

*Review*

# Assessing the Impact of Dietary Cation-Anion Differences on Productive and Reproductive Efficiency in Animal Agriculture

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Various nutritional tools have been used to improve the productive and reproductive performance of animals, among which difference between certain minerals, called dietary cation anion difference (DCAD) plays a pivotal role. Low or negative DCAD diets reduce blood pH and  $\text{HCO}_3^-$  and animal becomes acidotic. This improves Ca absorption from the intestinal tract. It also induces mobilization of Ca from bones which improves Ca status of the animal, thus preventing the occurrence of milk fever at the time of parturition. This may increase milk production and health in subsequent lactation. However, animals fed high DCAD diets before parturition may suffer from milk fever. Milk fever affected animals have increased plasma cortisol level that causes immunosuppression at calving. It is also positively associated with other problems like retained placenta, mastitis and udder edema. On the other hand, feeding high DCAD diet results in increased ruminal pH which is pre-requisite for optimal microbial activity as well as improving the feed intake of the animal. Improved dry matter intake (DMI) is positively correlated with milk yield by providing precursors for various milk constituents. High DCAD diet results in increased milk fat percent due to shifting of ruminal volatile fatty acid production towards acetic acid and butyric acid. It also improves energy balance of the animal which causes increased blood flow towards ovaries and increased progesterone synthesis and follicular development due to positive association between energy balance and postpartum ovulation, which leads to improved reproductive performance of the animal. While feeding low DCAD diet reduces feed intake which causes negative energy balance in early lactating animals that lessens conception rate and increases services per conception. In conclusion, feeding low DCAD diets prepartum prevents the occurrence of milk fever via improving Ca status while feeding high DCAD diets results in improved productive and reproductive performance in lactating animals.

**Key words:** Feed intake, milk yield, reproductive performance, hypocalcaemia, dietary cation anion difference.

## INTRODUCTION

Formulation of a ration according to physiological stage of animals plays a pivotal role in optimizing their productive and reproductive performance. By providing balanced ration, milk production can be improved. At the same time, it helps in reducing reproductive disorders

(Osmanu, 1979). This is especially important one month before parturition and during early lactation. Just after parturition, there is excessive loss of calcium (Ca) from the plasma pool to the formation of colostrum which must be replenished by increasing intestinal Ca absorption and bone Ca resorption. If the loss of Ca is not replaced, animal may suffer from milk fever. Animals with milk fever may result in depressed feed intake and decreased milk production (Block, 1984). Milk fever may also lead to other disorders like dystocia, retained placenta, ketosis, metritis, displaced abomasum and mastitis (Gröhn et al., 1989; Wilson and Stevenson, 1998) which affect the health of animal. During early lactation, animal requirement for nutrients increases manifolds due to increased milk

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**Abbreviations:** DCAD, Dietary cation anion difference; VFA, volatile fatty acids, NDF, neutral detergent fiber; ADF, acid detergent fiber; OM, organic matter; CP, crude protein; IGF-I, insulin like growth factor; DMI, dry matter intake; PTH, parathyroid hormone.

synthesis. Reduced feed intake during this period may lead to negative energy balance which affects animal productive and reproductive performance (Stevenson and Britt, 1980; Butler et al., 1981). Concentrate feeding is practiced to meet the nutrient requirement which decreases ruminal pH due to increased volatile fatty acids (VFA) production. It also depresses biosynthetic activities in mammary glands aimed to synthesize milk fat due to decreased acetate: propionate (Doreau et al., 1999; Bauman and Griinari, 2003).

Various nutritional tools have been used to combat these problems. Among these, manipulation of minerals in ration formulation is significant. Minerals are necessary to carry out various biological functions in animal's body. These may carry positive (cations) or negative (anions) charge. The difference between certain cations ( $\text{Na}^+$  and  $\text{K}^+$ ) and anions ( $\text{Cl}^-$  and  $\text{S}^{--}$ ), in milliequivalents, is usually referred to as dietary cation anion difference (DCAD). The concept of DCAD is based upon the maintenance of desirable acid base status. Dishington (1975) and Mongin (1981) were the first who used the concept of DCAD in livestock and poultry, respectively. Since then, it has been used in prepartum and postpartum animals due to its beneficial effect.

The strong cations and anions determine the body fluid pH (Stewart, 1981) and are used to calculate DCAD which is given as:

Cations – Anions = DCAD in milliequivalent per kilogram of dry matter (mEq/kg of DM).

Where

$\text{mEq} / 100 \text{ g} = [(\text{milligrams}) (\text{Valence}) / (\text{g atomic weight})]$

The equations below are mainly used to calculate DCAD

$(\text{Na}^+ + \text{K}^+) - (\text{Cl}^- + \text{S}^{--}) = \text{mEq}/100 \text{ gm of DM} \dots\dots\dots$   
(Tucker et al., 1992)

$2(\text{Na}^+ + \text{K}^+) - (\text{Cl}^-) = \text{mEq} / 100 \text{ gm of DM} \dots\dots\dots$   
(Mongin, 1981)

The DACD may also be calculated by using the dietary percent of respective minerals (on DM (dry matter) basis) with the following equation (Olson, 1991; West, 1993; Oetzel, 1993):

$\text{DCAD} = [(\text{Na}\% / 0.023) + (\text{K}\%/0.039)] - [\text{Cl}\% / 0.0355] + (\text{S}\% / 0.016)] \text{ mEq}/100 \text{ g DM}$

Various salts have been used to attain the desired level of DCAD. For example,  $\text{NaHCO}_3$ ,  $\text{KHCO}_3$  and  $\text{Na}_2\text{CO}_3$  are used to increase the DCAD level while calcium chloride ( $\text{CaCl}_2$ ) and magnesium sulphate ( $\text{MgSO}_4$ ) are used to decrease DCAD level. Sodium (Na), potassium (K) and chloride ( $\text{Cl}^-$ ) are believed to be completely absorbed,

where as sulfate is absorbed up to 60% in early, mid and late lactation as well as during the dry period (Delaquis and Block, 1995a, b, c).

