Glycerol and Other Energy Sources for Metabolism and Production of Transition Dairy Cows

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Introduction

Feeding the dairy cow around the time of calving poses unique nutritional challenges. Feed consumption during the week prior to calving declines 30% (Bertics et al., 1992), and feed intake is decreased compared with nutritional needs until 3 to 5 weeks after calving. During this time, the cow is in a negative energy balance with energy output in the form of milk exceeding energy intake. The single most important nutrient required for milk synthesis is glucose, yet nearly all glucose consumed by the dairy cow is degraded in the rumen to volatile fatty acids which are absorbed and delivered to the liver. The liver is responsible for converting propionate from glucose and starch fermentation in the rumen, glucogenic amino acids, and glycerol from adipose triglycerides into glucose which is exported and used primarily for milk synthesis in the mammary gland. When feed consumption, or supply of glucose precursors is insufficient to satisfy glucose demands for milk synthesis, the dairy cow mobilizes large amounts of body fat. When the delivery of mobilized body fat exceeds the liver’s ability to process and export it, the fat accumulates in the liver. The accumulation of fat within the liver results in impaired liver function leading to decreased blood glucose, increased production of ketone bodies, and ketosis.

Because of inability to overcome the intake depression observed around calving, dairymen have adopted the use of oral drenches and pastes as a means to deliver glucose precursors, such as calcium-propionate and propylene glycol. It has been known since the 1950’s that, when drenched, glycerol is an effective treatment for lactation ketosis in dairy cattle and because glycerol enters into the metabolic pathway much closer to glucose than do other glucose precursors, it may be more efficacious. Johnson (1954) reported the oral administration of 2000 grams of glycerol was the most effective means of supplying large quantities of glucose when compared with propylene glycol; however, until recently with the availability of glycerol from biodiesel production, its use was cost prohibitive. Because of past cost of glycerol, data regarding the use of glycerol for treatment of ketosis is largely absent.

As the demand for renewable energy resources, such as soydiesel, continues to rise, it is likely that glycerol will become an affordable ingredient in dairy cow diets. Glycerol could be the prophylactic of choice for treating and preventing ketosis as well as energy supplement in dairy cow diets.

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Glycerol

Background

Glycerol (glycerin) is a colorless, odorless, hygroscopic, sweet tasting, viscous liquid that is a by product of biodiesel production (Donkin and Doane, 2007). During biodiesel production fatty acids are hydrolyzed from the glycerol backbone of the triglyceride molecule by a transesterification process using methanol. After separation of the fatty acid esters, glycerol is removed containing excess methanol and salts from the reactions. Separation or purification of the glycerol can be variable depending upon the plant and the processes used. The potential range of values of contaminants is listed in Table 1.

Table 1. Composition of glycerol depending upon purity (Schröder and Südekum, 1999).

<table>
<thead>
<tr>
<th>Purity of glycerol</th>
<th>Low</th>
<th>Medium</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water, %</td>
<td>26.8</td>
<td>1.1</td>
<td>2.5</td>
</tr>
<tr>
<td>Glycerol</td>
<td>63.3</td>
<td>85.3</td>
<td>99.8</td>
</tr>
<tr>
<td>Ether extract</td>
<td>0.71</td>
<td>0.44</td>
<td>n.a.</td>
</tr>
<tr>
<td>P</td>
<td>1.05</td>
<td>2.36</td>
<td>n.a.</td>
</tr>
<tr>
<td>K</td>
<td>2.20</td>
<td>2.33</td>
<td>n.a.</td>
</tr>
<tr>
<td>Na</td>
<td>0.11</td>
<td>0.09</td>
<td>n.a.</td>
</tr>
<tr>
<td>Pb</td>
<td>0.0003</td>
<td>0.0002</td>
<td>n.a.</td>
</tr>
<tr>
<td>Methanol</td>
<td>26.7</td>
<td>0.04</td>
<td>n.a.</td>
</tr>
</tbody>
</table>

1 Concentrations of cadmium, mercury and arsenic were below the detection limit.
2 Not analysed.

Yield of glycerol from this process is approximately 1 unit of glycerol for each 10 units of biodiesel produced. With projected annual production of over 2.2 billion gallons of biodiesel by the end of 2008, about 220 million gallons of glycerol of 80% purity will become available annually.

