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Effect of niacin supplementation on milk yield and composition during heat stress in dairy cows: A review

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Abstract
Niacin has an affirmative role on curtailing heat, nutritional stress in lactating animals due to its role in the physical regulation of body temperature by vasodilatation besides its potent role in counteracting ketosis. As the component of coenzymes NAD and NADP, it is crucial in energy metabolism. Moreover, there is the synthesis of niacin by rumen microbes in ruminants, therefore, niacin reaching duodenum is higher than niacin fed. The niacin so formed will help in the growth of rumen microbes and will aid in fiber degradation favoring acetate production which may appear in milk as milk protein and milk fat, respectively. Also, it has a role in DNA repair and cell signaling. It has been indicated to have a role in the increased synthesis of heat shock protein (HSP) that are crucial in ameliorating heat stress. Niacin However, there are different opinions among researchers regarding the effect of niacin on the milk yield, composition and physiology of lactating dairy cows during hot weather. Therefore present review discusses the effect of niacin supplementation on milk yield, milk composition and physiological responses of lactating cows during heat stress.

Keywords: Niacin, nicotinamide (NAM), temperature humidity index, heat stress, milk

Introduction

Due to continuous rise in greenhouse gases linear increase in earth's atmospheric temperature (global warming) is being recorded and forecasted [1]. This rise in temperature is posing several threats to animals and their production performance [2]. A large increase in demand of animal products (*i.e.* milk, milk products and meat) is predicted for the coming decades by FAO. Heat stress on animals is one of the effect of global warming causes a major economic loss in the dairy industry. Annual losses occur due to reduced production potential, increased mortality, and lowered reproduction performance. Dairy animals experience heat stress when any combination of environmental conditions (temperature, relative humidity, solar radiation, air movement, and precipitation) causes the effective temperature of the environment to exceed the animal's thermo-neutral zone [3]. The high environmental temperature also increases respiration rate and water intake, which consequently reduces dry matter intake due to gut fill [4]. High producing dairy cows are more sensitive to heat stress because of their selection and breeding especially for higher milk yield, milk protein and fat. This is proportional to increase in body size and thereby feed intake of dairy cows leading to an increase in heat increment [5] that is a reason for easy susceptibility of dairy animals to heat stress. When high producing dairy cows are exposed to heat stress conditions, then their homeostasis get challenged. So to overcome this problem, heat stress alleviators like vitamin C, E, B complex group and selenium are being supplemented to dairy animals'.

Niacin (pyridine 3-carboxylic acid), also known as nicotinic acid (NA) is one of the water soluble B-complex vitamin popularly known for its role in prevention of pellagra in humans [6]. Another form of niacin, nicotinamide (NAM) is equivalent to nicotinic acid in biological terms. The difference between the two lies in the R-group. Nicotinic acid has a COOH group, while nicotinamide has a $CONH_2$ group in place of the carboxyl group [7]. These have a great importance in the metabolism due to their incorporation into coenzymes NAD and NADP, which is an essential coenzyme for many oxidation reactions in energy metabolism, but NAM is the sole reactive niacin form [7, 8]. While NA and NAM are synthesized naturally by bacteria and plants through condensation of 3-and 4-carbon units [9], NAM can also be formed during hydrolysis of NA under acidic conditions [10]. It is also synthesized in the body from amino acid tryptophan, requiring 34 to 86 mg of tryptophan to synthesize 1 mg of niacin [11, 12]. Most of the vertebrates are able to synthesize this vitamin from tryptophan [11, 12, 13] and quinolate [14]. In dairy cows, niacin is synthesized in the rumen by rumen microorganisms [15] and is also consumed though feed, feedstuff and B-vitamin supplements. Niacin synthesis by rumen microbes was estimated to be 1804 mg/d for a 650 kg cow producing 35 kg of 4% fat corrected milk/d [16].

Previously it has been assumed that niacin is synthesized at adequate amounts in the rumen to meet the needs of the dairy cow [15, 17]. However, due to the improvement in the genetic potential of dairy cows in recent years, their requirements tend to exceed the capacity of rumen microorganisms to synthesize sufficient vitamins B complex [18]. Various studies have been carried out with niacin supplementation during heat stress period [19, 20, 21]. Some studies showed positive responses to niacin supplementation, while in others administration of niacin did not have any effect. Therefore, in this context impact of niacin supplementation on cow's performance, physiology and milk composition during heat stress is discussed.