DCAD affects acid base status and Ca metabolism of the animal. Low DCAD diet results in decreased blood and urine pH and depressed bicarbonate ( $\text{HCO}_3^-$ ) concentration (Block, 1994). The decrease in blood  $\text{HCO}_3^-$  and urine pH works as a compensatory mechanism. It also increases blood  $\text{H}^+$  concentration which induces slight acidosis that improves Ca absorption (Moore et al., 2000). Slight metabolic acid situation due to feeding low DCAD diets in prepartum animals has been reported to stimulate parathyroid hormone (PTH) production which accelerates absorption of  $\text{Ca}^{++}$  from intestine. This plays key role in reducing the occurrence of hypocalcemia (Block, 1984; Fredeen et al., 1988b; Espino et al., 2003). Cows recovered from milk fever have 8 times more chances of ketosis, mastitis and uterine prolapse compared to non-milk fever cows (Curtis et al., 1983). On the other hand, feeding high DCAD diet during early lactation improves dry matter intake (DMI) (Tucker et al., 1988; Delaquis and Block, 1995b) and milk production (Hu and Murphy, 2004) by improving ruminal pH that favors optimum microbial activity (Roche et al., 2005). It can also improve the reproductive performance of the animal by improving the energy status.

Keeping in view the significance of DCAD on acid base status and animal productive and reproductive performance, the current attempt has been made to review and present the available possible information in lactating and gestating animals.

## NUTRIENT INTAKE

Hu and Murphy (2004) conducted a meta-analysis and observed a linear increase in DMI with increasing DCAD levels in the diet. They reported a positive correlation between DCAD and DMI. Similarly, findings were reported by Oetzel and Barmore (1993) who observed an increasing trend in DMI as DCAD was increased from – 109 to +313 mEq/kg DM. Hu et al. (2007) also supported these findings. Increased DMI at high DCAD diets might be due to increased rumen pH (Tucker et al., 1988; Sharif et al., 2009; Sharif et al., 2010) that makes the ruminal environment alkaline, which is pre-requisite for optimum ruminal microbial activity. Delaquis and Block (1995b) observed 15.2 and 16.2 kg/d DMI in early lactating cows fed 55.5 and 258.1 mEq/kg DCAD diets, respectively. Likewise, during mid lactation, DMI increased from 15.6 to 17.0 kg/d as DCAD level was increased from 140.2 to 372.7mEq/kg DCAD. They also recorded increased water consumption at high DCAD level in dairy cows during early and mid lactation. Similar findings were reported by West et al. (1992) who observed increased feed intake when DCAD level was increased from 12 to 46 mEq/100 g DM in heat stressed cows. However, Jackson et al.

(1992) reported a quadratic response in feed consumption in dairy calves fed diets containing DCAD 0, 21, 37 and 52 mEq/100 g DM. Minimum (3.79 kg/d) and maximum (4.41 kg/d) feed intake was observed in calves fed 0 and 37 mEq/100 g of DM, respectively, while a significant reduction (3.93 kg/d) was observed at 52 mEq/kg DM. This decrease in DMI with increasing DCAD might be attributed to the wide range (0 to 52 mEq/100 g of DM) of DCAD levels used in their study.

Spanghero (2004) reported a decrease in DMI by animals fed low DCAD diets. Similar findings have also been reported by Tucker et al. (1992) who determined the DCAD effect in heifers and mature cows. They observed decreased DMI in cows fed low DCAD diet. The plausible explanation for this decrease in DMI might be due to unpalatability of anionic salts (Goff et al., 1988; Shahzad et al., 2008a, b) used to reduce the DCAD level. Goff et al. (1991) also reported that feeding negative DCAD diets reduced feed consumption due to poor palatability of salts. Another plausible explanation might be that low DCAD induces slight metabolic acidosis, which reduces DMI (Block, 1994). These findings are consistent with other workers (Yen et al., 1981; Escobosa et al., 1984; Tucker et al., 1988; Sharif et al., 2009) who reported decreased DMI in cows with low DCAD diet when  $\text{CaCl}_2$  was used to attain the desired low DCAD level. Biological studies executed under different environment to know response of DCAD on ruminant animal performance reflects that the DCAD can enhance nutrients intake due to its favourable influence on rumen dynamics and blood chemistry. However, the extent of nutrients intake varies depending on the level of DCAD, diet composition, animal productive potential and environment.

## NUTRIENT DIGESTION

Influence of varying DCAD diets on nutrient digestibility was investigated by Delaquis and Block (1995a). They studied the effect of DCAD (481, 327 meq/kg of DM) on neutral detergent fiber (NDF) and acid detergent fiber (ADF) digestibilities in dry cows and reported that DCAD had non-significant effect on ADF and NDF digestibilities. In another study, Delaquis and Block (1995b) reported that during lactation period, DM digestibility was slightly higher in cows fed +55 compared to +375 mEq/kg DCAD diets, respectively. However, the difference was statistically non-significant. The NDF digestibility also remained unaltered by DCAD alteration. This might be attributed to the speculation that DCAD had no significant effect on ruminal fermentation pattern in lactating cows (Tucker et al., 1991).

