# Review Article

# Niacin for dairy cattle: a review

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Due to the incorporation of niacin into the coenzymes NAD and NADP, niacin is of great importance for the metabolism of man and animals. Apart from niacin in feed and endogenous formation, microbial niacin synthesis in the rumen is an important source for dairy cows. But the amount synthesised seems to differ greatly, which might be influenced by the ration fed. Many studies revealed a positive impact of a niacin supplementation on rumen protozoa, but microbial protein synthesis or volatile fatty acid production in the rumen showed inconsistent reactions to supplemental niacin. The amount of niacin reaching the duodenum is usually higher when niacin is fed. However, not the whole quantity supplemented reaches the duodenum, indicating degradation or absorption before the duodenal cannula. Furthermore, supplementation of niacin did not always lead to a higher niacin concentration in blood. Effects on other blood parameters have been inconsistent, but might be more obvious when cows are in a tense metabolic situation, for example, ketosis or if high amounts are infused post-ruminally, since ruminal degradation appears to be substantial. The same is valid for milk parameters. In the few studies where blood niacin and milk parameters have been investigated, enhanced niacin concentrations in blood did not necessarily affect milk production or composition. These results are discussed in the present review, gaps of knowledge of niacin's mode of action on the metabolism of dairy cows are identified and directions for future research are suggested.

Niacin: Dairy cows: Nicotinic acid: Nicotinamide

Niacin is of great importance in the metabolism due to its incorporation into the coenzymes NAD and NADP<sup>(1)</sup>. Both forms of niacin, nicotinic acid (NA) and nicotinamide (NAM), can be converted into the coenzymes, although they contain only NAM as a reactive component. Apart from feed as a source of niacin, nearly all species are able to synthesise the vitamin<sup>(1-3)</sup> from tryptophan<sup>(3)</sup> and quinolinate<sup>(4)</sup>. Since micro-organisms are able to produce niacin as well, ruminants have an additional supply due to their rumen microbes<sup>(5)</sup>. Ruminal synthesis of niacin was estimated to be 1804 mg/d for a 650 kg cow producing 35 kg of 4 % fatcorrected milk/d<sup>(6)</sup>. This seems to cover the requirement definitely, which was assumed to be 256 mg/d for tissues and 33 mg/d for milk production, thus 289 mg/d in total<sup>(6)</sup>. Therefore, it was concluded that a general supplementation could not be advised<sup>(6,7)</sup>. But tissue requirements are estimated based on data from lactating sows and have not been experimentally determined<sup>(6)</sup>. Furthermore, synthesis might vary, for example, when different feeding regimens are applied<sup>(8)</sup>. Indeed, numerous studies showed positive responses to a niacin supplementation. On the other hand, a lot of research

has been done where administration of niacin did not have any effect. Therefore current literature is reviewed here to distinguish the vitamin's impact on cow performance and metabolism. The aim of the present review is to present the state of knowledge on niacin synthesis in the rumen and the amount of niacin arriving at the duodenum, niacin's mode of action on ruminal and several blood parameters as well as its influence on milk production and composition. Where possible, conclusions are drawn from experiments and gaps of knowledge are identified. Cognition of these processes would facilitate a decision on necessity and time of a niacin supplementation.

To our knowledge, the last detailed review available on niacin (NA and NAM) in dairy cow nutrition was done in  $1993^{(9)}$ . Therefore in the present review studies newer than 1990 are used to show developments. But in some cases (rumen, duodenum), older literature was included as a comparison with few new results available. Only significant effects (P < 0.05) and tendencies (P < 0.10) are mentioned, unless otherwise noted. In all studies, supplemental niacin was not rumen-protected.

Abbreviations: BHBA, β-hydroxybutyrate; F:C ratio, forage:concentrate ratio; NA, nicotinic acid; NAM, nicotinamide; NFC, non-fibre carbohydrate; VFA, volatile fatty acid.

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#### Rumen

Niacin in the rumen

In Table 1, niacin concentrations in ruminal contents from several studies are summarised. In interpretation of the results, it has to be kept in mind that different analytical methods for niacin determination exist (for example, colorimetric, microbiological and HPLC methods<sup>(10)</sup>). This could lead to different results as was proven for cereal-based foods analysed by microbiological and HPLC methods<sup>(10)</sup>.

