Manipulation of the Rumen Microbial Environment to Improve Performance of Beef Cattle

Nicolas DiLorenzo[1]
North Florida Research and Education Center, University of Florida

Introduction

It is well known that rumen fermentation processes play a key role in ruminant nutrition, as it is this distinctive symbiotic feature between the host and the rumen micro-flora that lends the ruminant animal several advantages in digestive and metabolic processes over non-ruminants. The extent of complexity of interactions between diverse groups of microorganisms which inhabit the rumen is such that, even nowadays, some pathways and microorganisms involved are unknown. The possibility of controlling some of the metabolic processes in the rumen with the objective of achieving more efficient nutrient utilization has been an appealing concept to both nutritionists and rumen microbiologists. As a result of several decades of continuous research on ruminal fermentation, metabolism, and microbiology, the rumen is one of the most extensively studied microbial ecosystems. General objectives of ruminal fermentation manipulation can be summarized as follows (Nagaraja et al., 1997):

- To enhance beneficial processes
- To minimize, alter or eliminate inefficient processes
- To minimize, alter or eliminate processes that are harmful to the host

Since the approval of monensin as a feed additive for ruminant diets in the mid-1970s, research on the effects of ionophores on ruminal fermentation has multiplied rapidly. As a result, several ionophores have been discovered and approved as feed additives for beef cattle, and have greatly improved the efficiency of beef production. Because of the cost effectiveness of ionophores, their rate of adoption in beef cattle diets (particularly on feedlots) increased rapidly to the point that nowadays virtually all feedlots in the US include an ionophore in their supplements. Obvious exceptions are those feeding programs that target natural or organic beef production, for which alternative feed additive options are scarce.

As negative public perception over the use of antimicrobials in animal agriculture increased in the years following the approval of ionophores as feed additives, research efforts concentrated on the development of alternative types of additives such as probiotics, enzymes, essential oils, and organic acids. Although the development of feed additives that represent an alternative to the use of antibiotics as growth promoters continues to be a priority, food safety concerns in the past decade temporarily shifted

---

[1] Contact at: North Florida Research and Education Center, 3925 Hwy. 71, Marianna, FL 32446; Phone: 850-394-9124; Email: ndilorenzo@ufl.edu

the attention of researchers towards a new menace, *Escherichia coli* O157:H7. Increased foodborne illnesses due to this foodborne pathogen coupled with the fact that ruminants are the primary reservoir fueled recent research efforts to reduce pathogen shedding by cattle. Lastly, the debate over the contribution to greenhouse gas emissions from enteric fermentation by livestock has redirected what can be defined as the latest "wave" of research towards the development of modifiers of ruminal fermentation with the capacity to reduce methane production.

For the purpose of the present paper, different categories of modifiers of ruminal fermentation will be classified based on their predominant effect. Although the significant degree of overlapping that exists in the categories will be discussed, for simplicity the feed additives will be classified as: 1) Modifiers of the volatile fatty acid (**VFA**) profile, 2) Compounds that decrease the risk of acidosis, 3) Compounds that increase digestibility of nutrients, and 4) Compounds that decrease methane emissions. The objective of this review is to provide an overview of the fed additives with potential or proved efficacy to modify ruminal fermentation, with emphasis on the discussion of compounds that are in the experimental phases and may have a significant impact on ruminant nutrition in the future.

Modifiers of the VFA Profile

Because of the benefits for the host ruminant in terms of energetics, increasing molar proportions of propionate during ruminal fermentation has been a goal of beef nutritionists for decades. This specific objective of increasing the proportions of glucogenic (propionate) at the expense of acetogenic VFA (acetate and butyrate) is perhaps the only case in which a distinction needs to be made between the goals of beef and dairy nutritionists in manipulation of the ruminal fermentation. While increasing ruminal propionate is the most desired outcome for beef cattle, an excessive increase in propionate at the expense of butyrate and acetate can have detrimental consequences for the fat content of milk, which is one of the key determinants of the profitability of dairy production. The additives discussed in this section are primarily aimed at increasing ruminal concentrations of propionate, and thus are better suited for use in beef cattle diets.

Ionophores. This group of feed additives represent the "gold standard" because of the consistent response usually obtained both in vivo and in vitro. The mode of action of ionophores is related to their highly lipophilic nature and their capacity to alter the ion exchange gradient across the bacterial membrane, causing an energy spilling cycle in the bacteria in a futile intent to maintain the ion gradient (Russell and Strobel, 1989). The impermeability of the outer membrane of Gram-negative bacteria to several large molecules provides a protective barrier and is likely the cause of the selectiveness of ionophores. Although the mode of action of ionophores can vary slightly among compounds, the end result is often similar, a decrease in counts of Gram-positive bacteria in the rumen (Russell and Strobel, 1989; Coe et al., 1999). Because Gram-positive bacteria are for the most part lactate producers, and Gram-negative bacteria are for the most part propionate and succinate producers (Nagaraja et al., 1997), the inclusion of ionophores in ruminant diets often leads to a decrease in the acetate-to-propionate ratio (**A:P**). This reduction in A:P has been the hallmark of this category of additives and is believed to be partially responsible for the improved performance observed in feedlot cattle. In addition, because of the inhibition of ruminal lactate-producing bacteria, ionophores typically decrease the risk of metabolic disorders such as lactic acidosis (Owens et al., 1998), and this will be discussed in a subsequent section of this paper. Added benefits of ionophores include a decrease in ammonia production in the rumen, which in turn, can lead to a more efficient use of dietary protein (Russell et al., 1981), and a possible reduction in methane production. In the case of the ionophore monensin, although no direct inhibition of methanogenic bacteria has been observed, an indirect effect on methane reduction is possible due to the inhibition of protozoa, which produce hydrogen and are colonized by methanogens (Russell and Strobel, 1989; Guan et al., 2006). Because of their effect tends to be indirect, ionophores are not classified in this review as “compounds that decrease CH_4 emissions”.

