Calcium Propionate in Dairy Cows

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Calcium propionate is a safe and reliable food and feed additive. It can be metabolized and absorbed by humans and animals as a precursor for glucose synthesis. In addition, calcium propionate provides essential calcium to mammals. In the perinatal period of dairy cows, many cows cannot adjust to the tremendous metabolic, endocrine, and physiological changes, resulting in ketosis and fatty liver due to a negative energy balance (NEB) or milk fever induced by hypocalcemia. On hot weather days, cow feed (TMR or silage) is susceptible to mildew, which produces mycotoxins. These two issues are closely related to dairy health and performance. Propionic acid is the primary gluconeogenic precursor in dairy cows and one of the safest mold inhibitors. Therefore, calcium propionate, which can be hydrolyzed into propionic acid and Ca^{2+} in the rumen, may be a good feed additive for alleviating NEB and milk fever in the perinatal period of dairy cows. It can also be used to inhibit TMR or silage deterioration in hot weather and regulate rumen development in calves. This paper reviews the application of calcium propionate in dairy cows.

calcium propionate | negative energy balance | milk fever | aerobic stability | resist mildew

1. Introduction

There are many important challenges in dairy production, including reducing the feed intake and metabolic diseases caused by a negative energy balance (NEB)[1] and milk fever[2] during the perinatal period and mycotoxin pollution[3] of feed induced by environmental and climatic conditions, which have negative effects on milk production and quality and pose a potential threat to human health. In particular, ketosis and hypocalcemia represent two potentially devastating insults to the lactating dairy cow[4]. Appropriate dosages of calcium propionate as a feed additive can effectively alleviate these difficulties and serve the dairy industry.

Since calcium propionate does not inhibit yeast growth, it is one of the most useful antimicrobial preservatives in the fermented foods industry, especially in bread and fermented dairy products; in aqueous solution, it can dissociate to propionic acid (the active antifungal ingredient) and calcium ions[5]. It can be used as a feed preservative, growth promoter, intestinal microbiota enhancer, or appetite suppressant in animal nutrition[6]. In the dairy cow industry, calcium propionate can also be applied in many cases to inhibit mycotoxin production and as a metabolite precursor additive.

Propionic acid and Ca^{2+} are basic components in the rumen fluid[7], which means that calcium propionate is safe to add to the feed of dairy cows. It is approved by the World Health Organization (WHO) and the United Nations Food and Agriculture Organization (FAO) for use in food or feed additives. Therefore, it is used as a safe and valuable additive in the dairy cow industry. To update our knowledge on calcium propionate application for dairy cow performance and metabolism, we reviewed the effects of calcium propionate supplementation on decreasing feed mycotoxins, alleviating dairy cow NEB and milk fever, and promoting rumen development in dairy calves.

2. The Application of Calcium Propionate in Dairy Cows

As mentioned above, calcium propionate can be metabolized and absorbed by animals, providing them with essential calcium and glucose precursors, which are advantages that are not offered by other anti-mildew agents. Furthermore, it is generally regarded as safe (GRAS) in the United States, where upper limits only exist for its use in specific human food items[8]. Therefore, it is widely used in dairy cows as an antimicrobial agent, glucose precursor, and calcium provider.

2.1. Application in Silage to Resist Mildew

Silage is one of the most common ingredients in the diets of dairy cows and is an important source of nutrients. However, poorly made or contaminated silage can also be a source of pathogenic bacteria that may decrease the dairy cow performance, reduce the safety and quality of dairy products, and compromise animal and human health[9]. Molds identified in fermented feeds include *Aspergillus* sp., *Cladosporium* sp., *Fusarium* sp., *Mucor* sp., and *Penicillium* sp., and their adverse effects may occur through either their deleterious effects on the nutrient quality or their production of mycotoxins [10]. Several mycotoxins have been detected in corn silage, including aflatoxin B1, citrinin, deoxynivalenol, gliotoxin, and zearalenone[11].