Keeping in view the significance of sodium bicarbonate ( $\text{NaHCO}_3$ ) as cationic salt in DCAD studies, several researchers used this salt to divert the electrical composition of diet towards more alkaline to counteract

the slight ruminal acidosis which animals may experience when fed on nutrient rich diet. Canale and Stokes (1988) observed the influence of  $\text{NaHCO}_3$  supplementation on forage source and nutrient digestibility and reported that apparent dry matter digestibility of the corn silage based diet was greater than hay crop silage. The  $\text{NaHCO}_3$  supplementation improved the digestibility of NDF in both diets but did not significantly affect the digestion of other nutrients. These findings were consistent with other workers (DePeters et al., 1984; Eichelberger et al., 1985) who reported that buffer supplementation (0.25 to 1.2%  $\text{NaHCO}_3$ ) in alfalfa hay had no significant effect on nutrient digestion. Similarly, its supplementation in hay crop silage did not significantly affect nutrient digestion (Stokes and Bull, 1986). However, Rogers et al. (1985) reported that supplementation of  $\text{NaHCO}_3$  (1.4%) improved DM, organic matter (OM) and crude protein (CP) digestibilities in dairy cows fed alfalfa hay based diet. Stokes and Bull, (1986) also observed that supplementation of  $\text{NaHCO}_3$  in corn silage based diets enhanced the DM, OM, ADF, gross energy and cellulose digestibilities in early lactating cows. Other workers (Erdman et al., 1982; Snyder et al., 1983) also pointed out improved DM, OM, ADF and NDF digestibilities in dairy animals when  $\text{NaHCO}_3$  was supplemented in their diets. Rogers et al. (1982) observed that DM digestibility increased in cows when fed 2.0%  $\text{NaHCO}_3$  in a mixed ration of 75% concentrate and 25% corn silage diet. This improved DM and NDF digestibilities might be due to reduced flow rate at the duodenum level (Tagari et al., 1982).

Alkaline nature of high DCAD diet or sodium bicarbonate feeding may be used as a nutritional tool to enhance rumen ecology aimed to utilize nutrients more efficiently, however, its response in terms of nutrients utilization depends on the nature of diet, rumen dynamics (which may differ with age) and productive potential, etc.

## BLOOD ACID BASE STATUS

A positive linear relationship exists between blood acid base status and DCAD level (Jackson et al., 1992). It was observed that blood pH and  $\text{HCO}_3^-$  were lower in calves fed 0 DCAD diet than those fed 21, 37 and 52 mEq/100 g of DM DCAD diets (Jackson et al., 1992). Similarly, Roche et al. (2005) also reported that altering DCAD from 23 to 88 mEq/100 g of DM increased blood pH and  $\text{HCO}_3^-$  concentration in early lactating cows. The main reason for reduced blood pH and  $\text{HCO}_3^-$  at low DCAD diet is due to its acidic properties. Calcium chloride is primarily used as an anionic salt to reduce the DCAD level which has more absorption and acidifying properties compared to all other anionic salts. Chloride is absorbed from the posterior part of the intestine in exchange of  $\text{Na}^+$  and when it is in excess of  $\text{Na}^+$  then with  $\text{HCO}_3^-$  resulting in reduced blood bicarbonate and increased  $\text{H}^+$ . It might have overcome the capacity of kidneys to excrete  $\text{H}^+$  to

maintain a constant blood pH, following slight metabolic acidosis. Moreover, when the body faces an acid load, it is compensated through respiratory rate that reduced partial pressure of carbon (iv) oxide ( $p\text{CO}_2$ ) and carbonic acid ( $\text{H}_2\text{CO}_3$ ) (Hill, 1990). Other researchers (Borucki Castro et al., 2004; Chan et al., 2006; Apper-Bossard et al., 2006; Shahzad et al., 2007; Li et al., 2008; Sarwar et al., 2008) also reported similar findings.

Moore et al. (2000) reported that blood pH and  $\text{HCO}_3^-$  were lower in cows and heifers fed -15 DCAD diet than those fed 0 DCAD diet. Cows fed low DCAD diets (-40, -51 and -63 mEq/kg of DM) had reduced blood pH than those fed high DCAD diet (+203 mEq/kg of DM), although the difference was not significant (Vagnoni and Oetzel, 1998). Similarly, Roche et al. (2003a) also reported significant reduction in blood pH in cows fed +21 DCAD diet compared to those fed +45, +70 and +95 mEq/100 g DCAD diets. These studies were in line with Fredeen et al. (1988b) who reported that blood pH and  $\text{HCO}_3^-$  increased with increasing DCAD from 0.7 to 90 mEq/100 g DM in pregnant and lactating goats. High DCAD diets decreased blood  $\text{H}^+$  and thus resulted in increased blood  $\text{HCO}_3^-$  (Block, 1994) as blood  $\text{HCO}_3^-$  responses were inversely related to  $\text{H}^+$  changes that reflected the metabolic nature of the acid challenge at low DCAD diet. Outcome of the studies suggest significant influence of high DCAD diet on acid base status of the animals through modification in blood pH due to alteration in blood bicarbonate and  $\text{H}^+$  concentrations.

## BLOOD MINERALS

It has been observed that plasma Ca concentration was higher in prepartum cows fed low DCAD diet compared to those fed high DCAD diet (Tucker et al., 1992). Feeding anionic diets before and after parturition improved total Ca in cows (Oetzel et al., 1988). Other workers (Yen et al., 1981; Tucker et al., 1991; Li et al., 2008; Wu et al., 2008) also reported similar findings. Improved plasma Ca concentration is due to increased Ca absorption (Verdaris and Evans, 1975), Ca mobilization from bones (Fredeen et al., 1988a) and renal reabsorption of Ca due to slight metabolic acidosis induced by low DCAD diet (Ross, 1994b; Shahzad et al., 2008a, b; Sharif et al., 2010). Feeding a low DCAD diet increased the flow of Ca through the readily exchangeable Ca pool (Takagi and Block, 1988) which increased ionized Ca concentration in the blood (Oetzel et al., 1988). The improved Ca status of the animal helps in reducing the occurrence of milk fever at the time of calving.

