Review Article

Subacute ruminal acidosis in dairy herds: Microbiological and nutritional causes, consequences, and prevention strategies

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Abstract
Dairy cattle are frequently fed high-concentrate (HC) diets in modern intensive feeding systems, especially in the transition period. During this period, cows face many alterations that include hormonal changes and shifting to a lactating state. Switching to a HC diet that may disrupt the ruminal microbiota balance can lead to subacute ruminal acidosis (SARA). Moreover, the main factor shaping the rumen microbiota is dietary composition, especially the ratio of starch to fibrous carbohydrates. Feeding highly fermentable carbohydrate diets after adaptation to forage diets leads to a rumen fermentation rate that exceeds rumen absorption and buffering rates, resulting in a reduction in ruminal pH. As a result of Gram-negative bacterial cell lysis, an increase in harmful ruminal bacterial metabolites, including lipopolysaccharide, lactic acid, and histamine, is observed. The interactions between the host immune system and the ruminal microbiota play an essential role in many physiological processes and the development of the disorder. Progress in DNA sequencing and bioinformatics platforms provides new opportunities to investigate the composition of ruminal microbes and yields unique advances in understanding ecology of the rumen. Subacute ruminal acidosis is linked with a change in the ruminal microbiota structure and richness and with other metabolic disorders; such as rumenitis, milk fat depression, laminitis, and liver abscesses. Therefore, this review aims to explore a better understanding of the crosstalk between diet and microbiota in the prevalence of rumen acidosis and its consequences, which is crucial for control strategies such as feeding management, and supplementation with thiamine, prebiotics, and probiotics.

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1. Introduction
In the last 3 decades, global milk production has increased by more than 64%, from 538 million tonnes in 1989 to 883 million tonnes in 2019 (FAO, 2021). This improved milk production requires nutrients that cannot be met by forage alone (Hua et al., 2017). The general practice in the modern intensive management system is feeding ruminants with massive amounts of high-concentrate (HC) diets. As a consequence, these animals suffer from metabolic diseases. In a dairy herd, one or several metabolic disorders may affect one out of every 2 cows (Ametaj, 2010). Subacute ruminal acidosis (SARA) is among the most crucial metabolic diseases in intensively fed cows, sheep, and goats (Howard, 1981; Huo et al., 2014).

The ruminant’s gastrointestinal tract is an immune-dynamic organ continuously exposed to many microorganisms, toxins, and chemical stimuli. The complicated and varied microbial ecosystem is referred to as the microbiome or microbiota. Decades of studies have focused on the complex correlation between the host animal and its inhabitant microbiota, primarily to determine the variation in rumen bacterial communities with diet alterations that can lead to digestive disorders such as SARA. Consumption of a HC diet...
increases ruminal fermentation that produces short-chain fatty acids (SCFA), which causes a decrease in ruminal pH to a level below 5.6. The reduction in ruminal pH stimulates the Gram-negative bacteria to die and release lipopolysaccharide (LPS). When an animal fails to cope with the organic acid balance, SARA will occur (Herdt, 2000).

To date, the role of microbiota in SARA is not entirely understood. The functionality and capacity of gastrointestinal tract microorganisms to utilize the fractions of substrate resources are varied. Excessive microbiota richness, balance, and diversity are considered essential for promoting microbial stability through dietary challenge situations and allow the animals to utilize limited resources more effectively. This review outlines the current research performed on SARA to demonstrate the potential role of ruminal microbial alterations, consequences, and prevention strategies.