Niacin concentration in the rumen was enhanced if pure NA or NAM was supplemented (11,12), while the highest intake via feed components did not necessarily force the highest concentration in the rumen (8,13). Santschi *et al.* (8) found no difference in total niacin content in the rumen when comparing rations with a forage:concentrate ratio (F:C ratio) of 60:40 or 40:60. However, they noticed an effect on the concentrations of each vitamer. Although no NAM was present in the feed, it was found in the rumen. Furthermore, NAM was significantly increased with the low-forage ration. NA decreased numerically and hence total niacin content was not affected. Earlier work showed an effect of the F:C ratio on ruminal niacin concentrations, which was highest in the all-concentrate ration (14) (data not shown). Thus, there is evidence that ruminal niacin concentrations and/or the concentrations of each vitamer are influenced by niacin supplementation and the F:C ratio.

Some studies have been conducted to measure the ruminal synthesis of niacin. Micro-organisms use aspartate and dihydroxyacetone phosphate for niacin production<sup>(4)</sup>. It is extremely difficult to measure real synthesis; therefore apparent synthesis is calculated by subtracting the intake from the amount reaching the duodenum. Some data are given in Table 2. It can be assumed that there is an influence of type of feed. Zinn et al. (15) mentioned a stimulating effect of starch on the ruminal synthesis of all B vitamins. Schwab et al. (16) found a significant effect of the non-fibre carbohydrate (NFC) content of feed on niacin synthesis, while the F:C ratio had no effect. But the effect of NFC might also reflect large differences in niacin intake (Table 2). In the above-mentioned studies where an effect of the F:C ratio on ruminal niacin concentrations was found<sup>(8,14)</sup>, duodenal niacin flow was not measured, therefore it was not possible to calculate apparent synthesis to compare these values.

In all studies listed in Table 2, the ration with the highest niacin content within a study resulted in the lowest apparent niacin synthesis. It was stated that there seems to be an optimal concentration. Synthesis will occur below this level and above it, excess niacin is degraded by the bacteria<sup>(17)</sup>. This might be the reason why in two studies with cows and feedlot calves where 6 or  $2\,\mathrm{g}$  NA/d were supplemented  $^{(11,15)}$ , only  $2\,$ and 20%, respectively, of the amount added reached the duodenum. Santschi *et al.* <sup>(18)</sup> reported a ruminal disappearance rate for niacin of 98.5% as well. The fate of niacin that disappeared from the rumen is not clear. Zinn et al. (15) suggested either degradation or absorption. It is not completely clarified if absorption of vitamins could take place in the rumen. Erickson et al. (19) found free NAM to be absorbed at 0.98 g/h from a dilution in a washed rumen of cows. NA was not absorbed, because it is ionised under a physiological pH. But usually, most of the niacin is bound in the bacterial fraction<sup>(8,19,20)</sup> Therefore, under normal circumstances, no absorption should

take place from the rumen<sup>(18)</sup>. Yet it has to be kept in mind that with niacin supplementation, a high amount of usually free niacin reaches the rumen. Thus, some absorption might occur. However, in the work of Campbell *et al.* <sup>(12)</sup>, supplementation of NAM gave significantly higher duodenal values of niacin than NA. If only NAM is absorbed from the rumen at normal ruminal pH values<sup>(19)</sup>, the opposite would be expected. Consequently, ruminal degradation might be the reason for the high disappearance rate of supplemented niacin from the rumen. Another possible explanation could be that niacin is absorbed in the proximal duodenum, before the duodenal cannula. In man, niacin is absorbable from the stomach as well<sup>(21)</sup>. To our knowledge, no studies concerning absorption from the abomasum are available.

In summary, niacin concentrations and apparent synthesis in the rumen are affected by niacin supplementation and the ration fed. But it is not known which feed component most influences niacin in the rumen. If niacin is supplemented, only a small part reaches the duodenum. Ruminal absorption might occur, but does not seem to make a large contribution. Ruminal degradation or absorption in the abomasum or before the duodenal cannula seems more likely.

# Effect of niacin on rumen metabolism

In contrast to ruminal bacteria it is assumed that protozoa are not able to synthesise niacin and need to cover their requirements from feed or bacterial synthesis<sup>(22)</sup>. Doreau & Ottou<sup>(22)</sup> observed no effect of 6 g NA on bacteria, but an increase of protozoa<sup>(22)</sup>. This especially concerned *Ophryoscolecidae*, but *Isotrichidae* were not affected. Increasing protozoal numbers, especially *Entodinia* (family *Ophryoscolecidae*), may increase bacterial numbers as well, because *Entodinia* are able to regulate the ruminal environment by consuming starch<sup>(19)</sup>. Others also found a significant increase in total protozoa in the rumen fluid due to niacin feeding<sup>(23–25)</sup>, which was once primarily attributable to increases in numbers of *Entodinia* <sup>(25)</sup>. Therefore, an effect of niacin on the microbial population is likely, but might be mainly on protozoa.