Serum  $\text{Na}^+$  remained unaffected with varying levels of DCAD (West et al., 1991). Tucker et al. (1988) also observed non-significant effect on serum  $\text{Na}^+$  or  $\text{K}^+$  concentration but  $\text{Cl}^-$  concentration decreased with increasing DCAD. Similar findings were observed by West et al. (1992) who reported that serum  $\text{Na}^+$  and  $\text{K}^+$

were not altered when DCAD level was increased from 120.4 to 464.1 mEq/kg DM. A meta-analysis conducted by Hu and Murphy (2004) also revealed similar findings. The non-significant effect of high DCAD diet on  $\text{Na}^+$  and  $\text{K}^+$  might be due to their excessive excretion through kidney. However, Fredeen et al. (1988b) noticed that plasma  $\text{Na}^+$  concentration increased as DCAD was increased in the diet. Low DCAD diets resulted in increased  $\text{Cl}^-$  concentration in pregnant and lactating goats (Fredeen et al., 1988a) which reflects  $\text{Cl}^-$  content of the diet (Tucker et al., 1991). Its absorption takes place in ileum and colon part of large intestine in exchange of  $\text{HCO}_3^-$  (Ganong, 1983). A linear increase in serum cation anion difference was observed with increasing DCAD level in diet (West et al., 1991) which is due to its positive association with blood pH thus improving blood buffering capacity.

The DCAD had non-significant effect on serum Mg concentration (West et al., 1992). However, Roche et al. (2003a) observed a linear increase in renal excretion of Mg concentration as DCAD level was decreased in the diet. Other researchers (Fredeen et al., 1988b; Roche et al., 2005; Sarwar et al., 2007a, b) also observed similar findings. It might be due to metabolic acidosis induced by low or negative DCAD diet. The DCAD had non-significant effect on serum P concentration (West et al., 1992; Tucker et al., 1988). Contrary to this, Roche et al. (2005) reported increased plasma P concentration as DCAD was increased in the diet. Delaquis and Block (1995b) observed increased plasma sulfide ( $\text{S}^{2-}$ ) concentration with decreasing DCAD in the diet which might be due to renal regulation for its absorption. Studies on DCAD suggest that feeding low DCAD diets may increase serum Ca concentration which can be helpful in reducing the occurrence of milk fever at the time of calving.

## MINERAL BALANCE

Joyce et al. (1997) reported that urinary excretion of Ca was higher in cows fed -7 mEq/100 g DM DCAD diet compared to those fed +30 and +35 mEq/100 g DM DCAD diets. Other researchers (Borucki Castro et al., 2004; Li et al., 2008) also observed increased urinary excretion of Ca at low DCAD diet while it tended to decrease at high DCAD diet. The increase in urinary Ca at low DCAD was due to high plasma Ca concentration. This excess amount of plasma Ca is filtered through kidneys resulting in increased urinary excretion of Ca (Takagi and Block, 1988) as its concentration increased with increasing plasma Ca concentration, blood  $\text{H}^+$  and urine  $\text{H}^+$ . Moreover, higher plasma Ca concentration indicates greater availability of Ca for metabolic functions and is helpful to assess Ca status of the animal. Tucker et al. (1988) observed that urinary mineral composition was closely associated with dietary mineral composition. Urinary  $\text{Na}^+$  and  $\text{K}^+$  concentrations increased while  $\text{Cl}^-$

concentration decreased as DCAD increased from -10 to +20 mEq/100 g DM. Increased urinary  $\text{Cl}^-$  concentration in cows fed low DCAD (Tucker et al., 1992) might be attributed to increased  $\text{Cl}^-$  content of the diet (Tucker et al., 1988; 1992). West et al. (1992) also pointed out that urinary  $\text{Na}^+$  and  $\text{K}^+$  concentration increased in cows fed high DCAD diet while its reverse was true for  $\text{Cl}^-$  concentration.

The  $\text{Cl}^-$  content of the anionic diet induced acid load (Budde and Crenshaw, 2003) and it is also retained in excess quantity in the body. An increased  $\text{Cl}^-$  retention with increasing  $\text{Cl}^-$  intake was also observed by Golz and Crenshaw (1991) in young ones. Due to physiological regulation of osmotic pressure, the excess dietary  $\text{Cl}^-$  must either be excreted with a counter balance of cations or stored in a body compartment (bone) with a replacement of another anion. Urinary cation anion difference also tended to increase as DCAD level was increased from 120.4 to 464.1 mEq/kg DM (West et al., 1992). Similarly, West et al. (1991) observed a linear increase in urinary cation anion difference with increasing DCAD.

Tucker et al. (1988) also pointed out that increasing DCAD from -10 to +20 mEq/100 g DM increased urinary cation anion difference. This increased urinary cation anion difference at high DCAD diet might be attributed to decreased  $\text{Cl}^-$  content of the diet. Excretion of P tended to increase as DCAD level was decreased in the diet (Shahzad et al., 2008b). This is because urinary excretion of P is positively associated with increased  $\text{H}^+$  both in blood and urine (Tucker et al., 1992). They further pointed out that urinary excretion of Mg increased during first week postpartum in cows fed low DCAD diet. Other researchers (Oetzel et al., 1988; Gaynor et al., 1989) also reported similar results. The increase in urinary excretion of Mg is due to its positive association with plasma Mg concentration. When low DCAD diet is fed to the animals, it induces slight metabolic acidosis which results in increased plasma Mg concentration (Roche et al., 2003a), excreting more urinary Mg. It has been concluded that mineral composition of diet may have close association with urinary mineral composition. Feeding low DCAD diet can increase urinary Ca excretion due to slight metabolic acidosis. This increased amount of plasma Ca may be available for various metabolic processes.

