Role of niacin supplementation in dairy cattle: A review

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ABSTRACT
Niacin (Vitamin B₃) is significantly important for the metabolism of animals and human beings due to its incorporation into the coenzymes NAD and NADP. For dairy cows, the microbial synthesis of niacin in the rumen is an important source besides its availability from feed and endogenous formation. This vitamin is involved in various energy-yielding pathways and for synthesis of amino acid and fatty acid; for which it is important for milk production. Supplementation of niacin has beneficial effects on growth of cattle. The production performance of dairy cows fed with niacin at 6g/day may not be satisfactory, but supplementation of 12g of niacin per head per day can increase milk production by about 1lb. An optimistic return on asset is possible if the supplementation is limited to high producing early lactation cows. Supplementing the dairy animals with a dose of 6-12g of niacin will not only protect them from various metabolic diseases but will also help them defend from severe heat stress; ultimately leading to augmentation of their health, production potential and economy.

Key words: Growth, Heat Stress, Ketosis, Milk Production, Niacin.

INTRODUCTION
Dairy sector plays an important role in upliftment of socio-economic status of poor farmers and also contributes to nutritional requirement of human beings. Statistical analysis of BAHS-2015 (Basic animal husbandry statistics) evidenced that milk sector is growing at a faster rate with annual growth rate of 4.5%. As a result, the total milk production during the period has increased from 107.9 million tonnes in 2007-08 to 127.9 million tonnes in 2011-12. At the 2nd year of 12th Five Year Plan i.e. (2013-14), the total milk production was 137.7 million tonnes. Per capita availability has sharply increased from 225 gm per day in 2003-04 to 307 gm per day in 2013-14 with an annual growth rate of 3.7 %. If we analyze the species wise contribution, then buffalo contributes highest share i.e. 51% followed by 25%, 20% and 4% for Cow Exotic/Crossbred, Cow Indigenous/Non-Descript and Goats respectively.

Maintenance of animal health and production potential are the most important economic factors in the dairy industry. Supplementation of niacin (vitaminB₃) causes increased milk production, decreased incidence of ketosis and fatty liver syndrome, enhanced microbial protein synthesis and increased propionate production (Cervantes et al., 1996). Funk isolated this vitamin from yeast and rice polishing. Nicotinic acid was discovered for the treatment of black tongue in dogs and pellagra in human beings (Elvehjem et al., 1937). Niacin is the third B vitamin to be established after isolation of thiamine and riboflavin from the vitamin B complex.

Niacin is a generic name for pyridine 3-carboxylic acids and chemically, it is one of the simplest vitamins, having the empirical formula C₆H₅O₂NN. Niacin is present as nicotinic acid in plants and nicotinamide in animals. Both the physiologically active forms are derivatives of pyridine. Nicotinic acid and nicotinamide (niacinamide) possess the same activity, but in lactating cows the later has slightly higher activity (Jaster and Ward, 1990). Nicotinic acid is converted to nicotinamide in the rumen (Erickson et al., 1991). Nicotinamide functions as a component of two different coenzymes such as NAD (nicotinamide adenine dinucleotide) and NADP (nicotinamide adenine dinucleotide phosphate). NAD and NADP function in biological oxidation-reduction systems by virtue of their ability to serve as hydrogen–transfer agents. Tryptophan is the precursor of this vitamin and pyridoxine is required for its action.

Chemical structures:

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REQUIREMENTS

The variation in the response of ruminant livestock to supplemental niacin is due to variations in:

1. Endogenous niacin synthesis from tryptophan
2. Niacin supply and bioavailability in common feedstuffs
3. Rumen niacin synthesis and degradation

Young, pre-ruminant calves would be expected to have a dietary requirement for niacin. The dietary niacin requirement does not exist as long as dietary tryptophan is maintained near 0.2% of dry matter. In the absence of dietary tryptophan, 2.5 mg per liter of milk offered ad libitum was required to prevent deficiency symptoms. The minimum level of niacin recommended for calf milk replacers is 2.6 mg per kg (1.2 mg per lb). Niacin supplementation in milk replacer would be of more concern when the non-milk protein sources are used as an alternative to the primary protein source in milk replacer, due to low tryptophan content (Touchette et al., 2003).

