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ANIMAL SCIENCE

Effects of different additives on cattle feed intake and performance - a systematic review and meta-analysis

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Abstract: In the last few years, there has been a growing interest in the use of natural feed additives in animal feed. These can be used as replacements for antibiotics, to alter rumen fermentation and increase feed efficiency in ruminants. Therefore, the objective of this study is to evaluate the effects of adding different feed additives in the diet of beef and dairy cattle on their performance, dry matter intake (DMI) and feed efficiency, through a systematic review followed by meta-analysis. The systematic review suggested 43 peer-reviewed publications, according to the pre-established criteria. In beef cattle, the ionophore antibiotics reduced the DMI, improved the feed efficiency without interfering in the average daily gain (ADG). Non-ionophore antibiotics and propolis extract increased the ADG. In dairy cattle, the ionophores, yeast-based additives, and enzyme additives increased the feed efficiency, DMI, and daily milk production (MY), respectively. Essential oil supplementation in beef and dairy cattle had no effect on the feed intake and animal performance. The systematic review and meta-analysis allowed us to conclude that different feed additives have different effects on cattle performance, however, our results suggest that there are a few gaps regarding their effects on animal performance.

Key words: Antimicrobials, essential oil, feed efficiency, ionophores, nutrition, ruminants.

INTRODUCTION

Ruminant animals play an important role in supplying the current and growing demand for meat and milk consumed by humans (Malmuthuge & Guan 2017). With approximately 200 species described, ruminants constitute the most important group of large herbivorous terrestrial mammals (Fernández & Vrba 2005). The complex microbiota that inhabits the rumen of ruminant animals is responsible for the ability of these animals to convert indigestible vegetable mass into energy and protein for the animal (Jami & Mizrahi 2012, Soltis et al. 2023).

This microbial community can convert the otherwise unusable organic matter into usable protein and energy and provide up to 70% of the animal's protein and energy needs in the form of microbial protein and volatile organic acids (Abbas et al. 2020, Li et al. 2022). Therefore, the ruminal microbiota is a potential target for manipulation, to improve the productivity and health of ruminants (Li et al. 2019).

Ruminal fermentation manipulation is considered an important tool to improve production efficiency, which is the main objective of the studies on ruminant nutrition. Moreover, the use of feed additives is considered a direct strategy for ruminal fermentation manipulation (Stivari et al. 2014, Clemmons et al. 2019). Antibiotics, probiotics, and feed additives disrupt the microbial ecosystem of the rumen, which can provide targeted, immediate, and acute alterations to the rumen microbial profile (Clemmons et al. 2019). However, among the potential feed additives used in ruminant nutrition, the most widespread are ionophore antibiotics (El-Waziry et al. 2022).

In the last few years, there is a growing interest in the use of natural feed additives in animal feed, including probiotics, organic acids, exogenous enzymes, propolis extracts, and secondary plant metabolites, which can be used as replacements for antibiotics, to alter the rumen fermentation and increase feed efficiency in ruminants (Clemmons et al. 2019, Al-Suwaiegh et al. 2020).

Natural feed additives have the ability to modify microbial populations in the rumen or hindgut, change their fermentation pattern, increase the flow of nutrients to the small intestine, and enhance the digestibility of the feed (Clemmons et al. 2019, Gheller et al. 2020, Oliveira et al. 2023, Meenongyai et al. 2023, Varela et al. 2023). The supplementation of probiotics can enhance livestock performance through the maintenance of healthy rumen and enhancing breakdown of the fibrous feed in the rumen by improving the uptake of nutrients, thereby resulting in an increased yield of livestock products (Arowolo & He 2018). Yeast is a commonly used probiotic in ruminant nutrition and has been proven to be effective in restoring gut microbial balance, especially during digestive disorders (McAllister et al. 2011).

Therefore, as there is a growing interest in the use of alternative additives in cattle feed, there are a growing number of studies that analyze the effects of these feed additives in the diet of ruminants (Arriola et al. 2011, Gómez-Vázquez et al. 2011, Aguiar et al. 2012, Afzalani et al. 2015, Jesus et al. 2016, Aboagye et al. 2018, Al-Suwaiegh et al. 2020). Hence, it is important to evaluate, summarize, and draw conclusions from the information available through systematic reviews and meta-analytic methods.