Glycerin is generally recognized as safe when used in accordance with good manufacture and feeding practices (FDA, 2007, 21 C.F.R. 582.1320), though concerns have been expressed relative to contaminant levels in crude glycerol from residual methanol. The methanol content of crude glycerol should be less than 0.5%. A recent regulatory letter issued by FDA indicates that methanol levels higher than 150 ppm could be considered unsafe for animal feed (Donkin and Doane, 2007). The Office of the Texas State Chemist has established guidelines for labeling with minimal levels of glycerol and maximal levels of moisture, sulfur, ash and methanol. Methanol is not to exceed 1% in crude glycerol targeted for ruminants (Feedstuffs, 2007).
**Fermentation Characteristics**

Glycerol has been determined to be rapidly fermented by ruminal microbes. Garton et al. (1961) conducted in vitro incubations of glycerol and found that at 2 hours, nearly 25% of the glycerol had disappeared and by 8 hours nearly 90% of the glycerol was undetectable. Wright (1969) determined fermentation end-products of glycerol in vitro and found glycerol was fermented to 47.6, 20.8, 5.7, and 52.1% as acetate, propionate, butyrate, and carbon dioxide, respectively. More recent work by Remond et al. (1993) demonstrated that glycerol addition decreased pH much greater in fermenters fed starch when compared with addition to fermenters fed cellulose. Furthermore, the addition of glycerol led to a volatile fatty acid (VFA) mixture rich in butyrate which became as high as 31% of the molar proportion of VFA. According to data from Remond, butyrate molar percentages were higher in fermenters fed starch versus those fed cellulose. Results of fermentation studies both in vitro and in vivo indicate that glycerol is rapidly fermentable and, depending on the cows diet, will increase propionate and butyrate within ruminal fluid.

**Feeding Studies**

Glycerol as a feed supplement preventative for ketosis in dairy cows was evaluated by Fisher et al. (1973). Fifty-two Holstein cows were randomly assigned at calving to concentrates supplemented with 3% propylene glycol, 3% glycerol, 6% glycerol, or a control containing no supplement over an 8 week period. Cows fed the glycerol supplemented at 6% lost less body weight and remained in a more positive energy balance than those treated with the other treatments. Because the treatment differences in metabolites and performance were quite minimal, Fisher et al. (1973) concluded that glycerol’s effectiveness in the feed as an antiketogenic agent was questionable.

Schröder and Südekum (1999) determined the suitability of glycerol as an energy source in ruminant diets. Using wethers fed low- and high-starch concentrates, they added glycerol at 10, 15, or 20% of diet dry matter. With a low-starch concentrate diet, they observed no effect on digestibilities of organic matter, starch, and cell-wall components. Feeding the same concentrations of glycerol in high-starch concentrate diets resulted in a decrease in cell-wall digestibility with no effect on the digestion of organic matter or starch. It appears that glycerol would act similar to a carbohydrate (vs. a fat) in the rumen when formulated into a typical high forage, dairy diet. The authors determined the energy density of glycerol to be 0.90 to 1.03 Mcal/lb NE\textsubscript{L}.

Schröder and Südekum (1999) also used four, ruminally cannulated steers to evaluate ruminal effects of feeding glycerol. Steers consumed an average of 29.5 lb/d, of which 4.6 lb/d of starch for those fed control diets was substituted with 2.4 lb/d of glycerol and 3.1 lb/d of starch for steers fed treatments. Feeding glycerol did not affect diet digestibility, but decreased the acetate:propionate ratio, increased ruminal butyrate concentrations, and stimulated more water intake. These changes would be beneficial to the dairy cow because 1) increasing ruminal propionate would increase the supply of this gluconeogenic substrate to the liver, 2) increasing ruminal butyrate would support the growth of the ruminal epithelial tissue and perhaps increase nutrient
absorption from the rumen as indicated by Dirksen et al. (1985), finally and 3) increasing water intake would supply the mammary gland with the water necessary for milk synthesis.