2. Subacute ruminal acidosis

The current definition of SARA is a ruminal pH reduction from 5.5 to 5.0 for 111 to 180 min per 24 h (Jaramillo-López et al., 2017). SARA is also known as a subclinical rumen acidosis or chronic acidosis—lactic acidosis is a rare accidental pathalogy in which the ruminal ecosystem is completely disturbed. SARA is a predominant ruminant health and production problem that inflicts high economic losses on dairy herds by reducing dry matter intake, milk production, and profitability by increasing the loss of animals due to culling or death (Gozho et al., 2007). Field studies in Europe and the USA have estimated that SARA incidence is between 11% and 19% in cows in early lactation, and between 18% and 20% in cows in mid-lactation and at peak dietary dry matter intake (O’Grady et al., 2008; Enemark, 2008; Mao et al., 2013). Unlike acute ruminal acidosis, SARA is a more chronic status not associated with the increase in ruminal lactic acid. SARA is related to deleterious animal health problems, such as ruminal mucous epithelial damage, and decreased fibre degradation. Symptoms such as diarrhoea, poor body condition, weight loss, and reductions in dry matter intake and milk production appear (Lean, 2007; Plaizier et al., 2009).

SARA is associated with modifications in the ruminal microbial population and diet type (Calsamiglia et al., 2012). Previous evidence showed that feeding ruminants a 50% to 65% grain diet could induce SARA (Tao et al., 2014a, 2014b). Another important cause of SARA is the diet present in the diet, which can occur in excessive amounts of long particles, or be present at sufficient levels, but the long or inedible particles cause the animal to eat a portion of the feed in which the physically adequate fibre is low (Krause and Oetzel, 2006; Oetzel, 2007). Feeding fibre and grain diets separately appears to be a high risk for inducing SARA compared with feeding as mixed diets (Krause and Oetzel, 2006). In addition, animals fail to accommodate abrupt changes in the diet. Ruminal bacterial populations and papillae need more time to adapt to the digestion of HC diets and the absorption of the resultant high levels of volatile fatty acids (VFA) (Ghaffari et al., 2017).

In healthy cows, ruminal bacteria ferment starch into VFA, glucose, and lactic acid. Then, VFA and lactic acid are immediately absorbed by the ruminal wall papillae and enter the blood vessels, where they can be used in milk production. However, under acidic conditions, VFA and lactic acid accumulate in the rumen and contribute to acidosis. Furthermore, the rapid release of glucose in the rumen has subsequent negative consequences: (1) the growth of starch-digesting bacteria such as Streptococcus bovis (S. bovis) increases lactate production; (2) rapid growth with further domination of Gram-positive bacteria and defaunation killing of Gram-negative bacteria (e.g., Fibrobacter succinogenes, Ruminococcus flavefaciens) lead to the release of endotoxins such as LPS, and (3) the rumen osmolality and the accumulation of VFA and lactic acid increase.

3. Ruminal microbial changes associated with subacute ruminal acidosis

Until recently, traditional culture-based methods have been used for exploring the ruminal microbiome, but many microorganisms cannot be cultured. Moreover, quantitative polymerase chain reaction (PCR) techniques, which are based on a specific organism rather than all microbes, are limited. At the beginning of the 21st century, a series of DNA fragmentation procedures, such as terminal restriction fragment length polymorphism, became available for studying microbial diversity (Ghaffari et al., 2017).

The ruminal microbiota includes bacteria, archaea, ciliate protozoa, and fungi. A fibre-rich nutrient and a steady microbial population are essential for maintaining ruminant health. Various investigations have been carried out on ruminal microbiota changes related to ruminal acidosis, which have indicated that the most indispensable microbiotas are bacteria and ciliated protozoa that enhance the grain fermentation rate (Nagaraja and Titgemeyer, 2007). In SARA, the number of protozoa begins to decrease, followed by a further reduction in the number of Gram-negative bacteria (Howard, 1981), whereas Gram-positive bacteria tend to increase (Petri et al., 2013).