As a result of this probable effect of niacin on microbial population, ruminal N metabolism could also be affected. A stimulating effect of niacin on microbial protein synthesis has been observed *in vitro* <sup>(26)</sup> and *in vivo* <sup>(23,24)</sup>. In contrast, in some *in vivo* studies no influence was seen on microbial protein production, either on the total amount or on the efficiency <sup>(12,15)</sup>.

Whereas some *in vivo* trials<sup>(22,27,28)</sup> showed no niacin effect on ammonia concentration in the rumen, other *in vitro* <sup>(26)</sup> and *in vivo* <sup>(23,24)</sup> experiments showed a decreasing effect of niacin on rumen NH<sub>3</sub>-N. An interaction of fat and niacin towards increasing ammonia concentrations in the high-fat, and decreasing values in the low-fat, diet after niacin feeding was also found *in vivo* <sup>(27)</sup>. It is known that ammonia fixation of the rumen bacteria and fungi occurs largely via NADP- or NAD-linked glutamic dehydrogenase, and possible assimilation of ammonia via NAD<sup>+</sup>-dependent glutamic dehydrogenase was also shown for protozoa<sup>(29)</sup>. This might be favoured by a niacin supplementation.

The fermentation pattern of carbohydrates might also be altered due to a possible niacin effect on the microbial

Table 1. Niacin concentrations in the rumen of cattle

Reference	Feeding ration	Niacin content of feed (mg/kg DM)	Niacin intake (mg/d)	Niacin concentration in the rumen	Vitamer	Studied fraction
Riddell <i>et al.</i> (1985) <sup>(11)</sup>	55 % wheat straw, 45 % concentrate (corn starch, dextrose, soyabean meal)				NA and NAM†	Whole rumen content
	Without niacin	6	50	102-114 mg/kg DM <sup>a</sup> *		
	With 6 g NA	697	6060	119-155 mg/kg DM <sup>b</sup> *		
Abdouli & Schaefer (1986) <sup>(13)</sup>	27 % lucerne hay; 73 % barley	64	868	0.48 mg/l fluid + 2.32 mg NAD/l <sup>a</sup>	NA and NAM†	Rumen fluid
	29 % lucerne hay; 71 % oats	19	166	0-32 mg/l fluid + 1-51 mg NAD/lb		
Campbell <i>et al.</i> (1994) <sup>(12)</sup>	60 % forage (lucerne haylage, maize silage), 40 % concentrate (corn, soyabean hulls and meal)					Rumen fluid
	Without niacin	n.d.	_	0 mg/l fluid <sup>a</sup> 0 mg/l fluid	NA NAM	
	With 12 g NA	n.d.	+12 000 NA	14 mg/l fluid <sup>b</sup> 0 mg/l fluid	NA NAM	
	With 12 g NAM	n.d.	+12 000 NAM	14 mg/l fluid <sup>b</sup> 0 mg/l fluid	NA NAM	
	With 6g NA and 6g NAM	n.d.	+6000  NA + 6000  NAM	12 mg/l fluid <sup>b</sup> 0 mg/l fluid	NA NAM	
Santschi <i>et al.</i> (2005) <sup>(8)</sup>	60 % forage (mixed silage, maize silage), 40 % concentrate (corn, soyabean meal)	26	520	143 mg/kg DM 77 mg/kg DM <sup>a</sup>	NA NAM	Solid-associated bacteria
	40% forage (mixed silage, maize silage), 60% concentrate (corn, soyabean meal)	23	453	137 mg/kg DM 94 mg/kg DM <sup>b</sup>	NA NAM	
	60% forage (mixed silage, maize silage), 40% concentrate (corn, soyabean meal)	26	520	173 mg/kg DM 86 mg/kg DM <sup>a</sup>	NA NAM	Liquid-associated bacteria
	40% forage (mixed silage, maize silage), 60% concentrate (corn, soyabean meal)	23	453	161 mg/kg DM 123 mg/kg DM <sup>b</sup>	NA NAM	
	60 % forage (mixed silage, maize silage), 40 % concentrate (corn, soyabean meal)	26	520	0·08 mg/l fluid 0·53 mg/l fluid	NA NAM	Particle-free fluid
	40% forage (mixed silage, maize silage), 60% concentrate (corn, soyabean meal)	23	453	0·09 mg/l fluid 0·62 mg/l fluid	NA NAM	

NA, nicotinic acid; NAM, nicotinamide; n.d., not determined.