## NITROGEN BALANCE

The DCAD had non-significant effect on nitrogen intake and excretion in early lactating cows (Delaquis and Block, 1995b). Fecal nitrogen (N) concentration and total N excretion were similar at both DCAD levels (258.1, 55.5mEq/kg DM) that resulted in equal absorption of N. Although, there was significant increase in protein secretion in milk at high DCAD level but overall N balance was not affected during early lactation. During mid lactation, intake, absorption, retention and balance of N increased

in animals fed high DCAD diets that might be associated with increased feed intake (Delaquis and Block, 1995b). No effect of DCAD on N balance was observed during late lactation, which revealed that acid base perturbation was not sufficient to affect the protein metabolism. Similar results were also reported by other researchers (Phromphetcharat et al., 1981; Welbourne et al., 1988). It was observed that DCAD had no significant effect on N intake, digestibility and retention in dry cows (Delaquis and Block, 1995a), which might be due to small difference in DCAD level used in their study. Similarly, Delaquis and Block (1995c) ascribed that urine N was not affected from DCAD levels in cows fed alfalfa hay and corn silage based diets, although slight increase was observed in cows fed alfalfa hay based diets. The probable reason for this might be attributed to higher N content of alfalfa hay than corn silage.

In conclusion, nitrogen metabolism of animals receiving different DCAD concentrations may be influenced due to effect of DCAD on nitrogen utilization; however, it is governed by multiple factors like dietary nitrogen concentration and its utilization in rumen which may be modified by DCAD.

## ENERGY BALANCE

Moore et al. (2000) investigated the effect of various DCAD levels (+15, 0 and -15mEq/100 g DM) in prepartum cows. They reported that energy balance was higher (3.75 MCal/d) in heifers fed +15 mEq/100 g DM DCAD diet than those (0.09 MCal/d) fed -15 mEq/100 g DM DCAD diet. Similarly, cows fed high DCAD level (+15 mEq/100 g DM) showed better (8.42 Mcal/d) energy status when compared (6.01 Mcal/d) with cows fed low DCAD level (-15 mEq/100 g DM). This revealed that energy balance was higher both for heifers and cows fed 0 and +15 mEq/100 kg DM DCAD than those fed -15 mEq/100 DM DCAD diet. The decreased energy balance at low DCAD diet was due to reduced DMI. On the other hand, high DCAD diet increased rumen pH (Tucker et al., 1988) that eventually increased DMI leading to improved energy balance.

It has been observed that sodium bicarbonate supplementation in cows fed control rations (50% corn silage, 50% concentrate) improved energy balance than those cows which were fed control rations only (Vicini et al., 1988). The improved energy balance (21.5 vs 15.5 Mcal ME/d) in sodium bicarbonate supplemented cows was due to increased DMI. In short, feeding high DCAD diet may increase energy balance due to increase in dry matter intake and its utilization in ruminant animals.

## URINE pH

Urinary pH is generally used as an indicator of metabolic

acid or alkali load (Sanchez, 2003; Wu et al., 2008). Any change in urine pH is due to alteration in blood pH which reflects the ability of kidney to withstand change in metabolic challenge. However, there is a minimum (4.5) threshold limit for reduction in urine pH in the mammalian body (McGilvery, 1970; Houpt, 1993). Low DCAD diets resulted in decreased urine pH in goats (Stratton-Phelps and House, 2004). Manna et al. (1999) also observed a linear increase in urine pH as DCAD was increased from 98 to 270 mEq/kg DM. Hu et al. (2007) also reported increased urine pH with increasing DCAD level in the diet. These results were supported by other researchers (West et al., 1992; Pehrson et al., 1999). Decrease in urine pH in low or negative DCAD diets is associated with excess Cl and S inclusion in the diet. Golz and Crenshaw (1991) noticed similar findings when Cl was increased in the diet. Increased urine  $H^+$  at low DCAD diet was due to acidogenic properties of  $CaCl_2$  (Tucker et al., 1991). These findings were also supported by other researchers (Merck, 1983; Tucker et al., 1988). The findings reflect that increase or decrease in urine pH in DCAD fed animals was because of the alkaline or acidic nature of the diet, respectively, which is the function of salts used for the respective mineral composition.

## RESPIRATORY RATE

West et al. (1992) studied the effect of altering DCAD on respiration rate in cows. They observed that increasing DCAD level (120.4 to 456.0 mEq/kg DM) increased respiration rate (94 to 102 breaths/min). This is because  $pCO_2$  increased linearly with increasing DCAD that enhanced respiration rate. West et al. (1991) also observed increased respiratory rate with increasing DCAD level in the diet (from -79 to 324 mEq/kg DM). Whereas, low DCAD diet reduced blood  $pCO_2$ , which consequently decreased the respiration rate (Jackson et al., 1992; Ross et al., 1994a). Respiratory rate was also higher in cows fed diet rich in cations ( $Na^+$  and  $K^+$ ) (Schneider et al., 1988). This is due to high concentration of these minerals which neutralize the acidogenic effect of the diet resulting in increased respiration rate. Contrary to these, Fredeen et al. (1988b) reported that low DCAD diets reduced blood  $HCO_3^-$  concentration while  $H^+$  concentration increased which resulted in increased respiratory rate. Table 1 shows the effect of dietary cation-anion difference on dry matter intake, blood pH, plasma calcium and urinary Ca excretion, reported in various studies.

## MILK FEVER

Oetzel et al. (1988) noticed the effect of altering DCAD (187, -75 mEq/kg DM) on the prevention of milk fever in prepartum cows and reported that cows fed high DCAD diet (187 mEq/kg DM) had more incidences of milk fever compared to those fed low DCAD diet (-75 mEq/kg DM).