sources

The supply of niacin to the ruminant comes from three main sources: dietary niacin, conversion of tryptophan to niacin and ruminal synthesis of niacin. Niacin is widely distributed in feedstuffs of plants well asof animal origin. The by-products of animal and fish origin, distiller’s grains, yeast, various distillation and fermentation solubles and certain oilseed meals are good sources. The bound form of niacin in cereal grains and their by-products is largely unavailable to monogastric species of animals. By use of a rat bioassay procedure, it was shown that in eight samples of various mature cooked cereals like corn, wheat, rice and milo, only about 35% of the total niacin was available. Probably much of this niacin will also be unavailable to rumen microorganisms (Erickson et al., 1991). In calculating the niacin content of formulated diets, all niacin from cereal grain sources should be ignored or at least given a value no greater than one-third of the total niacin. Some bound forms of this vitamin are biologically available, but the niacin especially in corn is unavailable and is implicated in the etiology of pellagra in animals that consume large quantities of this grain. The tissue content of niacin is variable and dependant on strain, sex, age and treatment of animals (Hankes, 1984).

Niacin occurs as a part of biologically available coenzymes NAD and NADP, it is having great significance in the metabolism of human and animal species. Apart from niacin in feed ingredients and endogenous formation, microbial synthesis of niacin in the rumen is an important source for dairy cows but the amount synthesized seems to differ greatly, which might be influenced by the ration fed. There occurs a positive impact of niacin supplementation on rumen protozoa, but microbial protein synthesis or volatile fatty acid production in the rumen resulted inconsistent reactions to the supplemental niacin. The amount of niacin reaching the duodenum is generally higher when niacin is fed; however the whole quantity supplemented does not reach the duodenum, representing the degradation or absorption due to conversion of the essential amino acid tryptophan to niacin, the content of niacin and tryptophan in the diet are frequently considered together in expressing niacin values of feeds i.e. niacin equivalent. However, tryptophan is preferably used for protein synthesis and tryptophan content in several ruminant feed stuffs is lower. The rate at which tryptophan is converted to niacin is higher in chicken and pig as compared to cattle (Scott et al., 1982).

Synthesis of niacin can occur in the rumen; but the extent to which it occurs, particularly with commercial feedstuffs, and their contributions to the niacin supply are controversial. A concentration of niacin is comparatively higher in rumen dry matter than in the diet, which is an evidence of net synthesis of this vitaminin the rumen. However, in certain studies ruminants showed a positive response to supplemental niacin indicating that niacin supply is sometimes sub optimal (Tienken et al., 2015).

Niacin is commercially available in two forms, nicotinamide (niacinamide) and nicotinic acid. These two forms provide same biological activity. Positive response to the supplementation of either source resulted in a positive impact on dairy animals. In contrary to this, minor differences noted in metabolism of nicotinic acid and niacinamide in dairy cows (Campbell et al., 1994).

Nicotinic acid and nicotinamide are readily and efficiently absorbed by diffusion at either physiological or pharmacological doses. Blood transport of niacin is associated mainly with the red blood cells. Niacin rapidly leaves the blood stream and enters the kidney, liver and adipose tissues. The absorbed niacin is actively cycled through the NAD pathway to nicotinamide in the intestinal mucosa. Absorbed nicotinamide is taken up by tissues and incorporated into its coenzymes. The tissue content of niacin and its analogs, NAD and NADP, is variable and dependant on strain, sex, age and treatment of animals (Hankes, 1984). The liver is the site of greatest niacin concentration but the amount stored is not large enough. Urine is the primary pathway of excretion of absorbed niacin and its metabolites.