<sup>&</sup>lt;sup>a,b</sup> Values with unlike superscript letters within a study were significantly different ( $P \le 0.05$ ).

<sup>\*</sup>Depending on different sampling times after feeding (0 to 8 h), means were significantly different at 4 and 6 h after feeding.

<sup>†</sup>The vitamin content was determined via microbiological assay, where it is not possible to distinguish between the vitamers.

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Table 2. Apparent synthesis of piacin in the rumen of cattle and flow at the duodenum

Reference	Feeding ration	Niacin supplement (g/d)	DM intake (kg/d)	Niacin intake with feed (mg/d)	Duodenal niacin flow (mg/d)	Apparent synthesis (mg/d)†	
Riddell et al.	55% forage (wheat straw), 45% concentrate	0	8.7	50	85	35	
(1985) <sup>(11)</sup> ‡§	(corn starch, dextrose, soyabean meal)	6 NA	8.7	6060	138*	- 5922	
Miller et al.	12 % lucerne meal, 88 % maize grain, urea	0	6.7	204	589	386	
(1986) <sup>(32)</sup> ‡§	13 % lucerne meal, 87 % wheat grain	0	7.0	357	785	428	
	13% lucerne meal, 87% oat grain, urea	0	7.4	163	750	586	
	13% lucerne meal, 87% barley grain, urea	0	6⋅5	485	664	179	
	13 % lucerne meal, 87 % sorghum grain, urea	0	7.3	295	813	518	
	11 % lucerne meal, 89 % maize grain	0	6.2	93	557	485	
	70 % lucerne meal, 30 % maize grain	0	6.3	314	753	439	
Zinn <i>et al.</i>	45 % forage (lucerne hay, Sudan grass),	0	3.4	67	277	210	
(1987) <sup>(15)</sup> द	55 % concentrates (corn, molasses, fat)	0.2	3.4	267	207	- 60	
		2	3.4	2067	401	<b>- 1666</b>	
Campbell <i>et al.</i> (1994) <sup>(12)</sup> **	60% forage (lucerne haylage, maize silage), 40% concentrate (corn, soyabean hulls	0	19-9	n.d.	1716 NA 0 NAM		
	and meal)	12 NA	19-9	>12 000 NA	3187 NA†† 0 NAM		
		12 NAM	19.9	>12 000 NAM	4902 NA†† 0 NAM		
		6 NA + 6 NAM	19-9	>6000 NA + 6000 NAM	3922 NA†† 0 NAM		
Santschi <i>et al.</i> (2005) <sup>(18)</sup>	58 % forage (grass-legume silage, maize silage), 42 % concentrate (corn, soyabean meal, protein supplement)	0	19-8	465 NA 0 NAM	1334 NA 1242 NAM	912 NA 1259 NAN	
	B-vitamin blend infused post-ruminally	1·17 NAM	19-8	465 NA 1173 NAM	1815 NA 1140 NAM		
Schwab <i>et al.</i> (2006) <sup>(16)</sup>	35% forage (corn silage, Lucerne and grass hay), 65% concentrate (soyabeans hulls	0	21.3	620 NA‡‡§§	1209 NA	589 NA	
,	and meal, beet pulp), total 30 % NFC			1399 NAM‡‡§§	1256 NAM‡‡	− 143 NAM§§	
	35 % forage (corn silage, lucerne and grass hay), 65 % concentrate (corn, barley, soyabean hulls and meal, beet pulp), total 40 % NFC	0	22.2	489 NA‡‡§§ 838 NAM‡‡§§	1504 NA 1370 NAM‡‡	1015 NA 532 NAM§§	
	60 % forage (corn silage, lucerne and grass hay), 40 % concentrate (soyabean hulls and meal, beet pulp, blood meal, fat), total 30 % NFC	0	18-1	462 NA‡‡§§ 727 NAM‡‡§§	1016 NA 892 NAM‡‡	555 NA 165 NAM§§	
	60 % forage (corn silage, lucerne and grass hay), 40 % concentrate (corn, barley, soyabean hulls and meal, beet pulp, blood meal, fat), total 40 % NFC	0	19-8	363 NA‡‡§§ 221 NAM‡‡§§	1134 NA 837 NAM‡‡	771 NA 615 NAM§§	