It is hypothesized that antibiotics as feed additives can positively affect animal performance and that alternative additives to antibiotics are able to efficiently replace them. The objective of the present study is to evaluate the effects of adding different feed additives in the diet of beef and dairy cattle on their performance, dry matter intake (DMI) and feed efficiency, through a systematic review followed by meta-analysis.

Our results revealed that supplementation with ionophore antibiotics reduced DMI in beef cattle, and increased feed efficiency in beef and dairy cattle. Supplementation of beef cattle with non-ionophore antibiotics and propolis extract increased the average daily gain. Supplementation with yeast-based additives increased DMI and supplementation with enzyme additives decreased milk production in dairy cattle.

MATERIALS AND METHODS

Literary identification - systematic review

A systematic review of scientific studies was carried out to identify feed additives, antibiotics, and antibiotic substitutes used in cattle farming, as manipulators of ruminal fermentation and their impact on cattle performance. An electronic search in the Scopus database (https://www.scopus.com) was carried out from August to November 2020. The review was conducted based on the reported items used for systematic reviews and meta-analyses (Prisma) (Moher et al. 2009).

The search query consisted of combining the search terms and keywords, with the boolean operators (AND and OR). The terms that were sought for pursued the following criteria: (a) Terms related to the species or animal group (cattle, bovine, cow, steers, bulls, ruminants); (b) terms related to the evaluated characteristic (performance, “feed efficiency”, “milk production”, “weight gain”) and (c) terms related to the feed component evaluated (additive, “feed additive”). Thus, the combination between keywords and boolean operators used for the search was: cattle OR bovine OR cow OR steers OR bulls OR ruminant AND performance OR “feed efficiency” OR “milk production” OR “weight gain” AND additive OR “feed additive”.

Screening and evaluation of the studies

The selection of scientific studies started with the verification of the presence of at least one keyword of each search criterion in the title, abstract, or keywords of the studies. Studies that met this criterion were selected.

The second step was a screening of the selected studies, according to the following criteria: (1) The studies had to deal with the use of feed additives for ruminal manipulation; (2) the studies had to be published in English; (3) the full text of the studies had to be available; (4) the study should not be a literature review or meta-analysis; (5) the bovines used had to be of productive age, had to have females in lactation or males in growth or finishing, which were not being submitted to any sanitary challenge; (6) the animals should not have received any hormonal implants; (7) the studies had to present data on animal performance and dry matter intake; (8) the study had to have a control treatment group; and (9) the methodology used had to be provided.

Thus, the studies that met all the criteria described above were submitted to the full text review phase.

Data extraction

After reviewing the full text, the following data were extracted from the studies that met all these criteria: The group of feed additives used (ionophore antibiotics, non-ionophore antibiotics, essential oils or their active components, yeasts, tannins, enzymatic additives); the number of animals used (n); the experimental period (days); the age (months); and dry matter intake (DMI, kg/day) and feed efficiency. For studies referring to beef cattle, data on average daily gain (ADG, g/day) were extracted and for studies referring to dairy cows, data on daily milk production (MY, kg/day) were extracted.

Statistical analysis

In the meta-analysis, the Inverse Variance Method and the DerSimonian-Laird methods were used to estimate the variance between the studies (τ^2). The mean difference is given by the mean value of the variable for animals supplemented with different types of feed additives minus the mean value of the variable for non-supplemented animals (control). This was used as the measure of effect.

A fixed-effects or random-effects model was used for the meta-analysis, depending on the existence or non-existence of heterogeneity, was checked for significance at 5% of the test applied for the value of the Q statistic. The magnitude of heterogeneity (I^2) was interpreted as: Close to 0% indicated the absence of heterogeneity between studies, close to 25% indicated low heterogeneity, close to 50% indicated moderate heterogeneity, and close to 75% indicated high heterogeneity between the studies (Higgins et al. 2003, Santos & Cunha 2013).