Due to the incorporation of niacin into the coenzymes NAD and NADP, it is having great significance in the metabolism of human and animal species. Apart from niacin in feed ingredients and endogenous formation, microbial synthesis of niacin in the rumen is an important source for dairy cows but the amount synthesized seems to differ greatly, which might be influenced by the ration fed. There occurs a positive impact of niacin supplementation on rumen protozoa, but microbial protein synthesis or volatile fatty acid production in the rumen resulted inconsistent reactions to the supplemental niacin. The amount of niacin reaching the duodenum is generally higher when niacin is fed; however the whole quantity supplemented does not reach the duodenum, representing the degradation or absorption
of this vitamin. The supplementation of niacin did not always lead to a higher niacin concentration in blood. Inconsistent effects of niacin on other blood parameters were observed not only during ketosis but also during high amount of post-ruminal infusion, as the ruminal degradation appears to be significant. The similar condition is valid for milk parameters. Enhanced niacin concentrations in blood did not necessarily affect milk production or composition (Karkoodi et al., 2009).

Tryptophan is the precursor of niacin and the degree to which the metabolic requirement for niacin can be met from tryptophan will depend on the dietary availability of tryptophan and efficiency of conversion of tryptophan to niacin. At low levels of tryptophan intake, the efficiency of conversion is high. It decreases when niacin and tryptophan levels in the diet are increased. When animals have received deficient levels of tryptophan, increasing amounts of dietary tryptophan are used first to restore nitrogen balance, next to restore blood pyridine nucleotides and then to be excreted as niacin metabolites. Under starvation or energy restriction, efficiency of conversion is increased (Karkoodi et al., 2009).

![Niacin Metabolism Diagram](image)

**FUNCTIONS**

Niacin mainly functions in the coenzyme forms of nicotinamide i.e. NAD and NADP. Enzymes containing NAD and NADP are important links in a series of reactions associated with the metabolism of carbohydrate, protein and lipid. They are particularly important in the metabolic reactions that provide energy to the animal. The coenzymes act as an intermediate in most of the H+ transfers in metabolism. In biological oxidation-reduction systems NAD- and NADP-containing enzyme systems play an important role because of their capacity to serve as effective hydrogen-transfer agents. The transfer of hydrogen from the oxidizable substrate to oxygen occurs much efficiently through a chain of graded enzymatic hydrogen transfers. One such group of hydrogen transfer agents is included under different nicotinamide containing enzyme systems. Important metabolic reactions catalyzed by NAD and NADP are listed as follows:

a. Carbohydrate metabolism: Glycolysis (anaerobic and aerobic oxidation of glucose) and TCA (Krebs) cycle
b. Lipid metabolism: Glycerol synthesis and breakdown, Fatty acid oxidation and synthesis and Steroid synthesis
c. Protein metabolism: Degradation and synthesis of amino acids and Oxidation of carbon chains via the TCA cycle
d. Photosynthesis
e. Rhodopsin synthesis

In ruminants, niacin is particularly required for protein and energy metabolism, involving liver detoxification of portal blood NH3 to urea along with metabolism of ketones in liver during ketosis. It is quite evident that niacin can enhance microbial protein synthesis (Girard, 1998). This may facilitate an increased molar proportion of propionate in rumen volatile fatty acids which may cause an increased rate of flow of material through the rumen. The function of prime interest for dairy cows deals with the role of niacin in oxidation of fatty acid and glucose synthesis, particularly as a preventive and possible treatment for clinical and subclinical ketosis.

**RESPONSES TO NIACIN SUPPLEMENTATION — DAIRY COWS**

**Growth:** Supplementation of niacin was done @ 100, 200, 300 and 400 ppm in 5 groups of heifers and daily average gain of 443, 428, 443, 426 and 365 g, respectively was observed indicating no statistical significant difference in weight gain due to inclusion of different levels of niacin in the diet. In contrast to the above finding, another experiment showed increased live weight gain in calves supplemented with niacin (Chang et al., 1995), but simultaneous mixing of niacin with urea diet reflected better live weight gain in lambs and bulls which might be due to better utilization of urea by rumen microbes for their body protein synthesis and thus higher availability of microbial protein at the lower tract, in the presence of niacin, as niacin is involved intimately in energy metabolism (Horner et al., 1988). In agreement with the above findings, another trial was conducted in which 50-500 mg niacin was supplemented in the diet and effect of niacin on growth of cattle was observed and reports showed there were increased gains and feed efficiency by 9.7% and 10.9%, respectively (Byers, 1981). He concluded that Niacin supplementation during adaptation of cattle to feedlot diets was beneficial for growth. In another study, supplementation of 1g niacin/head/day in cattle showed 4% gain in body weight (Brethour, 1982).