All modifications in the ruminal fermentation profile by ionophores discussed previously typically lead to substantial improvements in productivity. Particularly in the case of the ionophore monensin, a decreased feed intake is typically observed by feedlot steers, leading to an improvement in feed efficiency in the order of 7.5% versus cattle not fed monensin (Goodrich et al., 1984). Similarly, response summaries have reported improvements in feed efficiency in feedlot cattle of 5.6, 7.5, and 8.1% when feeding laidlomycin propionate (Bauer et al., 1995), lasalocid (Berger et al., 1981), and salinomycin (Zinn, 1986), respectively.

Essential oils. This category of feed additives includes plant-derived compounds that typically exert an antimicrobial effect that leads to an alteration of the fermentation profile. Essential oils are blends of secondary metabolites produced by plants and, because of their volatile nature, they are typically recovered by steam distillation of plant materials (Calsamiglia et al., 2007). Since the prohibition of use of antibiotics as growth promoters in the European Union in January 2006 (Regulation 1831/2003/EC), research on the effects of essential oils has greatly increased.

The antimicrobial spectrum of most essential oils resembles that of ionophores in which, for the most part, Gram-positive bacteria are selectively inhibited (Busquet et al., 2006; Calsamiglia et al., 2007). Reasons for their selectiveness are also analogous to those of ionophores, in that the hydrophobic nature of the essential oils allows their interaction with the bacterial membrane altering the ion transport across the membrane (Busquet et al., 2006; Calsamiglia et al., 2007). Given the similarities with ionophores in terms of selectiveness and mode of action, it may be expected that one of the main effects of essential oils on ruminal fermentation would be a shift in the proportions of VFA towards a reduced A:P. However, this is not always the case, and in fact publications have reported no effects on VFA molar proportions (Benchaar et al., 2006 and 2007; Meyer et al., 2009), an increase in A:P (Castillejos et al., 2007), or a decrease in A:P (Busquet et al., 2006; Cardozo et al., 2006). It is evident from the literature that effects of essential oils on VFA molar proportions are largely dependent on the type of diet (or incubation substrate) used, and the type and dose of essential oil, and presence of active components. Busquet et al. (2006) conducted an in vitro screening study on the effects of 5 doses of 18 plant extracts and secondary metabolites, and reported mild effects on VFA molar proportions with moderate doses (30 to 300 mg/L), mostly tending to decrease A:P. Although higher doses (3,000 mg/L) increased the response, they are unlikely to be used in practice, being more than 10-fold greater than those used in vivo (Cardozo et al., 2006). This disproportion between the doses tested in vivo and in vitro is repeatedly found in the literature and represents a problem when testing new feed additives. Because the effect of any additive depends on the interaction between compounds and bacteria, the decreased concentration of bacteria in in vitro systems forces researchers to increase the doses tested in vitro to favor that interaction (Calsamiglia et al., 2007). Thus, caution must be exercised when extrapolating results found in vitro to in vivo situations.

When reviewing the literature on the effects of essential oils on ruminal fermentation, the discrepancy between large number of studies conducted in vitro versus the few conducted in vivo is apparent. While this is a logical approach to reduce the cost of research during exploratory phases of new additive testing, it is the opinion of this author that we may be ready to move to the next phase (in vivo studies) with some essential oils. Given the constraints associated with in vitro studies in terms of extrapolation of doses and palatability issues, the imperative for in vivo studies is considerable.

Most of the in vivo research conducted on the potential of essential oils as feed additives has been done in dairy cattle. Although several in vitro studies indicate a potential impact on ruminal fermentation, which could in theory lead to an increase in milk production, positive performance responses do not abound in the literature. Limited or no effects on milk production have been reported when feeding essential oils to lactating dairy cows (Benchaar et al., 2006; Benchaar et al., 2007; Tassoul and Shaver, 2009).

Research on the effects of essential oils in beef cattle diets is very limited. Meyer et al. (2009) reported improvements in feed efficiency by feedlot steers fed a mixture of essential oils (thymol, eugenol, vanillin, guaiacol, and limonene) and supplemented with tylosin. Interestingly, no effects on feed efficiency were found in the same study when the essential oil mix was fed without tylosin. Furthermore, none of the treatments affected ruminal fermentation characteristics. Cardozo et al. (2006) tested the effects of essential oils on ruminal fermentation in ruminally cannulated Holstein heifers. The authors found increased molar proportions of propionate when feeding anise oil or a mixture of cinnamaldehyde and eugenol. The changes in ruminal fermentation observed by Cardozo et al. (2006) may lead to improved growth performance but that particular study was not designed to test this hypothesis. A recent study conducted by Yang et al. (2010) tested the effects of cinnamaldehyde (3 doses) or monensin on feedlot cattle performance. Cinnamaldehyde or monensin had no effects on any of the performance variables with the exception of an increase in feed intake in steers fed the cinnamaldehyde diet instead of the control diet for the first 28 days on feed.

