REVIEW ARTICLE

Effect of Sodium Butyrate on Growth Performance of Dairy Calves: An Overview

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Abstract

Butyrate, a volatile fatty acid (VFA), is produced by microbial fermentation of feed carbohydrates in the stomach and large intestine. Butyrate, among the three primary volatile fatty acids (VFAs) generated within the gastrointestinal tract, is characterized by its relatively lower abundance. Nevertheless, it exhibits the most intricate and variable patterns of behavior and exerts significant physiological functions, particularly in the context of developing bovine calves. It is essential for promoting the growth of rumen, abomasum, and intestinal epithelia. Dietary butyrate supplementation can help to further speed up the growth of the gastrointestinal tract (GIT). There is proof that adding Na-butyrate to liquid feed at a higher dose rate of 45 g per day improved growth performance, feed efficiency, and antioxidant activity in dairy calves. It has been frequently demonstrated that adding sodium butyrate to a liquid diet at a modest level (0.3 percentage of DM) will enhance pre-weaned calves› growth, function, and GIT development and is also advisable due to a very strong, unpleasant smell. Future research should concentrate on how well Na-butyrate works to improve the growth performance of calves in Indian environments.

Key words: Butyrate, Dairy calves, Gastrointestinal tract, Volatile fatty acids.

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Introduction

The gastrointestinal tract (GIT) of calves especially the fore-stomach at birth is not fully developed to digest solid feed, it develops significantly during the early weeks of postnatal life (Heinrichs, 2005), resulting in consumption and efficient digestion of solid feed (Hill *et al.,* 2010). A calf's digestive system changes from a monogastric to a functional ruminant digestive system in the first month of its' lives which poses challenges (Steele *et al.,* 2016). A considerable anatomical and physiological changes are required in a very short time starting from single stomach digestion in the abomasum, to developing four compartments functional stomach within a few weeks (Gorka *et al.,* 2018). A well-developed functional rumen in dairy calves is essential to improve feed intake, growth, and feed efficiency (FE), which decreases the cost of raising replacement heifers. The higher solid feed intake in calves stimulates microbial growth in the rumen, which ferments carbohydrates (Bergman, 1990) more efficiently to volatile fatty acids-(VFAs) like acetate, propionate, and butyrate (major three) and others. The butyrate stimulates the growth of papillae embedded on the rumen epithelium surface. These papillae, supplied with blood vessels, are responsible for the absorption of microbial metabolites in the rumen. Thus, butyrate plays a vital role in supporting the development of the epithelia of the rumen, abomasum, and intestine. It has been shown in numerous studies that substantial acceleration of GIT development in calves can be obtained by dietary butyrate supplementation (Guilloteau *et al.,* 2009; Górka *et al.,* 2011). In this review, we summarize the current knowledge on the use of dietary butyrate for calves' performance.

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Butyrate: Need In Body & Action

Butyrate is the end product of microbial fermentation of carbohydrates. The higher butyrate production in the rumen results when ruminants are fed high starch and simple sugar diets. Butyrate is essential to stimulate and regulate the growth and function of ruminal epithelium over and above acts as an energy substrate (Penner *et al*., 2011). The injection of butyrate directly into the lumen of the developing rumen results in the proliferation of ruminal epithelial cells in pre-ruminant calves (Mentschel *et al*., 2001), with longer rumen papillae and a larger surface area for nutrient absorption (Malhi *et al.,* 2013). Butyrate also improves the metabolic activity of the ruminal epithelium (Wiese *et al.,* 2013), the abundance of transcript-encoding proteins mediating short chain fatty acid (SCFA) absorption (Dengler *et al.,* 2015), and epithelial blood flow to the gut and rumen.

The effect of butyrate supplementation in the liquid feed may affect gastrointestinal tract (GIT) development and function directly as a source of energy for GIT tissues (Drackley, 2008), or indirectly via secretion of GIT peptides, hormones, and vagal nerve stimulation (Guilloteau *et al.,* 2010). Butyrate supplementation in the solid feed also serves as readily accessible energy for the growing tissue in addition to the key energy source for the ruminal epithelial cells (Wiese *et al*., 2013). Butyrate indirectly also promotes the proliferation of ruminal epithelial cells as it influences the release of hormones and growth factors like insulin or IGF-1 (Baldwin *et al*., 2004; Penner *et al*., 2011). Shen *et al*. (2012), Steele *et al*. (2012) and Herrick *et al*. (2017) reported that this effect can be of both endocrine and paracrine origin.