NA, nicotinic acid; NAM, nicotinamide; n.d., not determined; NFC, non-fibre carbohydrates.

population, resulting in a change in volatile fatty acid (VFA) production in the rumen. Results for in vivo experiments are presented in Table 3. Butyrate was the VFA which was mostly but inconsistently affected, but there were also influences on acetic and propionic acid; in some surveys, no effect was seen at all. The effect of niacin on butyrate might be induced by the effect on rumen protozoa, since the presence of some protozoa species led to more butyrate produced<sup>(30)</sup> This would match with the work of Doreau & Ottou<sup>(22)</sup>, who observed higher protozoal counts and an increase in the

molar proportion of butyrate. But it is contrary to Samanta et al. (24), who observed higher protozoal counts and a decrease in the molar proportion of butyrate. Thus, the effect of niacin on protozoa might not be the main reason for its effect on VFA.

In total, the responses of ruminal parameters to niacin feeding vary greatly. Ottou & Doreau<sup>(31)</sup> concluded that response differences could be due to the level of niacin supplementation, but this was not obvious here, since niacin concentrations varied in an equal range in all studies.

<sup>\*</sup>Significant differences ( $P \le 0.05$ ) between control and niacin groups. In the paper of Santschi *et al.* (18), the level of significance was not declared; furthermore, Zinn *et al.* (15) and Miller *et al.* (32) did not calculate the apparent synthesis. Therefore it was not possible to characterise significances in these studies. † Apparent synthesis = duodenal flow - intake.

<sup>‡</sup> In these studies, apparent ruminal synthesis was not calculated by the authors, but daily intake and duodenal flows were given, therefore apparent synthesis was calculated by us. § The vitamin content was determined via microbiological assay, where it is not possible to distinguish between the vitamers. || Level of niacin intake differed significantly (P≤0.05).

<sup>¶</sup> In this study, the vitamer applied was not named. It was just stated that niacin was supplemented. But since the term niacin is occasionally also used as a synonym for NA<sup>(45)</sup>, it is assumed that NA was fed in this survey.

<sup>\*\*</sup> In this study, concentrations per litre duodenal digesta were given, but the authors stated that on average duodenal content had a DM content of 6.65 % and a daily DM flow of 16.3 kg. Based on this, the values presented here are calculated.

<sup>††</sup> Significant differences between control v. niacin and NA v. NAM (P≤0.05).

<sup>‡‡</sup> Significant effects of forage ( $P \le 0.05$ ).

<sup>§§</sup> Significant effects of NFC (P≤0.05).

Table 3. Effect of niacin on ruminal total volatile fatty acid (VFA) concentrations and molar proportions of individual VFA in cattle

Reference	Control ration	Niacin (per d)	Niacin effect
Campbell <i>et al.</i> (1994) <sup>(12)</sup>	60% forage (lucerne haylage, maize silage), 40% concentrate (soyabean hulls and meal, corn)	12g NA	No effect
	60% forage (lucerne haylage, maize silage), 40% concentrate (soyabean hulls and meal, corn)	12g NAM	No effect
	60% forage (lucerne haylage, maize silage), 40% concentrate (soyabean hulls and meal, corn)	$6\mathrm{g}\mathrm{NA} + 6\mathrm{g}\mathrm{NAM}$	No effect
Christensen <i>et al.</i> (1996) <sup>(27)</sup>	40 % forage (lucerne haylage, maize silage), 60 % concentrate (corn, soyabean hulls and meal), total 2-8 % fatty acids	12g NA	C <sub>2</sub> (↓), C <sub>4</sub> ↑ Interaction with fat
	40 % forage (lucerne haylage, maize silage), 60 % concentrate (corn, soyabean meal, whole raw soyabeans, tallow), total 5.9 % fatty acids	12g NA	$C_2(\downarrow)$
Doreau & Ottou (1996) <sup>(22)</sup>	60 % forage (corn silage, grass hay), 40 % concentrate (soyabean meal, rapeseed meal, urea)	6 g NA	C <sub>4</sub> †
Madison-Anderson et al. (1997) <sup>(28)</sup>	50% forage (lucerne hay, maize silage), 50% concentrate (corn, barley, soyabean meal)	12 g NA	No effect
	50% forage (lucerne hay, maize silage), 50% concentrate (corn, barley, extruded soyabeans), 3% of DM as unsaturated fat	12g NA	No effect
Samanta <i>et al.</i> (2000) <sup>(24)</sup>	Corn, ground nut-cake, wheat bran and straw as forage, amounts were not specified	400 mg NA/kg concentrate	Total VFA $\uparrow$ , C <sub>3</sub> $\uparrow$ , C <sub>4</sub> $\downarrow$
Kumar & Dass (2005) <sup>(23)</sup>	50 % forage (wheat straw), 50 % concentrate (soyabean cake, wheat bran, corn)	100 mg NA/kg feed	Total VFA ↑
	50 % forage (wheat straw), 50 % concentrate (soyabean cake, wheat bran, corn)	200 mg NA/kg feed	Total VFA ↑