Researchers at Purdue (Donkin and Doane, 2007) recently fed 0, 5, 10, and 15% glycerol (99.5% pure glycerol) of diet DM to lactating dairy cows replacing corn with glycerol and corn gluten feed. Feed intake was decreased with 15% glycerol during the first 7 d of the experiment but recovered thereafter. Milk production and composition was not affected other than MUN was decreased by glycerol. Cows fed 15% glycerol gained more weight after 8 wk on the diet than did cows fed other treatments. Energy calculated for the diets were 0.70, 0.70, 0.71, and 0.72 Mcal/lb and were not statistically different. The researchers concluded that glycerol can be fed at up to 15% of diet DM to lactating dairy cows.

In a transition cow experiment at Pennsylvania State University, a dry glycerol product (food grade, 65% glycerol) was fed from calving until 21 DIM in an experiment with 39 multiparous Holstein cows (Chung et al., 2008). Two hundred fifty gram of product was fed supplying 0.36 lb/d of glycerol. Feed intake, milk yield and components, and serum insulin concentrations were not affected by dry glycerol. Glycerin-supplemented cows exhibited a more positive energy status during the second week of lactation as indicated by greater concentrations of plasma glucose, lower concentrations of plasma β-hydroxybutyrate (BHBA), and lower concentrations of urine ketones. Researchers observed no differences in feed intake or milk yield during the first 3 wk of lactation. There was a tendency toward greater milk yield for glycerin-supplemented cows during wk 6 of lactation (114 vs. 101 lb/d) after the supplementation period had ended, suggesting a potential benefit of dry glycerin on energy status and subsequent milk production.

Multiparous Holstein cows were used in an experiment at Cornell to determine the effects of method of delivery of glycerol on performance and metabolism during the transition period (Ogborne, 2007). Cows were fed either a control diet or a diet containing glycerol (5% of DM) starting 21 d prepartum. After calving, cows were fed glycerol at 3.3% of DM or given glycerol in a drench at 500 ml/d for the first 5 DIM. Feeding glycerol during the prepartum period increased DMI, but feeding glycerol during the postpartum period tended to decrease DMI. Drenching glycerol for the first 5 d of lactation decreased DMI. Milk yield was not affected by feeding or drenching glycerol. Glycerol fed during the prepartum period resulted in no significant effects on plasma glucose, NEFA or BHBA concentrations. There was a trend for an increase in BHBA concentrations for cows drenched with glycerol. Intensive blood sampling performed on d 5 post calving demonstrated that a 500 ml oral bolus of crude glycerin significantly decreased plasma NEFA concentration with no significant effects on plasma glucose, BHBA, or insulin. The researcher concluded that incorporation of glycerol into the diets of transition cows or the short-term oral drench of glycerol at calving resulted in few positive performance responses and modest effects on metabolism.
Researchers at SDSU have been experimenting with glycerol in dairy cow diets since 2002. The first experiment was designed to test glycerol as a TMR top-dress for its ability to prevent ketosis (DeFrain et al., 2004). Twenty-one multiparous and nine primiparous Holstein cows were fed diets with topdresses of 1) 2 lb of corn starch, 2) 1 lb of corn starch + 1 lb of glycerol, or 3) 2 lb of glycerol. Treatments were fed from 21 d prepartum until 21 d after calving. Dosages of glycerol were selected based upon amounts shown to be effective in drenching studies (Goff and Horst, 2001). Treatments were topdressed, and hand-mixed into the upper 1/3 of the daily ration. Prepartum DMI was greater for control cows compared with those fed glycerol (29.3, 23.7, and 24.8 ± 1.1 lb/d, for 0, 1, and 2 lb of glycerol respectively). Prepartum plasma glucose, insulin, BHBA, NEFA, and ruminal VFA profiles were not affected by treatments. Rumen fluid collected postpartum showed cows fed glycerol had greater total VFA, greater molar proportions of propionate, and a decreased ratio of acetate to propionate. Butyrate tended to be greater for cows fed glycerol postpartum. Glucose concentrations in plasma were actually greatest for cows fed the control diet compared with those fed glycerol discounting the perception of the gluconeogenic effects of glycerol. Dry matter intakes, body weight, body condition, and liver lipid during the first 21 DIM were similar among treatments. Plasma NEFA and BHBA were decreased for cows fed 2 lb/d of glycerol at 7 DIM, but this effect disappeared by 14 DIM and at 21 DIM, when BHBA was greatest in cows fed glycerol. There were no cows that exhibited signs of ketosis on any of the treatments. Yield of energy-corrected milk during the first 70 DIM tended to be greatest for cows fed the control diet. Cows fed glycerol had decreased MUN concentrations. Our conclusion was that increased energy in the glycerol supplemented diets may have been beneficial to the cows, but feeding glycerol did not provide an increase in gluconeogenic precursors.