The meta-analysis was performed using the meta package (Schwarze 2007, Balduzzi et al. 2019) of the statistical software R (R Development Core Team 2020). Differences were considered significant at $P < 0.05$ and as trends when $0.05 \geq P < 0.10$.

RESULTS

The systematic search registered 1,770 scientific studies. After screening each title, abstract, and keyword, 325 studies were excluded for not presenting at least one keyword for each search criteria (Figure 1). Of the remaining 1,445 studies, 1,045 were excluded because they did not address the topic of interest (n = 974) or because they were review studies, meta-analysis, or they were not published in English (n = 71) (Figure 1). Of the remaining 400 studies, 357 studies were excluded because the full text was not available (n = 16) or because they did not meet the eligibility criteria (n = 341) (Figure 1). Finally, 43 publications were included in the meta-analysis (Figure 1 and Table I).

For studies referring to beef cattle (Table I), meta-analyses were performed on each group of feed additives, for each measure of interest: Average daily gain (ADG), dry matter intake (DMI), and feed efficiency. Likewise, for studies referring to dairy cattle (Table I), the measures of interest were: Daily milk yield (MY), dry matter intake (DMI), and feed efficiency.

In the evaluated studies, the inclusion of ionophore antibiotics in the diet reduced the DMI (MD = - 0.48 kg/day, P = 0.0004), and improved the feed efficiency (MD = 0.01, P = 0.0067) in beef cattle (Table II). When analyzing the studies with the inclusion of non-ionophore antibiotics (MD = 0.07 kg/day, P = 0.0128) and propolis extract (MD = 0.16 kg/day, P = 0.0350) in the diet, it was observed that both groups of feed additives increased the ADG of beef cattle (Table II).

Including ionophore antibiotics in the diet increased (MD = 0.06, P = 0.0079) the feed efficiency in dairy cattle (Table III). Yeast-based additives to the diet of dairy cows increased the DMI (MD = 0.59 kg/day, P = 0.0001) and the inclusion of enzyme additives increased the MY (MD = 0.69 kg/day, P = 0.0408) (Table III).