Despite the results reported thus far on performance of beef cattle, essential oils are currently one of the best alternatives to the use of ionophores. Research on the effects of new compounds and to gain better understanding of their mode of action will likely continue in the years to come. Given the changes in ruminal fermentation patterns of beef cattle discussed previously, the limited number of studies designed to test animal performance when feeding essential oils is puzzling.

Nonionic surfactants. Nonionic surfactants (**NIS**) have been proposed as a feed additive with the potential to modify ruminal fermentation. The proposed mode of action of NIA is the stimulation of enzyme production by fungi and bacteria, as well as the improvement in the affinity of enzymes to their substrates (Wang et al., 2004; Cong et al., 2009). When polyoxyethylene sorbitan monooleate (Tween 80) was added to in vitro incubations in combination with monensin, a synergistic enhancement in the reduction of A:P was observed along with an increased enzymatic activity, and increased in vitro digestibility of the substrates (Wang et al., 2004). Cong et al. (2009) tested the effects of 3 ionic surfactants on in vitro fermentations and concluded, based on the changes observed in the fermentation profile, that NIS have the potential to improve the digestion of plant material in the rumen. Yuan et al. (2010) tested the effect of alkyl polyglycoside, one of the surfactants used by Cong et al. (2009), on nutrient digestion and ruminal fermentation in goats and reported that it increased ruminal activity of carboxymethyl cellulase and xylanase, and increased total tract digestibility of organic matter (**OM**) and neutral detergent fiber (**NDF**). Although these findings could lead to a potential enhancement in growth performance, no studies have been conducted to test the effects of NIS on beef cattle.

Prevention of Acidosis

In order to maintain high levels of productivity, beef cattle diets have evolved from being predominantly forage-based, at the beginnings of the cattle industry in the U.S., to contain increased proportions of cereal grains and their byproducts. While this has been a cost-effective practice, it also contributes to the development of digestive disorders such as ruminal acidosis. For a comprehensive review of the etiology and physiology related to acidosis, readers are referred to the comprehensive papers by Owens et al., (1998) and Nagaraja and Titgemeyer (2007).

Ionophores. The effect of ionophores on ruminal fermentation discussed in the previous section contributes to prevention of acidosis. A reduction in ruminal counts of Gram-positive lactate-producing bacteria when feeding ionophores is believed to be the principal cause of acidosis prevention (Owens et al., 1998; Coe et al., 1999). In particular with the ionophore monensin, decreased feed intake and fed intake variation are commonly observed. Although the mechanism associated with these effects on intake is not known, they seem to play a key role in the prevention of digestive disorders.

Studying the effects of ionophores (or any other feed additive) on acidosis prevention often requires the experimental induction of acidosis, which can be extremely challenging (Nagaraja and Titgemeyer, 2007). Virginiamycin or monensin were equally effective in decreasing ruminal counts of lactate-producing bacteria and increasing pH in steers during the transition to a high-grain diet; however, once steers were adapted to the high-grain diet for 21 d, no effects were observed on ruminal pH (Coe et al., 1999). Similarly, Ives et al. (2002) compared monensin plus tylosin, virginiamycin, or no antibiotic in steers adapted to high-grain diets and found no differences in ruminal pH or VFA concentrations among treatments. Thus, it appears that the greatest impact of ionophores on acidosis prevention is achieved by modulation of feed intake, rather than in vivo changes in ruminal fermentation patterns and pH (Bauer et al., 1995; Coe et al., 1999; Salinas-Chavira et al., 2009).

Probiotics. In terms of acidosis prevention and enhancement of growth performance, the inclusion of probiotics in beef cattle diets is perhaps the second most adopted practice after ionophores. Although not fully understood, the mode of action of probiotic feeding is believed to be to adapt the rumen to the presence of large quantities of lactic acid, whether directly, by feeding lactate-utilizing bacteria, or indirectly by feeding lactate-producing bacteria, which in turn will stimulate the growth of lactate-utilizers (Beauchemin et al., 2003; Krehbiel et al., 2003). Once lactate-utilizing bacteria counts increase, the ability to metabolize lactate derived from rapid carbohydrate fermentation also increases, preventing or reducing the risk of acidosis. Minimizing the incidence of acidosis in feedlot cattle, especially during the transition from high-forage to high-grain diets may lead to improved growth performance. However, improvements in performance have not been consistently achieved when feeding probiotics to feedlot cattle. Beauchemin et al. (2003) reported limited effects on ruminal acidosis prevention or changes in digestive function when ruminally cannulated steers were supplemented with the lactate-producing bacterium *Enterococcus faecium* with or without yeasts (*Saccharomyces cerevisiae*). Elam et al. (2003) indicated that growth performance by feedlot cattle was not greatly affected when feeding *L. acidophilus* (strains NP45 and NP51) plus *Propionibacterium freudenreichii* (strain NP24), but Vasconelos et al. (2008) reported a 2% increase in G:F when feedlot cattle received the same probiotics and strains.

Recently, the use of the lactate-utilizing bacterium *Megasphaera elsdenii* as a probiotic has yielded interesting results in acidosis prevention and performance enhancement. Drenching *M. elsdenii* intraruminally has been effective in increasing ruminal pH and decreasing lactate concentrations during a rapid transition from a high forage to a high concentrate diet (Henning et al., 2010a,b). Interestingly, a link between ruminal abundance of *M. elsdenii* and milk fat depression has been recently identified (Palmonari et al., 2010), which can be extremely important in the future development of probiotics with application in dairy diets. The main limitation to using *M. elsdenii* as a probiotic is the fact that strict anaerobiosis is required to maintain a viable culture. Nevertheless, the promising results in terms of acidosis prevention warrant further research.