**Milk Production:** The effect of niacin on milk production and composition in dairy cows has been changeable (Table 1). More positive results appear possibly in high-producing early lactating cows, but responses are approximately never observed in mid- and late lactation cows (Girard, 1998). In agreement to this finding, another report suggested that the
It has been found that a reduction of milk protein percentage and protein yield resulted in dairy cows when it comes to feeding of whole cottonseed and most other dietary fat sources to these precious animals. Diets supplemented with niacin (6 g niacin per 20.45 kg of dry matter) increased milk protein percentage in diets with 15% whole cottonseed (Horner et al., 1986). Milk protein depression with whole cottonseed was alleviated by niacin because of stimulation of mammary casein synthesis. In contrary to this, another study reported that supplemental niacin increased milk production by 3% with no effect on dry matter intake (Horner et al., 1988); though beneficial effect of niacin on milk casein synthesis was found for cows fed whole cottonseed, which may have been due to their late stage of lactation (Lanham et al., 1992). Another experiment suggested that feeding niacin to cows receiving heat-treated soybeans rectified a dietary oil-induced milk protein depression (Driver et al., 1990); however feeding cows 12 g of niacin daily increased milk protein yield and reduced plasma ketones (Erickson et al., 1992).

Considering the cows in mid-lactation, it was observed that feeding 12 g of nicotinamide daily increased milk yield and milk protein production, decreased milk fat percentage and had no significant effect on blood glucose or beta-hydroxybutyrate (Cervantes et al., 1996). The study regarding the feeding of 0 or 12 g of nicotinic acid daily with or without supplemental fat from extruded soybeans showed that milk yield was 3.3 Kg/d higher for cows fed niacin (Madison-Anderson et al., 1997). The supplementation of niacin exerted some effects on fatty acid composition of milk, increasing the proportion of unsaturated and long-chain fatty acids whereas another report suggested that milk oleic acid concentration was increased by duodenal infusion of 6g of nicotinic acid daily with no other effects on milk yield or composition (Wagner et al., 1997).

During the study of effects of supplementary niacin (0 or 12g per day) fed with either high or moderate levels of nonstructural carbohydrate in the ration, starting 19 days prepartum and continuing through week 40 of lactation, it was found that niacin had no significant effects on production parameters or blood metabolites (Minor et al., 1998). In contrary to this, another experimental trial was conducted using similar rations with or without supplemental fat (whole soybeans and animal fat), and supplementing either 0 or 12 g of nicotinic acid daily for weeks four through 43 of lactation, reported an increase in milk production (6.2% to 7.2%), lower milk casein concentration and a tendency toward higher milk protein yield in cows fed niacin (Drackley et al., 1998).

A significant increase in milk production was recorded (Al-Abbay, 2013) when Friesian cows were fed 6 g and 12g niacin in two experimental groups(Table 2). This may be due to increase in energy use and also increase in

### Table 1: Summary of studies evaluating milk yield responses to supplemental niacin.

<table>
<thead>
<tr>
<th></th>
<th>No. of studies</th>
<th>Mean increase</th>
<th>Range in responses</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Early-lactation cows</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Significant increase</td>
<td>3</td>
<td>6.7%</td>
<td>4 to 10%</td>
</tr>
<tr>
<td>Increase trend</td>
<td>5</td>
<td>6.3%</td>
<td>3 to 9%</td>
</tr>
<tr>
<td>No effect</td>
<td>5</td>
<td>0%</td>
<td>——</td>
</tr>
<tr>
<td>All studies</td>
<td>13</td>
<td>4%</td>
<td>——</td>
</tr>
<tr>
<td><strong>Mid-lactation cows</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Significant increase</td>
<td>3</td>
<td>3.9%</td>
<td>2 to 7%</td>
</tr>
<tr>
<td>No effect</td>
<td>7</td>
<td>0%</td>
<td>——</td>
</tr>
<tr>
<td>All studies</td>
<td>10</td>
<td>1.2%</td>
<td>——</td>
</tr>
<tr>
<td><strong>Late-lactation cows</strong></td>
<td></td>
<td></td>
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<tr>
<td>No effect</td>
<td>2</td>
<td>0%</td>
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</tr>
</tbody>
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Note: Niacin was usually fed at about 6 g/day (Girard, 1998) and positive metabolic effects of niacin supplementation have resulted in an improved milk yield (3-4%) especially during early lactation (Niehoff et al., 2009).