Because of results from the DeFrain experiment, it was decided to test glycerol at similar feeding amounts in mid-lactation cows as an energy supplement (Linke et al., 2004). Six primiparous Holstein and six primiparous Brown Swiss cows (192 DIM; SD ± 150) were assigned to one of three diets in a Latin square with four week periods. The diets were: 1) Control diet containing no glycerol, 2) Low glycerol with 1.1 lb of glycerol, and 3) High glycerol with 2.2 lb of glycerol. Rumen VFA profiles showed that molar proportions of acetate were not changed in rumens of cows fed glycerol. Propionate tended to be increased for cows fed glycerol, and butyrate was increased linearly as the amount of glycerol fed increased. Dry matter intakes, milk yield, and 4% FCM yield were not significantly changed by glycerol supplementation. Feed efficiency, however, was increased by glycerol supplementation with milk to feed ratios of 1.46, 1.59, and 1.60 lb of FCM/lb of DMI for 0, 1.1, and 2.2 lb of glycerol, respectively. Milk composition was not changed except, as before, MUN concentrations were decreased with the addition of glycerol. We surmised by the increased feed efficiency and decreased MUN that the addition of glycerol may have improved rumen microbial efficiency. Based upon differences in feed efficiency, we calculated the energy value of glycerol to be about 20% greater than that of corn yielding an NE_{L} of about 1.05 mcal/lb, similar to the estimate by Schröder and Südekum (1999).
Drenching Studies

Goff and Horst (2001) evaluated an oral glycerol drench as an aid in the treatment of ketosis in two experiments. In the first, cows were administered 1, 2, or 3 L of glycerol via esophageal pump. Thirty minutes after dosing, concentrations of blood glucose increased by 16, 20, and 25% for cows treated with 1, 2, or 3 L, respectively. Similar to observations by Schröder and Südekum (1999), Goff and Horst (2001) indicated that drenching with glycerol had no affect on ruminal pH. In the second experiment, two cows diagnosed with clinical ketosis were treated with 1 L of a glycerol drench. Both cows responded with higher concentrations of glucose in blood, decreased urinary ketone body excretion, and an increased milk production. These data further support the potential role glycerol could play as a glucose precursor in diets for transition dairy cows.

Researchers at Iowa State University have been investigating the usefulness of drenching glycerol in combination with glucagon, a hormone to stimulate gluconeogenesis, in prevention of ketosis and fatty liver (Osman et. al., 2006) Five hundred milliliters of glycerol was administered daily for 14 d after calving to 12 cows with or without glucagon treatment. Glucagon plus glycerol treatment increased plasma glucose concentrations on d 1, 7, and 13 postpartum by more than 40 mg/dL greater than that of the control group and maintained it at an elevated concentration for a longer time than did other treatments. Glycerol alone increased blood glucose on d 7 and 13. Plasma NEFA concentration was decreased by glucagon plus glycerol and glycerol treatments on all three sampling days. Glycerol treatment maintained plasma NEFA low for longer time than did glucagon plus glycerol treatment on d 7 and 13 postpartum. Researchers at ISU determined drenching glycerol was an effective tool for prevention of fatty liver and ketosis, particularly when combined with hormonal therapy.