Effect of niacin on milk yield and its components

Milk production or yield

Dairy industry in tropical countries like India faces several economic losses due to various reasons; one among them is heat stress that causes decreased milk yield to the tune of 10-35% [21, 22] and altered milk composition [21, 23]. Lactating cows demonstrated a decrease in milk production when temperature humidity index (THI) exceeded 72 [3]. Zimbleman [24] reported that the threshold in milk production of high producing cows (milk yield > 35kg/day) was shown to be reduced at THI 68. Decreased feed intake during heat stress is the major reason for reduced milk production in dairy cows. When the temperature was above 25 ºC, three breeds of dairy cows (Jersey, Holstein and Brown Swiss) showed a marked decrease in feed intake and milk production [21, 25]. Heat stressed dairy cows in chamber experiments (room temperature at 29.4 to 38.9 ºC) decreased dry matter intake (DMI) 28% and milk yield 29% compared to cows in the thermal neutral environment (room temperature at 20 ºC) [26]. Baumgard and Rhoads [26] reported that heat-induced reduction in nutrient intake accounted for approximately 35-50% of the reduction in milk yield and *vis a vis* milk composition. Although many reports indicated that decreased feed intake at high ambient temperatures was the major reason for depressed milk yield, forced feeding of lactating cows though rumen fistulas showed that milk yield was still reduced 10% at an ambient temperature of 31 °C compared to the same cows at an ambient temperature of 18 °C. These data suggest that there are other factors involved in decreased milk yield [27]. Other factors that cause decreased milk yield during heat stress include an increase in maintenance requirements, retarded rumination and thereby, reduced nutrient absorption, [28] resulting in a decrease of available nutrients from the diet to produce milk [26]. This reduced nutrient availability and consumption have negative impact on milk yield in terms of reduced milk yield.

In lactation, heat stress down-regulates milk production by the plasminogen-plasmin system, an enzymatic mechanism in milk including plasminogen activator, plasminogen and plasmin [29]. This mechanism acts on β-casein to form a fragment, β-casein fragment 1-28. So formed fragment binds to the apical aspects of mammary epithelial cells and inhibits ion channel synthesis resulting in reduced secretion of lactose (directly related to milk production because of its osmotic effect in udder) and monovalent ions into the lumen of the mammary gland, leading to a decrease in milk secretion [30]. Heat stress, dehydration and stress hormones, such as glucocorticoids, are able to activate plasmin activity leading to increased β-casein fragment 1-28 resulting in a reduction of milk yield [29, 30, 31].

Niacin is involved in most energy-yielding pathways *vis a vis* amino acid and fatty acid synthesis therefore it is imperative for milk production. There are many reports that indicate niacin supplementation increases milk production [21, 22, 32]. Dufva *et al*. [33] demonstrated that niacin supplemented at 3, 6, 12g /cow/day for 10 weeks postpartum slightly increased milk production over control group. Muller *et al.* [17] reported that supplemental niacin at 6 g/d increased milk production by 2.4 kg in cows producing greater than 34 kg. Schwab *et al*. [34] also presented data demonstrating that niacin supplementation at 12 g/d increased milk 0.5 kg/d. There also are many reports that show niacin has no effect on milk production. Jaster *et al*. [35] reported that niacin supplemented at 12 g/day did not affect milk production, but serum nicotinic acid concentrations increased for cows fed niacin. Costanzo *et al.* [19] demonstrated that 12, 24, and 36 g/d of supplemental niacin for cows during heat stress didn't significantly increase milk production. Madison-Anderson *et al*. [36] indicated that niacin supplemented at 12 g/d had no substantial influence on milk production and only a minor influence on milk fatty acid content.

In summary, dietary supplementation of niacin may have a beneficial effect on milk yield possibly because of the increase in microbial protein and function of niacin in lipid and energy mechanism. This may explain how niacin increased milk yield. However, Niehoff *et al.* [37] speculated that the reason niacin doesn't increase milk production in some studies may be because cows in those studies were not in negative energy balance when fed niacin. Also, it can be attributed to the environmental condition in which feeding trial was conducted as it has positive impact in stressed animals. The negative energy balance that occurs in the first 2 weeks postpartum is the critical time for metabolic disease such as ketosis and fatty liver [38]. Cows that suffer from these metabolic diseases have shown decreased milk yield. Niacin has anti-lipolytic effect resulting in decreased NEFA and preventing fatty liver.