Diets containing -100 to -150 mEq/kg of DM DCAD helped in the prevention of milk fever (Sanchez and Blauwickel, 1994). Goff et al. (1991) also reported similar findings. Prepartum diet supplemented with anionic salts improved Ca metabolism which is responsible for the prevention of hypocalcemia at calving (Dishington, 1975; Block, 1984). Cows fed anionic diet had no milk fever while those fed cationic diet had 47.4% incidence of milk fever (Block, 1984). Feeding low DCAD diet in late gestation reduces milk fever by enhancing mobilization of Ca from bones, thus increasing availability of Ca after calving compared with high DCAD diets (Dishington, 1975; Gaynor et al., 1989). This is necessary as serum plasma Ca concentration is reduced at the time of parturition due to entrance from the extracellular fluid to mammary glands for the synthesis of colostrum. This excessive loss of Ca from the extracellular fluid must be replenished by absorbing Ca either from the intestines or from the mobilization of bones. Most of the cows are able to meet the Ca requirements from the onset of lactation but in some animals, this homeostatic mechanism fails and these animals show signs of hypocalcemia. If the calcium need is not met from the external source, the animal may develop milk fever. The homeostatic mechanism depends upon animal age, breed, dietary Ca before parturition and DCAD (Goff et al., 1991). High Ca concentration in animal feed such as alfalfa hay may also cause parturient paresis. Actually, Ca being cationic in nature increases the alkalinity of diet and thus reduces the parathyroid hormone (PTH) activity on bone and kidney cell which are required to maintain normal calcium level. While, low DCAD diet increases Ca mobilization from bones by releasing Ca from amorphous Ca-phosphates and Ca-carbonates on bone surfaces (Bushinsky et al., 1985), preventing milk fever.

However, the exact physiological mechanism for prevention of parturient paresis at low DCAD is not clear. There are various views about it. One is that feeding low DCAD diet might have increased Ca absorption due to acidity induced by the diet (Vagg and Payne, 1970; Fredeen et al., 1988a). While, Block (1984) pointed out that increased bone mobilization of Ca rather than increased Ca absorption from the intestinal tract is the primary means by which anionic salts improve Ca metabolism at parturition. This is because PTH and its receptors are located on the surface of bone and renal tissue cells that result in "lock and key" system and PTH stimulates the target cells. At high DCAD level, blood pH becomes alkaline that results in conformational changes in PTH receptors and as a result of which PTH does not recognize its receptors and thus is unable to work on the tissues efficiently. As a result, blood Ca level decreases and hypocalcemia occurs. Cows suffering from milk fever have increased plasma cortisol level (Littledike et al., 1970; Horst and Jorgensen, 1982) that causes immunosuppression at calving. Hypocalcaemia is also associated with loss of uterine muscle tone that leads to uterine

**Table 1.** The effect of dietary cation-anion difference on dry matter intake, blood pH, plasma calcium and urinary Ca excretion, reported in various studies.

S/N	DCAD (mEq/100 g of DM)	Dry matter intake (kg/d)		Blood pH		Urine pH		Plasma Ca (mg/dL)		Urinary Ca excretion (g/d)		Reference
		At low DCAD	At high DCAD	At low DCAD	At high DCAD	At low DCAD	At high DCAD	At low DCAD	At high DCAD	At low DCAD	At high DCAD	
1	-10, +20	16.8	18.6	7.37	7.43	6.1	7.6	---	---	---	---	Tucker et al., 1988
2	-11.66, +31.24	10.7	15.9	7.32	7.42	5.38	8.30	9.63	9.23	---	---	West et al., 1991
3	+12.04, +45.6	16.4	18.1	7.45	7.49	6.33	8.19	10.54	10.35	---	---	West et al., 1992
4	0, +52	3.79	3.93	7.34	7.38	6.1	8.1	10.10	10.72	5.5	0.17	Jackson et al., 1992
5	0, +45	7.31	7.56	7.38	7.42	---	---	5.33	5.38	---	---	Ross et al., 1994a
6	+32.72, +48.18	10.1	10.2	7.39	7.40	8.51	8.68	---	---	---	---	Delaquis and Block, 1995a
7	-7, +35	---	---	7.42	7.45	7.59	8.35	4.31	3.87	4.23	0.38	Joyce et al., 1997
8	-6.3, +20.3	14.9	16.0	7.39	7.42	7.20	8.33	9.86	9.20	6.87	0.92	Vagnoni and Oetzel, 1998
9	0, +200	3.56	3.61	7.38	7.39	6.80	8.09	11.5	11.5	---	---	Jackson et al., 2001
10	+12.4, +33.3	6.72	10.01	---	---	---	---	---	---	---	---	Mueller et al., 2001
11	-12, +69	---	---	7.40	7.40	7.76	7.90	---	---	---	---	Roche et al., 2003b
12	+14, +45	20.1	20.1	7.42	7.45	7.73	8.36	---	---	2.8	0.64	Borucki Castro et al., 2004
13	-5.57, -6.02	11.8	10.6	---	---	7.15	7.21	9.25	9.02	18.36	15.93	Chan et al., 2006
14	-22, +22	12.09	13.95	7.34	7.43	5.95	7.81	10.98	9.43	1.16	0.78	Sharif, 2007
15	+26.8, +56.1	22.5	22.0	7.42	7.44	---	---	10.5	10.5	---	---	Wildman et al., 2007
16	+5.6, +14	---	---	---	---	6.21	7.28	7.98	7.70	---	---	Roux et al., 2008
17	-26.5, +22.4	13	11.5	7.35	7.95	6.21	8.60	2.18	2.38	17.1	10.4	Li et al., 2008
18	-15, +15	11.87	12.06	7.37	7.41	5.75	7.67	9.02	8.55	---	---	Wu et al., 2008
19	-11, +33	10.2	13.2	7.30	7.50	6.0	8.0	9.90	8.92	1.25	0.788	Shahzad et al., 2008b

prolapse (Risco et al., 1984). Cows recovered from milk fever have 8 times more chances of ketosis and mastitis compared to non-milk fever affected cows. Dystocia, retained placenta, displacement of abomasum and uterine prolapse also increased due to the occurrence of milk fever (Curtis et al., 1983). Thus, low DCAD diet in prepartum animals may be used as an effective practical nutritional tool in reducing the incidence of milk fever and other problems associated with productivity. Table 2 shows the effect of dietary cation-anion difference on occurrence of milk fever observed in various studies.