3.1. Ruminal bacteria

The ruminant gastrointestinal tract accommodates more than 5,000 bacterial species, which changes according to diets, feeding approaches, and geographical regions (Chauceyras-Durand and Ossa, 2014; Khafipour et al., 2016). Feeding cows with a SARA induction diet is related to a decline in the ruminal bacterial richness and diversity (Ametaj, 2010; Khafipour et al., 2009; Mao et al., 2013; Plaizier et al., 2017; Hua et al., 2017). Many investigations have been conducted on ruminal microbial alterations related to SARA (Table 1). In the rumen, the most dominant bacterial phyla are Bacteroidetes and Firmicutes (Kong et al., 2010; Khafipour et al., 2016). An earlier study assessed the alterations in the ruminal bacterial communities of dairy cows following adaptation to SARA, which showed that a SARA induction diet decreases Bacteroidetes but increases Firmicutes (Mao et al., 2013). This result agrees with the results of Mao et al. (2016) and Hua et al. (2017) on the influence of HC feeding on the reduction in Bacteroidetes and the increase in Firmicutes. Bacteroidetes are the primary degraders of complex polysaccharides in the plant cell walls. However, a HC diet raises the ratio of Firmicutes to Bacteroidetes, which is undesirable (Khafipour et al., 2016). In contrast, Hook et al. (2011a), Hua et al. (2017), and Zhang et al. (2017) found that the most dominant bacteria at the phylum level were Firmicutes and Bacteroidetes when feeding HC diets to ruminants. This difference in Bacteroidetes and Firmicutes abundance may be due to the resilience of the bacteria to dietary changes, the susceptibility of the ruminants, and/or differences in the starch content in the diet.

The increased level of concentrate directly reduced the relative dominance of the cellulolytic bacteria of the genus Fibrobacter (Zhang et al., 2017; Mickdam et al., 2016) and Ruminococcus (Mickdam et al., 2016). In contrast, SARA induction is associated with a Ruminococcus abundance (Mao et al., 2013; McCann et al., 2016). However, the relative abundance of Megasphaera elsdenii (M. elsdenii), which is a lactic acid utilizer, was shown to be increased in mild grain-induced SARA as reported by Khafipour et al. (2009), in vitro severe SARA induction as reported by Mickdam et al. (2016), and in SARA induced using pellets of ground wheat and barley as reported by Plaizier et al. (2017). In contrast,
Table 1
Changes in the ruminal bacteria associated with the subacute ruminal acidosis (SARA).

| Model     | SARA induction diet | Rumen bacteria change                                                                 | 16S rRNA region and sequencing platform | Citation                      |
|-----------|---------------------|---------------------------------------------------------------------------------------|----------------------------------------|-------------------------------|
| Cow       | Hay (week 0)        | Bacteroidetes were decreased with SARA, whereas *Megasphaera elsdenii* was found to dominate mild grain-induced SARA. There was a significant decrease in bacterial species variety in mild grain-induced SARA. Moreover, high-grain feeding increased the communities of ruminal pathogenic *Escherichia coli* and *Clostridium perfringens*. | V1–V2 (TRFLP and real-time PCR)         | Hook et al. (2011a)         |
| Cow       | Hay (week 4 to 6)   | Bacterial density was significantly reduced in the rumen solids with a HC diet. The most common bacteria were *Lactobacillus* spp. and *Streptococcus bovis*. | Real-time PCR                          | Hook et al. (2011a)         |
| Goat      | Hay (week 4 to 6)   | The percentages of Proteobacteria and Bacteroidetes were decreased, whereas those of Firmicutes and Actinobacteria were increased. | V1–V3 (454 pyrosequencing)             | Mao et al. (2013)           |
| Cow       | HC diet             | Relative dominance of the genera *Prevotella, Ruminococcus, Streptococcus* and *Lactobacillus* within the ruminal sample liquid fraction was detected, while Firmicutes was the abundant phylum in the solid fraction. | V4 (MiSeq Illumina platform)           | McCann et al. (2016)       |
| Goat      | HC diet             | Under a severe SARA situation, the relative dominance of the fibrolytic *Ruminococcus albus*, *Fibrobacter succinogenes*, and *Ruminobacter amylophilus* was reduced. In contrast, the relative abundances of *Prevotella, Lactobacillus* group, *M. elsdenii* and *Entodinium* spp. were increased. | Real-time quantitative PCR              | McCann et al. (2016)       |
| Cow       | Pellets of ground wheat and barley | The level of Firmicutes and Bacteroidetes were increased. In addition, a notable change in the Cyanobacteria and Verrucomicrobia was demonstrated. The dominance of the ruminal Bacteroidetes and Tenericutes was decreased by a diet of pellets of ground wheat and barley but not by pellets of ground alfalfa. Only pellets of ground wheat and barley could increase ruminal *M. elsdenii*. Additionally, both challenges reduced the dominance of *S. bovis*. | V3–V4 (454 pyrosequencing and qRT--PCR) | Hua et al. (2017)          |
| Heifer    | Pellets of ground alfalfa | The Bacteroidetes and Firmicutes were significantly increased, and the relative abundance of cellulolytic bacteria (*Fibrobacter* and *Succinimonas*) was reduced. | V3–V4 (Illumina MiSeq sequencing)       | Zhang et al. (2017)        |