Milk protein

Niacin's effect on milk protein is still unclear. Some researchers reported niacin caused an increase in milk protein such as Erickson *et al.* [39] and Schwab *et al*. [34] but some researchers indicated niacin had no effect such as Dufva *et al*. [33], Skaar *et al.* [40] and Campbell *et al*. [10]. The authors explained that a niacin increase in milk protein might result from niacin increased microbial protein synthesis [37]. Study by Riddell *et al*. [32] showed that supplementation of niacin has increased microbial protein synthesis that will ultimately result in improved milk protein synthesis. However, the experiments using encapsulated niacin (fed 12 to 24 g/d) showed niacin has no effect on milk protein yield [21, 38, 41]. As there are several discrepancies in data related to any direct or indirect effect of niacin supplementation on milk protein therefore, it can be said that there may be improved milk protein or may not be.

Milk fat

Previous published papers indicated that raw niacin supplementation had no effect on milk fat yield [10, 17, 21, 33, 36, 40]. However, there are a few studies that indicate supplemental raw niacin causes increased milk fat concentration and yield [34, 42]. The authors explained that raw niacin increased fiber degrading microbial population in the rumen resulting in increased fiber digestion and thereby increased acetate production for milk fat synthesis.

Current studies, using encapsulated niacin in lactating dairy cows have shown no effect on milk fat yield [21, 38, 41]. However, cows fed encapsulated niacin had a numerically decreased milk fat yield. Fatty acids used for milk fat synthesis are derived from circulating lipoprotein (absorption from digestive tract) and NEFA (mobilization from body fat). Normally, NEFA accounts for < 10% of fatty acids in milk [43]. However, cows use more NEFAs to synthesize milk fat when they are in negative energy balance. These data indicate milk fat synthesis in cows fed niacin depends on a degree of negative energy balance and fats absorbed from the digestive tract. If cows are not in negative energy balance, the effect of niacin on milk fat yield is more difficult to detect. But, higher incidence of negative energy balance during postpartum period is not uncommon wherein, supplementation of niacin can be effective for improving milk fat synthesis besides its role in prevention of ketosis [44].

Effect of niacin on physiological parameters

The therapeutic concentrations of niacin causes peripheral and internal vasodilatation, that enhances heat transfer from core to skin sites and generate the temperature gradient favoring heat loss from skin to environment [20, 45, 46]. Several workers have reported a significant reduction in skin and body temperatures during periods of mild or severe heat stress in niacin supplemented group compared to control group [19, 20, 21, 47]. Another possible mechanism of niacin at the cellular level is an increase in Heat shock protein (HSP) production [21]. These proteins protect cells against heat stress by refolding proteins in the cytoplasm which have been denatured by high temperatures. The expression of Hsp70 is increased up to 20 fold when subjected to chronic thermal stress [48].

The temperature humidity index (THI) is commonly used to determine the level of heat stress in dairy cows. Lactating dairy cows start suffering mild heat stress at THI of 72, moderate heat stress at THI > 80 and severe heat stress at THI > 90 [3, 49]. West *et al.* [50] reported that increased THI resulted in decreased dry matter intake and thereby reduced milk yield. An increase in body temperature usually accompanies this rise in ambient temperature and is the primary stimulus for reduction in both feed intake and milk production [22, 51]. Moreover high-producing cows are extremely vulnerable to high ambient temperatures and humidity because at higher levels of milk yield metabolic heat production, DMI for higher production and thereby, increased heat increment that increases metabolism [5] causing heat stress on dairy animals.

Small [52] found that supplementation of 0, 6 and 12 g/d encapsulated niacin to multiparous Holstein cows had no effects on skin temperature (Table 1). Zimbelman *et al.* [20] conducted a study in twelve multiparous Holstein cows, given either 0g/d niacin or 12g/d of encapsulated niacin, and exposed to thermoneutral or heat stress conditions in climate controlled chambers, the temperature humidity index (THI) during thermoneutral conditions (TN) never exceeded 72, whereas, heat Stress (HS) conditions consists of circadian temperature range in which THI index exceeded 72 for 12 h/d and found that average evaporative heat loss for shaved and unshaved skin for control and niacin supplemented treatments was higher during HS (Table 1). The niacin fed cows had decreased rectal temperatures during heat stress compared with the control diet fed cows (38.17 vs. 38.34 °C). This mechanism of dairy animals towards better acclimation to heat stress may be attributed to the vasodilatory and heat shock protein enhancing property of niacin.