NA, nicotinic acid; NAM, nicotinamide; C2, acetic acid; C3, propionic acid; C4, butyric acid; (1), tendency; ↑, increase; 1, decrease.

Furthermore, Ottou & Doreau<sup>(31)</sup> listed dietary conditions, diurnal variations in the concentration of rumen protozoa, micronutrients and other growth factors as an explanation. It must also be kept in mind that measuring ruminal concentrations is dependent on time after feeding, which was not equal for all the studies cited. This might explain some of the differences obtained and it cannot be excluded that some of the observed niacin effects are rather due to high diurnal variations in the rumen than a response to niacin.

### **Duodenum**

The amount of niacin reaching the duodenum varies less than does the concentration in the rumen. Duodenal flow values for niacin are given in Table 2. From these data it can be concluded that a niacin supplementation led to higher niacin values reaching the duodenum<sup>(11,12,15,18)</sup>. But the extent to which this occurs varies and is low. A loss of niacin occurs even when the vitamin is infused into the abomasum<sup>(18)</sup> but to a lower extent. This indicates abomasal or duodenal absorption before the duodenal cannula. Niacin flow at the duodenum was higher than daily niacin intake after postruminal niacin supplementation, even if the total amount given did not reach the duodenum<sup>(18)</sup>. This was not the case when niacin was added to the ration<sup>(11,12,15)</sup>. Therefore, it is likely that an oral niacin supplementation is highly degraded in the rumen and might also suppress niacin synthesis. A higher amount seems to reach the duodenum when it is infused post-ruminally.

The type of feed might modify the amount of niacin reaching the duodenum. Schwab *et al.* <sup>(16)</sup> found an effect of the F:C ratio. The high-forage ration decreased NAM content in duodenal fluid significantly, and tended to decrease

NA content. The NFC content had no effect. Apparent synthesis of niacin in the rumen was affected by NFC, but not by the F:C ratio. This further indicates that the NFC effect on apparent synthesis might be due to different niacin intake, and that the F:C ratio could be important. But more information is lacking.

Even if given post-ruminally, NAM seems to convert to NA. After NAM supplementation only the amount of NA was enhanced at the duodenum, while NAM was even lower than in the control group<sup>(18)</sup>. The authors concluded that this was due to the acidic environment in the abomasum which may transform NAM to NA. Additionally, supplementation of NAM in feed enhanced the amount of niacin arriving at the duodenum to a higher extent than did NA<sup>(12)</sup>.

Apparent absorption of niacin in the duodenum was not influenced by the type of feed<sup>(32)</sup> and accounted for 67%<sup>(32)</sup>, 79%<sup>(15)</sup> and 84% (73% of the NA and 94% of the NAM)<sup>(18)</sup> of the amount reaching the duodenum. When supplemental niacin was fed, Riddell *et al.*<sup>(11)</sup> observed a higher amount of niacin reaching the duodenum, but excretion with faeces was equal. Therefore, the authors concluded that absorption in the duodenum must have been higher in the supplemented group. But no measurements were taken in the large intestine, thus results could also be due to a higher degradation or absorption in the large intestine. In other studies, a B vitamin blend was supplemented, either in the feed or post-ruminally, but did not influence absorption in the duodenum<sup>(18)</sup>.

