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Feed aditives for beef cattle

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INTRODUCTION

The enhancement in ruminant nutrition knowledge and the increased adoption of technologies by Brazilian farmers reveal knowledge gaps that need to be filled to provide the most accurate estimates of cattle nutrient requirements. In this context, the use of feed additives that alter ruminal fermentation in beef cattle diets are examples of these technologies.

According to surveys carried out on nutritional recommendations and management practices adopted in Brazilian feedlots, nearly 100% of the feedlots evaluated used some type of feed additive in the diets (Oliveira and Millen, 2014; Pinto and Millen, 2019; Silvestre and Millen, 2021). In addition, the latest survey (Silvestre and Millen, 2021) demonstrated that monensin (ionophore) was the primary feed additive used. Other feed additives commonly used in beef cattle diets include buffers, alkalizers, non-ionophore antibiotics, live yeast, exogenous enzymes, and plant extracts (e.g., essential and functional oils).

Feed additives are mainly used in beef cattle diets to beneficially alter rumen fermentation, prevent rumen acidosis, and improve nutrient utilization (Beauchemin et al., 2018). The effects of feed additives that alter ruminal fermentation (mainly ionophores) in beef cattle raised under temperate conditions have been extensively studied. It is well known that ionophores alter ruminal fermentation by limiting the growth of gram-positive bacteria and shift rumen fermentation towards more propionate and less acetate and butyrate (Bergen and Bates, 1984; NASEM, 2016; Beauchemin et al., 2018). In addition, reduced metabolic disorders incidence, methane production and rumen protein degradation are also effects of most feed additives (Beauchemin et al., 2018). Hence, the use of feed additives in ruminant diets may affect feed intake, ruminal parameters, and energy and protein metabolism, and, consequently, may influence cattle nutrient requirements and performance.

However, the effects of feed additives reported have not always been consistent. For example, reduced dry matter intake (DMI) and improved feed efficiency (FE), with either no effect or an increase in average daily gain (ADG), have been observed in feedlot cattle fed monensin (Raun et al., 1976; Maturana Filho et al., 2010; Melo et al., 2020), whereas some studies have not found significant effects on DMI and FE for cattle in either feedlot or pasture production systems (McGinn et al., 2004; Zawadzki et al., 2011; Maciel et al., 2019).

Furthermore, some recent studies have found the combination of a blend of essential oils (EO) with exogenous α-amylase in feedlot diets to increase feed intake and improve animal growth performance compared to monensin, without affecting FE (Gouvêa et al., 2019; Meschiatti et al., 2019). Nevertheless, in a study conducted by Toseti et al. (2020), including a blend of EO with exogenous α-amylase in feedlot diets improved animal growth performance compared to animals fed monensin, with no differences in DMI and FE. The variations among experimental conditions (i.e., dosage of feed additive; basal diet, experimental duration, sex, breed, age, among others) may impair the comparison of the effects of feed additives obtained in different studies. Thus, meta-analysis can be used to summarize effects of different feed additives across studies and to investigate factors explaining potential heterogeneity of response (Duffield et al., 2012).

However, authors are not aware of any meta-analytical study addressing the effects of feed additive on the productive performance and ruminal parameters of cattle raised under Brazilian conditions. In addition, the last edition of BR-CORTE (BR-CORTE, 2016) did not recommend any correction factor to estimate the nutrient requirements of cattle fed feed additives. Therefore, the committee of BR-CORTE current edition proposed a new chapter regarding the effects of feed additives on the productive performance and ruminal parameters of cattle raised under Brazilian conditions.

In this way, the first section of this chapter is composed by a review of the main feed additives currently available for cattle in Brazil. Subsequently, a meta-analysis regarding the effects of monensin and functional oils on the productive performance and ruminal parameters of feedlot cattle raised under Brazilian conditions is presented.

FEED ADDITIVES AVAILABLE IN BRAZIL

According to the Normative Nº. 13 of November 30, 2004 of the Ministry of Agriculture, Livestock and Supplying (MAPA), feed additives are defined as "products destinated to animal feeding such as substance, microorganisms, or formulated products, which are not commonly used as feed ingredients". Also, such products may or may not have nutritional value; and are usually used to improve the characteristics of products destinated to animal feeding or to animal products themselves, improve growth performance of healthy animals, meet animals' nutrient requirements, or have anticoccidial effect. However, although several feed additives have nutritional value, they are not fed to meet the ruminant nutrient requirements, instead, they are usually fed to alter ruminal or post-ruminal metabolism to improve nutrient utilization and animal productivity.

Many feed additives are available for use in the Brazilian beef industry (the list of feed additives allowed by the Brazilian legislation can be seen at https://www.gov.br/agricultura/pt-br/assuntos/insumos-agropecuarios/insumos-pecuarios/alimentacao-animal/aditivos), with many different formulations and commercial brands for each one. In practice, they can be classified into general categories, such as: ionophore antibiotics, non-ionophore antibiotics, probiotics, exogenous enzymes, buffers and alkalinizes, plant extracts, among others. Some feed additives such as ionophores have been extensively studied (at least under temperate conditions), while others lack robust evaluation. In this context, it can be hard for producers and consultants to balance all the information and decide on which feed additives to use. A brief description of the main feed additives used for beef cattle will be presented below.

Buffers and alkalizers

Ruminal acidosis is a major challenge when large amounts of readily fermentable starch are fed to cattle. Decreased DMI, animal performance, and FE (subacute acidosis), and in severe cases, animal death (acute acidosis) may occur if ruminal acidosis is not properly managed. An option to reduce the potential for acidosis is adding buffer agents, such as sodium ($NaHCO_3$) and potassium ($KHCO_3$) bicarbonate, and/or alkalizer agents, such as sodium (Na_2CO_3) and potassium carbonates (K_2CO_3) and magnesium oxide (MgO), to the diet. Magnesium ($MgCO_3$), calcium ($CaCO_3$), and calcium magnesium ($CaMg(CO_3)_2$) carbonates are other buffer and alkalizer agents used for preventing ruminal acidosis.

Technically, buffer and alkalizer agents are different. Buffer agents reduce the fluctuations in ruminal pH; meanwhile alkalizer agents increase the ruminal pH. Nevertheless, both agents have a direct effect on rumen fluid pH through chemical changes in the rumen as they neutralize acidity through H^+ sequestration and increase buffering capacity of ruminal fluid (Hernández et al., 2014). Moreover, some side effects of supplementing buffer or alkalizer agents may include improved DM and fiber digestibility (Peirce et al., 1983;

Stroud et al., 1985; Kovacik et al., 1986), acetate:propionate ratio (Okeke et al., 1983; Ghorbani et al., 1989; González et al., 2008), and cattle productive performance (Wise et al., 1965; Stroud et al., 1985; Zinn, 1991). Buffers and alkalizers are supposed to benefit ruminants that eat large amounts of readily fermentable carbohydrates. Therefore, they have been used in Brazilian feedlot diets to avoid or mitigate the occurrence of metabolic disorders (Millen et al., 2009).

Sodium bicarbonate is the most used buffer in ruminant diets. This feed additive is considered a true buffer as its pKa is close to the physiological pH of the rumen and it has excellent solubility in the rumen, besides being naturally the main buffer in saliva and ruminal fluid (Kohn and Dunlap, 1998). In addition, $NaHCO_3$ can elevate ruminal pH (Rogers and Davis, 1982; Ghorbani et al., 1989; Zinn, 1991) as it is a strong buffer (Kohn and Dunlap, 1998), and increase the dilution of ruminal contents, and, therefore, the flow of acids and fermentable carbohydrate from the rumen (Rogers and Davis, 1982; Okeke et al., 1983; Russell and Chow, 1993), although these responses are not detected in all studies (Kellaway et al., 1978; Zinn and Borques, 1993; Paton et al., 2006; Calsamiglia et al., 2012). Such increase in the rumen outflow may prevent severe decline in rumen pH, and consequently, be beneficial for feedlot cattle consuming high-concentrate diets.

Responses on growth performance to supplemental $NaHCO_3$ have been variable. Increase in DMI, ADG, and/or FE have been reported in cattle fed high concentrate diets containing $NaHCO_3$ at levels of 0.75% (Zinn, 1991), 1% (Thomas and Hall, 1984; Stroud et al., 1985; Brethour et al., 1986), and 3% of diet DM (Nicholson et al., 1963). Furthermore, experiments have shown similar growth performance responses by adding $NaHCO_3$ or monensin (0.75, 2.5, and 5% $NaHCO_3$ *vs.* 33 mg/kg monensin or 1.14 % $NaHCO_3$ *vs.* 34 mg/kg monensin) in finishing diets, with no further benefit when both were included together to the diet (Kargaard and Van Niekerk, 1980; Zinn and Borques, 1993; Oliveira et al., 2013).

In contrast, the addition of 0.75, 1.5, 2.25, and 5% (McKnight et al., 1979) or 1.0, 1.25, 2.5, and 5% $NaHCO_3$ (González et al., 2008) to high concentrate diets did not influence DMI, ADG, and FE or DMI and ruminal pH of Holstein steers and heifers, respectively. Similarly, the inclusion of 5.7% $NaHCO_3$ in all concentrate diets did not improve feed intake, ADG, or FE of Hereford steers (Nicholson et al., 1962). Furthermore, Thomas and Hall (1984) found that the inclusion of 1 and 1.25 % $NaHCO_3$ to roughage-based diets had no effect on ruminal pH, DMI, ADG, and FE of feedlot steers. Increased saliva production due to increased chewing and ruminating time, and consequently greater endogenous buffering capacity is expected when roughage-based diets are fed to cattle (Bailey, 1961; Maekawa et al., 2002). Such greater buffering capacity along with a reduced rate of volatile fatty acids (VFA) production, may reduce the effectiveness and requirements of dietary buffer supplementation.

In general, no effect on carcass traits has been observed when $NaHCO_3$ is supplemented in feedlot diets (Nicholson et al., 1962; McKnight et al., 1979; Kargaard and Van Niekerk, 1980); although small negative effects of $NaHCO_3$ inclusion at 0.75 and 1.2 % $NaHCO_3$ on carcass traits (retail yield, *Longissimus* muscle area, and fat thickness) have been described in some studies (Russell et al., 1980; Zinn, 1991; Zinn and Borques, 1993).

Nevertheless, there are many instances in the literature that describe only short-term effects of supplemented diets, where inclusion of 0.9, 1.1 and 1.2 % $NaHCO_3$ in high, moderate or low concentrate diets, respectively, enhanced growth performance of cattle during the first 28 days of feeding with no benefit for the entire feeding period (Russell et al., 1980; Worley et al., 1986; Lanna and Boin, 1990). These findings may corroborate the inconsistencies of the effects of $NaHCO_3$ supplementation on growth performance when the whole feeding period was considered.

Alkalizers may also contribute to the control of ruminal acidosis, with magnesium oxide (MgO) being the most used. Magnesium oxide is a strong alkalinizer agent but has lower solubility in normal rumen pH range (Erdman et al., 1982; Schaefer et al., 1982; Erdman, 1988). The inclusion of MgO at levels of 0.4, 0.69 and 1.37% in moderate concentrate diets or 0.5, 0.69, and 1.05% in high concentrate diets have increased ruminal and/or fecal pH (Schaefer et al., 1982; Peirce et al., 1983; Christiansen and Webb, 1990), diet DM digestibility (Erdman et al., 1982; Peirce et al., 1983), acetate molar concentration (Emery et al., 1965), and acetate:propionate ratio (Teh et al., 1985) of beef and dairy cattle.