The inconsistency reported in growth performance responses to probiotics likely reflects the differences in strains and doses used. Despite this inconsistency, the relatively low cost of inclusion of probiotics in cattle diets has driven an increase in the adoption rate, especially in feedlot cattle.

Acarbose. Acarbose is an α-amylase and glucosidase inhibitor that slows the rate of degradation of starch to glucose. It is commercially available and typically used to control blood glucose in diabetic patients (McLaughlin et al., 2009a). Because of the effect of acarbose on glucose metabolism, researchers from Pfizer Animal Health have studied the potential of this compound in acidosis prevention by using it to decrease the rate of VFA production, thus maintaining a higher ruminal pH. When acute acidosis was experimentally induced in Holstein steers, feeding 1.07 or 2.14 mg of acarbose/kg of body weight was effective at preventing acute acidosis by decreasing ruminal lactate concentrations and maintaining a higher pH (McLaughlin et al., 2009a). A subsequent study conducted by the same researchers showed that when 0.75 g/d of acarbose was fed to dairy cows in early lactation, feed intake and fat corrected milk yield were increased versus the control treatment (McLaughlin et al., 2009b). Furthermore, when cows were fasted for 3 h prior to the morning feeding to simulate an unplanned delay in feed delivery, those fed acarbose increased feed intake and fat-corrected milk yield. In conclusion, acarbose successfully prevented acidosis and the associated drop in milk fat percentage that is typical in dairy cows. Undoubtedly, this feed additive represents a promising technology in modification of the ruminal fermentation to prevent acidosis.

Polyclonal antibody preparations. The mode of action of these novel feed additives is based on the concept of passive immunization against lactate-producing ruminal bacteria. Providing oral doses of an avian-derived antibody against key bacteria involved in the development of acidosis decreases their ruminal counts preventing the onset of acidosis. Feeding a polyclonal antibody preparation (**PAP**) made from eggs of hens immunized against *Streptococcus bovis* was successful at decreasing ruminal counts of target bacteria and increasing pH in ruminally-cannulated steers (DiLorenzo et al., 2006 and 2008). Furthermore, DiLorenzo et al. (2008), observed an increased gain to feed ratio (live weight basis) when feeding 2.5 mL/d of a PAP against *S. bovis* to feedlot cattle during a two-year study. Blanch et al. (2009) tested the effects of a multivalent PAP against *S. bovis* (predominantly) and several other ruminal bacteria on acidosis prevention in heifers. Feeding 10 mL of PAP/d for 10 d prior to the experimental induction of acidosis was effective at reducing the incidence of ruminal acidosis, although no major changes were observed in the fermentation profile (Blanch et al., 2009). In conclusion the use of passive immunization strategies with avian antibodies appears to have potential for acidosis mitigation. More in vivo studies are needed to confirm these findings, and to provide a more precise description of the doses needed to obtain a response. Furthermore, this technology could be utilized to target other microorganisms of interest such as *E. coli* O157:H7 or methanogenic bacteria.

Increase in Digestibility of Nutrients

Achieving an increase in ruminal or total tract digestion by means of manipulating ruminal fermentation has proved to be one of the most challenging tasks for nutritionists. Despite the success in modification of the ruminal fermentation profile observed with some of the compounds described previously, transforming that into improved digestibility of nutrient is rarely the case. Perhaps the only feed additives that could be classified in this category with a certain degree of success are exogenous enzymes.

Exogenous enzymes. If indeed the enzymatic activity in the gastrointestinal tract is limiting the extent of digestion of feeds, addition of exogenous enzymes to enhance digestions seems a logical approach. Inclusion of exogenous amylase in feedlot diets was hypothesized to increase digestion of one of the most expensive ingredients in the diet, cereal grains. However, addition of exogenous amylase in feedlot diets did not improve digestibility of nutrients (DiLorenzo et al., 2010) or increase the gain to feed ratio in feedlot steers (Tricarico et al., 2007). Feeding exogenous amylase increased dry matter (**DM**) intake and consequently average daily gain in the early stages of the finishing period in feedlot steers fed cottonseed hulls as the roughage source (Tricarico et al., 2007). However, another experiment by the same authors found no differences in growth performance over the entire feeding period when steers received cracked corn or high moisture corn (Tricarico et al., 2007). When exogenous amylase was fed to lactating dairy cows, no effects on starch digestion were found, but apparent total tract digestibility of OM and NDF were increased (Klingerman et al., 2009). Similarly, Gencoglu et al. (2010) found increased apparent total tract digestibility of OM, crude protein (**CP**), and NDF when supplementing exogenous amylase to lactating dairy cows. Reasons for the different response to amylase supplementation in beef and dairy cattle are not obvious, but it is possible that the ruminal microbial ecology of cattle fed high-forage diets differs from that of animals fed high-grain diets in their response to changes in fermentation products associated with feeding exogenous amylase.