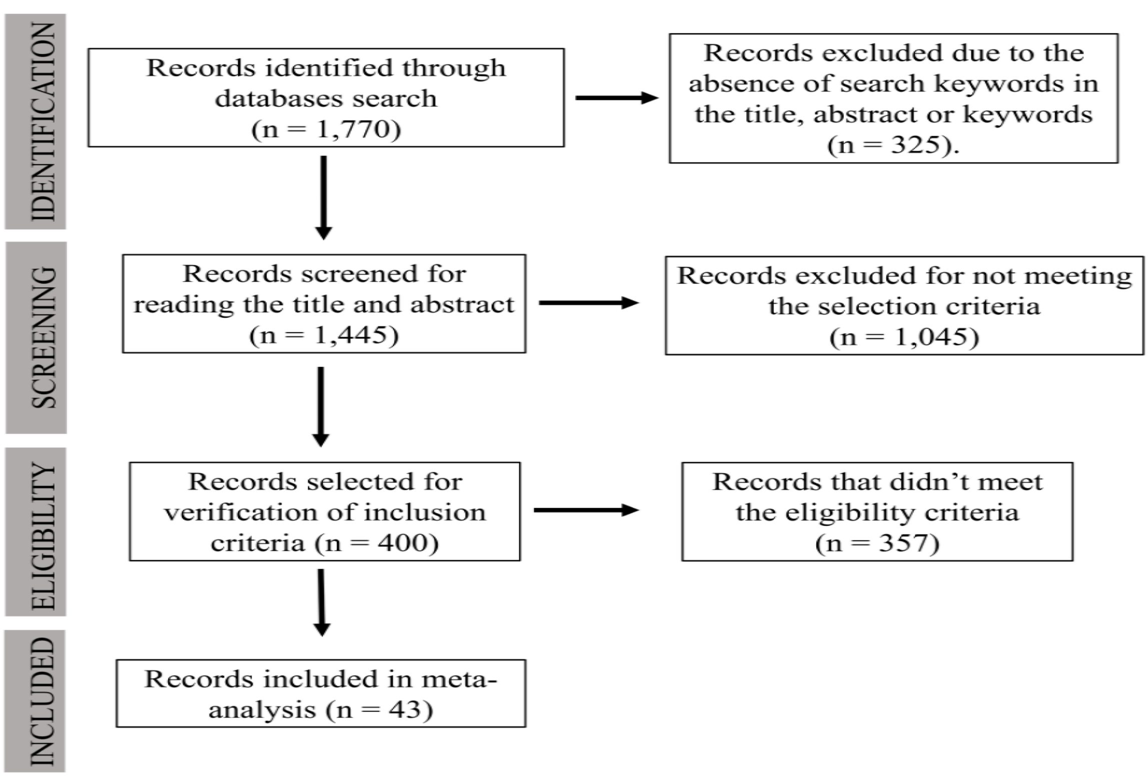

Figure 1. PRISMA flow diagram of all the records searched and included in the meta-analysis.

Table I. Summary of the studies included in the meta-analysis.

	Animal class[1]	Experimental period (day)	Experimental desing	Treatments[2]
Afzalani et al. (2015)	Beef	60	Randomized block	Control (1); Essential oils* (4);
Arelovich et al. (2008)	Beef	77	Completely randomized design	Control (1); Ionophore antibiotics (1);
Avila et al. (2020)	Dairy	20	Latin square	Control (1); Condensed Tannins (4);
Bagheri et al. (2009)	Dairy	84	Latin square	Control (1); Yeast-based aditives (1)
Benatti et al. (2017)	Beef	110	Randomized block	Control (1); Ionophore antibiotics (1);
Beauchemin et al. (1999)	Dairy	92	Latin square	Control (2); Enzyme additives (2);
Benchaar et al. (2006)	Dairy	112	Latin square	Control (1); Ionophore antibiotics (1); Essential oils* (1);
Benchaar et al. (2012)	Dairy	112	Latin square	Control (2); Essential oils* (2);
Benchaar (2016)	Dairy	112	Latin square	Control (1); Ionophore antibiotics (1); Essential oils* (2);
Benchaar (2020)	Dairy	112	Latin square	Control (1); Ionophore antibiotics (1); Essential oils* (2);
Berger et al. (1981)	Beef	120, 130, 130	-	Control (3); Ionophore antibiotics (7);
Braun et al. (2019)	Dairy	80	Crossover	Control (1); Essential oils* (1);
Elcoso et al. (2019)	Dairy	56	Completely randomized design	Control (1); Essential oils* (1);
Faehnrich et al. (2019)	Dairy	150	-	Control (1); Essential oils* (1);
Flores et al. (2013)	Dairy	63	Completely randomized design	Control (1); Essential oils* (3);
Focant et al. (2019)	Dairy	63	Latin square	Control (1); Condensed Tannins (1);
Fonseca et al. (2019)	Beef	70	Completely randomized design	Control (1); Ionophore antibiotics (1); Non-ionophore antibiotics (1);
Fugita et al. (2017)	Beef	94	Completely randomized design	Control (1); Essential oils* (2);
Ghizzi et al. (2018)	Dairy	42	Randomized block	Control (1); Ionophore antibiotics (1); Essential oils* (1);
Holtshausen et al. (2011)	Dairy	84	Randomized block	Control (1); Enzyme additives (2);

Table I. Continuation.