However, responses to MgO supplementation on productive performance of cattle in general were limited or variable. No effect of MgO supplementation at levels of 0.4, 0.8 and 1.37 % was observed on DMI (Erdman et al., 1982; Teh et al., 1985; Arambel et al., 1988), ADG (Schaefer et al., 1982), or milk production (Erdman et al., 1982; Arambel et al., 1988) of cattle. Furthermore, reduced DMI has been also reported in dairy cattle studies as a result of MgO supplementation (Thomas and Emery, 1969a; Erdman, 1988). Nevertheless, several studies have reported increased milk fat content when MgO was added to lactating cow diets (Emery et al., 1965; Thomas and Emery, 1969b; Erdman et al., 1982), with this effect being smaller as the fiber content of the diet increased (Erdman, 1988).

Because alkalizers act raising ruminal pH and buffers resisting to changes in pH, some studies were performed to evaluate the possibility of an additive or synergistic effect of combining $NaHCO_3$ and MgO. Some authors have reported increased DMI for both beef and dairy cattle with the combination of $NaHCO_3$ and MgO in the early period following the transition from a high forage to a high concentrate diet (Erdman et al., 1980; Peirce et al., 1983; Teh et al., 1985). Moreover, Erdman (1988) reviewed several publications and tested the interaction of $NaHCO_3$ and MgO on milk fat content and stated that their effect was additive and could be used for preventing the reduction in milk fat content. However, no apparent additive beneficial effect was observed on milk production with these two additives combined (Teh et al., 1985; Erdman, 1988; Cabrita et al., 2009).

It seems that the inclusion of buffers and/or alkalizers to diets containing high levels of fermentable carbohydrates have some benefits for cattle, at least at the beginning of feeding period or adaptation to high-concentrate diets. However, the cost-benefit ratio must be evaluated before use, since other feed additives that promote similar or even more consistent improvement in ruminal conditions and growth performance are also commercially available.

Ionophores

Ionophores are the primary feed additive used in finishing diets in Brazil (Oliveira and Millen, 2014; Pinto and Millen, 2019; Silvestre and Millen, 2021). These feed additives are a class of antimicrobial compounds, which do not include medically important drugs for humans. They are carboxylic polyester compounds, which are usually included in growing and finishing cattle diets to improve ruminal fermentation, allowing increased FE and decreased risk of acidosis and bloat (Bergen and Bates, 1984). More than 120 types of ionophores are known, mainly produced by bacteria of the genus *Streptomyces*. There are many ionophores currently licensed for use in animal nutrition in Brazil, such as: monensin, lasalocid, narasin, and salinomycin.

The mechanism of action is similar among the different ionophores compounds. They have the ability to interact with cations, usually sodium ions (Na^+), serving as a carrier by which these ions can be transported across the cell membrane of some ruminal microorganisms (Bergen and Bates, 1984). Nevertheless, it is noteworthy that some ionophores may have higher or similar affinity for other ions such as potassium (K^+) and calcium (Ca^{2+}) (Bergen and Bates, 1984; NASEM, 2016). This disruption in ionic gradients results in increased proton pump activity and, consequently, depletion of energy reserve (ATP), causing impaired cell division, and probable death of the microorganism (Bergen and Bates, 1984; Russel and Strobel, 1989). In this context, ionophores selectively inhibit Gram-positive bacteria while preserving many Gram-negative bacteria, whose sensitivity is related to their different cell wall structure (Bergen and Bates, 1984; Russel and Strobel, 1989; NASEM, 2016). Gram-negative bacteria present an external membrane which is usually impermeable to ionophores (molecular size usually greater than 500 Daltons) and other macromolecules (Russel and Strobel, 1989). Thus, ionophores alter the profile of the microbial population in rumen and, thereby, the pattern of ruminal fermentation.

It is well known that ionophores alter ruminal fermentation by limiting the growth of Gram-positive bacteria and shift rumen fermentation towards more propionate (glucose precursor) and less acetate and butyrate (Bergen and Bates, 1984; NASEM, 2016; Beauchemin et al., 2018). Consequently, less H^+ is available for methane producer bacteria, leading to a reduced methane production (Nagaraja et al., 1997; NASEM, 2016). Thus, the reduced energy loss, through reduced methane production, and the increased input of glucose precursors for gluconeogenesis in the liver result in a greater energy supply to the animal (improve energy use efficiency). In addition, reduced metabolic disorders incidence (ruminal acidosis and bloat) and rumen protein degradation to ammonia (improve N use efficiency in the rumen) are also effects attributed to the use of ionophores (Bergen and Bates, 1984; Nagaraja et al., 1997; Beauchemin et al., 2018). Such effects are usually attributed to their anticoccidial effect and inhibition of ruminal lactate producers and obligate amino acid fermenting bacteria without inhibiting lactate users (Bergen and Bates, 1984; Beauchemin et al., 2018). Therefore, an enhanced productive performance would be expected from the improved retention of energy and N in the rumen fermentation. Nevertheless, the effects of feeding ionophores on animal performance seem to be dependent on animal, dose, and dietary factors (Tedeschi et al., 2003; Bretschneider et al., 2008; Duffield et al., 2012).

Monensin is the most widely studied and is also the most used ionophore in Brazil (Silvestre and Millen, 2021). Monensin generally depresses feed intake with a little or no effect on ADG. FE is improved when diets containing high levels of readily fermentable carbohydrates are fed to cattle (Maturana Filho et al., 2010; Duffield et al., 2012; Melo et al., 2020). In diets with greater forage content or in grazing systems, monensin does not decrease intake, and ADG is usually improved, resulting in improved FE (Bretschneider et al., 2008; Prado et al., 2010; Maciel et al., 2019; Gadberry et al., 2022a). Nonetheless, it is important to highlight that most of the research conducted to date with ionophores has focused on high concentrate diets; thus, information about the effects of these feed additives in cattle fed high-forage diets is still limited.

In fact, research data have shown a consistent improvement in FE of cattle raised in feedlot receiving monensin by improving or maintaining ADG and decreasing DMI. Goodrich et al (1984) summarized 228 trials in which monensin was added to feedlot cattle diets at 31.8 mg/kg DM, on average. These authors concluded that monensin increased ADG and FE by 1.6 and 6.5%, respectively, and decreased DMI by 6.4%. Moreover, carcass traits were not influenced by monensin. Subsequently, a meta-analysis of the impact of monensin on growing and finishing beef cattle was performed by Duffield et al. (2012). This study comprised data from 40 peer-reviewed articles and 24 trial reports. The average dose of monensin was 28.1 mg/kg DM. Authors stated that monensin improved both ADG and FE in approximately 2.5 and 6.4%, respectively, and decreased DMI by 3%. However, authors highlighted that the improvement in FE was influenced by the decade of the study, where the improvement of monensin in FE decreased from 8.1% in the 1970s to 2.3 to 3.5% in the 1990s to 2000s, respectively. Authors also pointed out that this reduced effect of monensin on FE may be associated with the increasing level of concentrate (and energy content) in feedlot diets over the decades.

Bretschneider et al. (2008) summarized results from 48 references in a review regarding the effects of antibiotic growth promoters (AGP) in beef cattle receiving forage-based diets. Monensin and lasalocid were among the AGP compounds evaluated, whose doses averaged 70 and 68 mg/100 kg BW, respectively. Authors observed an increase of 12.1 and 10.3 % in ADG when monensin and lasalocid were used, respectively. However, no effect of monesin or lasalocid was observed on DMI. Likewise, FE was improved as a result of the improvement in ADG. In all reviews (Goodrich et al., 1984; Bretschneider et al., 2008; Duffield et al., 2012), the improvement in ADG of cattle receiving monensin decreased as the ADG of cattle fed the control diet (without monensin) increased. Nevertheless, Bretschneider et al. (2008) reported increased response to lasalocid with increasing ADG of cattle fed high forage diets.

Recently, Gadberry et al. (2022ab) performed two metanalytical studies regarding the effects of monensin supplementation on the performance of beef cows (21 experiments), developing replacement heifers (18 experiments), and growing cattle on high forage diets (38 experiments). Monensin supplementation at doses from 125 to 200 mg/d did not affect BW or body condition score (BCS) of beef cows. However, beef cows presented a reduction of 8% on forage intake and 18 d to first estrous, while the percentage of cows with estrous prior the breeding season increased by 19% and milk production increased by 5.4% when monensin was offered. These results suggested an increase in energy availability when monensin was fed to beef cows.

Furthermore, monensin increased ADG by 5%, FE by 14%, and percentage cycling before the breeding season by 15.9%; while decreasing DMI by 4.3%, and age at puberty by 8.9 d in replacement heifers (Gadberry et al., 2022b). In growing cattle, average improvement in ADG due to monensin supplementaion was of 11%, although this response was negatively affected by the duration of the feeding period (Gadberry et al., 2022a). Besides, monensin supplementation decreased the incidence of bloat by 20%.

Similar responses have been observed for other ionophores such as narasin and salinomycin. No change on DMI, increased ADG from 6.7 to 24.8% and improved FE from 5.8 to 25.1% were documented for cattle fed forage-based diets containing narasin at doses of 7.3, 13, 15.3, and 20 mg/kg DM (Silva, 2016; Polizel et al., 2017; Polizel et al., 2020; Limede et al., 2021). Furthermore, DMI has been reduced from 4 to 6% and FE was increased from 6 to 14.8% in cattle fed high concentrate diets at 11 to 50 mg/kg DM levels of supplementation of salinomycin (Wagner, 1984; Merchen and Berger, 1985; Zinn, 1986a). However, some studies have shown no change in DMI of feedlot cattle with the addition of 11 and 12.6 mg/kg DM of salinomycin (Zinn, 1986b; Neumann et al., 2016) or 10.6 mg/kg DM of narasin (Gobato et al., 2017). Nonetheless, it is noteworthy that narasin and salinomycin seem to be effective in improving FE at a smaller dosage than lasalocid and monensin (Bergen and Bates, 1984).

Several studies have evaluated the main effects of monensin and other feed additives on beef cattle growth performance raised in temperate climates (Goodrich et al., 1984; Bretschneider et al., 2008; Khiaosa-Ard and Zebeli, 2013), and general recommendations have been made to adjust the nutrient requirements of beef cattle fed feed additives by the North American System (NASEM, 2016). Based on a review of the literature, NASEM (2016) recommended: 1) 3% reduction in DMI when monensin is fed regardless of the diet composition with no decrease when lasalocid or laidlomycin are fed; and 2) 3.5% improvement in FE when both monensin and lasalocid are fed; and 3) improved metabolizable energy availability by 2.3% and 1.5% when monensin and lasalocid or laidlomycin are fed, respectively.

However, no recommendations on dietary energy or animal performance adjustments were proposed in the previous edition of BR-CORTE (Valadares Filho et al., 2016) due to ionophores utilization in beef cattle diets. Unfortunately, there were only few data regarding the effects of ionophores from studies performed in Brazilian conditions to make any recommendation. In the current edition, the committee has performed a meta-analysis regarding the main effects of monensin on ruminal characteristics and productive performance of cattle raised in Brazilian conditions, which will be discussed further in this chapter.

Non-ionophores antibiotics

Like ionophores, non-ionophores antibiotics used as growth promoters, selectively modify microbial population in the rumen, resulting in changes in the proportions of VFA produced (towards more propionate and less acetate), reduced deamination of amino acids (increasing amino acids supply for the host animal), and inhibition of ruminal lactate producing bacteria; thus, improving FE, animal health, and productive performance (Nagaraja and Taylor, 1987; Nagaraja, 1995; Harfoot and Hazlewood, 2016). Virginiamycin and flavomycin are non-ionophores antibiotics available for use in animal diets in Brazil. However, the means by which specific compounds exert their antimicrobial effect differ.