### MILK YIELD AND COMPOSITION

The effects of dietary cation-anion difference on milk yield as reported in various studies are shown in Table 3. Tucker et al. (1988) observed increased milk yield (18.5 to 20.1 kg) in lactating cows as DCAD level was increased from -10 to +20 mEq/100 g DM. Increasing DCAD improved milk yield, milk fat and milk lactose contents (Mooney and Allen, 2002). Other researchers (West et al., 1991; Delaquis and block, 1995b; Apper-Bossard et al., 2006) also reported similar findings. Hu and Murphy (2004) conducted a

meat-analysis and observed optimum milk production at 34 and 40 mEq/100 g DM DCAD. This work was also supported by other data analyzed by Sanchez and Beede (1994) who stated that optimum milk yield can be obtained from lactating animals if the DCAD level is kept in the range of 25 and 50 mEq/100 g DM. Improved milk production at higher DCAD level is due to the reason that a positive correlation exists between DCAD and milk yield (Sanchez et al., 2002) which might be due to improved DMI. It has been observed that higher metabolic activities make cellular environment acidic due to more production

**Table 2.** The effect of dietary cation-anion difference on occurrence of milk fever, observed in various studies.

S/N	DCAD (mEq/100 g of DM)	Milk fever % incidence or number of cases		Reference
		At low DCAD	At high DCAD	
1	-11.9, +34.6	16.7%	85.7%	Dishington, 1975
2	-17.2, +44.9	0%	47.4%	Block, 1984
3	-7.5, +18.9	4%	17%	Oetzel et al., 1988
4	-3.0, +9.0	4/60	5/60	Tucker et al., 1992
5	-7, +35	2/15	3/15	Joyce et al., 1997
6	-22, +22	0	40%	Sharif, 2007
7	-11, 33	0	33%	Shahzad et al., 2008b
8	-15, +15	0/10	0/10	Wu et al., 2008

**Table 3.** The effect of dietary cation-anion difference on milk yield, reported in various studies.

S/N	DCAD (mEq/100g of DM)	Milk yield (kg/d)		Reference
		At low DCAD	At high DCAD	
1	-10, +20	18.5	20.1	Tucker et al., 1988
2	-11.66, +31.24	16.4	19.7	West et al., 1991
3	+12.04, +45.6	22.4	22.0	West et al., 1992
4	-7, +35	29.1	28.9	Joyce et al., 1997
5	+21, +127	25.4	23.2	Roche et al., 2003a
6	+14, +45	29.2	30.3	Borucki Castro et al., 2004
7	+20, +50	25.5	22.4	Chan et al., 2005
8	+0.4, +30.6	29.2	29.3	Apper-Bossard et al., 2006
9	+36.5, +58.5	27.5	27.4	Wildman et al., 2007
10	-15, +15	35.60	33.23	Wu et al., 2008
11	-11, +33	12.60	15.30	Shahzad et al., 2008a

of CO<sub>2</sub> in lactating dairy cows. Feeding high DCAD diet neutralizes the acidity due to its alkalogenic property, which improves cellular glucose intake (Block, 1994) thus improving productive performance of the animal.

Fredeen et al. (1988b) observed the effect of diets containing -2.8, -38.3 and 33.1 mEq/100 g DM DCAD in goats. They reported that milk yield was slightly higher at low DCAD. Similar findings were also reported by Block (1984) who observed 6.8% depression in milk yield in cows fed high DCAD diet (33.05 mEq/100 g DM) than those fed low DCAD diet (-12.85 mEq/100 g DM). This might be attributed to milk fever problem at high DCAD diet during parturition that was responsible for decreased productive span (Block, 1984). Feeding low DCAD diet to close up cows has favorable effect on animal health and production. These diets are helpful in preventing milk fever and associated problems. It has been observed that cows that suffered from milk fever have reduced milk production in subsequent lactations than cows which never suffered from the problem (Moore et al., 2000). Joyce et al. (1997) also reported increased milk

production during first few weeks of lactation in cows fed negative DCAD diet (-7 mEq/100 g DM) compared to those fed high DCAD diet (+35 mEq/100 g DM). The probable explanation for this might be the improved Ca status of cows fed low DCAD diet.

Milk protein remained unaffected by DCAD level (Tucker et al., 1988). Aramblé et al. (1988) also pointed out that milk protein percent remained unaltered with supplementation of NaHCO<sub>3</sub>. Roche et al. (2005) observed improved milk fat with increasing DCAD levels in the diet. West et al. (1992) also reported similar findings. This might be due to the reason that high DCAD diet, being alkaline in nature, might have shifted the rumen fermentation pattern to acetate and butyrate production (Kaufmann et al., 1980; Klover and de Veth, 2002) that enhanced *DE NOVO* fatty acids synthesis which led to improved milk fat synthesis. It has been concluded that feeding high DCAD diet may improve milk yield due to increased dry matter intake. It can also be helpful in improving milk fat synthesis due to shifting of rumen fermentation towards acetate and butyrate production in



animals fed on high DCAD.