Sources and Importance of Butyrate

The are two main sources of butyrate ie internal, naturally occurring sources, and exogenous sources. Milk naturally contains butyrate and the microbial fermentation of carbohydrates is the second most significant source of butyrate for ruminants (Bergman, 1990) which hastens the development of the fore-stomach in calves. Ruminants also ferment feed to create butyrate in the distal portion of the small and large intestines, just like monogastric animals (Bergman, 1990). The external source is butyrate salts (calcium, sodium, potassium, or magnesium) or butyrins (esters of butyrate and glycerol*, i.e.,* mono-, di-, or tri-butyrin), which can be supplied in feed. Sodium butyrate (SB) is the most widely utilized dietary source due to its wide availability, affordable price, and ease of dissolving in water. The dietary sodium butyrate quickly dissociates in the stomach and is probably entirely absorbed (Guilloteau *et al*., 2009). The more pronounced effect of butyrate in the small intestine and abomasum results when added to solid feeds than to liquid feeds.

Natural Internal Sources

Butyrate in milk is the newborn calf›s main supply prior to the establishment of the rumen, though the free butyrate in whole milk is not very high (0.16 g/L in cow›s milk), it may be enough to impact GIT growth and functions (Guilloteau *et al*., 2010). Additionally, pregastric lipase also releases butyrate from milk fat in the abomasum in newborn calves (Drackley, 2008). The primary source of butyrate in dairy cows is the microbial fermentation of carbohydrates in the rumen (Bergman, 1990). The concentration of butyrate can range from 4 mol to more than 10 mol, which is more than 10% of the daily SCFA production in the rumen depending on the stage of lactation and the food (Dieho *et al*., 2016). The ruminal butyrate of up to 90% is directly absorbed from the rumen, and the ruminal epithelium metabolizes the majority of this pool (Bergman, 1990). Butyrate also produces in the large and distal intestines in Ruminants much like monogastric animals (Bergman, 1990) and in mature ruminants, its content in the large intestine digesta can resemble that of the rumen fluid (Li *et al*., 2012).

External Sources

Salts or butyrins can be used as external feed supplements with benefits simpler to handle, less offensive, and more stable, over-free butyric acid in feed manufacturing (Gorka *et al*., 2018). Sodium butyrate (SB) is the most popular source of dietary butyrate due to its wide availability, low cost, and ease of dissolving in water. The dietary sodium butyrate quickly dissociates in the stomach (fore-stomach, abomasum) and is likely entirely absorbed there. Calcium butyrate is less soluble in water in comparison to sodium butyrate (Mallo *et al*., 2012), and is reasonable to assume that some of the butyrate administered will reach the small intestine. The minor sources of butyrate salts are potassium, and magnesium, which are not currently employed in animal nutrition.

Dietary Supplementation of Butyrate

The intake of solid feed is quite low early in a calf›s life, and the rumen bacteria are developing the butyrate content in the immature rumen is very low and utilization of milk replacer (MR) to economize rearing in place of whole milk again lowers the butyrate content (Flaga *et al*., 2015). Again, liquid feed (milk or MR) feeding, enters the abomasum instead of the rumen in pre-ruminants (Górka *et al*., 2011) and reduces butyrate. These conditions necessitate the feed supplementation of butyrate. The effects of butyrate on rumen development are anticipated to be greatest when added to solid feed, and addition in liquid feeds impact more the abomasum and small intestine development (Górka *et al*., 2011). The known effects both in liquid and solid feeds on the structure and function of the lower GIT, faster fore-stomach development in newborn ruminants (Guilloteau *et al*., 2009) necessitate supplementation both through the liquid and solid feed in the young calves (Górka *et al*., 2014).