Virginiamycin is produced during the fermentation of *Streptomyces virginiae*, and is an antibiotic of the streptogramin class. This antibiotic is composed of two main factors (M and S) that work synergistically (Boom and Dewart, 1974) and are able to bind specifically and irreversibly to ribosomal units (Cocito, 1979). Such binding inhibits protein synthesis, causing reduction in growth or even death of Gram-positive bacteria, mainly (Cocito, 1979). Flavomycin is a polypeptide antibiotic that inhibits the peptidoglycan formation, and therefore, cell wall formation in Gram-positive bacteria (Aarestrup et al., 1998). Virginiamycin can be used within the production system without withdrawal periods.

The benefits of including non-ionophores antibiotics in cattle diets are well documented. Molar proportions of propionate increased and acetate and butyrate decreased when virginiamycin is supplemented in forage and concentrate-based diets (Nagaraja et al., 1987; Harfoot and Hazlewood, 2016). Moreover, it is claimed to increase ADG and/or FE in growing and finishing cattle fed high forage or concentrate diets as well as to prevent liver abscesses in feedlot cattle (Fiems et al., 1992; Harfoot and Hazlewood, 2016; Tedeschi and Gorocica-Buenfil, 2018). Rogers et al. (1995) observed a linear improvement in ADG and FE and a decrease in the overall incidence and severity of liver abscesses in feedlot cattle as the supplemented dose of virginiamycin increased from 11 to 27.6 mg/kg DM. Authors stated that the effective dose range for virginiamycin in feedlot diets was 19.3 to 27.3 mg/kg DM to increase ADG, 13.2 to 19.3 mg/kg DM to improve FE, and 16.5 to 19.3 mg/kg DM to reduce the incidence of liver abscess.

Similarly, results from a meta-analytical study performed by Tedeschi and Gorocica-Buenfil (2018) demonstrated that liver abscesses incidence decreased linearly as virginiamycin dosage increased. Furthermore, these authors observed that virginiamycin was approximately 2.3 times more effective in improving ADG than monensin for the same dosage and feeding period (2.08 g/d per ppm compared to 0.92 g/d per ppm for monensin). Nonetheless, non-ionophores antibiotics had little or no effect on DMI and carcass traits (Lemos et al., 2016; Gorocica and Tedeschi, 2017; Castagnino et al., 2018).

Because of their similar selective effects on rumen microorganisms and complementary mechanism of action, several studies have hypothesized an additive feeding effect of ionophores and non-ionophores antibiotics for beef cattle. Recent studies performed under different conditions have shown improved productive performance (increase in ADG and FE) when virginiamycin and monensin were used in combination compared to monensin alone in high concentrate diets (Benatti et al., 2017; Heker et al., 2018; Neumann et al., 2020). Similarly, Nunez et al. (2013)

suggested that the combination of virginiamycin and salinomycin in high concentrate diets at doses of 15 and 13 mg/kg DM, respectively, improved the efficiency of dietary energy utilization efficiency when compared to cattle fed only salinomycin.

In contrast, Rigueiro et al. (2020), evaluating feedlot performance of Nellore bulls receiving different combinations of virginiamycin (25 mg/kg of DM) and monensin (30 mg/kg of DM) during the adaptation and finishing periods, observed an improvement in overall productive performance when bulls were fed the additive combination only during the adaptation period; with no benefits when the combination was supplemented during the finishing period or the entire feeding period (adaptation and finishing). The authors postulated that their results reflected the absence of the negative impact of monensin on DMI, since bulls were supplemented with ionophore for the shortest period. Furthermore, no evidence of benefits was found to support the supplementation of virginiamycin combined with monensin to cattle fed high forage diets (Maciel et al., 2019).

Concern about antimicrobial resistance has led to greater control over the use of antimicrobial agents in animal production. In this context, many countries have banned the use of antimicrobial agents as feed additives to improve animal performance, such as those in the European Union. In Brazil, the use of antimicrobial compounds and other growth promoters in animal production has been gradually restricted (Rabello et al., 2020). This has increased interest in alternative and more natural feed additives, such as yeast, essential and functional oils, and exogenous enzymes.

Yeasts

The increasing demand for natural products as an alternative to antibiotics, with potential to improve productive efficiency in ruminants, is increasing the interest in feed additives such as live cells, microorganisms, and/or their metabolites. In this regard, yeast (*Saccharomyces cerevisiae*) has been increasingly used in cattle diets to improve FE, productive performance and health. Nevertheless, studies evaluating the effects of yeast supplementation on the productive performance of beef cattle are recent.

Yeast (*Saccharomyces cerevisiae)* is usually supplied as dry preparations of live cells (live yeast) and, in some products, the cells are mixed with their growth medium (yeast culture). Products containing dead cells are also commercially available and, as they do not contain viable cells, they are used as a nutritional ingredient. Yeasts are composed by high quality proteins, carbohydrates, lipids, and B-complex vitamins, making them advantageous in relation to other feed additives. Moreover, commercially available products vary widely in the strain of *Saccharomyces cerevisiae* used, and in the number of yeast cells present.

In general, yeasts action has been related to the promotion of better ruminal conditions through: 1) removal of traces of oxygen, improving ruminal anaerobiosis; 2) competition with lactate-producing (e.g. *Streptococcus bovis and Lactobacillus*) bacteria for readily fermentable carbohydrates and, therefore, contribution to ruminal pH regulation; 3) stimulation of the growth of fiber digesting bacteria (e.g. *Fibrobacter succinogenes and Ruminococcus flavefaciens*) and growth of lactate-utilizing bacteria (e.g. *Megasphaera elsdenii*), which can be related to the probiotic effect of yeasts (Wallace and Newbold, 1992; Jouany and Morgavi, 2007; Chaucheyras-Durand et al., 2008).

Therefore, there are several instances in the literature that have related the supplementation of diets for growing and finishing cattle with yeast (*Saccharomyces cerevisiae*) to improve productive performance and health (Finck et al., 2014; Geng et al., 2016; Peng et al., 2020). Improved productive responses (DMI, ADG, final BW, and/or FE) attributed to yeast are usually related to increased ruminal pH and VFA concentrations, fiber digestion, and microbial protein flow from the rumen due to the inhibitory activity of rumen proteolytic bacteria (Jouany and

Morgavi, 2007; Chaucheyras-Durand et al., 2008; Amin and Mao, 2021). These effects may be particularly important when high grain diets are fed to cattle.

However, the effects of yeast supplementation are not reported as consistent in the literature. Some studies have shown no benefits of adding yeast to beef cattle diets on digestive parameters or growth performance (Adams et al., 1981; Edwards et al., 1990; Gattass et al., 2008). The discrepancies in responses of yeast supplementation seem to be dependent on different interaction factors, such as diet type, yeast strain, and dose.

The positive effects of adding yeast are more evident when diets with higher concentrate levels are fed, which may be associated with the ability of yeast to modulate ruminal pH. Carro et al. (1992) reported greater *in vitro* digestibility of DM and NDF when yeast was supplemented to high-concentrate diets, but no effect of yeast supplementation was observed with medium- and low-concentrate diets. Likewise, Desnoyers et al. (2009) performed a meta-analysis on the influence of yeast supplementation on ruminal parameters and performance of ruminants (beef and dairy cattle, goats, sheep, and buffaloes) and concluded that beneficial responses to DMI, ruminal pH, ruminal VFA and lactate concentrations, and milk yield were more pronounced in ruminants fed higher levels of concentrate in the diet.

Also, the effectiveness of yeast seems to be dependent on the relationship between the diet composition and the nutritional demands of the animal. The effectiveness of yeast on a low protein diet and high protein diet was investigated for dairy cows in early lactation and the results obtained revealed that yeast supplementation improved the milk yield of cows fed low protein diets, but had no effect on milk yield of cows fed high protein diets (Putnam et al., 1997).

Different strains and doses of yeast differ in their effectiveness in stimulating rumen fermentation and growth performance. The variability in the response to yeast supplementation regarding strain type may be related to differences in their metabolic activity and should be considered in the selection of yeasts for ruminants (Newbold et al., 1995; Jouany and Morgavi, 2007; Sartori et al., 2017). The effect of different dosages (0, 2×10^6; 4×10^6; and 6×10^6 CFU of the total dietary substrate) of yeast in different forage:concentrate ratio diets (80:20, 60:40, 40:60, and 20:80) on *in vitro* digestibility were investigated and the results revealed that the maximum DM and OM digestibility was achieved with the highest dose of yeast (Phesatcha et al., 2020). The inclusion of a higher dose of yeast (4 g/d) improved feed intake, ADG, and FE of calves, whereas the inclusion of a lower dose (1% dry yeast/kg DM) had no effect on calves' performance (Lesmeister et al., 2004). In a meta-analysis, Desnoyers et al. (2009) observed that ruminal pH, VFA concentration, organic matter digestibility and milk yield increased linearly with yeast dose supplemented to ruminants. Similarly, a linear increase in ADG was observed for beef heifers when yeast supplementation was increased from 5 to 20 g/d in the diet (Greene, 2002).

Essential and functional oils

This type of feed additives includes plant extracts that usually have an antimicrobial effect, causing changes in the fermentation profile. Most plant extracts have been associated with essential oils (EO). Essential oils are a diverse group of plant secondary metabolites obtained from volatile aromatic fractions of plants (e.g., thymol, carvacrol and eugenol), which have antimicrobial properties (Patra and Saxena, 2010). However, some plant oils cannot be classified as EO because they are not derived from aromatic portions. Instead, these oils are referred to as functional oils (FO) because they have functions beyond their nutritional value. Anarcardic and ricinoleic acids (main group of phenolic lipids) are examples of FO. Although they can be classified differently, a variety of positive health effects such as antitumor, antioxidant, gastroprotective, and antimicrobial properties have been attributed to these plant extracts (Dahham et al., 2015; Salehi et al., 2020). Thus, EO and FO are part of a natural alternative to improve animal health and productive performance, reducing the use of antimicrobials in livestock. As FO is a broader classification than EO, both types of plant extracts have increasingly been described just as FO.

The antimicrobial effect of most EO and FO is believed to be similar to that of ionophores in which most Gram-positive bacteria are selectively inhibited (Calsamiglia et al., 2007; Watanabe et al., 2010). This selectiveness is also analogous to that of ionophores, as the hydrophobic nature of the oils allows their interaction with the bacterial membrane, resulting in altered ion transport and gradient (Calsamiglia et al., 2007; Watanabe et al., 2010). Nevertheless, it is noteworthy that these plant extracts may also be effective against some Gram-negative bacteria (although they are less sensitive than Gram-positive bacteria) and some compounds have other modes of action, acting in the cytoplasm or organelles of microbial cells (Burt, 2004; Benchaar and Greathead, 2011).

Thus, the main effects of these oils on ruminal fermentation can be expected to include a shift in the proportions of VFA towards less acetate and more propionate, and, thereby, decreased methane production in the rumen; decreased protein degradation; and improved nutrient utilization and FE. Many studies have been performed to evaluate the benefits of supplementing EO and FO as well as their components in ruminant diets. These studies have been using a wide range experimental procedures, compounds, doses, and diets; thus, results have been inconsistent.