*M. elsdenii* was shown to decrease in the study of Wang et al. (2015). SARA induction is dominated by *Prevotella* (Khaipour et al., 2009; McCann et al., 2016; Mickdam et al., 2016), which is known for the utilization of starch and protein. The most common bacteria discovered in the cow’s rumen related to SARA are starch-utilizing bacteria such as *Lactobacillus* spp. and *S. bovis* (Hook et al., 2011a; McCann et al., 2016; Wang et al., 2015). Moreover, feeding a HC diet was shown to increase the pathogenic *Clostridium perfringens* and *Escherichia coli* (Khaipour et al., 2016). These increases were limited when increased grain feeding did not lead to severe rumen and hindgut acidosis, indicating that *C. perfringens* and *E. coli* might be factors contributing to severe rumen and hindgut acidosis onset.

### 3.2. Ruminal archaea

A study of nonlactating dairy cattle fed a HC diet to induce SARA was conducted to assess alterations in methanogen (methane-producing archaea) diversity and community structure (Hook et al., 2011b). These authors found no significant influence of feed on the ruminal methanogen density. This is in line with the results investigating the effect of an increased dietary fibre to grain concentration ratio on the archaeal community (Zhang et al., 2017). These authors found that a different dietary fibre to grain concentration ratio did not affect the archaeal communities. This is in contrast to the study that examined the influence of increased dietary grain (0%, 25%, and 50% maize grain) on archaea in goats, in which HC feeding reduced the richness of the archaeal community and increased the methanogen community (Mao et al., 2016). Ruminal archaeal changes are illustrated in Table 2.

### 3.3. Ruminal protozoa

An alteration in rumen protozoa density was determined in a study on nonlactating dairy cows transitioned to a HC diet (Hook et al., 2011b). SARA was induced during week 1 of the experiment. Up through week 3, there was a significant increase in the abundance of protozoa in the ruminal solids and fluid, followed by a significant decrease in ruminal fluid protozoa when the cattle transitioned back to a hay diet in week 6. Similarly, Mao et al. (2016) examined the influence of increased dietary grain (0%, 25%, and 50% maize grain) on goat ruminal protozoa and observed that HC feeding increased the ciliate community. In contrast, feeding lactating cows with diet-induced SARA reduced the ruminal protozoa diversity (Ishaq et al., 2017). Increasing the concentration level linearly reduced the relative dominance of ciliates, namely, *Polyplostron* and *Ostracodinium*, and linearly increased the relative dominance of *Entodinium* (a nonfibrous carbohydrate degrader) (Zhang et al., 2017). Ruminal protozoa changes are illustrated in Table 3.