Effect of Sodium Butyrate on Growth and Feed Conversion

The diet enriched with 0.3% Na-butyrate to calves resulted in enhanced feed intake, body weight gain, improved feed conversion, and significant modifications in GIT architecture and functioning (Guilloteau *et al.,* 2009) probably due to improved digestibility. The incremental adding Na-butyrate (15, 30,45 g/d) to liquid diets (milk, milk replacer, and a combination of both) resulted in a linear drop in the feed-to-gain ratio, and a linear increase in daily weight gain, wither height, body length and dry matter intake in calves (Liu *et al*., 2021). The researcher's report is available suggesting that adding Na-butyrate to the diet could boost animal growth, stimulate the development of the duodenal mucosa (Hu and Guo, 2007), improve feed intake, daily gain, and feed conversion ratio (Mazzoni *et al*., 2008) of young calves. O›Hara *et al.* (2018) put up the theory of enhanced calves› performance may be due to altering the rumen and hindgut microbiota, particularly the caecal microbiota.

Effect of Butyrate on GIT Development and Rumen Fermentation

Sodium-butyrate (Na-butyrate) supplementation in milk formula (MF) and/or starter diet intake of neonatal calves improved the relative rumeno-reticule weight, produced larger rumen papillae length and width, and suggested an improvement of the rumen (Slusarczyk *et al.,* 2010; Gorka *et al.,* 2009, 2011). The accelerated papillae growth and development in neonatal calves were verified (Mentschel *et al.,* 2001; Kato *et al.,* 2011). Butyrate supplementation also improves intestinal tight junctions, epithelial energy mobilization, and volatile fatty acids absorption capacity in the rumen, all of which are protective effects (Baldwin *et al.,* 2012; Laarman *et al.,* 2013). The rumen pH reduction effect of butyric acid may also encourage the colonization of the gastrointestinal tract with helpful bacteria (Galfi and Bokori, 1990; Laarman *et al.,* 2013). Because butyrate is well known for its bioactivity in numerous tissues (Hamer *et al.,* 2008; Gorka *et al.,* 2018), it is a popular choice for enhancing rumen function.

The supplementation of 1% wt/wt rumen-protected butyrate in the diet of post-wean calves tended to have a lower total VFA concentration, a higher proportion of propionate, and lower rumen pH for a longer duration (McCurdy *et al.,* 2019). Despite unclear mechanisms of action, these results support the report of Gorka *et al.* (2009) of improved weaning performance with rumen-protected butyrate. Recently, one study found that rumen pH, concentrations of individual and total VFAs, or acetate: propionate ratio were not affected by supplementation of sodium butyrate in liquid feeds (milk, milk replacer, and the mixture of both) in dairy calves (Liu *et al.,* 2021). This is likely because most of the Na-butyrate and the ingested liquid feed bypassed the rumen and may be due to improved absorption of volatile fatty acids in the rumen on account of the larger surface area of rumen papillae in another case. The mechanism through which Na-butyrate increases the generation and absorption of VFAs should be the subject of further study. Nonetheless, the observed rumen pH levels in their study do not appear to pose a detriment to rumen growth. However, Koch *et al.,(* 2019), demonstrated that supplementation of sodium butyrate via a rumen cannula leads to a reduction in pH levels and an elevation in the production of volatile fatty acids.

Effect of Butyrate on Health, Antioxidant and Immune Status

The potential effect of Na-butyrate supplementation on health can be measured directly as faecal consistency score, frequency, and duration of diarrhoea, and coughing score. More detail and bodily investigation can also be carried out by measuring anti-oxidant components in serum, immunoglobulin and related components in the serum of calves.

The calves fed Na-butyrate in the liquid feed had the fewest scours and didn›t need any electrolyte therapy, thicker faeces, and fewer electrolyte treatments are signs that the SB supplementation in the milk replacer group tended to have a positive impact on calves› health throughout the first two weeks of the study (Hill *et al.,* 2007; Gorka *et al.,* 2009; Guilloteau *et al.,* 2009; Górka *et al.,* 2011; Sun *et al.,* 2019). Diarrhoea and respiratory disorders, *i.e.,* more faecal fluidity and less coughing were impacted by feeding non-medicated milk replacer containing sodium butyrate and active probiotic *Bacillus amyloliquefaciens* (Vazquez-Mendoza *et al.,* 2020) in Holstein dairy calves. Additionally, Wanat *et al.* (2015) noted that adding sodium butyrate to the beginning feed (starter feed) enhanced faecal fluidity when the dose was raised. However, in that study, the number of days with diarrhoea did not rise linearly with the dose, suggesting that feeding sodium butyrate may be associated with watery faeces apart from diarrhoea.