Several *in vitro* studies have indicated the potential of EO and their components in the beneficial manipulation of rumen fermentation (McIntosh et al., 2003; Castillejos et al., 2005; Benchaar et al., 2008). An increase in total VFA concentration and/or propionate:acetate ratio, as well as a decrease in ammonia N concentration and methane production has been described when different EO and their components and doses were included in readily fermentable and medium and high-fiber diets/substrates (Cardozo et al., 2005; Busquet et al., 2006; Chaudhry and Khan, 2012). Nevertheless, positive results have been shown for substrate/diet, EO and/or their components or mixtures, dose applied, and pH dependent. For example, Busquet et al (2006) showed *in vitro* that propionate molar proportion increased and acetate molar proportion decreased when garlic oil was included in a 50:50 forage:concentrate diet at doses of 300 and 3000 mg/L but not at 3 or 30 mg/L. Moreover, other EO, such as ginger, cade, capsicum, and yucca oils had no effect on propionate or acetate molar proportions at all inclusion doses tested in the same study (3, 30, 300 and 3000 mg/L). In some cases, beneficial effects on VFA proportions, ruminal N metabolism, and *in vitro* methane were achieved only at high concentrations of some EO supplemented (Busquet et al., 2006; Benchaar et al., 2008; Benchaar and Greathead, 2011), which may also inhibit the process of ruminal fermentation (decreasing feed digestion and total VFA production) and are unlikely to be used in practice (*in vivo*). The effects can also be transient due to an adaptation of the microbiota to the EO (Benchaar et al., 2008).

Additive, antagonistic and synergistic effects have been suggested among different plant extracts and their components (Burt, 2004; Toroglu, 2007; Fandiño et al., 2020), which have resulted in a variety of commercial products combining different EO, FO, or their components currently available for ruminants in the market. Nonetheless, published studies on the effects of feeding EO and FO to beef cattle are limited when compared to the number of studies performed in dairy cattle.

Overall, results from feeding studies are inconsistent depending on the type of plant extract, source, diet, and doses evaluated. Nevertheless, there are some instances in the literature that describe potential benefits of feeding EO and FO to beef cattle. In a study, Yang et al. (2010) reported a linear increase in propionate molar proportion and a linear decrease in acetate:propionate ratio with increasing dose of EO (0, 400, 800, 1600 mg/d of eugenol) in the diet of growing beef cattle. Ornaghi et al. (2017) showed greater DMI, ADG, and final body and carcass weight in finishing feedlot cattle fed clove and cinnamon EO. Moreover, the authors also stated that responses for most of these variables increased linearly as the dose of EO increased from 3.5 to 7 g/d.

Similarly, greater ADG and FE were reported for feedlot Nellore heifers receiving protected EO blends (composed of eugenol, thymol, and vanillin plus clove EO or eugenol, thymol, and vanillin plus rosemary and clove

EO) (Souza et al., 2019). Moreover, Valero et al. (2014) documented improvement in growth performance (final weight, ADG, and FE) and carcass weight in feedlot bulls fed diets supplemented with FO (blend of castor oil acid and cashew nut shell liquid). These results may increase expectation regarding the use of EO and FO in beef cattle nutrition. In contrast, other studies have shown no effect on rumen fermentation parameters, growth performance, carcass traits or FE of cattle fed high, medium and low concentrate diets containing different commercial blends of EO and FO at different dosages (Beauchemin et al., 2006; Silva et al., 2019; Melo et al., 2020; Wang et al., 2020; Wilson et al., 2020).

In a meta-analytic study, Khiaosa-Ard and Zebeli (2013) investigated the effects of different EO and their compounds on ruminal fermentation, productive performance, and FE in ruminants (beef, dairy, and small ruminants). Although dose-dependent, the results indicated an overall improvement in ruminal fermentation (VFA production and individual VFA concentration) with EO supplementation in ruminants. Nevertheless, positive responses on VFA composition and methane production were more pronounced in beef cattle when compared to dairy cattle and small ruminants. The authors attributed the better response of beef cattle to a synergistic effect between EO and their low ruminal pH, since the reduction in ruminal pH is commonly observed in feedlot systems due to the high-grain diets used. No beneficial effects on ruminal protein degradation or productive performance and FE of dairy cattle were attributed to EO supplementation. The effects of EO supplementation on the productive performance of beef cattle and small ruminants were not evaluated due to the limited number of studies to date. Thus, it seems that manipulation of ruminal fermentation towards more energetically efficient routes is the most consistent benefit of utilizing EO in ruminants.

Despite the limited and inconsistent results reported so far on the productive performance of beef cattle, EO and FO are currently one of the best alternatives to the use of ionophores antibiotics. In this context, Torres et al. (2021) performed a meta-analysis evaluating the effects of different EO as an alternative to monensin in beef cattle diets. These authors reported that the replacement of monensin by EO had no influence on growth performance parameters, but positively affected dressing percentage, rib eye area, and subcutaneous fat thickness of beef cattle fed high grain diets. However, the authors also concluded that EO presented low effectiveness in preventing liver abscesses in these animals.

Likewise, Purevjav et al. (2013) evaluated the effects of FO (blend of castor oil acid and cashew nut shell liquid) with or without monensin on the growth performance and carcass traits of feedlot steers. The authors described improvement in carcass traits (dressing percentage, rib eye area, and prime grade classification) in cattle receiving only FO supplementation; however, they also presented a higher incidence of liver abscess, especially at the highest dose applied (500 mg/kg DM). Although further evaluation is still needed, published data suggest that there is still potential of replacing ionophores antibiotics by EO or FO in beef cattle diets.

For the authors, knowledge on the potential use of these plant extracts in beef cattle, particularly those raised under Brazilian conditions, is still very limited. Therefore, the committee carried out a meta-analysis on the main effects of FO on ruminal characteristics and productive performance of cattle raised in Brazilian production systems, which will be discussed later in this chapter.

Exogenous enzymes

Exogenous enzymes are another class of natural feed additives that have potential to replace growth promoters such as ionophore antibiotics. Enzyme additives are complex bacterial (e.g., *Bacillus*) or fungal (e.g., *Aspergillus, Trichoderma*) fermentation extracts with specific activities of enzymes such as amylases, xylanases, cellulases, and proteases. Enzymes are proteins that are ultimately digested or excreted by the animal, leaving no residues in meat or milk.

In ruminants, exogenous enzymes aid the microbial population of the rumen by performing part of the feed digestion, mainly. Thus, these compounds have potential to enhance the digestion of feed ingredients in the rumen and nutrient availability, and improve FE (Beauchemin et al., 2004; NASEM, 2016; Beauchemin et al., 2018). In addition, they can be used to supplement the enzymes produced by young animals which, because of an immature digestive system, may have an inadequate enzyme production. The mode of action of the exogenous enzymes is not well understood. Nevertheless, the proposed mode of action of exogenous enzymes includes direct hydrolysis, stimulation of microbial population, synergism with microbial enzymes, and improved microbial adherence to feed particles (Beauchemin et al., 2004; Salem et al., 2013).

Most research in ruminants has examined the potential effects of exogenous fibrolytic enzymes (e.g., xylanase and cellulase) to improve fiber digestibility in the rumen (NASEM, 2016; Beauchemin et al., 2018), because increased fiber digestibility may increase the energy intake by the animal. Moreover, improved fiber digestibility in the rumen stimulates microbial growth, which usually increases the supply of metabolizable protein to the animal. As a result, higher productivity and FE may be achieved. Few studies have been conducted regarding other types of exogenous enzymes, such as amylases and proteases.

Research evaluated several enzymes products which were applied at various doses in different ways (e.g., sprayed on to forage, added to concentrate, etc.) to different types of diets fed to different types of animal (dairy cattle, beef cattle, and small ruminants) and categories (e.g., growing and finishing beef cattle, lactating dairy cows, etc.); thus, results have shown high variability. For example, increased digestibility (particularly fiber), productive performance (ADG, final BW, and/or FE), and/or carcass traits have been reported in some studies (Salem et al., 2013; Neumann et al., 2018; Lourenco et al., 2020) but not in others (ZoBell et al., 2000; Miller et al., 2008; Encinas et al., 2018) when exogenous fibrolytic enzymes were supplemented to high forage and high concentrate diets fed to growing and finishing cattle.

In a meta-analytical study, Tirado-González et al. (2018) evaluated the effects of using exogenous fibrolytic enzymes in ruminant diets with variable content of forage (grass or legume) on the productive performance of lactating dairy cow, growing beef cattle, and sheep. Research included data from 74 journal articles. Overall, results suggested that the inclusion of exogenous fibrolytic enzymes improve the productive performance of dairy and beef cattle, but responses were dependent on enzyme activity (cellulases, xylanases, or different mixtures of both) according to the diet composition (type of forage and forage to concentrate ratio). It is noteworthy that exogenous fibrolytic enzymes improved the productive performance of dairy cattle when they were supplemented in high forage diets, whereas increased productive responses in beef cattle were observed when exogenous fibrolytic enzymes were added to low forage diets. The effects of exogenous fibrolytic enzymes supplementation on the productive performance of sheep were inconsistent. It seems that responses to exogenous fibrolytic enzymes are greater when energy limits animal productivity, which is often the case of lactating dairy cows and growing beef cattle.

Although research has hypothesized that the digestion of starch and protein would not be limited within the rumen, some studies performed with supplementation of exogenous enzymes with amylolytic (Tricarico et al., 2007; DiLorenzo et al., 2011; de Oliveira et al., 2015) and proteolytic activities (Licitra et al., 1999; Vera et al., 2012; Amaro et al., 2021) have evaluated the potential of these exogenous enzymes to improve theproductive performance. Overall, the use of exogenous amylases and proteases seems to have potential to improve feed digestion and the productive performance of cattle, especially when added to high grain diets (Tricarico et al., 2007; Vera et al., 2012; Jolly-Breithaupt et al., 2019).

Furthermore, recent studies (Gouvêa et al., 2019; Meschiatti et al., 2019; Toseti et al., 2020) have suggested a positive synergistic effect on DMI and starch digestibility, and, consequently improved animal growth performance when EO and exogenous α-amylase were included in feedlot diets compared to other feed additives such as monensin.

The use of enzymes additives is expected to increase as the use of antibiotics in ruminant diets decreases. However, results from experiments with exogenous enzymes in ruminants are still inconsistent or limited.

Therefore, although much progress has been made in exogenous enzyme technology, it cannot be concluded at the moment that enzyme supplementation may be an effective way to enhance ruminant productivity.

3-nitrooxypropanol (3-NOP)

3-nitrooxypropanol (3-NOP; DSM Nutritional Products Ltd., Kaiseraugst, Switzerland), marketed as Bovaer® since 2021 in Brazil, is a ruminal CH_4 inhibitor through the inactivation of the enzyme methyl-coenzyme M reductase used by archaea (Duin et al., 2016). Feeding 3-NOP to cattle seems to have no adverse effects on animal or other ruminal microorganisms (Jayanegara et al., 2018; Honan et al., 2022). Moreover, residues of 3-NOP in milk and meat are minimal or inexistent (Thiel et al., 2019), with apparently low safety risks.

Results of CH_4 mitigation by 3-NOP have been promising. Vyas et al. (2016) reported that 200 mg/kg DM of 3-NOP supplementation reduced CH_4 production in backgrounding and finishing beef cattle by 37.6% and 84.3%, respectively, when compared to the control group. Similarly, Alemu et al. (2021) reported a decrease in CH_4 production of 25.7%, on average, in growing steers supplemented with increasing doses of 3-NOP (from 150 to 200 mg/kg of DM), whereas McGuinn et al. (2019), using the supplementation level of 125 mg/kg DM for finishing beef cattle, found a reduction of approximately 70% in CH_4 production. In a metanalysis, Hristov et al. (2022) demonstrated a consistent decrease of 28 to 32% in CH_4 emissions in dairy cows fed 3-NOP at doses ranging from 40 to 200 mg/kg DM, with no effect on DMI, milk production, body weight, or body weight change, and a slight increase in milk fat concentration (0,19%) and yield (90 g/d).

In fact, the effects of 3-NOP appear to depend on the dose, animal type, diet characteristics and feeding duration. In a metanalysis regarding the effects of 3-NOP on dairy and beef cattle, Dijkstra et al. (2018) concluded that CH_4 mitigation effect of this compound was dose-dependent and was less pronounced in beef (22% reduction) than in dairy (39% reduction) cattle. Furthermore, they concluded that increasing diet NDF content decreased the effectiveness of the additive. Therefore, in the same cattle category and dose applied, the mitigation effect of 3-NOP has been greater in higher concentrate diets.