### 3.4. Ruminal fungi

High-concentrate diet feeding decreased anaerobic fungal density in male goats (Mao et al., 2016) but increased fungal diversity in dairy cows (Ishaq et al., 2017). The predominant anaerobic fungi were *Neocallimastigomycota* and *Ascomycota*, whereas 4 diets with different dietary forage to concentrate ratios did not affect the density and diversity of anaerobic fungal communities in heifers (Zhang et al., 2017). The anaerobic fungal resistance in the 4 treatment diets might be due to the coexistence of HC and high forage diets among the treatments, which balance cellulose and carbohydrate degradation. Ruminal fungal changes are illustrated in Table 4.

### 4. Inflammatory and immune responses associated with subacute ruminal acidosis

The lower ruminal pH may trigger the cell lysis of Gram-negative bacteria that is associated with the release of free LPS.
Lipopolysaccharide is a portion of the Gram-negative bacterial outer membrane cell wall that acts as an immunogenic compound (Bilal et al., 2016; Ghaftari et al., 2017). Moreover, free ruminal LPS can also result from bacterial cell lysis due to excessive autolytic enzymes that enhance bacterial growth during the rapid growth phase (Gozho et al., 2007; Plaizier et al., 2009). Increased ruminal permeability may be an adaptive response to HC diets to increase SCFA uptake (Zebeli and Metzler-Zebeli, 2012) or acidification or hyperosmolality (Emmanuel et al., 2007; Schweigel et al., 2005). Depending on the failure of the ruminal epithelial barrier in decreased ruminal pH conditions, LPS may be translocated into the bloodstream and promote systemic inflammation by stimulating the release of proinflammatory cytokines, such as tumour necrosis factor-α, interleukin-1β, and interleukin-6, which may be a key causative factor in SARA (Xia et al., 2020). In addition, there is an increase in acute-phase proteins such as serum amyloid A, haptoglobin, LPS-binding protein, C-reactive protein, and alpha-1-acid glycoprotein in peripheral blood (Eckel and Ametaj, 2016; Gozho et al., 2007; Zebeli and Metzler-Zebeli, 2012). Other harmful compounds, such as biogenic amines and ethanol, may be produced during SARA (Ametaj, 2010). Histamine is a biogenic amine produced during SARA that is either absorbed from the gut or generated endogenously through inflammation and has been suggested to play a crucial role in laminitis progression.

Ruminal and intestinal epithelia, in addition to their functions as a selective barrier, help immune functions by their interactions with gut-associated lymphoid tissue (Goto and Kiyono, 2012). The microbial effects on mucosal functions and gut-associated lymphoid tissue occur through linear microbial component interactions with receptors and by-products of symbiotic microbiota, including SCFA (Brestoff and Artis, 2013). In an investigation, isolated rumen and colon tissue from steers showed that LPS and reduced pH worked synergistically to lower barrier function (Emmanuel et al., 2007). Once the epithelium is breached, gut-associated lymphoid tissue cells may respond by triggering local inflammation and altering the generation of cytokines; this may further enhance permeability, potentiate colonization by pathogenic organisms, increase the transfer of bacteria and toxins across the epithelium, and increase the inflammatory response (Kurashima et al., 2013; Mani et al., 2012).

5. Subacute ruminal acidosis consequences

Potential SARA consequences that may occur are rumenitis, milk fat depression (MFD), laminitis, and liver abscesses (Lean, 2007; Plaizier et al., 2009), which are illustrated in Fig. 1.

5.1. Rumenitis

Rumenitis is a common consequence of rumen acidosis (Enemark et al., 2002). The pathogenesis of rumenitis involves LPS resulting from rumen acidosis over-activating the nuclear factor-
kappa B and mitogen-activated protein kinase inflammatory pathways in the ruminal epithelium. Consequently, this significantly increases the synthesis and expression of proinflammatory cytokines, thereby partly inducing rumenitis (Zhao et al., 2018).