The absence of a niacin effect may be explained in that cows were too far into lactation and thus not in a negative energy balance (Ottou et al., 1995). The milk constituents were generally un influenced or only minimally improved. Causes for the high fluctuations of results are differences in ration formulation, level of milk production, stage of lactation, age, body conditions of cows, level and duration of niacin supplementation and specific experimental conditions. Niacin supplemented cows lost less body weight during early lactation, was less days open and required fewer pellets per pregnancy.

Under some conditions, supplemental niacin at 6 to 12 g per cow per day has had a favourable effect on milk production in early lactation and when fed to ketogenic cows (Al-Abbsay et al., 2013). Milk production of niacin-supplemented cows peaked earlier, and milk production of high-producing cows in first lactation was greater with slight increase in milk fat percentage when they received 3-6g of supplemental niacin (Jaster et al., 1983). In contrast to the former finding, another experimental trial suggested that supplementing 6 g of niacin per day had no effect on milk production or milk composition where as a 12 g of supplemental niacin per day resulted an increase in fat yield up to 26g/d, milk protein yield 17 g/d and 3.5% fat-corrected milk increased about 11b/d (Schwab et al., 2005). The feeding of nicotinamide during the close-up period decreased early lactation culling and enhanced fat-corrected milk yield (FCM). It would appear that niacin supplementation of about 6g/animal/d (200-400 mg per kg dry matter) for the first 60 to 100 days of lactation may be helpful in specific high producing cows or heifers; however a 4% increase in milk production over the entire lactation was noticed in response to feeding 6g of niacin per day (Muller et al., 1986).
blood sugar level. Niacin also had positive impact on milk production due to its direct relationship with tryptophan. However a decrease in plasma tryptophan concentration was noted in a study which may be due to utilization by rumen microbes for niacin synthesis (Horner et al., 1988). So this indirectly increases milk production by increasing level of NAD and NADP which are prerequisites for carbohydrate, protein and fat metabolism. This was also supported by another experiment which concluded that increase in milk production may be due to enhanced microbial protein synthesis, increase in volatile fatty acids composition, appetite, food intake and increased blood sugar levels (Hutjens, 1984).

The variation in response to supplemental niacin in dairy cows is quite complicated to explain. The tryptophan status in animals may be involved in some of the milk production responses if supplemental niacin is able to spare tryptophan for use by the mammary gland. An experimental report suggested a trend for elevated plasma levels of free tryptophan in niacin-supplemented cows (Horner et al., 1986). In relation to this, an apparent effect of niacin was observed in decreasing plasma calcium and increasing plasma phosphorus concentration (Dufva et al., 1983). This has led to as assumption that marginal dietary calcium levels may limit the response to supplementary niacin which is directly associated with the production potential of dairy animals. It is concluded that niacin can be considered as a supplemental nutrient at 6 to 12 g per day in high-producing cows during early lactation, particularly with higher fat diets (>6% fat).

**Ketosis:** Ketosis is a metabolic disease, in which there occurs an increase in quantity of ketone bodies (acetoacetate, ß-hydroxybutyrate, and acetone) and free fatty acids in the blood-plasma, while the glucose concentration decreases. More than 50% of the high yielding dairy cows suffer from sub-clinical ketosis. In case of ketosis appetite, feed-intake, live weight and milk production of the animal decreases. Niacin is beneficial during late gestation and early lactation when ketosis may be a problem as it is involved in the breakdown of body fat and ketones. Body fat mobilization is highest during early lactation when energy demand for milk production is in peak. Recent research suggests that microbial production of niacin may not be sufficient for the requirements of high yielders. The niacin supplementation in early lactating cows may decrease the rate of fat mobilization, concentration of ketones in blood along with increase the level of blood glucose. Niacin supplementation may enhance the propionate concentration and diminish the butyrate concentration in rumen liquor.