Supplementation with fibrolytic enzymes to cattle fed high-forage diets has shown some potential at enhancing fiber digestibility both in vivo and in vitro. Krause et al. (1998) reported increased total tract digestibility of acid detergent fiber and decreased A:P when feedlot cattle fed barley-based diets were supplemented with fibrolytic enzymes. Pinos-Rodriguez et al. (2002) reported increased apparent digestibility of hemicellulose, CP, and NDF in sheep consuming alfalfa hay. Krueger et al. (2008) tested different methods of applying fibrolytic enzymes and found that even though all treatments increased DM digestibility, the application of enzymes immediately after cutting was the most promising method and was almost as effective as ammoniation for enhancing forage quality. Lewis et al. (1996) also reported increased total tract digestibility of DM and NDF when feeding fibrolytic enzymes to beef steers.

Given the promising results obtained with fibrolytic enzymes, coupled with the abundance of forage resources and a scenario of increasing prices of cereal grains, research in this area should continue to be a priority. Furthermore, research on the application of fibrolytic enzymes in cattle feeding will be greatly enhanced in the years to come as new developments arise from ongoing research in the area of cellulosic biofuels.

Reduction in Methane Emissions

Methane produced from enteric fermentation represents both a loss of feed energy and a threat to the environment. A logical approach to decrease greenhouse gas emissions would, thus, be a reduction or elimination of methanogenic bacteria in the gastrointestinal tract of cattle, however the solution to this problem may not be as simple as it appears. Methanogenic bacteria are essential to ruminal metabolism as they are responsible for removing the H_2 produced during microbial fermentation. The continuous removal of H_2 allows the fermentation process to continue towards the digestion of OM and production of VFA. Thus, decreasing methane production must be accompanied by providing an alternative hydrogen sink or by minimizing the proportion of H_2 released (e.g., altering VFA proportions towards increased propionate). Providing alternative electron sinks that are also safe to feed to cattle can prove quite challenging, and very few options are available. A recent study was successful at using supplemental nitrate and sulfate in sheep diets as an alternative electron sink, thereby decreasing methane emissions and methanogenic bacteria counts (van Zijderveld et al., 2010).

This is an active area of research and several additives have been identified as potential greenhouse gas mitigation strategies. However, as with previous approaches, the majority of the studies were conducted in vitro and require in vivo validation.

Essential oils. As discussed previously, essential oils can be effective at altering the VFA proportions in the rumen. Increasing propionate and decreasing acetate molar proportions leads to a reduction in methane because propionate production consumes reducing equivalents.

Several in vitro studies have reported methane reductions due to addition of essentials oils. A recent study showed the potential antimethanogenic properties of cashew nut shell liquid when added to batch cultures at a the rate of 200 µg/mL of incubated volume (Watanabe et al., 2010). The antimicrobial properties of cashew nut shell extract are related to their content of anacardic acid, cardanol, and cardol, which are salicylic acid derivatives with a C-15 alkyl group (Watanabe et al., 2010). When ground rhizomes of rhubarb (*Rheum spp.*) were added to rumen-simulating fermenters (Rusitec), a reduction in methane was observed (Garcia-Gonzalez et al., 2010).

As with other new feed additives, in vivo studies showing the efficacy of essential oils are uncommon in the literature. A commercial blend of essential oils failed to decrease methane production in vivo despite decreasing the digestibility of all nutrients (Beauchemin and McGinn, 2006). Mohammed et al. (2004) evaluated the effect of Japanese horseradish oil on methane emissions and diet digestibility. The Japanese horseradish oil contains volatile compounds similar to those of mustard seed oil (allyl isothiocyanate) that have been reported to decrease methane productionin vitro. However because of the pungent odor, these compounds are not palatable for cattle, imposing a practical obstacle for their use. Mohammed et al. (2004) coated Japanese horseradish oil with cyclodextrin to prevent rejection by cattle and fed it to Holstein steers, and reported a 19% decrease in methane production along with a decrease in methanogenic bacteria counts.

Fatty acids and organic acids. Fumaric acid has been proposed as a potential feed additive in methane mitigation as it provides an alternative electron sink and is a metabolic precursor of propionate. The stoichiometry of fumarate metabolism in ruminal fermentations indicates potentially promising results (Ungerfeld et al., 2007), however fumarate has not been consistently effective at decreasing methane productionin vivo (McGinn et al., 2004; Beauchemin and McGinn, 2006).

Dietary addition of polyunsaturated oils has been demonstrated to decrease methane emissions, but often such reductions are achieved with doses that would also cause a reduction in forage digestibility, which would be undesirable (McGinn et al., 2004).

Other Feed Additives

This section is reserved to the discussion of products/compounds that would not fall under any of the categories previously discussed. Passive immunization with avian-derived antibodies against specific bacteria or digestive enzymes has been proposed to enhance digestive function in ruminants. Targeting ruminal bacteria to reduce the incidence of acidosis was already discussed in a previous section. The use of passive immunization to target enzymes involved in the acute phase response cascade has been proposed as a means of decreasing an over reactive inflammatory event, which can be costly to the host in terms of energy and protein expenditure (Cook, 2010). Intestinal secretory phospholipase A_2 ($sPLA_2$) is an enzyme that hydrolyzes the sn-2 position ester bond of phospholipids and liberates arachidonic acid from cellular membranes. Arachidonic acid is then metabolized to produce prostaglandins and leukotrienes, the key mediators of the gut inflammatory response (Cook, 2010). Thus blocking $sPLA_2$ can reduce the inflammatory response, preventing the diversion of energy and protein that could otherwise be used for growth. Although sound in theory, this approach has never been tested as a potential feed additive in beef cattle diets.