Little knowledge is available concerning the mechanism of absorption. New research in human subjects suggests that the mechanism for NA absorptions in physiological amounts is dependent on an acidic pH and a specialised Na<sup>+</sup>-independent carrier-mediated system<sup>(33)</sup>. In higher concentrations,

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diffusion was observed to be the main mechanism in rats<sup>(34)</sup>. For NAM, absorption was suggested to occur via diffusion at twice the rate of NA<sup>(35)</sup>, but new research on NAM absorption is not available. Furthermore, it is not known if the same mechanisms take place in ruminants.

Briefly, niacin feeding enhances the amount reaching the duodenum. But not the whole quantity supplemented reaches the duodenum, even after post-ruminal infusion. This provides evidence for abomasal or duodenal absorption before the duodenal cannula. Furthermore, there might be influences of the type of feed and vitamer given. Apparent absorption in the duodenum seems to be high, but the mechanism of absorption has not yet been studied in ruminants.

#### **Blood**

Niacin in blood

Data concerning blood niacin concentrations are given in Table 4. Obviously, concentrations vary in a wide range. A reason for this might lie in difficulties of vitamin analysis and/or in different blood fractions examined.

There is disagreement about the existence of NA in blood. Whereas Campbell *et al.* (12) found both vitamers, Kollenkirchen *et al.* (36) stated that only NAM was present in the blood of sheep. In two studies, only values for NAM were named (37,38). It was not stated whether only NAM was found, or if only NAM was analysed. The metabolism of niacin in the body might provide an explanation for this discrepancy. There appears to be no direct conversion of NA to NAM. NA is first converted to NAD, and NAM is then produced from the hydrolysis of excess NAD (39). Part of the NAM formed is reutilised to NAD, but NAM is produced in excess to supply extra-hepatic organs with niacin (40). Therefore, NAM seems to be the main transport form of niacin in blood (4), although the NA that escaped liver metabolism is also transported to various cell types in the body (41).

The difference in niacin content of the analysed blood fractions between control and niacin-supplemented groups was significant in three studies<sup>(37,38,42)</sup>, but not in the others<sup>(12,43,44)</sup>. Campbell *et al.* <sup>(12)</sup> found a significant difference between the vitamers. The addition of NA enhanced both NA and NAM, while feeding NAM had a decreasing impact on blood NA and NAM concentrations. This was not expected, since the NAM-supplemented group had the highest duodenal values of niacin; at this point it is not explainable why this should result in the lowest niacin content of plasma. For rats, it was demonstrated that NAM is also able to pass from the bloodstream back to the lumen<sup>(34)</sup>. This could explain the previously mentioned results in the NAM group<sup>(12)</sup>, should it occur in ruminants as well. But the reasons for and physiological role of such a process remain unclear<sup>(34)</sup>.

In sheep, the NAM concentration of whole blood was not influenced by NA or NAM supplementation<sup>(36)</sup>. Hence the conclusion was drawn that concentrations in blood appeared to be unaffected by supplementation, even though the amount reaching the duodenum was increased. In contrast, Ottou *et al.* <sup>(42)</sup> infused 6 g niacin into the proximal duodenum and observed an increase in the niacin content of whole blood. The results of this study also lead to the conclusion that

ruminal absorption could be excluded as a reason for observed differences in blood niacin content, because changes occurred after post-ruminal infusion. In other studies as well there was no obvious relationship between ruminal and blood niacin concentrations<sup>(12,36)</sup>.

In humans, there seems to be a kind of homeostasis of niacin in blood<sup>(45)</sup>. Excess niacin gets converted into a storage form of NAD in the liver. Pires & Grummer<sup>(46)</sup> conducted an experiment with different amounts of NA infused in the abomasum and concluded from effects on blood metabolites that some build-up of NA in blood or adipose tissue might have occurred. If some homeostasis system exists also in ruminants, it would explain studies without an effect on blood niacin, but would fail to elucidate observed differences in the others.

# Effect on blood metabolites

The effect of niacin on several blood parameters (glucose, NEFA and  $\beta$ -hydroxybutyrate (BHBA) as the main ketone body) has been studied extensively in dairy cattle (Table 5). Only surveys including glucose, NEFA and BHBA are incorporated in this Table. One study mentioned separate results for several lactation weeks<sup>(47)</sup>, and so values for week 2 were included in Table 5 as the earliest sampling time.