Feeding six grams of niacin per head daily during the last two weeks of gestation and in early lactation increases the glucose concentration of the blood plasma and the rate of fat metabolism, which in turn prevent synthesis of ketone bodies, particularly in over conditioned cows. Feeding 12 grams of niacin per head daily to cows with ketosis has shown positive responses (Fronk and Schultz, 1979).

Two levels of niacin was supplemented in postpartum Friesian cows and a significant decrease in the serum ß-hydroxybutyrate and acetone level were observed (Al-Abbasy, 2013) which are the good indicators of ketosis which is a very rampant metabolic disease in lactating cows due to negative energy balance (Table 3, 4).
Due to niacin’s involvement with fat metabolism, it may be helpful in using supplemental dietary niacin when adding fat to diets of lactating animals. Niacin is utilized both in the rumen and in the small intestine and has positive effect on rumen fermentation, N-metabolism as well as on prevention of several metabolic diseases like acidosis, ketosis. Ruminal microbial protein synthesis was enhanced by niacin. Endogenous synthesis of niacin is slowed down by ketones and enhanced by corticosteroids, leading to the fact that a part of the beneficial effect of adrenal corticoids on ketosis is derived from increased niacin synthesis. This suggests that niacin may be a helpful adjunct to glucocorticoid therapy for ketosis. Supplemental niacin has been reported to increase plasma insulin and glucose response to beta-agonists (Chilliard and Ottou, 1995).

Increased plasma non-esterified fatty acid (NEFA) concentration has been associated with insulin resistance in Holstein cows. Reduction of plasma NEFA concentration by nicotinic acid was found to increase the response to insulin in feed-restricted Holstein cows (Pires et al., 2007). A reduction in lipolysis in response to epinephrine challenge was found in cows fed 12 g per day of either nicotinic acid or nicotinamide (Erickson et al., 1991); however no significant effect of niacin on hepatic lipidosis observed during the periparturient period in dairy cows (Skára et al., 1989).

**Heat Stress:** Constant exposure of productive animals to high temperature and high humidity is directly concerned with the feed and water intake leading to not only reduction in growth but also decreased production potential of the animals.

An experimental trial was conducted on lactating Holstein cows in which encapsulated niacin was administered to study the vitamin’s affect on heat stress (Zimbelman et al., 2010). Cows receiving niacin had increased dry matter intake. A comparatively higher sweating rate and lower vaginal temperature was observed in cows supplemented with niacin.

**DEFICIENCY AND TOXICITY**

In the pre-ruminant calf, a niacin free and low tryptophan diet produced several deficiency signs like sudden anorexia, severe diarrhea, ataxia and dehydration, followed by sudden death. Supplementation of 2.5 mg of nicotinic acid per liter of milk, offered ad libitum twice daily, prevented the deficiency. Basing on the above results, the daily niacin requirement for calves from all sources would be 10 to 15 mg per day. Microbial protein synthesis may be enhanced by the effect of niacin; however a number of experiments indicated no significant effects. Differences between these studies may reflect the amount and availability of niacin in the unsupplemented diet, the niacin status of the microbes, or both of these (NRC, 2001).

There is a broad margin of safety for use of this vitamin. The toxic effects of nicotinic acid can occur only at levels far in excess of requirements. Nicotinic acid and nicotinamide are toxic at dietary intakes greater than about 350 mg per kg (160 mg per lb) body weight per day. The Nicotinamide is two- to three-times more toxic than the free acid. The nicotinic acid and nicaminamide tolerance for ruminants has not been determined.

**CONCLUSION**

The production performance of dairy animals fed with niacin at 6g/day may not be satisfactory, but supplementation of 12g of niacin/h/d can increase milk production by about 1lb. An optimistic return on asset is possible if the supplementation is limited to high producing early lactation cows. Supplementing the dairy animals a dose of 6-12g of niacin will not only protect them from various metabolic diseases but will also defend them from severe heat stress; ultimately leading to augmentation of their health, production potential and economy.

**REFERENCES**