A more recent metanalytical study reported that increasing the dose of 3-NOP linearly decreased CH_4 yield (g/kg DMI), regardless of animal type and feeding period, as well as the proportion of acetate and acetate to propionate ratio (A:P) in both dairy and beef cattle (Kim et al., 2020). Furthermore, authors also observed a trend for decreased DMI in beef but not in dairy cattle with increasing dose of 3-NOP, whereas increasing 3-NOP supplementation tended to decrease milk yield (kg/d) and increased milk fat (%) and protein (%). The effects of 3-NOP supplementation on ADG, BW or FE of beef cattle were not evaluated in the study.

In contrast, although CH_4 emissions decreased linearly, increasing 3-NOP supplementation had no effect on ruminants DMI (dairy cows, beef cattle, and sheep; Jayanegara et al., 2018). Moreover, the production performance of dairy and beef cattle was influenced by feeding 3-NOP in this study, except for FE and milk fat (%). Both FE and milk fat (%) were improved by 3-NOP supplementation, which may suggest greater energy availability as a result of reduced CH_4 emissions. There are instances in the literature that support these findings, in which improved milk fat and FE without change in milk yield and ADG were observed when feeding 3-NOP to dairy and beef cattle, respectively (Vyas et al., 2018; Hristov et al., 2022). However, reduction in DMI of beef cattle fed high forage diet has been often observed (Romero-Perez et al., 2014; Vyas et al., 2016; Vyas et al., 2018).

Other factors may affect the response to 3-NOP supplementation, such as the method used to measure CH_4 emissions (chambers, SF_6 tracer technique, and Greenfeed system) and interaction effects when 3-NOP was combined with other mitigation strategies. Results from Gruninger et al. (2022) showed that the combination of 3-NOP with canola oil in a high forage diet for beef cattle resulted in an additive reduction in CH_4 yield (g/kg DM; 3-NOP = -28%; canola oil = -24%; 3-NOP + canola oil = -52%).

3-NOP seems to be an effective strategy to mitigate CH_4 emissions from ruminants. However, results on animal performance (especially DMI) have been more variable. In addition, little is known regarding the effectiveness of 3-NOP for grazing animals and its long-term impacts. Furthermore, the authors are not aware of any published studies evaluating 3-NOP under Brazilian conditions. Thus, further information is still needed on the use of 3-NOP in a broad range of feeding systems and for longer durations.

METANALYSIS

The use of additive products to beef cattle diets could improve productive performance. However, the literature shows inconsistent results for most feed additives available. Furthermore, most research regarding the effects of feed additives supplementation to cattle was conducted under temperate conditions. In this context, since meta-analysis could summarize results of different studies, the committee of BR-CORTE current edition evaluated the effects of monensin and FO on the productive performance and ruminal parameters of cattle raised under Brazilian conditions through a meta-analytical method.

Database

A literature search and screening process was conducted using public data search engines, such as Google Scholar, Science direct, and Scielo, to create a dataset of feed additives manuscripts conducted in Brazil using the keywords: "feed additives, cattle, and Brazil", "additive, cattle, and Brazil", "monensin, cattle, and Brazil", "essential oils, cattle, and Brazil" or "functional oils, cattle, and Brazil". The same keywords were also searched in Portuguese. No date restrictions were used on the search; thus, the entire time feed additives in cattle studies conducted in Brazil have been available for research. In addition, Brazilian research and organizations were asked for unpublished and/or published data that might be used for this analysis. Experiments were treated individually even though they were published within the same study.

All unpublished data and peer-reviewed manuscripts were initially evaluated for acceptability by determining whether the research was conducted in Brazil and which feed additive was used. Articles investigating the effects of EO and FO as well as their specific bioactive compounds and blends were eligible for inclusion in the database in the category of FO, as FO is a more general term. Thus, hereafter, EO, FO, bioactive compounds, and their blends are referred to as FO. Initial screening of trial reports and manuscripts was conducted by two authors. Any rejections and inclusions were reviewed by one of the authors and confirmed by other two authors. Studies were required to be randomized trials (completely randomized, complete block, or factorial designs) performed under Brazilian conditions and to contain a control treatment to be eligible for analysis. Each treatment (control, monensin, and functional oils) required report of the number of animals/pens per treatment, mean for the treatment, and a measure of dispersion. As a result, a total of 22 peer-reviewed manuscripts and unpublished data were reached (Table 16.1). The complete list of experiments used in this metanalytic study can be found in Appendix 16.1. Data from different animal class (bulls, steers, heifers, and dry cows) from different genetic groups (*Bos taurus taurus*, *Bos taurus indicus*, or crossbred), raised in feedlot, were included. Other factors that could influence the outcomes of interest were included in the data extraction process, including physiological status (growing, finishing, or dry cow), treatment dose (mg/kg feed of DM), days on feed, forage:concentrate ratio, type of paper (peer-reviewed [J] or not [U]), and animal condition (cannulated or not).

Table 16.1 - Description of the experiments included in the database

Study	Source type: J = Journal U = unpublished	Treatment n	Animal class	Genetic group	Production system	Canullated Y = Yes N = No	Physiological status	Days on feed	Replicates per treatment	Feed additive: MON = monensin FO = functional oils	Doses tested (mg/kg DM)	Outcomes[1]
Chagas, L. J.	U	4	Bull	*Bos taurus indicus*	Feedlot	No	Finishing	124	10	MON, FO	MON = 30 FO = 300 and 500	DMI, BW, ADG, CW, G:F
Fonseca et al.	J	4	Bull	Crossbred	Feedlot	No	Growing	70	5	MON	22	DMI, ADG, G:F
Mogentale et al.	J	3	Cow	Crossbred	Feedlot	Yes	Dry cow	21	4	MON	26.5	DMI, ruminal pH, NH_3, VFA, acetate, propionate, butyrate, acetate:propionate ratio
Gomes et al.	J	4	Steer	*Bos taurus indicus*	Feedlot	No	Finishing	84	18	MON	30	DMI, BW, ADG
Maturana Filho et al.	J	3	Steer	*Bos taurus indicus*	Feedlot	No	Finishing	84	6	MON	30.8	DMI, BW, ADG, G:F
Pereira, M. C. S.	U	5	Bull	*Bos taurus indicus*	Feedlot	No	Finishing	70	12	MON	9, 18, 27, and 36	DMI, BW, ADG, CW, G:F
Prado et al.	J	4	Steer	*Bos taurus taurus*	Feedlot	Yes	Growing	21	4	MON	32.8	DMI, ruminal pH, NH_3, VFA, acetate, propionate, butyrate, acetate:propionate ratio
Ribeiro, F. G.	U	4	Heifer	*Bos taurus taurus*	Feedlot	No	Finishing	84	16	MON	13.3	DMI, BW, ADG, CW, G:F
Segabinazzi, L. R.	U	3	Cow	Crossbred	Feedlot	No	Dry cow	64	8	MON	24.2	DMI, BW, ADG, G:F
Sitta, C.	U	5	Bull	*Bos taurus indicus*	Feedlot	No	Finishing	102	22	MON	30	DMI, BW, ADG, G:F
Sitta, C.	U	5	Bull	*Bos taurus indicus*	Feedlot	No	Finishing	109	23	MON	30	BW, ADG, G:F
Zawadzki et al.	J	3	Bull	*Bos taurus indicus*	Feedlot	No	Finishing	84	11	MON	32.8	DMI, BW, ADG, CW, G:F
Souza, K. A.	U	5	Heifer	*Bos taurus indicus*	Feedlot	No	Finishing	73	8	FO	789, 640, 678, and 644	DMI, BW, ADG, CW, G:F

[1]DMI = dry matter intake; BW = body weight; ADG = average daily gain; CW = carcass weight; G:F = gain to feed ratio; NH = ruminal ammonia; VFA = volatile fatty acids.

Table 16.1 - Description of the experiments included in the database (continued)

Study	Source type: J = Journal U = unpublished	Treatment n	Animal class	Genetic group	Production system	Canullated Y = Yes N = No	Physiological status	Days on feed	Replicates per treatment	Feed additive: MON = monensin FO = functional oils	Doses tested (mg/kg DM)	Outcomes[1]
Zotti, C. A.	U	4	Steer	*Bos taurus indicus*	Feedlot	Yes	Finishing	21	6	MON, FO	MON = 30 and 40 FO = 400	DMI, ruminal pH, NH_3, VFA, acetate, propionate, butyrate, acetate:propionate ratio
Almeida et. al.	J	5	Steer	*Bos taurus indicus*	Feedlot	Yes	Finishing	21	5	MON, FO	MON = 30 FO = 500	DMI, acetate, propionate, butyrate, acetate:propionate ratio
Fugita et al.	J	4	Bull	Crossbred	Feedlot	No	Finishing	-	12	FO	485	DMI, BW, ADG, CW, G:F
Martinele et al.	J	4	Cow	Crossbred	Feedlot	Yes	Dry cow	21	4	MON	33	DMI, ruminal pH, NH_3, VFA, acetate, propionate, butyrate, acetate:propionate ratio
Melo et al.	J	4	Bull	*Bos taurus indicus*	Feedlot	No	Finishing	89	6	MON, FO	MON = 27 FO = 500	DMI, BW, ADG, CW, G:F
Perna Júnior et al.	J	3	Cow	*Bos taurus taurus*	Feedlot	Yes	Dry cow	30	6	MON	17.8	DMI, ruminal pH
Chagas, L. J.	U	4	Steer	*Bos taurus indicus*	Feedlot	Yes	Finishing	21	4	MON, FO	MON = 25 FO = 300	DMI, ruminal pH, NH_3, VFA, acetate, propionate, butyrate
Figueira, D.	U	5	Bull	*Bos taurus indicus*	Feedlot	No	Finishing	112	7	MON	20	DMI, BW, ADG, CW, G:F
Benatti, J. M. B.	U	4	Bull	*Bos taurus indicus*	Feedlot	No	Finishing	84	11	MON	7	DMI, BW, ADG, CW, G:F

[1]DMI = dry matter intake; BW = body weight; ADG = average daily gain; CW = carcass weight; G:F = gain to feed ratio; NH = ruminal ammonia; VFA = volatile fatty acids.

All response variables were not available in each feed additive and in all observations, leading to many missing data. Therefore, sub datasets for each feed additive tested were constructed according to each dependent variables: DMI, BW, ADG, FE (gain:feed ratio), carcass weight, ruminal pH, ruminal N-NH_3, total VFA, acetate (% of total VFA), propionate (% of total VFA), butyrate (% of total VFA), and acetate: propionate ratio. Moreover, due to the limited number of studies obtained and to avoid bias that may occur from differences regarding experimental conditions (genetic groups, animal class, mean BW, etc.) the analyzes of each variable within each feed additive were conducted on changes adjusted according to their corresponding control values (change = (value in feed additive treatment – control value)/ control value). This removed any interstudy bias effect (Ellis et al., 2012).

Statistical analysis

A meta-analysis was conducted through the MIXED procedure of SAS (version 9.4, Inst. Inc., Cary, NC, USA). A fixed effect model was first conducted for each parameter within each feed additive evaluated to estimate the effect size (ES), 95% confidence interval (CI), and statistical significance of effect size. Treatments differences relative to control were weighed by the inverse of variance (weighted mean differences; WMD).