Conclusions

The development of feed additives with the capacity of modifying ruminal fermentation and gastrointestinal tract metabolism has been an active area of research in past years and likely will continue to be. Research efforts appear to have been concentrated on alternatives to use of the proven cost-effective ionophores that are commonly used in beef diets. Efforts have been reported in the screening of plant extracts with antimicrobial activity, and as a result,numerous publications testing their effects in vitro exist. A recurring theme in all the feed additives discussed in this review is the much greater number of in vitro studies conducted versus in vivo studies. While this is understandable from a cost of research standpoint, the imperative to validate in vitro experiments is great given practical issues such as delivery of additives, intake, and palatability. Decreasing methane emissions seems to be a research priority as reflected by the large number of studies in this area. The use of enzymes and passive immunization approaches appear amongst the most promising new technologies to enhance digestive function and growth. Particularly in the case of fibrolytic enzymes, a great opportunity exists for animal scientists to partner with researchers in the area of biofuels to enhance and expand the resources currently available.

References

Bauer, M. L., D. W. Herold, R. A. Britton, R. A. Stock, T. J. Klopfenstein, and D. A. Yates. 1995. Efficacy of laidlomycin propionate to reduce ruminal acidosis in cattle. J. Anim. Sci. 73:3445-3454.

Beauchemin, K. A., W. Z. Yang, D. P. Morgavi, G. R. Ghorbani, W. Kautz, and J. A. Z. Leedle. 2003. Effects of bacterial direct-fed microbials and yeast on site and extent of digestion, blood chemistry, and subclinical ruminal acidosis in feedlot cattle. J. Anim. Sci. 81:1628-1640.

Beauchemin, K. A., and S. M. McGinn. 2006. Methane emissions from beef cattle: Effects of fumaric acid, essential oil, and canola oil. J. Anim. Sci. 84:1489-1496.

Benchaar, C., H. V. Petit, R. Berthiaume, T. D. Whyte, and P. Y. Chouinard. 2006. Effects of dietary addition of essential oils and monensin premix on digestion, ruminal fermentation characteristics, milk production, and milk composition in dairy cows. J. Dairy Sci. 89:4352-4364.

Benchaar, C., H. V. Petit, R. Berthiaume, D. R. Ouellet, J. Chiquette, and P. Y. Chouinard. 2007. Effects of essential oils on digestion, ruminal fermentation, rumen microbial populations, milk production, and milk composition in dairy cows fed alfalfa silage or corn silage. J. Dairy Sci. 90:886-897.

Berger, L. L., S. C. Ricke, and G. C. Fahey, Jr. 1981. Comparison of two forms and two levels of lasalocid with monensin on feedlot cattle performance. J. Anim. Sci. 53:1440-1445.

Blanch, M., Calsamiglia, S., N. DiLorenzo, A. DiCostanzo, S. Muetzel, and R. J. Wallace. 2009. Physiological changes in rumen fermentation during acidosis induction and its control using a multivalent polyclonal antibody preparation in heifers. J. Anim. Sci. 87:1722-1730.

Busquet, M., S. Calsamiglia, A. Ferret, and C. Kamel. 2006. Plant extracts affect in vitro rumen microbial fermentation. J. Dairy Sci. 89:761-771.

Calsamiglia, S., M. Busquet, P. W. Cardozo, L. Castillejos, and A. Ferret. 2007. Invited Review: Essential oils as modifiers of rumen microbial fermentation. J. Dairy Sci. 90:2580-2595.

Cardozo, P. W., Calsamiglia, S., Ferret, A. & Kamel, C. 2006. Effects of natural plant extracts at different pH on in vitro rumen microbial fermentation of a high-concentrate diet for beef cattle. J. Anim. Sci. 84:2801-2808.

Castillejos, L., S. Calsamiglia, A. Ferret, and R. Losa. 2007. Effects of dose and adaptation time of a specific blend of essential oils compounds on rumen fermentation. Anim. Feed Sci. Technol. 132:186-201.

Coe, M. L., T. G. Nagaraja, Y. D. Sun, N. Wallace, E. G. Towne, K. E. Kemp, and J. P. Hutcheson. 1999. Effect of virginiamycin on ruminal fermentation in cattle during adaptation to a high concentration diet and during an induced acidosis. J. Anim. Sci. 77:2259-2268.

Cong, Z. H., S. X. Tang, Z. L. Tan, Z. H. Sun, C. S. Zhou, X. F. Han, M. Wang, and G. P. Ren. 2009. Effects of different nonionic surfactants on in vitro fermentation characteristics of cereal straws. J. Anim. Sci. 87:1085-1096.

Cook, M. E. 2010. A review of science leading to host-targeted antibody strategies for preventing growth depression due to microbial colonization. J. Anim. Sci. doi: 10.2527/jas.2010-3375.

DiLorenzo, N., F. Diez-Gonzalez, and A. DiCostanzo. 2006. Effects of feeding polyclonal antibody preparations on rumen bacterial populations and ruminal pH of steers fed high-grain diets. J. Anim. Sci. 84:2178-2185.

DiLorenzo, N., C. R. Dahlen, F. Diez-Gonzalez, G. C. Lamb, J. E. Larson, and A. DiCostanzo. 2008. Effects of feeding polyclonal antibody preparations on rumen fermentation patterns, performance, and carcass characteristics of feedlot steers. J. Anim. Sci. 86:3023-3032.