Jesus et al. (2016)	Dairy	63	Latin square	Control (1); Ionophore antibiotics (1); Essential oils* (1);
Joch et al. (2019)	Dairy	105	Completely randomized design	Control (1); Essential oils* (1);
Kozerski et al. (2017)	Dairy	28	Crossover	Control (1); Ionophore antibiotics (1);
Kung et al. (2008)	Dairy	77	Completely randomized design	Control (1); Essential oils* (1);
Melo et al. (2020)	Beef	105	Completely randomized design	Control (1); Ionophore antibiotics (1); Essential oils* (1);
Matloup et al. (2017)	Dairy	63	Completely randomized design	Control (1); Ionophore antibiotics (1); Essential oils* (1);
Neto et al. (2018)	Beef	108	Randomized block	Control (1); Non-ionophore antibiotics (3);
Neumann et al. (2016)	Beef	112	Completely randomized design	Control (1); Ionophore antibiotics (1);
Oh et al. (2019)	Dairy	84	Latin square	Control (1); Yeast-based aditives (1); Enzyme additives (1);
Oliveira et al. (2015)	Dairy	84	Latin square	Control (1); Ionophore antibiotics (1);
Orlandi et al. (2020)	Dairy	49	Randomized block	Control (1); Condensed Tannins (1);
Orlandi et al. (2020)	Dairy	49	Randomized block	Control (1); Condensed Tannins (1);
Pereira et al. (2019)	Beef	84	Randomized block	Control (1); Ionophore antibiotics (4);
Sallam et al. (2019)	Dairy	98	Completely randomized design	Control (1); Yeast-based aditives (1); Enzyme additives (1);
Santos et al. (2019)	Dairy	84	Latin square	Control (1); Ionophore antibiotics (4);
Silva et al. (2018)	Dairy	84	Latin square	Control (1); Ionophore antibiotics (1); Essential oils* (1);
Tager & Krause (2011)	Dairy	84	Incomplete Latin rectangle	Control (1); Essential oils* (3);
Takiya et al. (2017)	Dairy	84	Latin square	Control (1); Enzyme additives (3);
Valero et al. (2014)	Beef	55	Completely randomized design	Control (1); Essential oils* (1); Propolis extract (1);

Table I. Continuation.

Valero et al. (2015)	Beef	70	-	Control (1); Ionophore antibiotics (1); Propolis extract (1);
Wall et al. (2014)	Dairy	42	-	Control (1); Essential oils* (1);
Weiss & Amiet (1990)	Dairy	98	Randomized block	Control (1); Ionophore antibiotics (1);
Yang et al. (2007)	Dairy	84	Latin square	Control (1); Ionophore antibiotics (1); Essential oils* (1);

[1]Beef = beef cattle; Dairy = dairy cattle; [2]Treatments included in the meta-analysis = Feed additive; [*]Essential oils or bioactive compounds.

DISCUSSION

Ionophore or non-ionophore antibiotics, methane (CH_4) inhibitors, defaunating agents, and other chemical additives in ruminant diets have been explored to modulate rumen fermentation, enhance salivary secretions, regulate ruminal pH, prevent metabolic disorders, increase growth and milk production, as well as increase intake and feed efficiency (Kholif & Olafadehan 2021, Rivera-Chacon et al. 2022). The significant effects of ionophore antibiotics are increased feed efficiency, increased rate of weight gain, and decreased dry matter intake. However, some studies found no increase in weight gain or feed efficiency (Ensley 2020).

Among the studies with the inclusion of ionophore antibiotics in the diet of beef cattle, 75% used sodium monensin (Table I). This ionophore is the most used among those available for use in beef production, in Brazil (Neumann et al. 2016). When the studies with the inclusion of ionophore antibiotics in the diet of dairy cattle were analyzed, it was observed that 78.6% of them used sodium monensin (Table I).

According to Silva et al. (2018), monensin is the main ionophore antibiotic used in dairy cow diets, with the objective of improving feed efficiency or decreasing the risk of metabolic disorders, such as, acidosis and ketosis. An increase in feed efficiency was observed with the inclusion of ionophore antibiotics in the diet of dairy cows (Table III).

According to Ensley (2020), the increase in the rate of gain and feed efficiency when ionophores are used is due to changes in the production of volatile organic acids in the rumen. Laidlomycin, monensin, narasin, salinomycin, and lasalocide alter the molar ratio of volatile organic acids produced by the rumen bacteria, increasing the production of propionic acid, and reducing the production of butyric and acetic acids, without changing the total production of volatile organic acids in cattle or altering fermentation (Ensley 2020). In addition, there are reports in the literature that ionophores reduce ruminal methane production, reduce protein digestion. and ammonia utilization by ruminal bacteria, increasing nitrogen retention and absorption (Ensley 2020). Ionophores are also related to the delay of digestive disturbances resulting from abnormal ruminal fermentation, such as ruminal acidosis and ruminal bloat (Azzaz et al. 2015).