5.2. Milk fat depression

Milk fat depression is a reduction in milk fat yield or percentage in response to highly fermentable diets and diets with high polyunsaturated fatty acids (Weimer et al., 2010). A depression in the milk fat concentration in cows induced by SARA has been demonstrated, due to alterations in ruminal fermentation patterns (Kleen et al., 2003). Milk fat depression illustrates the interactions among dietary feed, gastrointestinal microbiota, and tissue physiology (Pitta et al., 2018). Dietary components, particularly alterations in neutral detergent fibre and starch concentrations in the diet, can affect ruminal microbiota by modifying the ruminal environment (Lourenço et al., 2010).

During microbial fermentation in the rumen, polyunsaturated fatty acids undergo biohydrogenation to form saturated fatty acids with less toxic to microbes (Lourenço et al., 2010). Elevated concentrations of polyunsaturated fatty acids are considered toxic to rumen microbes because they form complexes with the cell walls of ruminal microbes and interfere with ruminal fermentation. Alterations in biohydrogenation pathways due to higher concentrations of polyunsaturated fatty acids and starch in the diet can lead to MFD.

Diet-induced MFD in dairy cows is commonly associated with alterations in the rumen microbe community due to the accumulation of VFA. Furthermore, it is associated with an increase in S. bovis, M. elsdenii, and Selenomonas ruminantium (Rico et al., 2015), an increase in specific genus levels of Actinobacteria and Firmicutes, such as unclassified Lachnospiraceae, Butyrivibrio, Bulleidia, and Coriobacteriaceae (Pitta et al., 2018), and a rise in the relative dominance of Prevotella (Zeng et al., 2019). In contrast, a reduction in the dominance of Prevotella bryantii, Fibrobacter succinogenes, and the Butyrivibrio fibrisolvens/Pseudobutyrivibrio group (Rico et al., 2015), a reduction in the members of Bacteroidetes and Fibrobacteres (Pitta et al., 2018), and a decline in the relative abundance of unclassified Lachnospiraceae, Orbitbacterium, Veillonellaceae and Pseudobutyrivibrio in the ruminal fluid tend to occur (Zeng et al., 2019). In addition, the total number of ciliated protozoa and fungi was shown to rapidly decrease by more than 90% during the induction of MFD (Rico et al., 2015).

5.3. Laminitis

Laminitis is a clinical sign associated with SARA (Kleen et al., 2003; Krause and Oetzel, 2006). Laminitis is characterized by attachment loss between the distal phalanx and the inner hoof wall that causes the bone to be pressed down into the hoof, damaging the surrounding blood vessels and subsequently breaking the sole corium and the coronet (Li et al., 2017). Laminitis is considered the major cause of significant production loss due to compulsory culling and deaths (Oetzel, 2007; Thoefner et al., 2005). Recently, it was found that the disturbance of ruminal microbiota plays a crucial role in laminitis onset (Li et al., 2017). Increasing levels of LPS, histamine, and lactic acid in the bloodstream during SARA play vital roles in causing laminitis. Feeding diets rich in HC has been identified as playing an important role in the pathogenesis of laminitis. Oligofructose administration was shown to induce a significant change in the ruminal microbiota and cause acute laminitis. Microbial data investigations have shown that oligofructose infusion increases the proportion of the phylum Firmicutes and the genera Lactobacillus and Streptococcus, and reduces the abundance of the phyla Bacteroidetes, Fibrobacteres, and the genera Butyrivibrio and Ruminococcus (Li et al., 2017).
5.4. Liver abscesses

Another indication of SARA at time of slaughter is liver abscess, which may reach a prevalence of 32% of the community, with more than half of the cases categorized as severe (Rezac et al., 2014). Liver abscess is a common disease of grain-fed cattle at all ages and within all types. The prevalence is most common in feedlots and is influenced by several dietary and management factors (Nagaraja and Chengappa, 1998). Liver abscess is often secondary to rumen acidosis, rumenitis, and rumen parakeratosis in cattle fed a grain diet. Liver abscesses are diet-induced, and the level of fibres negatively influence their predominance and severity.

