistent results from yeast inclusion in beef cattle diet. Therefore, despite the lack of evidence for publication bias, we did not evaluate the grey literature (thesis, dissertation, proceedings, and government or research station report). This could be considered a methodological limitation in our systematic review meta-analysis. Thus, to obtain consistent responses about the supplementation of yeast in beef cattle, we might consider the various factors and interactions. Otherwise, their recommendation is mere speculation of possible results. In summary, the challenge in animal nutrition is to try and understand the many interactions of the use of yeast in beef cattle performance.

In conclusion, the inclusion of *S. cerevisiae* yeast in diets for beef cattle reduces DMI without affecting the ADG. However, these effects depend on the diet composition, strain used and dose supplied.

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Appendix

Appendix A. List of relevant publications excluded from the final database

Reference	Country	Outcome parameter	Reason for exclusion
Beeson and Perry (1952)	USA	ADG and DMI	Only median was presented
Adams et al. (1981)	Mexico	DMI	Inconsistent information
Olson et al. (1994)	USA	ADG	Insufficient data for this study
Kuss et al. (2009)	Brazil	ADG and DMI	Only median was presented
Chuelong et al. (2011)	Thailand	ADG and DMI	Insufficient data for this study
Neumann et al. (2013)	Brazil	ADG and DMI	Only median was presented

Note. ADG = average daily gain; DMI = dry matter intake.

Appendix B. Risk of bias (classified as low, unclear, and high) of the 12 studies included in the meta-analysis of yeast supplementation in beef cattle

Reference	Outcome evaluated	Selection bias		Performance bias	Detection bias	Attrition bias	Reporting bias
		Sequence generation	Allocation concealment	Personnel blinding	Blinding of outcome assessment	Incomplete outcome data	Selective outcome reporting
Z. Mir and P. S. Mir (1994)	ADG and DMI	Low	Unclear	Unclear	Low	Low	Unclear
P. S. Mir and Z. Mir (1994)	ADG and DMI	Low	Unclear	Unclear	Low	Low	Unclear
Singh et al. (1998)	ADG and DMI	Low	Unclear	Unclear	Low	Low	Unclear
Hinman et al. (1998)	ADG and DMI	Low	Unclear	Unclear	Low	Low	Unclear
Cabrera et al. (2000)	ADG and DMI	Low	Unclear	Unclear	Low	Low	Unclear
Kamra et al. (2001)	ADG and DMI	Low	Unclear	Unclear	Low	Low	Unclear
Gattas et al. (2008)	ADG and DMI	Low	Unclear	Unclear	Low	Low	Unclear
Gomes et al. (2011)	ADG and DMI	Low	Unclear	Unclear	Low	Low	Unclear
Rodrigues et al. (2013)	ADG and DMI	Low	Unclear	Unclear	Low	Low	Unclear
Prohmann et al. (2013)	ADG	Low	Unclear	Unclear	Low	Low	Unclear
Vyas et al. (2014)	DMI	Low	Unclear	Unclear	Low	Low	Unclear
Swyera, et al. (2014)	ADG and DMI	Low	Low	Unclear	Low	Low	Unclear

Note. ADG = average daily gain; DMI = dry matter intake.

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