Between-study heterogeneity was quantified using the I^2 statistic (Higgins et al., 2003), which describes the percentage of total variation across experiments that is due to heterogeneity rather than chance. Uncertainty intervals for I^2 were calculated. Negative values of I^2 were put to equal to 0 (Duffield et al., 2012; Torres et al., 2021). Consequently, I^2 lies between 0 and 1. A value greater than 0.5 was considered substantial heterogeneity (Duffield et al., 2012). If there was evidence of heterogeneity, a random effects model was used. A level of 0.05 was established as the critical level of probability for a type I error.

Results

The summary of the experiments used for this metanalytic study is provided in Table 16.1 and a descriptive statistic from the database used to evaluate the effects of monensin and FO is available in Table 16.2. The total number of cattle included in this study regarding the effects of monensin and FO on growth performance and ruminal fermentation parameters were: 448 and 153 for DMI; 353 and 118 for BW; 363 and 118 for ADG; 327 and 118 for FE (G:F ratio);196 and 118 for carcass weight; 70 and 20 for ruminal pH; 58 and 20 for ruminal N-NH_3; 73 and 35 for total VFA, acetate (% total VFA), propionate (% total VFA), and butyrate (% total VFA); and 65 and 27 for acetate:propionate ratio (A:P), respectively. The average dose of monensin tested was 24.3 mg/kg DM, with a range of 7 to 40 mg/kg DM, whereas the average dose of FO evaluated was 488 mg/kg DM, with a rage of 300 to 789 mg/kg DM. All studies utilized the Total Mixed Ration (TMR) system in the feeding operations, forage:concentrate ratio varied from 72.5:27.5 to 7.75:92.25 in monensin studies and from 50:50 to 12:88 in FO studies.

Table 16.2 - Descriptive statistics of database used to evaluate the effects of monensin and functional oils on growth performance and ruminal characteristics of cattle under Brazilian conditions

Item[1]	Studies	n	Mean	SD	Maximum	Minimum
Monensin						
Dry matter intake (kg)	20	448	10.5	2.80	18.0	6.10
Body weight (kg)	12	353	504	43.0	597	426
Average daily gain (kg/d)	13	363	1.33	0.187	1.58	0.87
Gain to feed ratio (G:F)	13	327	0.13	0.028	0.22	0.09
Hot carcass weight (kg)	7	196	283	34.0	341	223
Ruminal pH	6	70	6.21	0.324	6.75	5.74
Ruminal $N\text{-}NH_3$ (mg/dL)	5	58	11.6	5.54	20.5	6.72
Total VFA (mM)	6	73	109	15.2	142	81.0
Acetate (% total VFA)	6	73	60.1	9.08	71.7	46.4
Propionate (% total VFA)	6	73	27.6	5.09	37.3	19.9
Butyrate (% total VFA)	6	73	9.37	3.674	14.6	5.32
Acetate:propionate ratio	5	65	2.52	0.879	4.23	1.31
Functional oils						
Dry matter intake (kg)	7	153	8.24	1.699	10.3	5.07
Body weight (kg)	4	118	439	69.6	506	343
Average daily gain (kg/d)	4	118	1.17	0.357	1.76	0.47
Gain to feed ratio (G:F)	4	118	0.14	0.032	0.19	0.09
Hot carcass weight (kg)	4	118	238	40.1	282	186
Ruminal pH	2	20	5.87	0.128	6.06	5.79
Ruminal $N\text{-}NH_3$ (mg/dL)	2	20	13.9	6.97	20.3	7.32
Total VFA (mM)	3	35	124	20.0	147	101
Acetate (% total VFA)	3	35	56.9	8.86	69.1	45.6
Propionate (% total VFA)	3	35	29.0	5.84	37.3	23.0
Butyrate (% total VFA)	3	35	11.3	3.94	14.7	6.2
Acetate:propionate ratio (A:P)	2	27	1.85	0.632	2.59	1.27

[1]VFA = volatile fatty acids.

Monensin

The sumary of meta-analysis for each monensin supplementation outcome is presented in Table 16.3. There was between-study heterogeneity in the response of monensin on A:P (I^2 = 0.75; IC = 0, 0.87). According to Higgins et al. (2003), values of I^2 statistic above 0.5 denote high heterogeneity. Thus, the model for A:P was evaluated using a random effect of experiment. In this context, if the between-study variance was not considered in the model, this would inflate the residual variance. Consequently, increased residual variance would promote a greater type II error rate. That is, the error that occurs when accepting a null hypothesis that is actually false (false negative response).

Table 16.3 - Summary of effect size estimates of monensin on growth performance and ruminal characteristics outcomes in cattle raised under Brazilian conditions derived from meta-analysis

Outcomes[1]	Weighed mean difference for control (95% CI)[2]	% Change	Trials	n	I^2 (95% uncertainty interval)[3]	Effect size P-value
Dry matter intake (kg/d)	-0.45 (-0.58,-0.32)	-4.96	20	448	0 (0, 0.28)	<0.001
Body weight (kg)	-1.03 (-4.57, 2.52)	-0.22	12	353	0 (0, 0.01)	0.838
Average daily gain (kg/d)	-0.007 (-0.04, 0.03)	-0.58	13	363	0 (0, 0.01)	0.932
Gain to feed ratio (G:F)	0.0003 (-0.004,0.004)	0.93	13	327	0 (0, 0.05)	0.991
Carcass weight (kg)	-1.67 (-5.57, 2.23)	-0.69	7	196	0 (0, 0.01)	0.672
Ruminal pH	-0.06 (-0.08, -0.03)	-0.96	6	70	0 (0, 0.01)	0.001
Ruminal $N\text{-}NH_3$ (mg/dL)	0.26 (-0.10, 0.63)	-3.30	5	58	0 (0, 0.01)	0.322
Total VFA (mM)	-3.38 (-6.65, -0.10)	-2.99	6	73	0.06 (0, 0.43)	0.123
Acetate (% total VFA)	-3.07 (-3.96, -2.18)	-5.28	6	73	0 (0, 0.30)	<0.001
Propionate (% total VFA)	4.08 (3.17, 4.99)	22.2	6	73	0 (0, 0.27)	<0.001
Butyrate (% total VFA)	-0.13 (-0.62, 0.37)	-1.60	6	73	0.10 (0, 0.38)	0.860
Acetate:propionate ratio (A:P)	-0.33 (-0.64, -0.02)	-10.3	5	65	0.75 (0, 0.87)	0.062

[1]VFA = volatile fatty acids.
[2]Weighted mean difference of treatment relative to control, where the weights used were the inverse of the variance in the differences in means; CI = confidence interval.
[3]I^2 is a measure of variation beyond chance (Higgins et al., 2003).

Monensin supplementation decreased DMI (– 0.45 kg; % Change = -4.96; P < 0.001), ruminal pH (– 0.06; % Change = -0.96; P = 0.001), and acetate concentration (WMD = – 0.45; % Change = -0.96; P < 0.001). Propionate concentration was increased with the inclusion of monensin in diets (4.08; % Change = 22.2; P < 0.001). However, there was no effect of diet supplementation with monensin on BW, ADG, FE (gain:feed ratio), carcass weight, ruminal $N\text{-}NH_3$ concentration, total VFA, butyrate concentration, or A:P (P ≥ 0.062).

Functional oils

Results of the meta-analysis regarding the effects of including FO in cattle diets are described in Table 16.4. High between-study heterogeneity was observed when the effects of FO on ADG, ruminal pH, and A:P were evaluated in the present study (I^2 = 0.54 e IC = 0, 0.73 for ADG; I^2 = 0.53 e IC = 0, 0.53 for ruminal pH; and I^2 = 0.71 e IC = 0, 0.74 for A:P). Therefore, the models for ADG, ruminal pH, and A:P were evaluated using a random effect of experiment. As discussed in the previous section, if this between-study variance were not considered in the model, it would increase the probability of occurrence of type II error.

Feeding FO increased BW (12.9 kg; % Change = 3.75; P = 0.047) and hot carcass weight 7.21 kg; % Change = 3.80; P = 0.017) and decreased ruminal concentration of $N\text{-}NH_3$ (- 0.81 mg/dL; % Change = 4.40; P = 0.009) and total VFA (- 3.62 mM; % Change = - 3.01; P = 0.022). Nevertheless, no effects of FO supplementation were observed on DMI, ADG, FE (gain:feed), ruminal pH, A:P or concentrations of acetate, propionate, and butyrate in the rumen (P ≥ 0.157)

Table 16.4 - Summary of effect size estimates of functional oils on growth performance and ruminal characteristics outcomes in cattle raised under Brazilian conditions derived from meta-analysis

Outcomes[1]	Weighed mean difference for control (95% CI)[2]	% Change	Trials	n	I^2 (95% uncertainty interval)[3]	Effect size P-value
Dry matter intake (kg/d)	0.24 (-0.02, 0.50)	4.05	7	153	0.04 (0; 0.37)	0.157
Body weight (kg)	12.9 (3.05, 22.8)	3.75	4	118	0 (0; 0.01)	0.047
Average daily gain (kg/d)	0.09 (-0.05, 0.24)	12.5	4	118	0.54 (0; 0.73)	0.364
Gain to feed ratio (G:F)	0.0008 (-0.004, 0.006)	0.04	4	118	0 (0; 0.01)	0.941
Carcass weight (kg)	7.21 (2.76, 11.7)	3.80	4	118	0 (0; 0.01)	0.017
Ruminal pH	-0.02 (-0.59, 0.56)	-0.26	2	20	0.53 (0; 0.53)	0.944
Ruminal $N\text{-}NH_3$ (mg/dL)	-0.81 (-1.05, -0.57)	-4.40	2	20	0 (0; 0.01)	0.009
Total VFA (mM)	-3.62 (-5.81, -1.42)	-3.01	3	35	0 (0; 0.01)	0.022
Acetate (% total VFA)	-0.70 (-2.74, 1.34)	-14.6	3	35	0 (0; 0.01)	0.697
Propionate (% total VFA)	0.08 (0.36, 0.73)	1.10	3	35	0 (0; 0.01)	0.996
Butyrate (% total VFA)	0.04 (-0.92, 1.00)	-0.01	3	35	0 (0; 0.18)	0.994
Acetate:propionate ratio (A:P)	0.07 (-0.41, 0.56)	6.70	2	27	0.71 (0; 0.74)	0.832

[1]VFA = volatile fatty acids.
[2]Weighted mean difference of treatment relative to control, where the weights used were the inverse of the variance in the differences in means; CI = confidence interval.
[3]I^2 is a measure of variation beyond chance (Higgins et al., 2003).

Discussion

To the authors' knowledge, this is the first attempt to summarize studies evaluating the effects of monensin and FO in cattle diets that were conducted under Brazilian conditions. Although the limited number of studies in the database, the main results seem to corroborate previously published data regarding the effects of monensin or FO in cattle diets worldwide.

The main results obtained for the monensin analysis agreed with its main effects reported for feedlot cattle in the literature, which include altered ruminal fermentation towards more propionate and less acetate and decreased feed intake with little or no effect on ADG (Maturana Filho et al., 2010; Ellis et al., 2012; Melo et al., 2020). In the present study, cattle receiving monensin presented a decrease of approximately 5% in DMI and acetate concentration and an increase of 22% in propionate concentration. Likewise, Goodrich et al. (1984) and Duffield et al. (2012) concluded in two metanalytic studies that the inclusion of monensin at average doses of 31.8 and 28.1 mg/kg DM in beef cattle diets reduced DMI in 6.4 and 3%, respectively. Furthermore, similar ruminal fermentation responses to monensin were obtained by McGinn et al. (2004) and Tomkins et al. (2015). These authors described an increase in propionate concentrations of 18 and 23.7% and decreasing in acetate concentrations of 3.6 and 5% when monensin was added to high concentrate and high forage diets, respectively. Nevertheless, unlikely the results reported in Goodrich et al. (1984) and Duffield et al. (2012) meta-analyses, no effect of monensin was observed on ADG or FE in the current study.