Costanzo *et al.* [19] Studied the effect of niacin supplementation on thermo-regulation in 26 Holstein cows beginning at approximately 90 days under heat stress conditions ranging between THI values of 63.1 and 85.1 (Table 1). Niacin supplementation among the cows receiving treatment increased in concentration over three consecutive 17-day periods from 12 g/cow/d to 24 g/cow/d to 36 g/cow/d NA. Treatments did not affect rectal temperature. They used an infrared thermometer to measure daily skin temperatures from shaved areas on the tail and rump of each cow. It was determined that cows supplemented with niacin had lower skin temperatures on the rump during the first 17-day period, and the tail skin temperatures followed the same trend. Tail skin temperatures were also significantly lower during the second 17-day period. There were no differences from control during the third 17-day period. Rectal temperatures during all three periods remained constant and authors proposed two explanations for the reduced skin temperatures with constant rectal temperatures: (1) heat transfer was reduced so the cows gained less heat from the environment while maintaining a stable core body temperature, or (2) evaporative heat loss was increased while heat gain was regulated such that cows maintained a stable core body temperature. Pineda *et al.* [53] reported that dietary supplementation of rumen protected niacin @ 15 g/cow/d during higher ambient temperature and higher mean THI improved milk yield and lowered vaginal temperatures. Lohölter *et al.* [54] reported that feeding combination of rumen protected niacin and high concentrate (60%) diet to primiparous dairy cows increased milk production and respiration rate, indicating evaporative heat loss from lungs.

Conclusions

Niacin supplementation during heat stress in dairy animals leads to inconsistent results, therefore it is still impossible to define dose and effect of niacin during heat stress period. However, it is obvious that supplementation of niacin is beneficial in postpartum dairy animals under heat stress and negative energy balance, but economics need to be given due share. There are certain gaps in knowledge which needs to be resolved by conducting more trials with this vitamin during hot weather regarding production and digestibility.

Table 1: Effect of niacin supplementation on physiological parameters during hot weather

Reference	Niacin Supplement (g/d)	Body temperature (◦C)	Respiration rate (bpm)
Yuan *et al.* 2012	0	38.4 (Rectal temperature)	-
	12 (RPN)	38.5	-
Zimbelman *et al.* 2010	0	38.34* (Rectal temperature)	50.8
	12 (RPN)	38.17*	54.5
	0	34.3 (shoulder, shaved)	
	12 (RPN)	34.1	
	0	33.1 (shoulder, unshaved)	
	12 (RPN)	33.6	
	0	33.8 (Rump, shaved)	
	12 (RPN)	33.7	
	0	33.4 (Tail head, shaved)	
	12 (RPN)	33.7	
	0	32.8 (Tail head, non-shaved)	
	12 (RPN)	32.6	
	0	92.4* (EHL($g/m^2/h$), shaved)	
	12 (RPN)	114.4*	
	0	87.2* (EHL($g/m^2/h$),unshaved)	
	12 (RPN)	101.7*	
Small, 2010	0	34.6 (Skin temperature)	-
	6 (RPN)	34.2	-
	12 (RPN)	34.4	-
Di Costanzo *et al*. 1997	0^a	34.1* (Rump temperature)	55
	12 (RPN)	33.7*	54
	0^b	35.6	72
	24 (RPN)	35.4	68
	0^c	31.7	47
	36 (RPN)	31.6	46
	0^a	34.0 (Tail temperature)	
	12 (RPN)	33.7	
	0^b	35.3*	
	24 (RPN)	35.0*	
	0^c	31.4	
	36 (RPN)	31.2	
	0^a	38.3 (Rectal temperature)	
	12 (RPN)	38.3	
	0^b	38.9	
	24 (RPN)	38.9	
	0^c	38.1	
	36 (RPN)	38.1	

RPN- rumen protected niacin, bpm- breaths per minute,
*significant differences ($P \leq 0.05$) have been observed for these parameters, EHL- evaporative heat loss superscript
A, b, c corresponds to period of mild stress, moderate stress and high stress respectively

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