## OVARIAN ACTIVITY AND HORMONAL PROFILE

It is well documented that a positive linear relationship exists between energy balance and ovarian activity and a high energy balance stimulates the ovarian functions (Pate, 1999). Feeding high DCAD diets perk up energy balance due to increased DMI which in turn improve ovarian activity (Sharif, 2007). At high DCAD diets, trace minerals enhance reproductive performance in cows by decreasing days to first service, days to conception and services per conception (Uchida et al., 2001). High DCAD diet tended to increase insulin like growth factor (IGF-I) in animals through increased DMI (Moore et al., 2000). The IGF-I is considered an indicator of energy status in dairy animals (Pate, 1999). It has stimulatory effect on granulosa cells to produce more estradiol which in turn improves the ovarian activity (Spicer et al., 1990). High DCAD diets might also have activated steroidogenic enzymes necessary for the synthesis of reproductive hormones such as progesterone and estrogen. These hormones are secreted mainly from follicles and corpus luteum and are responsible for ovulation and pregnancy, respectively.

Low DCAD diet is responsible for reduced ovarian efficiency due to depressed DMI (Sharif et al., 2009). Decreased DMI also increases the occurrence of negative energy balance and postpartum anovulation (Canfield and Butler, 1991; Beam, 1996; Zurek et al., 1995). Negative energy balance causes less secretion of leutinizing hormone (Schillo, 1992) which results in reduced follicular growth and ovulation. During negative energy balance, estrus is delayed due to less hormonal concentrations and their activity. It also reduces functions of corpus luteum. However, feeding low DCAD diet prepartum has favorable effect on reproductive performance. Beede et al. (1991) observed that prepartum cows offered low DCAD diets had 71% conception rate while those fed high DCAD diets had 54% in the coming oestrous. They further observed 124 and 138 days open for low and high DCAD diets, respectively. Wang et al. (1991) also found that prepartum cows fed low DCAD diets had higher pregnancy rate compared to those fed high DCAD diets. It might be due to sufficient Ca availability, which not only met body needs but also quickened the involution process that resultantly increased the conception rate and reduced the days open. In short, feeding high DCAD diet improved energy balance due to increased DMI which may stimulate the ovarian functions thus, improving the reproductive performance of the animal.

## MASTITIS AND UDDER EDEMA

Low DCAD diets reduced the incidence of mastitis; metritis

and displacement of abomasum compared to those cows fed high DCAD diets (Goff and Horst, 1997, 1998). These diets increased serum Ca status of the animal. Melendez et al. (2002) reported that cows offered anionic salts had higher plasma Ca concentration compared to those offered high DCAD diets. Adequate Ca level is very essential for normal physiological and muscular functions of the animal. Low DCAD diet prepartum has positive effect on Ca metabolism, prepartum health and postpartum productive and reproductive performance (Horst et al., 1997). If the animal is hypocalcemic at parturition, it will impair smooth muscles contraction that is very imperative for the closing of teat sphincter after milking. Smith et al. (1985) reported that animals are more prone to mastitis during first week of the dry period or first month of lactation which may be due to failure of the bacteria to flush from the teat canal. Metabolic disorders like milk fever and ketosis are also closely associated with retained placenta, mastitis and metritis (Dohoo and Martin, 1984; Correa et al., 1993).

Lema et al. (1992) reported that prepartum cows fed high DCAD diets developed severe udder edema compared to those fed  $\text{CaCl}_2$  diet. Removal of  $\text{CaCl}_2$  from the diet increased the chances of udder edema. Heifers fed high amounts of  $\text{NaCl}$  and  $\text{KHCO}_3$  tended to develop edema promptly compared to those fed low amounts of these salts (Nestor et al., 1988). Excess intake of Na or K (high DCAD diets) may be the major cause of udder edema (Al-Ani and Vestweber, 1986; Vestweber and Al Ani, 1983). Other researchers (Randall et al., 1974; Conway et al., 1977; Sanders and Sanders, 1981; Jones et al., 1984) also reported that high DCAD diet is the major cause of udder edema and its restriction to pregnant heifers reduce the severity of the problem. Occurrence of udder edema at high DCAD diet might be due to immune suppression in affected animals, manifested by increased plasma cortisol concentration (Littledike et al., 1970). The effect of dietary cation-anion difference on udder edema and mastitis as observed in various studies is shown in Table 4. It has been concluded that mastitis and udder edema can be controlled through manipulation of DCAD levels in the diet.

## CONCLUSION AND PERSPECTIVE

Studies on DCAD have confirmed its significant influence in systemic acid base status which has direct and indirect association with not only productive and reproductive performance on ruminants but also, with their well being. However, concentration of DCAD in ruminants differs as per animal productive potential, physiological stage, environmental conditions, diet composition and breed, etc. Furthermore, consequences of feeding DCAD in ruminants for longer period of time on productivity and well being are still areas which need to be investigated in order to harvest real benefits associated with animal agriculture enterprise.

**Table 4.** The effect of dietary cation-anion difference on udder edema and mastitis, observed in various studies.

Item	DCAD (mEq/100g of DM)	Incidence or number of cases		Reference
		At low DCAD	At high DCAD	
<sup>1</sup> Udder edema	-22, +22	0	6.5	Sharif, 2007
Udder edema	-15, +15	1/10	2/10	Wu et al., 2008
<sup>2</sup> Mastitis	-22, +22	0	2.5	Sharif, 2007
Mastitis	-15, +15	1/10	1/10	Wu et al., 2008

<sup>1</sup>0 = No problem, 10 = severe problem.

<sup>2</sup>0 = no problem, 3 = severe problem.

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