As previously discussed, results on the effects of FO on the productive performance and rumen fermentation parameters of cattle varied due to many influential factors such as FO type, application rates and diet composition. In fact, between-study heterogeneity was more pronounced in the FO outcomes when compared to monensin results in the current study. The greater between-study heterogeneity along with the limited number of studies in the database may have impaired obtaining significant differences even when large numerical changes due FO supplementation occurred, such as for ADG outcome (12% increase). Nevertheless, significant effects of FO supplementation observed herein agreed with previous findings in cattle.

Some studies have described improved ADG, final BW, and/or carcass weight when FO was included in beef cattle diets, which was usually associated to increased DMI and lack of effect on FE (Valero et al., 2014; Ornaghi et al., 2017; Silva et al., 2019). These positive effects of feeding FO partially corroborate with our findings, as FE (G:F) was not affected and an approximately 3.8% increase in body and carcass weight were observed for cattle fed FO. However, no significant effect of FO supplementation on DMI or ADG was observed in the current study.

Many studies available in the literature on FO supplementation in ruminants indicate that the total VFA concentration may remain unaltered rather than improving or even decreasing (Khorrami et al., 2015; Tomkins et al., 2015; Ghizzi et al., 2018), which is not consistent with the present findings. Nonetheless, the unchanged total VFA concentration due to FO may still be beneficial if ruminal $N\text{-}NH_3$ concentration decreases.

In the present study, inclusion of FO decreased ruminal $N\text{-}NH_3$ concentration by 4.4%, indicating that FO can be effective in reducing the loss of dietary protein due to less rumen degradation. Accordingly, some studies have associated the inclusion of FO in the diet with a reduction in ruminal protein and amino acid degradation (McIntosh et al., 2003; Cardozo et al., 2006; Bodas et al., 2012), resulting in reduced ruminal concentrations of ammonia and increased passage of protein to the small intestine.

As previously discussed, several studies have evaluated the effects of feed additives such as monensin and FO on the productivity of cattle raised in temperate climates (Goodrich et al., 1984; Duffield et al., 2012; Khiaosa-Ard and Zebeli, 2013), and general recommendations by the North American System (NASEM, 2016) have been made to adjust the nutrient requirements of beef cattle fed feed additives.

Our findings suggested that monensin and FO may positively affect ruminal metabolism and productive performance. The committee recommends reducing predicted DMI by 5% when monensin is included in feedlot diets. Although the inclusion of FO in cattle diets numerically increased DMI and ADG by approximately 4 and 12.5%, respectively, no adjustments are proposed by the current BR-CORTE committee, as these effects were not significant. Further research is needed to establish the effects of FO on DMI and ADG of cattle raised under Brazilian conditions.

It is noteworthy that the increase of about 22% in propionate and the reduction of approximately 5% in acetate concentrations promoted by monensin may have improved cattle energy utilization. Stoichiometrically, gas production (carbon dioxide and methane), and consequently, energy loss in rumen is usually reduced when fermentation is driven towards more propionate than acetate (Wolin et al., 1997). During the formation of propionate, no gas is generated but unlike acetate and butyrate, part of the excess hydrogen generated during their production is used to form propionate.

OTHER BRAZILIAN STUDIES WITH FEED ADDITIVES

Unfortunately, it was not possible to gather enough data to perform metanalytic studies regarding the use of other feed additives in Brazilian conditions. Nevertheless, a literature screening similar to that reported in the previous topic for monensin and FO was performed, and the data obtained are described in Table 16.5 (The list of studies is available in Appendix 16.2).

Table16.5 - Numerical mean difference for the control of different feed additives for dry matter intake (DMI), body weight (BW), average daily gain (ADG), gain to feed ratio (G:F), and carcass weight (CW)

Item	Study	DMI (kg/d)	BW (kg)	ADG (kg/d)	G:F	CW (kg)
Lasalocid	Cortada Neto, I. M.; Gonçalves, P. H.; Maturana Filho et al.	-0.08	-0.52	-0.01	0.003	4.00
Monensin + functional oils	Melo et al.; Chagas, L. J.	-1.15	0.00	0.00	0.02	0.00
Monensin + virginamycin	Fonseca et al.; Sitta, C.	-0.82	8.90	-0.08	0.004	-
Narasin	Gobato et al.	-	3.35	0.03	-	-
Salinomycin	Cortada Neto, I. M.; Ferreira et al.	-0.28	9.50	0.06	-	-
Salinomycin + virginamycin	Sitta, C.	-	-1.20	-0.01	-0.009	-
Virginamycin	Cortada Neto, I. M.; Fonseca et al.; Guimarães, K. L.; Sitta, C.; Ferreira et al.	-0.27	11.3	0.03	0.011	-
Yeast	Gomes et al.; Guimarães, K. L.; Sitta, C.; Fugita et al.; Benatti, J. M. B.	0.29	1.04	-0.002	-0.003	0.30
Yeast + monensin	Gomes et al.; Benatti, J. M. B.	-0.84	-6.05	-0.05	0.013	-7.00
Yeast + virginamycin	Guimarães, K. L.	-	14.1	0.13	-	-

In general, numerical reduction of 1.15, 0.83, and 0.85 kg/d in DMI were observed when monensin was utilized in association with FO, virginiamycin, and yeast, respectively. Moreover, a numerical increase in BW of 11.3, 8.90, and 14.1 kg when virginiamycin was included in cattle diets alone or in association with monensin or yeast, respectively.

The inclusion of virginiamycin combined with monensin numerically reduced ADG by 0.090 kg/d, whereas the association of virginimycin and yeast numerically increased ADG by 0.13 kg/d. Furthermore, addition of salinomycin in cattle diets numerically increased BW and ADG by 9.5 kg and 0.060 kg/d, respectively. Nevertheless, great numerical increase in G:F was only observed when monensin in association with FO or yeast was included in cattle diets. It seems that these preliminary results corroborate the discussion performed in the previous topics of this chapter. Nonetheless, more experimental results are needed to draw any conclusion regarding the effects of these feed additives in cattle diets.

PRACTICAL EVALUATION OF FEED ADDITIVES IN BRAZILIAN FEEDLOT DIETS

Two studies were concomitantly conducted to evaluate the effects of diets containing different feed additives on metabolism (Study 1) and growth performance (Study 2) of Nellore bulls raised under Brazilian conditions. Therefore, feed intake, nutrient digestibility, and rumen parameters of Nellore bulls fed diets containing different feed additives were evaluated in study 1 (Silva et al., 2021). In study 2, the effects of different feed additives supplementation on feed intake, ADG, and FE (G:F) were evaluated in finishing Nellore bulls (Pacheco, unpublished).

In both studies, bulls were fed a basal diet composed of 30% corn silage and 70% concentrate (DM basis). The treatments evaluated in both cases consisted of the addition of six feed additives (DM basis): 1.4% bicarbonate and magnesium oxide in a 3:1 ratio (BOX); 36 mg/kg DM lasalocid sodium (LAS); 30 mg/kg DM monensin sodium (MON); 25 mg/kg DM virginiamycin (VIR); 30 mg/kg DM monensin sodium plus 25 mg/kg DM virginiamycin (MV); and 3.15%

commercial mineral supplement containing D-limonene and exogenous α-amylase (EOA).

Study 1

In this study, six rumen-cannulated Nellore bulls (age = 8 ± 1.0 months; initial BW = 225 ± 13.2 kg) were distributed in a 6 × 6 Latin square design, with six treatments (different feed additives) and six periods. The experiment lasted 144 d, with six periods of 24 d. Each period consisted of 14 d for dietary adaptation, 3 d for total collection of feces and urine, and 7 d for omasal and ruminal digesta collection. The main results are described below (Figure 16.1 and Table 16.6). More details can be obtained in Silva et al. (2021).

Dry matter and other intakes (organic matter, starch, NDF and CP) were greater in bulls fed the BOX diet when compared to all other treatments (LAS, MON, VIR, MV, and EOA; Figure 16.1 A and B). It is noteworthy that improvement of DMI in bulls fed diets with BOX compared to those fed other diets was approximately 17.5%. There are instances in the literature that corroborate our finding in which greater feed intake was observed for beef cattle receiving diets containing BOX in relation to those fed no additive or other feed additives, such as MON (Adams et al., 1981; Peirce et al., 1983), since MON reduces DMI.

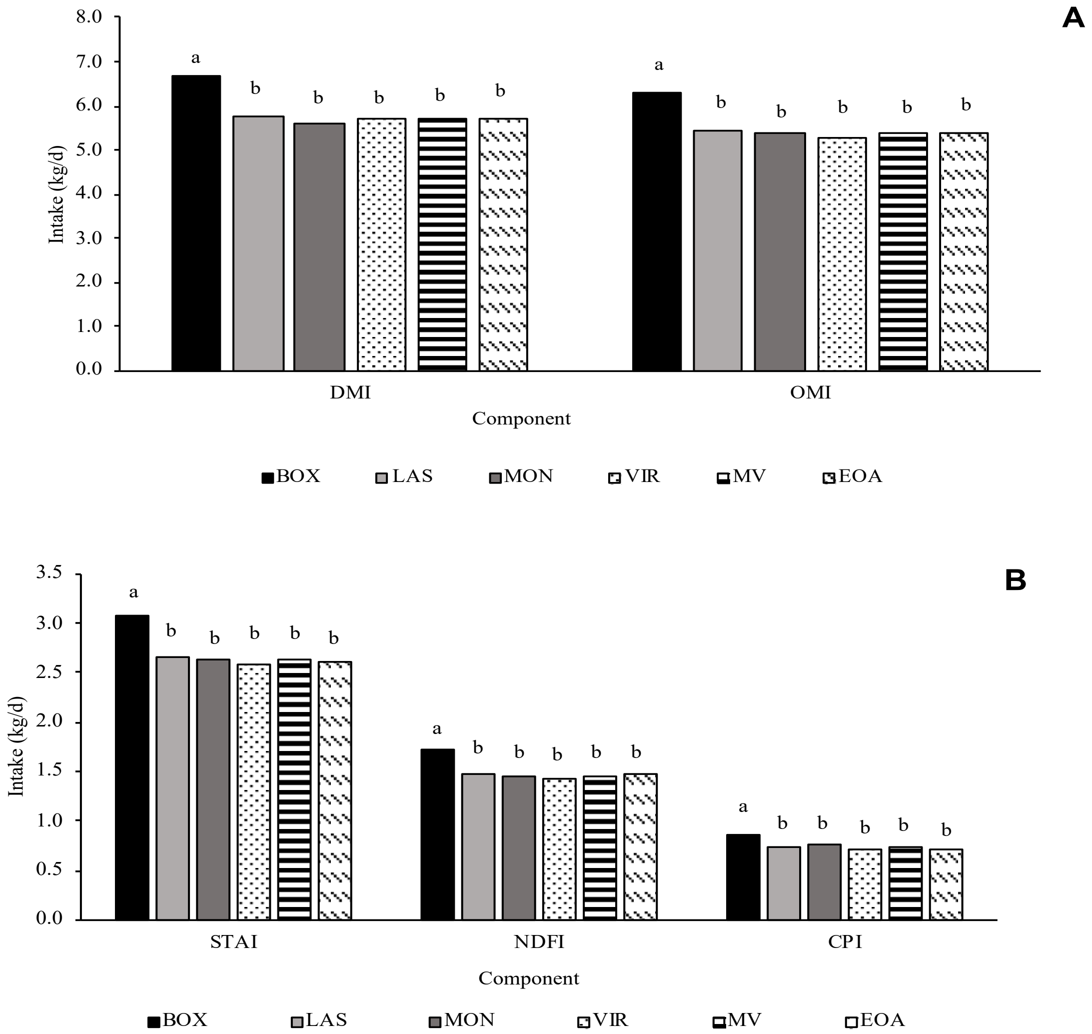

Figure 16.1 - Effect of different feed additives on dry matter intake (DMI; A), organic matter intake (OMI; A), starch intake(STAI; B), neutral detergent fiber intake (NDF; B), and crude protein intake (CPI; B) of Nellore bulls. Treatments were (DM basis): BOX = 1.4% bicarbonate and magnesium oxide in 3:1 ratio; LAS = 36 mg/kg DM lasalocid sodium; MON = 30 mg/kg DM monensin sodium; VIR = 25 mg/kg DM virginiamycin; MV = 30 mg/kg DM monensin sodium plus 25 mg/kg DM virginiamycin; and EOA = 3.15% commercial mineral supplement containing D-limonene and exogenous α-amylase [Adapted from Silva et al. (2021)].