DiLorenzo, N., D. R. Smith, M. J. Quinn, M. L. May, C. H. Ponce, W. Steinberg, M. A. Ensgtrom, and M. L. Galyean. 2010. Effects of grain processing and supplementation with exogenous amylase on nutrient digestibility in feedlot diets. Livest. Sci. (In Press).

Elam, N. A., J. F. Gleghorn, J. D. Rivera, M. L. Galyean, P. J. Defoor, M. M. Brashears, and S. M. Younts-Dahl. 2003. Effects of live cultures of *Lactobacillus acidophilus* (strains NP45 and NP51) and *Propionibacterium freudenreichii* on performance, carcass, and intestinal characteristics, and *Escherichia coli* O157 shedding of finishing beef steers. J. Anim. Sci. 81:2686-2698.

García-Gonzalez, R., J. S. Gonzalez, and S. Lopez. 2010. Decrease of ruminal methane production in Rusitec fermenters through the addition of plant material from rhubarb (*Rheum* spp.) and alder buckthorn (*Frangula alnus*). J. Dairy Sci. 93:3755-3763.

Gencoglu, H., R. D. Shaver, W. Steinberg, J. Ensink, L. F. Ferraretto, S. J. Bertics, J. C. Lopes, and M. S. Akins. 2010. Effect of feeding a reduced-starch diet with or without amylase addition on lactation performance in dairy cows. J. Dairy Sci. 93:723-732.

Goodrich, R. D., J. E. Garrett, D. R. Gast, M. A. Kirick, D. A. Larson, and J. C. Meiske. 1984. Influence of monensin on the performance of cattle. J. Anim. Sci. 58:1484-1498.

Guan, H., K. M. Wittenberg, K. H. Ominski, and D. O. Krause. 2006. Efficacy of ionophores in cattle diets for mitigation of enteric methane. J. Anim. Sci. 84:1896-1906.

Henning, P.H., C.H. Horn, D.G. Steyn, H.H. Meissner, and F.M. Hagg. 2010a. The potential of *Megasphaera elsdenii* isolates to control ruminal acidosis. Anim. Feed Sci. Technol. 157:13-19.

Henning, P.H., C.H. Horn, K.-J. Leeuw, H.H. Meissner, and F.M. Hagg. 2010b. Effect of ruminal administration of the lactate-utilizing strain *Megasphaera elsdenii* (Me) NCIMB 41125 on abrupt or gradual transition from forage to concentrate diets. Anim. Feed Sci. Technol. 157:20-29.

Ives, S. E., E. C. Titgemeyer, T. G. Nagaraja, A. del Barrio, D. J. Bindel, and L. C. Hollis. 2002. Effects of virginiamycin and monensin plus tylosin on ruminal protein metabolism in steers fed corn-based finishing diets with or without wet corn gluten feed. J. Anim. Sci. 80:3005-3015.

Klingerman, C. M., W. Hu, E. E. McDonell, M. C. DerBedrosian, and L. Kung, Jr. 2009. An evaluation of exogenous enzymes with amylolytic activity for dairy cows. J. Dairy Sci. 92:1050-1059.

Krause, M., K. A. Beauchemin, L. M. Rode, B. I. Farr, and P. Norgaard. 1998. Fibrolytic enzyme treatment of barley grain and source of forage in high-grain diets fed to growing cattle. J. Anim. Sci. 76:2912-2920.

Krehbiel, C. R., S. R. Rust, G. Zhang, and S. E. Gilliland. 2003. Bacterial direct-fed microbials in ruminant diets: Performance response and mode of action. J. Anim. Sci. 81 (E. Suppl. 2):E120-E132.

Krueger, N. A., A. T. Adesogan, C. R. Staples, W. K. Krueger, S. C. Kim, R. C. Littell, and L. E. Sollenberger. 2008. Effect of method of applying fibrolytic enzymes or ammonia to Bermudagrass hay on feed intake, digestion, and growth of beef steers. J. Anim. Sci. 86:882-889.

Lewis, G. E., C. W. Hunt, W. K. Sanchez, R. Treacher, G. T. Pritchard, and P. Feng. 1996. Effect of direct-fed fibrolytic enzymes on the digestive characteristics of a forage-based diet fed to beef steers. J. Anim. Sci. 74:3020-3028.

McGinn, S. M., K. A. Beauchemin, T. Coates, and D. Colombatto. 2004. Methane emissions from beef cattle: Effects of monensin, sunflower oil, enzymes, yeast, and furmaric acid. J. Anim. Sci. 82:3346-3356.

McLaughlin, C.L., A. Thompson, K. Greenwood, J. Sherington, and C. Bruce. 2009a. Effect of acarbose on acute acidosis. J. Dairy Sci. 92:2758-2766.

McLaughlin, C.L., A. Thompson, K. Greenwood, J. Sherington, and C. Bruce. 2009b. Effect of acarbose on milk yield and composition in early-lactation dairy cattle fed a ration to induce subacute ruminal acidosis. J. Dairy Sci. 29:4481-4488.

Meyer, N. F., G. E. Erickson, T. J. Klopfenstein, M. A. Greenquist, M. K. Luebbe, P. Williams, and M. A. Engstrom. 2009. Effect of essential oils, tylosin, and monensin on finishing steer performance, carcass characteristics, liver abscesses, ruminal fermentation, and digestibility. J. Anim. Sci. 87:2346-2354.