SDSU - Drenching vs Feeding Responses

To better explain discrepancies in results obtained from feeding and drenching studies, Linke at SDSU used four high producing Holstein dairy cows in a Latin square with 1-wk periods to evaluate the effect of methods of oral delivery versus feeding of glycerol on ruminal VFA and plasma concentrations of glucose, BHBA, NEFA, and insulin. Cows were 132 DIM and producing an average of 132 lb of milk/d. To create a mild negative energy balance, all cows were fed only grass hay for ad libitum consumption during 12 h before the experiment. This regimen was successful at elevating plasma NEFA concentrations similar to that observed in cows during the first 2 d after calving (Figure 1). At 0800 h the next morning (time 0) all cows were fed 11 lb of cracked corn. Refeeding dropped NEFA concentrations in all cows. Treatments administered at time 0 were: 1) control, corn alone with no glycerol; 2) 2.2 lb of glycerol solution (80% glycerol) added to the corn; 3) 2.2 lb of glycerol solution in 1.1 qt of water and delivered as oral drench with a drenching bottle; and 4) 2.2 lb of glycerol in 2.5 gal of water and delivered into the rumen via a McGraff pump and an esophageal tube. Blood samples were collected at -1, -0.5, 0, 0.25, 0.5, 0.75, 1, 1.5, 2, 4, 6, 8, 12, and 24 h after administering glycerol. Rumen samples were collected at 0, 2, 4, and 6 h. After administration of glycerol, concentrations of acetate decreased in
rubens of all cows given glycerol regardless of method of delivery (Figure 2). Likewise, propionate and butyrate were increased by glycerol in all forms with peak concentrations at 4 h (Figures 3 and 4). In plasma, concentrations of glucose were increased for cows that were drenched with glycerol or received tube delivery of glycerol into the rumen compared with both the control and feeding glycerol (Figure 5). Glucose reached peak concentrations at 1.5 and 3 h for drenching and tubing, respectively. Glucose response expressed as area under the curve over baseline for 6 h was greater for drenching or tube delivery but not feeding glycerol compared with control. Insulin concentrations in plasma were also increased for drenching and tubing reaching peak concentrations at 1.4 and 1.1 h (Figure 6). Finally, the BHBA was increased in plasma of all cows receiving glycerol (Figure 7), reaching peak concentrations at 2.5, 2.4, and 1.6 for drenching, tubing, and feeding, respectively.

Conclusions from this research are that to be glucogenic, glycerol must either be delivered in water to associate with the liquid fraction of the rumen contents or be able to "bypass" the rumen in some form to be absorbed as glycerol and converted to glucose by the liver. Glycerol that is available to rumen microbes will be converted to propionic and butyric acids. The fraction converted to butyrate is metabolized to BHBA by the ruminal epithelium, thus glycerol that is fed is actually ketogenic rather than glucogenic.

**Comparison with Other Glucogenic Supplements**

**Propylene glycol (PG)**

Recently, PG has received the most scrutiny of the glucogenic supplements. Reported effects of PG are increased blood glucose (Studer et al., 1993; Grummer et al., 1994), increased insulin and lower NEFA (Studer et al., 1993; Grummer et al., 1994; Christensen et al., 1997), and lower BHBA (Studer et al., 1993; Grummer et al., 1994; Fisher et al., 1971a). Notable findings are presented below.