Among the studies used in this meta-analysis that dealt with the inclusion of non-ionophore antibiotics in the diet of beef cattle, 100% used virginiamycin (VM) (Table I). Although it should be carefully interpreted, due to the small number of studies, as the results showed

Table II. **Performance of beef cattle supplemented with different types of feed additives.**

Variable	Treatments	MD	95% CI	*P*-value	Heterogeneity		Model
					I^2 (%)	*Q*	
Ionophoric Antibiotics							
ADG (kg/day)	16	0.00	[-0.06; 0.06]	0.9756	43	0.0350	Random-effects
DMI (kg/day)	16	-0.48	[-0.74; -0.21]	0.0004	41	0.0439	Random-effects
Feed efficiency	16	0.01	[0.00; 0.01]	0.0067	63	0.0004	Random-effects
Non-Ionophoric Antibiotics							
ADG (kg/day)	5	0.07	[0.01; 0.12]	0.0128	35	0.1898	Fixed-effect
DMI (kg/day)	5	-0.12	[-0.75; 0.52]	0.7182	0	0.7786	Fixed-effect
Feed efficiency	2	-0.01	[-0.02; 0.00]	0.1833	0	0.4898	Fixed-effect
Essencial oils							
ADG (kg/day)	8	0.06	[-0.01; 0.14]	0.1155	74	0.0003	Random-effects
DMI (kg/day)	8	0.14	[-0.19; 0.47]	0.3955	0	0.7792	Fixed-effect
Feed efficiency	4	0.00	[-0.01; 0.01]	0.6323	0	0.5419	Fixed-effect
Propolis extract							
ADG (kg/day)	2	0.16	[0.01; 0.31]	0.0350	0	0.7921	Fixed-effect
DMI (kg/day)	2	0.15	[-0.36; 0.66]	0.5563	0	0.9431	Fixed-effect
Feed efficiency	2	0.01	[-0.01; 0.03]	0.3961	0	1.0000	Fixed-effect

MD: mean difference (effect size); 95% CI = 95% confidence interval; ADG: average daily gain; DMI: dry matter intake.

that VM influenced the ADG of animals, however, it did not influence the DMI and feed efficiency (Table II). Most VM treatments used grazing cattle or cattle fed on a large proportion of forage in the diet. In the literature, most studies evaluating VM supplementation were carried out in animals that were confined, receiving diets rich in grains, or supplemented with non-structural carbohydrate sources (Costa et al. 2018). However, little is known about the effects of VM where pasture is the source of nitrogen and energy (Costa et al. 2018). According to Neto et al. (2018), there are no studies evaluating the optimal dose-response to VM in cattle on tropical pastures.

Despite the lack of effect on feed efficiency and DMI, there was an effect on ADG, which could be explained by the production of ammonia and butyrate, as VM did not affect the acetate: propionate ratio produced in the rumen (Neto et al. 2018). For grazing animals, the increased availability of ammonia nitrogen in the rumen improves the production of microbial enzymes, because ammonia nitrogen is preferentially used by fibrolytic microorganisms as a precursor for amino acid synthesis (Detmann et al. 2014). Butyrate contributes to approximately 70% of the daily metabolizable energy requirements of ruminants and is the main source of energy for the rumen epithelial cells (Li et al. 2012).

Oliveira et al. (2017) and Lemos et al. (2016), also demonstrated that VM has the potential to stabilize ruminal fermentation, because it controls the production of lactate and methane,

Table III. Performance of dairy cows supplemented with different types of feed additives.