To enhance the quality of silage, fermentation and the aerobic stability can be improved by adding silage additives. Propionic acid-based products, which are compatible with microbial inoculants, can be used as a silage additive. The combined use of propionic acid-based products and microbial inoculants can result in improvements in silage fermentation and the aerobic stability[12]. Propionic acid has excellent antifungal activity and has little impact on the activity of lactic acid bacteria. The application of propionic acid presents some problems due to its corrosive and hazardous nature, but its salt—calcium propionate—also has antimicrobial effects; additionally, it is safe and easy to handle[13]. Calcium propionate is an effective tool for suppressing the germination, growth rate, and aflatoxin production of *Aspergillus flavus* (A-2092) in different substrates[14]. Therefore, calcium propionate has the potential, as an additive in silage, to inhibit the growth of molds and decrease the mycotoxin contents in silage.

2.2. Application in TMR to Increase the Aerobic Stability

Warm and humid conditions are favorable for mold growth and can result in increased mycotoxin production. The spoilage of TMR in summer is an important factor affecting the production efficiency. To reduce the influence of TMR mold growth and its metabolites on the production performance, health, and milk quality of cows, appropriate methods, including chemical additives, water content control, increasing the number of fresh feed deliveries per day, and the timely cleaning of leftovers, must be used. As mentioned above, calcium propionate is a safe and effective inhibitor of mold, and can improve the aerobic stability of feed. Mold growth can be prevented in coarse texture feeds and other high moisture feeds by the addition of calcium propionate[15]. The addition of calcium propionate to TMR inhibits feed spoilage. Therefore, the proper addition of calcium propionate in TMR feed may have the function of preventing feed corruption. However, research on the recommended amount of calcium propionate added to TMR to prevent feed spoilage is needs to be further explored.

2.3. Application as a Gluconeogenic Precursor to Alleviate NEB in the Perinatal Period

The perinatal period from late pregnancy to early lactation is a critical period in a dairy cow's life due to the rapidly increased drain of nutrients from the mother towards the fetus and into the colostrum and milk[16]. After calving, with a high yield of milk, the nutrient intake of dairy cows is large under the need to supply the output of milk, resulting in a negative nutrient balance that requires the mobilization of body reserves. The metabolic diseases fatty liver and ketosis are due to the extent of glucose deficit that induces the excessive mobilization of body fat. In addition, during the perinatal period, the dry matter intake of dairy cows is reduced due to the diminution in rumen volume induced by the growth of the fetus and other hormonal changes[17]. The high energy demands of lactation, coupled with a reduction in the dry matter intake around calving, means that the majority of dairy cows enter the state of NEB in early lactation[18]. Cows showing excessive NEB utilize their body fat as a source of energy to maintain the rapidly increasing milk yield, which leads to excessive body fat mobilization, ketosis, and fatty liver syndrome. Metabolic or infectious diseases, including fatty liver syndrome and ketosis, affect dairy cow production during the perinatal period[19] and further impact the welfare, productive lifespan, and economic outcomes of dairy cows[16].

Strategies for supplying energy are one way of mitigating NEB. Based on a large amount of data on cattle and other species, glucose is known to reduce the fatty acids mobilized from adipose tissue [20]. The failure of cows to meet their glucose demands for lactation leads to an impaired immune response and an increased risk of disease that may affect milk production and profitability[21]. For cow rearing, the dietary energy can be improved through fat or concentrate supplementation to alleviate NEB, but excess fat supplementation inhibits rumen microbial growth, decreases the rumen pH value, and increases the rate of subclinical ruminal acidosis[22].

2.4. Application as a Source of Calcium to Prevent Milk Fever in the Perinatal Period

Milk fever is a metabolic disease characterized by clinical symptoms due to a reduction in the blood calcium concentration (hypocalcemia) during peripartum, which affects high-yielding multiparous cows[23]. It is one of the most common periparturient abnormalities afflicting dairy cows[24]. Milk fever can decrease the dry matter intake, milk production, and reproductive performance and increase the risk of secondary diseases, such as ketosis, a retained placenta, displaced abomasum, mastitis, and the incidence of dystocia and uterine disorders[25][26]. When the concentration of blood calcium falls below a critical threshold, it results in clinical and subclinical milk fever[26][27]. Serum calcium levels of 2 and 1.4 mmol/L have been proposed as thresholds of subclinical and clinical hypocalcemia, respectively, but the external signs may not be displayed in dairy cows[28]. Improving the mobilization of calcium from bone and the absorption of calcium from the diet are two major processes that prevent the decrease in blood calcium in dairy cows. The mobilization of calcium from bone can be accomplished by feeding a calcium-deficient diet or negative dietary cation-anion difference in the pre-calving period[29]. In addition, the infusion of 5-hydroxytryptophan can also improve blood calcium concentrations around parturition[30].