Fisher et al. (1971b) studied the effects of feeding glucose precursors on feed intake and determined their mode of action. Four Holstein cows were arranged in a Latin square design so that each cow was able to consume each of the three treatments under two feeding conditions: ad libitum (free-choice) and limited access. Treatments of glutamate, propylene glycol, and glycerol were mixed with the concentrate portion of the ration. Intakes of glutamate, propylene glycol, and glycerol averaged 432, 378, and 472 grams per day, respectively. Ruminal fluid from cows fed the propylene glycol-supplemented concentrate offered ad libitum contained significantly less butyrate than the other treatments and accordingly concentrations of BHBA in blood were decreased. From this, Fisher et al. (1971b) concluded that one of the modes of action for dietary propylene glycol was its tendency to reduce the production of ruminal butyrate, and accordingly the occurrence of ketosis. It was further concluded that because cows consumed more of the glycerol-supplemented concentrate, glycerol’s mode of action is primarily attributable to its ability to stimulate appetite and subsequently supply more glucogenic substrate. From these data, one
could conclude that feeding glycerol vs. propylene glycol could potentially improve intakes if delivered as a topdress.

In another experiment, dry multiparous cows were used to investigate the effects on intake, production, and metabolism of either a supplement containing 55% dry propylene glycol, a prilled fat supplement, or calcium soaps of fatty acid supplement (Moallem et al., 2007). Diets of cows in the PG group were supplemented with 500 g/d of dry PG until 21 DIM. Plasma glucose concentrations pre- and postpartum were greater for cows fed PG than for those fed fats, but were similar to those in the control group. No significant differences were observed in DMI, plasma glucose, NEFA, and BHBA concentrations between the control and PG groups.

Studer et al. (1993) drenched 1 kg of PG prepartum and observed increased blood glucose and insulin and decreased NEFA and BHBA prepartum and decreased NEFA and liver lipids postpartum compared with controls. Grummer et al. (1994) fed PG prepartum to heifers in a Latin square design and reported increased glucose and insulin and decreased NEFA and BHBA. As the dose was increased, the acetate to propionate ratio declined, indicating ruminal conversion of PG to propionate.

Christensen et al. (1997), using prepartum heifers with DMI restricted to 50% of ad libitum, evaluated PG delivered as a drench, in the concentrate, or TMR. Heifers fed PG showed decreased NEFA in blood, and insulin was elevated compared with controls. In the feeding study reported, Fisher et al. (1971a) observed a decrease of blood BHBA of dairy cows fed PG postpartum. Bahaa et al. (1997) induced postpartum ketosis via DMI restriction and reported no difference in effectiveness between oral PG and infused glucose. Emery et al. (1964) fed over 2000 g/cow/d of PG and saw no adverse effect. Emery concluded that PG was absorbed intact and not converted to propionate in the rumen. These workers summarized their research of over two years in three milking herds by reporting that oral PG decreased ketone bodies 75% of the time and increased milk 50% of the time. Fisher et al. (1973) observed no consistent effect of PG on DMI, body weight, or feed efficiency. Sauer et al. (1973) stated that PG fed at 3 and 6% of concentrate prepartum slightly increased milk production, had a tendency to depress butterfat, and markedly decreased the incidence of ketosis.

Bobe et al. (2004), conducted a review of preventatives for fatty liver and ketosis and reported that effectiveness of propylene glycol for increasing plasma glucose concentrations depends on the dosage and the mode of administration. Greatest response to PG is achieved when cows are given greater dietary concentrations dosages or when PG is administered as an oral drench (Pehrson, 1972; Christensen et al., 1997). Responses to feeding are related to changes in ruminal fermentation and VFA production in favor of propionate at the expense of acetate and butyrate (Pehrson, 1972; Christensen et al., 1997).

The use of PG as a drench and for extended periods should be approached with caution. High concentrations of propylene glycol appear toxic for some ruminal
bacteria species (Pehrson, 1972). It can also be toxic to the animal; a 1.8-kg dose of propylene glycol via a rumen tube or 2 to 3 L of glycerol administered orally can be neurotoxic (Johnson, 1954).

Propionic acid

Propionate as a feed additive has been reported to increase glucose (Baird et al., 1980; Shultz, 1958; Schmidt and Shultz, 1958) and decrease BHBA in blood (Goff et al., 1996; Schultz, 1958; Schmidt and Schultz, 1958). Propionate is the principle glucogenic VFA from the rumen and is estimated to be extracted from the blood by the liver with up to 95% efficiency (Bergman, 1990). Baird et al. (1980) showed that during glucose infusion, hepatic uptake of propionate in the lactating cow was efficient enough to account for the entire hepatic output of glucose. Propionate is also antiketogenic and has been documented to decrease liver oxidation of NEFA (Armentano et al., 1991; Jesse et al., 1986; Lomax et al., 1983). In the ruminant, propionate causes an increase in insulin in blood, but unlike other glucogenic substrates, efficiency of hepatic uptake is not decreased by insulin (Brockman, 1990).