Mohammed, N., N. Ajisaka, Z. A. Lila, Koji Hara, K. Mikuni, K. Hara, S. Kanda, and H. Itabashi. 2004. Effect of Japanese horseradish oil on methane production and ruminal fermentation in vitro and in steers. J. Anim. Sci. 82:1839-1846.

Nagaraja, T. G., C. J. Newbold, C. J. Van Nevel, and D. I. Demeyer. 1997. Manipulation of ruminal fermentation. Pages 523-632 in The Rumen Microbial Ecosystem. P. N. Hobson and C. S. Stewart, ed. Chapman and Hall, London, UK.

Nagaraja, T. G., and E. C. Titgemeyer. 2007. Ruminal acidosis in beef cattle: The current microbiological and nutritional outlook. J. Dairy Sci. 90(E. Suppl.):E17-E38.

Owens, F. N., D. S. Secrist, W. J. Hill, and D. R. Gill. 1998. Acidosis in cattle: A review. J. Anim. Sci. 76:275-286.

Palmonari , A., D. M. Stevenson, D. R. Mertens, C. W. Cruywagen , and P. J. Weimer. 2010. pH dynamics and bacterial community composition in the rumen of lactating dairy cows. J. Dairy Sci. 93:279-287.

Pinos-Rodríguez, J. M., S. S. González, G. D. Mendoza, R. Bárcena, M. A. Cobos, A. Hernández, and M. E. Ortega. 2002. Effect of exogenous fibrolytic enzyme on ruminal fermentation and digestibility of alfalfa and rye-grass hay fed to lambs. J. Anim. Sci. 80:3016-3020.

Russell, J. B., and H. J. Strobel. 1989. Minireview: The effect of ionophores on ruminal fermentation. Appl. Environ. Microbiol. 55:1-6.

Russell, J. B., W. G. Bottje, and M. A. Cotta. 1981. Degradation of protein by mixed cultures of rumen bacteria: Identification of *Streptococcus bovis* as an actively proteolytic rumen bacterium. J. Anim. Sci. 53:242-252.

Salinas-Chavira, J., J. Lenin, E. Ponce, U. Sanchez, N. Torrentera, and R. A. Zinn. 2009. Comparative effects of virginiamycin supplementation on characteristics of growth-performance, dietary energetics, and digestion of calf-fed Holstein steers. J. Anim. Sci. 87:4101-4108.

Tassoul, M. D., and R. D. Shaver. 2009. Effect of a mixture of supplemental dietary plant essential oils on performance of periparturient and early lactation dairy cows. J. Dairy Sci. 92:1734-1740.

Tricarico, J. M., M. D. Abney, M. L. Galyean, J. D. Rivera, K. C. Hanson, K. R. McLeod, and D. L. Harmon. 2007. Effects of a dietary *Aspergillus oryzae* extract containing α-amylase activity on performance and carcass characteristics of finishing beef cattle. J. Anim. Sci. 85:802-811.

Ungerfeld, E. M., R. A. Kohn, R. J. Wallace, and C. J. Newbold. 2007. A meta-analysis of fumarate effects on methane production in ruminal batch cultures. J. Anim. Sci. 85:2556-2563.

Wang, Y., T. W. Alexander, and T. A. McAllister. 2004. In vitro effects of monensin and Tween 80 on ruminal fermentation of barley grain:barley silage-based diets for beef cattle. Anim. Feed Sci. Technol. 116:197-209.

Watanabe, Y., R. Suzuki, S. Koike, K. Nagashima, M. Mochizuki, R. J. Forster, Y. Kobayashi. 2010. In vitro evaluation of cashew nut shell liquid as a methane-inhibiting and propionate-enhancing agent for ruminants. J. Dairy Sci. 93:5258-5267.

Yang, W. Z., B. N. Ametaj, C. Benchaar, M. L. He, and K. A. Beauchemin. 2010. Cinnamaldehyde in feedlot cattle diets: Intake, growth performance, carcass characteristics, and blood metabolites. J. Anim. Sci. 88:1082-1092.

Yuan, Z. Q., S. X. Tang, B. Zeng, M. Wang, Z. L. Tan, Z. H. Sun, C. S. Zhou, X. F. Han, and M. A. Bamikole. 2010. Effects of dietary supplementation with alkyl polyglycoside, a nonionic surfactant, on nutrient digestion and ruminal fermentation in goats. J. Anim. Sci. 88:3984-3991.

van Zijderveld, S. M., W. J. J. Gerrits, J. A. Apajalahti, J. R. Newbold, J. Dijkstra, R. A. Leng, H. B. Perdok. 2010. Nitrate and sulfate: Effective alternative hydrogen sinks for mitigation of ruminal methane production in sheep. J. Dairy Sci. 93:5856-5866.

Vasconcelos, J. T., N. A. Elam, M. M. Brashears, and M. L. Galyean. 2008. Effects of increasing dose of live cultures of *Lactobacillus acidophilus* (Strain NP 51) combined with a single dose of *Propionibacterium freudenreichii* (Strain NP 24) on performance and carcass characteristics of finishing beef steers. J. Anim. Sci. 86:756-762.

Zinn, R. A. 1986. Effect of salinomycin supplementation on characteristics of digestion and feedlot performance of cattle. J. Anim. Sci. 63:1996-2004.

SESSION NOTES