2.5. Application in Dairy Calves to Regulate Rumen Development or Improve Growth

The rumen is a vital digestive organ that plays a key role in the growth, production performance, and health of ruminants. Therefore, promoting rumen development has always been a key target of calf nutrition[31]. The papilla length of the rumen is the most important factor for the evaluation of rumen development[31]. Rumen epithelium development plays a very important role in the absorption, metabolism, and transportation of volatile fatty acids (VFAs). VFAs, such as propionic and butyric, provide the main chemical stimuli for the proliferation of the rumen epithelium if the amount is sufficient[32], indicating that additives of propionate may be used in calf feed as rumen growth promoters. As one kind of propionate, the additive of calcium propionate may also stimulate the epithelium development of calves. G protein-coupled receptors (GPRs) are integral membrane proteins which are activated by an external signal in the form of a ligand or other signal mediator[7]. Zhang et al.[7] found that calves supplemented with 5% calcium propionate (mixed in milk replacer and starter ration) in the diet had a greater rumen papillae length and improved mRNA expression of G protein-coupled receptor 41 (GPR41), GPR43, and cyclin D1 after feeding for 160 days, which indicated that propionate acted as a signaling molecule to improve the rumen epithelium. Propionate can be converted into glucose in the liver, and higher glucose concentrations mean that high energy can be used to increase the body weight of calves. Zhang et al.[33] pointed out that there were no differences in DMI with the different feeding levels of calcium propionate, but the addition of calcium propionate improved the growth performance and gastrointestinal tract traits of Jersey calves; thus, adding 10% calcium propionate to the feed before 90 days and 5% for 90 to 160 days was beneficial for calves. Cao et al.[34] also verified that calcium propionate supplementation (5% dry matter) can improve body weight gain and rumen growth both pre- and postweaning. Monensin is an ion carrier that can change the number of rumen microorganisms, reduce the amount of methane production, increase propionate in the rumen, decrease the intake of dry matter, and improve the efficiency of milk production and weight gain of dairy cows[35]. However, as an antibiotic, the use of monensin in animal feed as a growth promoter may enhance the risk of antibiotic-resistant strains, so it is important to seek alternatives to this compound[36]. Ferrerra and Bittar[37] revealed that employing calcium propionate as an additive in starter feeds of calves resulted in an equal animal performance before and after weaning in comparison to that of sodium monensin, which suggests that sodium monensin may be replaced by calcium propionate. Therefore, calcium propionate can be used as a good additive to promote the rumen development and growth of dairy calves.

3. Limitation of Calcium Propionate in Application

However, the use of calcium propionate in dairy cows should be controlled at appropriate doses because an overdose has a hypophagic effect in ruminants[38] and may decrease the DMI of dairy cows. It has also been reported that calcium propionate induces a negative causation state while reducing the feed intake in broiler breeders[6], rats[39], and steers[40] at high doses. The metabolic feedback theory contends that when the absorption of nutrients, principally energy and protein, exceeds the requirements, negative metabolic feedback impacts DMI. Calcium propionate is an important energy provider when working as an additive to alleviate NEB in dairy cows. Therefore, propionic acid is the fuel most likely to stimulate satiety and reduce the feed intake in dairy cows[41] because it has a high energy concentration. Propionic acid can stimulate the oxidation of acetyl CoA in the liver[42]. According to the oxidation theory, the oxidation of fuels in the liver can stimulate satiety by transmitting signals via hepatic vagal afferents to feeding centers in the brain[43]. Oba and Allen[44] confirmed that a propionate infusion linearly decreased the DMI of dairy cows at higher doses. When feeding calcium propionate at a high level, the TCA cycle intermediates increase, stimulating the oxidation of acetyl CoA, likely affecting the feeding behavior and satisfaction. However, propionate had a smaller hypophagic effect at low plasma glucose concentrations and had a greater hypophagic effect at elevated plasma glucose concentrations[45]. Therefore, when appetite reduction occurs in cows, the supply of calcium propionate suppresses the requirement for gluconeogenesis. However, the maximum dose available in cows remains to be determined.

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