Fusobacterium necrophorum, an anaerobic ruminal bacterium, is the primary cause of liver abscesses (Nagaraja and Chengappa, 1998). The amount of F. necrophorum is influenced by feed and some antimicrobial feed additives. Its role in ruminal fermentation is lactic acid metabolism of feed and epithelial protein degradation. It increases when cows are fed grain rather than forage. Ruminal F. necrophorum enters the portal circulation, is trapped by the liver, and then leads to the formation of abscesses. The term ‘rumenitis-liver abscess complex’ is usually used because of the close relationship between the ruminal pathology incidence and cattle liver abscesses (Tadepalli et al., 2008). Ruminal injuries occurring in acidosis are usually accepted as predisposing agents for liver abscesses (Nagaraja and Lechtenberg, 2007). The second most prevalent bacteria isolated from liver abscesses are Arcanobacterium pyogenes, which exist as a commensal microbe on the mucus membranes of the animal ruminal wall (Nagaraja and Lechtenberg, 2007).

6. Recent advanced studies in ruminal acidosis prevention

6.1. Feeding management strategies

The basic principles of prevention are a gradual adaptation to HC feeds, an adequate fibre source in the diet, and a reduction in concentrate amounts consumed by animals in a diet (Enemark, 2008; Krause and Oetzel, 2006). A well-balanced dietary fibre and starch content, and ratio of physically effective neutral detergent fibre to ruminal degradable starch, should be obtainable in diet formulations for high-producing ruminants (Xu et al., 2018). Approximately 15% of rumen-degradable starch from grains in total mixed rations may be considered a general optimum to assure normal rumen conditions and digestion, depending on the fibre content of the diet. The content of physically effective neutral detergent fibre >1.18 mm (expressed inclusive of particles-dry matter >1.18 mm) in the diet at approximately 30% to 32% is sufficient for maintaining a daily mean ruminal pH of 6.2, lowering the risk of SARA. In addition, a ratio of physically effective neutral detergent fibre >1.18 mm to ruminal degradable starch of grain that is lower than approximately 1.45 mm should be avoided (Zebeli et al., 2010). Feeding management requires a combination of proper diet formulation and good feed bunk management, including sufficient long-fibre particles in the feed (between 7% and 15% of the total mixed ration), which decreases SARA prevalence by enhancing salivation and increasing rumination (Oetzel, 2003; Ishaq et al., 2017).

6.2. Supplementation with buffer salts and organic acids

Supplementation with buffer salts has a direct effect on managing ruminal fluid pH. Supplementation of adequate buffer in the diet, such as sodium bicarbonate (from 110 to 225 g/day), neutralizes the ruminal pH changes and may prevent the overgrowth of acid-tolerant lactobacilli (Enemark, 2008). Additionally, adding alkanizing substances such as potassium carbonate or magnesium oxide from 270 to 410 and 50 to 90 g/day, respectively, increases ruminal pH (Enemark, 2008; Hernández et al., 2014). However, sodium bicarbonate supplementation may cause concern by upsetting the balance of ions in the body of ruminants. In addition, organic acids, such as malic acid, tannic acid and citric acid, which stimulate lactate utilization, are used directly as feed additives or through pre-treated (steeped) cereal grain (Krause and Oetzel, 2006; Zhao et al., 2021; Shen et al., 2019).

6.3. Supplementation with plant-derived extracts

Plant-derived extracts, e.g., alkaloids, terpenoids, and essential oils, have received extensive consideration from researchers due to their efficiency in maintaining ruminal pH and improving ruminal fermentation. Beta-sitosterol, a plant compound known as phytosterol, has the potential to relieve the inflammatory response and alter rumen fermentation in HC-intensive ruminant production (Xia et al., 2020). Supplementation with plant-derived alkaloids increases SCFA concentrations, which suggests advantages in improving gluconeogenesis and fermentation in ruminants (Mickdam et al., 2016).