Baird et al. (1980) infused propionate into lactating and dry cows and observed increased blood glucose in the cows, with no change in insulin, while in dry cows, propionate infusion had no effect on blood glucose, but increased insulin. Schultz (1958) reported that feeding 113 g of sodium propionate from 0-42 DIM significantly increased milk production and blood glucose at 21 and 35 DIM, and significantly lowered blood ketones at 7, 21, 35 and 49 DIM. Schmidt and Schultz (1958) fed 227 g of sodium propionate to 10 cows in a Latin square protocol switching treatments every 14 days. At 7 DIM, propionate-fed cows had greater concentrations of glucose and decreased ketones in blood. Milk production was identical between treatments, but butterfat was greater for controls (5.2 vs 4.2%) indicating greater mobilization of body fat. Schultz and Smith (1951) demonstrated in the goat that 15 g of oral propionate increased blood glucose 20% in 15 min, with return to baseline in 30 min. If dripped into the rumen, blood glucose peaked in 30 min. Goff et al. (1996) reported a tendency for calcium propionate dosed Jersey cows to have decreased blood BHBA at 2 and 10 DIM.

Propionate decreases feed intake in most but not all studies (Oba and Allen, 2003). Higher dosages of sodium propionate (0.5 kg) can cause diarrhea and increase water intake because sodium ions alter electrolyte concentrations in blood (Shaw, 1956; Pehrson, 1972; Oba and Allen, 2003). Therefore, the daily dosage of sodium propionate to treat ketosis and fatty liver should be increased slowly over days of administration (Schultz, 1952).

Feeding Propionate at SDSU

To investigate the usefulness of combining dietary propionate with fat, 40 multiparous Holstein cows were fed 0.7 lb/d of corn starch as a control, 0.25 lb of propionate as calcium propionate, 0.25 lb of propionate with 0.20 lb of Ca salts of fatty acids, or 0.40 lb of propionate and 0.33 lb of CA salts of fatty acids (DeFrain et al., 2005). Treatments were hand-mixed into the upper 1/3 of the TMR from 2 wk pre-
through 3 wk postpartum. Pre- and postpartum DMI did not differ among treatments. Cows fed the greater level of propionate and fat consumed 2 kg/d less DM during the 2\textsuperscript{nd} wk of lactation compared with other treatments. Milk yields were not significantly affected by treatments. Milk fat yield from cows fed propionate alone tended to be greater than those fed propionate plus fat indicating greater mobilization of body fat. Plasma glucose, insulin, and BHBA were not affected by treatments. The treatment with the greatest amount of propionate and fat decreased NEFA in plasma over all times measured during the first 21 DIM. Relative to other treatments, feeding propionate and fat at the greater level in this experiment improved energy balance postpartum as evidenced by decreased concentrations of plasma NEFA. Propionate alone at 0.25 lb/d was not effective at improving energy balance.

**Glucose (dextrose)**

Bobe (2004) summarized effects of glucose infusions with the following: “The efficacy of intravenous infusions of glucose to prevent ketosis is low (Gruchy et al., 1963). Blood glucose is increased for only 80 to 100 min after infusion is stopped (Shaw, 1956). Some cows do not react to glucose infusions, because they have developed insulin resistance (Ohtsuka et al., 2001). Compounds other than glucose that have been tried include intravenous administrations of 250 g of carbohydrates such as fructose, mixtures of glucose and fructose all of which have some potential compared with glucose alone.”