Variable	Treatments	MD	95% CI	*P*-value	Heterogeneity		Model
					I^2 (%)	Q	
Ionophoric Antibiotics							
MY (kg/day)	14	0.22	[-0.36; 0.81]	0.4508	49	0.0205	Random-effects
DMI (kg/day)	14	-0.67	[-1.46; 0.12]	0.0971	94	< 0.0001	Random-effects
Feed efficiency	9	0.06	[0.02; 0.10]	0.0079	89	< 0.0001	Random-effects
Tannins							
MY (kg/day)	7	0.27	[-0.65; 1.19]	0.5622	0	0.9711	Fixed-effect
DMI (kg/day)	7	-0.08	[-1.18; 1.02]	0.8884	77	0.0002	Random-effects
Feed efficiency	0	-	-	-	-	-	-
Essencial oils							
MY (kg/day)	24	0.16	[-0.28; 0.61]	0.4717	42	0.0178	Random-effects
DMI (kg/day)	25	0.13	[-0.27; 0.54]	0.5192	75	< 0.0001	Random-effects
Feed efficiency	10	0.01	[-0.02; 0.03]	0.6545	18	0.2773	Fixed-effect
Yeast-based Additives							
MY (kg/day)	3	0.25	[-0.67; 1.17]	0.5919	0	0.8257	Fixed-effect
DMI (kg/day)	3	0.59	[0.29; 0.89]	0.0001	0	0.9495	Fixed-effect
Feed efficiency	3	0.00	[-0.05; 0.05]	0.9894	0	0.5626	Fixed-effect
Enzyme Additives							
MY (kg/day)	9	0.69	[0.03; 1.35]	0.0408	0	0.9180	Fixed-effect
DMI (kg/day)	9	-0.24	[-1.20; 0.72]	0.6261	80	< 0.0001	Random-effects
Feed efficiency	7	0.00	[-0.03; 0.03]	0.9295	44	0.0986	Fixed-effect

MD: mean difference (effect size); 95% CI = 95% confidence interval; MY: daily milk yield; DMI: dry matter intake.

as VM acts directly on the ruminal microbial species that produce lactate and methane.

There is growing interest in the use of natural feed additives in animal feed, including probiotics (Astuti et al. 2022, Meenongyai et al. 2023), organic acids (Gheller et al. 2020), exogenous enzymes (Bugoni et al. 2023), propolis (Varela et al. 2023), and secondary plant compounds (Al-Suwaiegh et al. 2020, Oliveira et al. 2023). These compounds can be used as antibiotic replacements to alter ruminal fermentation and increase feed efficiency in ruminants (Al-Suwaiegh et al. 2020). The antibiotic substitutes likely to be found in this systematic review were: propolis, essential oils and their active components, tannins, yeast-based additives, and enzyme additives.

The inclusion of propolis in the diet of beef cattle had a positive effect on the ADG of the animals, however, it did not influence the DMI and feed efficiency (Table II). According to Aguiar et al. (2012), the inclusion of propolis in the diet of crossbred bulls did not influence P > 0.05) DMI, ADG, and feed conversion (FC).

However, Zawadzki et al. (2011), when using the same propolis-based product used by Aguiar et al. (2012), in a higher dosage (0.0054 mg/g), in bulls finished in the feedlot, found higher ADG and better FC (P < 0.05) in animals that received propolis in the diet.

Varela et al. (2023), found that supplementation with 64 mL/day of propolis extract in dairy cows increased feeding time, milk production, and feed efficiency. and did not influence dry matter intake, crude protein intake, neutral detergent-insoluble fiber intake, milk composition, or blood parameters. Thus, it is possible to assume that the dosage of propolis administered to animals has an influence on the results and needs to contain a sufficient quantity of phenolic compounds, so that there is an effect on the ruminal microbiota, and consequently, on animal performance.

With the wide variation in the bioactive composition of propolis, it is still a challenge to optimize the dosage and obtain consistent results (Soltan & Patra 2020). The concentration of propolis and the alcohol content used in the extraction of active substances can also influence the chemical composition of the propolis extract (Cottica et al. 2011, Morsy et al. 2021).