The calves› oxidative stress defence systems study must include antioxidative enzymes like superoxide dismutase (SOD), catalase (CAT) glutathione peroxidase (GSH-Px), and maleic dialdehyde (MDA) concentration in the blood serum. MDA is a marker for oxidative stress, and the content of MDA in the serum may be impacted by Na-butyrate (Georgieva *et al.,* 2011). The benefits of supplementing with Na-butyrate to help the calves deal with the oxidative stress they experience in their early lives as shown by the improved GSH-Px activity and lower MDA concentration (Liu *et al.,* 2021), while serum activities of SOD or CAT were not affected. This suggests that the Na-butyrate supplementation might have strengthened the body›s natural defences against oxidative stress, and also reducing oxidative stress.

Three crucial antibodies like IgA, IgG, and IgM of the immune system can enhance animal immunity, activate the complement system, and protect against a variety of pathogens and viruses (Horton and Vidarsson, 2013). Liu *et al.* (2021) measured the serum immunoglobin (Ig) concentration of calves given various amounts of sodium butyrate and discovered that the calves› blood concentrations of IgA, IgG, or IgM were unaffected ($p > 0.05$). In general agreement with the finding that supplementing with SB in acidified milk did not affect the serum immunoglobulin concentration in calves. Sun *et al. (*2019) found that supplementing liquid feeds with Na-butyrate in the presence of three antibodies in the calves did not affect their serum concentrations. It is necessary to conduct additional studies to determine the effect of butyrate on the operation of the immune system in calves using immunological tests including another test than those for the three Ig.

Effect of Butyrate on Blood Parameters

The greater plasma concentration of glucose in calves fed sodium butyrate in the early stages of life is beneficial as glucose is the preferred energy source for pre-ruminant calves (Gorka *et al.,* 2011; Nazari *et al.,* 2012), and increased serum total protein levels, indicating greater accessibility of proteins for the developing organism (Gorka *et al.,* 2011). This increase in blood glucose and serum total protein level is considered good for the growth and health of newborn calves.

The supplementation of Na-butyrate has a non-significant effect on serum glucose levels (Eskandary *et al.,* 2021). The blood glucose and serum BHB levels in calves supplemental fed Na-butyrate (Ślusarczyk *et al.,* 2010; McCurdy *et al.,* 2019; Ghaffari *et al.,* 2021) may be due to enhanced tissue sensitivity to insulin that reduces blood glucose levels which will not allow increasing the blood levels in calves in supplementing Na-butyrate (Kato *et al.,* 2011; Frieten *et al.,* 2017).

Recommended Doses

The recommended level of supplemental Na-butyrate in calves' feeds is low (0.3% of DM) in liquid feed as it exerted a stimulatory effect on the GIT development, and function and improves growth performance (Guilloteau *et al.,* 2009; Górka *et al.,* 2011). Even supplementation at three times higher levels was well tolerated by calves (Kato *et al.,* 2011; Hill *et al.,* 2007). Sodium butyrate is usually found as a white, water-soluble, crystalline solid with a very strong, unpleasant smell that needs to keep the dose rate lower, so the dose rate of 0.3 % of dry matter will work without a negative effect on intake. Need to reconstruct the above paras

Conclusions

The supplementation of dietary Na-butyrate in liquid feed and solid feed can contribute to the GIT development in calves. Sodium butyrate supplementation in liquid feed at a low level (0.3% of DM) can stimulate GIT development, and function as well as growth performance of pre-weaned calves. The faecal consistency improves and scours frequency and duration reduce. It can also improve growth, and antioxidant ability in pre-weaned dairy calves. Therefore, Na-butyrate supplementation is beneficial to improve the growth performance of calves.

The growth rate of calves of Indian cattle and buffalo is lower than that of exotic cattle and the effectiveness of Na-butyrate to improve growth in Indian conditions is useful and needed to improve performance. The farm-level large scale studies to evaluate the effect of Na-butyrate on growth rate also need to be conducted in Indian conditions. Mechanistic studies and technologies are also required to elucidate how butyrate enhances growth and antioxidant function in calves.

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