6.4. Ionophores and probiotics

Supplementation with ionophores aims to inhibit lactate-producing bacteria, mainly S. bovis and Lactobacillus spp. Ionophores are a class of antibiotics that are not used in human medicine but may have more potential for animals. Administering ionophore rumin modifiers, such as monensin, may decrease the risk of rumen acidosis by controlling lactate production and reducing meal size. More than a decade ago, monensin has been approved for use in lactating dairy cattle in the US (Oetzel, 2007). Nevertheless, the European Union and China have banned antibiotic use in feed animals, and it has been limited in other countries due to antibiotic resistance and government concerns regarding food safety (Blanch et al., 2009; Xia et al., 2020). To enhance ruminal lactate utilization that may decrease the risk of SARA, diets can be supplemented with probiotics or direct microbial strains, such as M. elsdenii, or yeasts such as Saccharomyces cerevisiae, which stimulate the growth of ruminal protozoa, improve cellulolytic bacterial activity and suppress the proliferation of lactic acid-producing bacteria. Fungi such as Aspergillus oryzae have been proposed to improve rumen performance, normalize rumen fermentation, increase ruminal bacterial activity, and inhibit lactic acid production (Hernández et al., 2014).

6.5. Thiamine supplementation

Thiamine supplementation is a novel strategy to relieve SARA in animals fed HC diets, which can change rumen microbial communities and mitigate HC-induced local inflammation and ruminal epithelial disruption. It reduced the relative protein expression of interleukin-1β, nuclear factor-kappa B unit p65, and phosphorylated nuclear factor-kappa B unit p65 in the ruminal epithelium (Ma et al., 2021; Wang et al., 2015; Zhang et al., 2020).

6.6. Immunization

Antibodies and vaccines against ruminal lactate-producing bacteria have successfully engendered a higher rumen pH and reduced the lactate concentration. In addition, the development of polyclonal antibodies against target bacteria may be effective in controlling rumen acidosis during a rapid transition to the HC diet (Blanch et al., 2009; Hernández et al., 2014).
7. Conclusion
SARA is a well-known metabolic disorder in early- and mid-lactation of high-producing dairy herds that harms animal production and health. Feeding animals HC diets leads to a reduction in the ruminal pH < 5.5 and thus affects the ruminal microbial diversity and population. High-throughput sequencing, multivariate statistical techniques and bioinformatics advances, which are more accurate and sensitive, were used to estimate and monitor microbiota alterations in the rumen. Such approaches enable us to distinguish microbiota that may be numerically less abundant but functionally have an important role in the causes of the disorder. Additionally, we elucidated bacterial interactions with the host animal, which allowed us to use the power of the microbial diversity to improve animal productivity, health, and feed protection. The evidence shows that the ruminal microbiota plays a substantial role in SARA incidence, with cellulosytic bacteria decreasing and acid-tolerant bacteria such as *Streptococcus* and *Lactobacillus* spp. increasing. Free ruminal LPS resulting from Gram-negative bacterial cell lysis and histamine play a crucial role in the SARA prevalence, and consequences such as rumenitis, MFD, laminitis, and liver abscesses affect animal production and health. Understanding the dietary and microbial causes of SARA and coordinating efforts between feed and microbial management will help us develop prevention strategies. This understanding may provide further guidelines for strategies to maintain the fine balance between high growth performance and good host health. The research to date has focused on the bacterial microbiome role in SARA. However, more research is needed to fill the gaps in our knowledge on the role of the protozoal, fungal and archael microbiomes as potential factors in metabolic acidosis. In addition, we require further studies on the mechanisms by which they may contribute to disease.

Author contributions
Hongrong Wang reviewed, added intellectual content, and approved the final version of the manuscript to be published. Mawda E. Elmhadi: writing, reviewing, and editing. Darien K. Ali and Mawabi K. Khogali critically revised the manuscript.

Declaration of competing interest
We declare that we have no financial and personal relationships with other people or organizations that can inappropriately influence our work, and there is no professional or personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the content of this paper.

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