Both essential oils and tannins, the so-called phytochemicals or secondary plant metabolites, have antimicrobial properties that make them attractive feed additives to alter rumen fermentation and improve dietary utilization and animal performance (Morsy et al. 2018). It was possible to observe the absence of effects on any of the variables in question, both in beef cattle and dairy cows, with the inclusion of essential oils or their active components in the animals' diet (Tables II, III). Likewise, no difference was observed in MY and DMI of tannin-fed dairy cattle (Table III).

Oliveira et al. (2023), demonstrated that supplementation with different doses (0, 0.14, 0.29, or 0.43% of the diet based on DM) of tannin extract in dairy cattle had no effect on DMI, milk production, or composition. However, a linear increase in the molar proportion of butyrate and reduction in the molar proportion of propionate was observed.

Kholif & Olafadehan (2021), point out that many factors determine the effectiveness of phytochemicals (including essential oils and tannins) in altering dietary digestion and ruminal fermentation. Consequently, it can include animal performance, which depends on diet digestion and ruminal fermentation. Among the factors, are the type and concentration of compounds in the plant, the solvent used to extract them, and the dilution and extraction conditions, the dose used, the type of diet, the age of the animals, the physiological state, and the infestation load by worms, among others (Kholif & Olafadehan 2021). The results of *in vivo* experiments are variable and need further experimentation before practical application in livestock production (Alemneh & Getabalew 2019).

Yeasts are an important source for obtaining products with probiotic activity, whether they are live strains or derived from their cell walls (Elghandour et al. 2020, Gunun et al. 2022). For many years, yeast and live yeast cultures have been used to stabilize rumen fermentation and prevent metabolic disturbances, increase feed intake, nutrient digestibility, lactational performance, and to improve carcass characteristics (Sallam et al. 2019, Amin & Mao 2021).

It is believed that yeasts stimulate the growth of microorganisms that digest fiber and cellulose, and that use lactate, resulting in increased feed intake and improved animal performance (Amin & Mao 2021). It was confirmed that the addition of yeast-based additives to the diet of dairy cows increased DMI, however, no effects were observed on the MY and feed efficiency (Table III). In the literature, there are still many inconsistent results with the use of yeast in ruminant nutrition, and its mechanism of action is not fully understood, which makes it difficult to draw conclusions about its effects (Amin & Mao 2021).

According to Meale et al. (2014) and Bugoni et al. (2023), exogenous enzymes are increasingly considered as a means of improving feed efficiency and milk yield, as they improve fiber and starch digestibility, and apparently have minor effects on ruminal fermentation. However, the production responses obtained are still highly variable. In the present meta-analysis, the inclusion of enzyme additives, enzymes, and yeast fermentation extracts in the diet of dairy cows increased the MY, without modifying the DMI and feed efficiency (Table III).

Although commercial enzyme preparations are commonly referred to as cellulases and xylanases, the activities of secondary enzymes such as amylases, proteases, esterases, and pectinases are invariably present, as these preparations rarely consist of a single pure enzyme (McAllister et al. 2001). According to Meale et al. (2014), it is virtually impossible to compare exogenous enzyme preparations on an equal activity basis, as there is a clear lack of standardization in the methodology used to assess enzyme activities across laboratories. Even though the same methods are used, it is difficult to standardize enzyme products, as they contain several activities and can only be standardized for one or two activities at a time (Meale et al. 2014).

Another common limitation of the enzyme literature is the lack of repeatability of the effects and repeated investigations of a common exogenous enzyme preparation, as most of them are only examined in a single experiment (Meale et al. 2014, Bugoni et al. 2023).

The present systematic review and meta-analysis concluded that supplementation with ionophore antibiotics reduced dry matter intake in beef cattle, and increased feed efficiency in beef and dairy cattle. Supplementation of beef cattle with non-ionophore antibiotics and propolis extract increased the average daily gain. Supplementation with yeast-based additives increased dry matter intake and supplementation with enzyme additives decreased daily milk production in dairy cattle. Benefits of including additives in the diet of cattle reported in the literature range from the prevention of metabolic disorders, improvement in performance, and reduction of enteric methane emissions. However, the results found in the present study suggest that there are still gaps regarding the effects of the supplementation of these additives on animal performance.

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