**Comparison of Metabolism**

Glycerol is an efficient glucogenic substrate because it enters the gluconeogenesis pathway at the triose phosphate level and, therefore, is not affected by two of the rate-limiting gluconeogenic enzymes. Logically, the dairy cow in negative energy balance has pathways activated for utilization of glycerol liberated from mobilization and hydrolysis of triglycerides from body fat. This activity is dependant upon absorption of glycerol rather than fermentation to propionate and butyrate, which is somewhat counterproductive as the ketogenic nature of butyrate. If absorbed intact, glycerol is a highly efficient glucogenic substrate.

Propylene glycol has been proven efficacious for treatment of ketosis. Its glucogenic activity will occur whether it is fermented to propionate in the rumen or absorbed and metabolized by the liver intact. Hepatic metabolism of propylene glycol is dependent upon the activity of lactate dehydrogenase with conversion to pyruvate. Pyruvate will replenish citric acid cycle intermediates allowing for increased gluconeogenesis.

Propionate is the primary glucogenic substrate in the dairy cow, thus pathways for use of this glucose precursor are stimulated in the dairy cow. Conversion of propionate to glucose depends upon conversion to propionyl co-A and to succinyl co-A before entry into the citric acid cycle and subsequently into the gluconeogenic pathway by the activity of phosphoenol pyruvate carboxykinase.
Taken together, each of these compounds has a different route for conversion to glucose. Thus combination therapies may be best suited for taking full advantage of the liver’s ability to make glucose. Indeed, a study by Pehrson (1972) showed that a combination of 75 g of sodium propionate, 125 g of glycerol, and 100 g of propylene glycerol proved to be effective for treatment of ketosis.

**Conclusions and Recommendations**

Use of glycerol in dairy cow nutrition programs will depend upon desired outcomes. When fed, glycerol provides a supplement that is essentially “pure energy.” It will enhance fermentation characteristics and possible feeding efficiencies. Attributes that make glycerol a suitable feed additive include the following:

- Provides “stick” to complete diets
- Enhances palatability at low amounts
- Increases water consumption
- Aids in pelleting – may act as antifungal
- Serves as antifreeze in liquid feeds – increased flowability
- Aids in keeping materials in suspension in liquids

As a preventative or treatment for ketosis, glycerol should be delivered in a form to associate with the liquid fraction in the rumen. Goff et al. (2001) showed that the ideal concentration for drenching will be about 1 L (2.2 lb /d). Daily drenching for up to 14 d has proven most effective at prevention, though treatments as low as 2 times during the first week of lactation have been effective at decreasing incidence and severity of ketosis. For treatment of severe ketosis, we have had success with alternating glycerol and propylene glycol drenches, thus avoiding the negative effects of overdosing with PG and taking advantage of the alternative pathways of glucose production.

**References**


Figure 1. Concentrations of NEFA in plasma of cows receiving glycerol via: No glycerol (diamonds), glycerol via drench (open squares), fed glycerol (triangles), and tubed glycerol (open circles).

Figure 2. Molar percentages of acetate in rumen fluid of cows receiving glycerol via: No glycerol (diamonds), glycerol via drench (open squares), fed glycerol (triangles), and tubed glycerol (open circles).

Figure 3. Molar percentages of propionate in rumen fluid of cows receiving glycerol via: No glycerol (diamonds), glycerol via drench (open squares), fed glycerol (triangles), and tubed glycerol (open circles).

Figure 4. Molar percentages of butyrate in rumen fluid of cows receiving glycerol via: No glycerol (diamonds), glycerol via drench (open squares), fed glycerol (triangles), and tubed glycerol (open circles).
Figure 5. Concentrations of glucose in plasma of cows receiving glycerol via: No glycerol (diamonds), glycerol via drench (open squares), fed glycerol (triangles), and tubed glycerol (open circles).

Figure 6. Concentrations of insulin in plasma of cows receiving glycerol via: No glycerol (diamonds), glycerol via drench (open squares), fed glycerol (triangles), and tubed glycerol (open circles).

Figure 7. Concentrations of BHBA in plasma of cows receiving glycerol via: No glycerol (diamonds), glycerol via drench (open squares), fed glycerol (triangles), and tubed glycerol (open circles).