In general, ruminal and intestinal digestibility of most nutrients were similar among all feed additives, except for starch rumen digestibility. Bulls fed EOA showed approximately 4.1% greater (trend; $P = 0.09$) ruminal digestibility of starch compared to those fed diets BOX, LAS, MON, VIR, or MV (Table 16.6).

Moreover, bulls fed EOA diet presented approximately 6.5 % greater ($P < 0.05$) total tract digestibility of DM compared to animals fed diets with BOX, LAS, MON, VIR, or MV. In agreement, the potential for exogenous α-amylase to improve ruminal starch digestibility has been reported in the literature (Nozière et al., 2014; Andreazzi et al., 2018).

Table 16.6 - Effects of different feed additives on starch digestibility, microbial efficiency, and rumen pH of Nellore bulls [Adapted from Silva et al. (2021)]

Item	Treatment[1]						SEM	P-value
	BOX	LAS	MON	VIR	MV	EOA		
Dry matter digestion (%)								
Rumen	50.2	48.4	81.4	50.2	50.0	52.3	2.53	0.897
Intestines	21.0	23.9	25.0	24.4	24.1	26.4	2.84	0.813
Total tract	71.2c	72.2bc	75.2b	74.5bc	73.4bc	78.7a	1.49	0.012
Starch digestion (%)								
Rumen	78.4	79.5	81.4	81.3	79.8	83.3	1.13	0.090
Intestines	10.7	9.13	8.11	8.59	9.39	8.72	1.187	0.717
Total tract	89.1	88.6	89.5	89.9	89.2	92.0	1.42	0.514
Microbial efficiency (g MCP/kg TDN)	125	125	121	127	125	124	5.2	0.978
Mean rumen pH	6.27	5.96	6.05	6.03	6.01	5.95	<0.001	0.634
Duration pH (min/d)								
pH > 5.6	1308	1089	1223	1161	1215	1129	139.4	0.887
5.6 < pH < 5.2	132	351	217	279	225	311	137.9	0.888
pH < 5.2	0.00	0.00	0.00	0.00	0.00	0.00	-	-

[1]Treatments were (DM basis): BOX = 1.4% bicarbonate and magnesium oxide in 3:1 ratio/ LAS = 36 mg/kg DM lasalocid sodium; MON = 30 mg/kg DM monensin sodium; VIR = 25 mg/kg DM virginiamycin; MV = 30 mg/kg DM monensin sodium plus 25 mg/kg DM virginiamycin; and EOA = 3.15% commercial mineral supplement containing D-limonene and exogenous α-amylase.

However, no effect of feed additive was observed ($P > 0.05$) on the intestinal or total tract digestibility of starch, microbial efficiency, or ruminal pH. Mean rumen pH varied between 6.0 and 6.3 for all diets. Moreover, the duration of pH between 5.6 and 5.2 was low and rumen pH values below 5.2 were absent, suggesting that all feed additives evaluated were efficient at controlling ruminal pH and preventing acute and/or subacute acidosis.

In summary, it seems that diets containing monensin, virginiamycin, monensin plus virginiamycin, and essential oils plus exogenous α-amylase reduced DM and nutrient intake of Nellore bulls compared to diets with the combination of sodium bicarbonate and magnesium oxide. Furthermore, the results of this study suggest that no major differences in digestive parameters seem to occur for the evaluated feed additives (BOX, LAS, MON, VIR, MV, and EOA). Nonetheless, this study results on rumen pH confirm that all the evaluated feed additives may be used in feedlot diets to minimize metabolic disorders, and consequently, the negative impacts on digestive parameters.

Study 2

Forty-two Nellore bulls (age = 8 ± 1.0 months; initial BW = 257 ± 26.3 kg) were randomly distributed in six groups with seven animals each and allocated in feedlot. The six treatments previously describred for Study 1 were randomly distributed for each group. This study lasted 140 d, which was consisted of five sub-experimental periods of 28 d each: d 1-28 , d 29-56, d 57-84; d 85-112, and d 113-140. Main growth performance results are described below.

No differences ($P \geq 0.38$) were observed in overall (d 1 to 140) DMI, ADG, or G:F (Figure 16.2). However, feed additive affected ($P \leq 0.017$) DMI and ADG during the d 1-28 intermediate period evaluated. Bulls fed BOX had the greatest ($P < 0.05$) DMI (Figure 16.2; A), while bulls fed LAS had the lowest ($P < 0.05$) DMI; bulls fed MON, VIR, MV, and EOA had intermediate DMI and were not different ($P > 0.05$) from the other treatments. Average daily gain (Figure 16.2; B) on d 1-28 period was the greatest ($P < 0.05$) in bulls fed BOX and EOA comparing to animals fed LAS, VIR, and MV ($P < 0.05$). Bulls fed MON were intermediate and not different ($P > 0.05$) from the other treatments.

It is well documented in the literature that feeding MON to feedlot cattle decreases DMI (Maturana Filho et al., 2010; Duffield et al., 2012; Melo et al., 2020). In addition, there are instances in the literature that describe greater DMI for beef cattle fed BOX or EOA compared to those fed no additive or other feed additives, such as MON (Peirce et al., 1983; Gouvêa et al., 2019; Meschiatti et al., 2019). Also, no additional benefit of using the combination of monensin and virginiamycin (MV) to cattle diets have been reported recently (Fonseca et al., 2016; Lemos et al., 2016; Maciel et al., 2019).

Moreover, BOX and EOA diets resulted in the greatest ADG, whereas bulls fed LAS, VIR, and MV presented the lowest ADG during the d 1-28 period. Thus, the results suggest that adding BOX and EOA to feedlot diets may have some increase in feed intake, whereas LAS presented the lowest feed intake, at the begging of the feeding period to Nellore bulls.

CONSIDERATIONS ABOUT STUDIES 1 AND 2

In general, results from studies 1 and 2 suggested:

1 – All the evaluated feed additives were efficient in controlling ruminal pH and preventing acute and/or subacute acidosis; therefore, all feed additives are recommended for such purpose.

2 – In the long term (140 d of feedlot period), all tested feed additives presented similar effects on overall (d 1 to 140) DMI, ADG, or G:F.

3 – In the short term (first 28 d of feedlot period), animals fed BOX presented greater DMI in relation to those fed LAS.

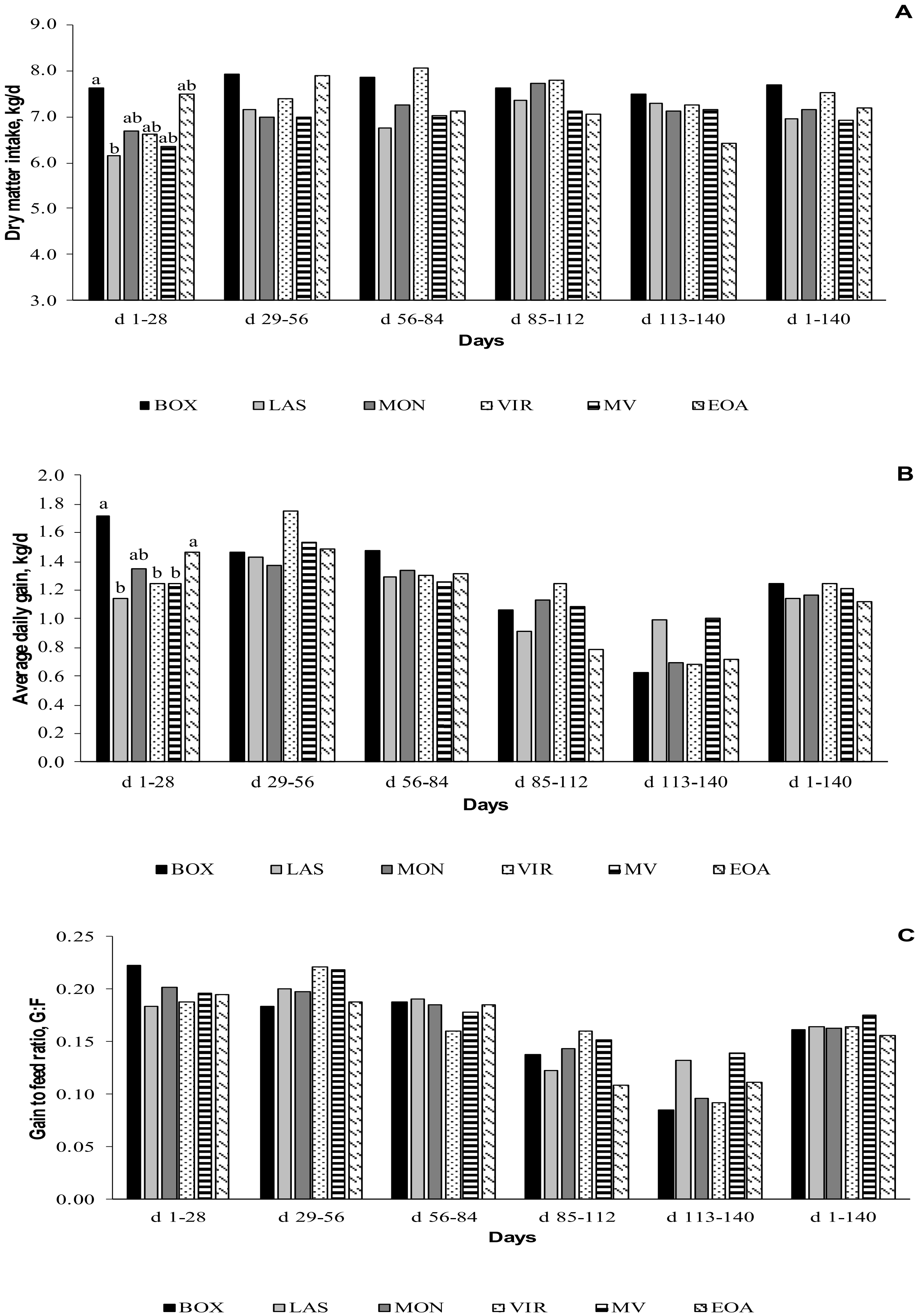

Figure 16.2 - Effect of different feed additives on dry matter intake (DMI; A), average daily gain (ADG; kg/d; B) and feed efficiency (gain to feed ratio; G:F; C) of finishing Nellore bulls. Treatments were (DM basis): BOX = 1.4% bicarbonate and magnesium oxide in 3:1 ratio/ LAS = 36 mg/kg DM lasalocid sodium; MON = 30 mg/kg DM monensin sodium; VIR = 25 mg/kg DM virginiamycin; MV = 30 mg/kg DM monensin sodium plus 25 mg/kg DM virginiamycin; and EOA = 3.15% commercial mineral supplement containing D-limonene and exogenous α-amylase.

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APPENDIX 16.1

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