# Non-esterified fatty acids

In Table 5, the only significant effect of a niacin supplementation was an increase of NEFA in the niacin group (43). This was not expected, since niacin is thought to be anti-lipolytic, which would result in a lower NEFA concentration. The authors proposed that this was due to increased lipoprotein lipase activity, which is stimulated by NA, thus resulting in decreased plasma TAG content and increases in NEFA. Apart from this effect, significant interactions between niacin and fat supplementation were observed, resulting in an increase in NEFA when niacin was supplemented, while NEFA decreased when niacin and fat were given<sup>(48)</sup>. If only studies are considered where niacin was given to periparturient cows (treatment started 2 weeks before or within 2 weeks after calving), there was no effect of a niacin supplementation (Table 5) as was described by Chamberlain & French<sup>(49)</sup> as well. Jaster & Ward<sup>(47)</sup> also analysed influences in other lactation weeks (not included in Table 5), where a decreasing effect of niacin on NEFA in week 4 was observed. Therefore, if given orally, it is not clear that niacin acts more on NEFA in periparturient than other cows.

NA was used as a lipid-lowering agent in humans for decades, but, until recently, cellular mechanisms have not been well understood<sup>(50)</sup>. In 2003, the receptor HM74A was identified in adipose tissue, to which NA is a high-affinity ligand<sup>(51)</sup>. Activation of the receptor starts an inhibitory G-protein signal that reduces adipocyte cAMP concentrations by repressing adenyl cyclase activity, which inhibits lipolysis. The endogenous ligand of HM74A is not known<sup>(50)</sup>. But NAM acted only as a very weak agonist on HM74A and seems therefore not to affect plasma lipid profiles<sup>(51)</sup>. For humans it was concluded that the endogenous level of NA is too low to impact on receptor activity<sup>(52)</sup>, but supplementation might enhance this level.

Table 4. Niacin concentrations in blood of cattle

Reference	Feeding ration	Niacin supplement (g/d)	DM intake (kg/d)	Niacin intake (g/d)	Niacin concen- tration of blood (μg/ml)	Blood fraction
Driver <i>et al.</i> (1990) <sup>(38)</sup> †	45% forage (lucerne hay and silage), 55% concentrate (ground maize and oats,	0	21.4		0.7 NAM	Plasma
(, 1	heat-treated soyabean meal)	6	20.1		1.0 NAM*	
	45% forage (lucerne hay and silage),	0	19.3		0.6 NAM	
	55% concentrate (ground corn, and oats, heat-treated whole soyabeans)	6	20-4		1-0 NAM*	
Martinez et al.	40 % chopped lucerne hay, 60 % concentrate	0	23.8		14.3	Whole blood
(1991) <sup>(43)</sup> †‡	(beet pulp, whole cottonseed and -meal, corn, wheat, molasses), total 2 % fat	12	23.3		17.3	
	40 % chopped lucerne hay, 60 % concentrate	0	23.6		8.1	
	(beet pulp, whole cottonseed and -meal, corn, wheat, molasses, fat), total 4% fat	12	23.2		9.7	
Lanham <i>et al.</i> (1992) <sup>(44)</sup> †‡	40% forage (corn silage, Bermuda grass hay), 60% concentrate (corn, soyabean meal)	0	19-8	0.69	1.1	Plasma
		Approximately 6§	16.7	5.14	1.3	
	40% forage (corn silage, Bermuda grass hay),	0	17.4	0.56	1.3	
	60% concentrate (corn, soyabean meal, whole cottonseed)	Approximately 6§	17.2	5.23	1.3	
Campbell <i>et al.</i> (1994) <sup>(12)</sup>	60% forage (lucerne haylage, maize silage), 40% concentrate (corn, soyabean hulls and	0	19-9		0·9 NA + 1·2 NAM	Plasma
	meal)	12 NA	19.9		1.3  NA + 1.3  NAM	
		12 NAM	19.9		0.6  NA + 0.9  NAM	
		6  NA + 6  NAM	19.9		1.0  NA + 1.0  NAM	
Ottou <i>et al.</i> (1995) <sup>(42)</sup> ‡	79% forage (corn silage, hay), 21% concentrate (beet pulp, wheat, barley, rapeseed meal, soyabean meal, molasses)	0	18-4		0.6	Plasma
	With niacin infused into the proximal duodenum	6 NA	19⋅3		2.5*	
	77% forage (corn silage, hay), 19% concentrate (rapeseed meal, soyabean meal) With 3.5% rapeseed oil infused into the proximal duodenum	0	17.9		0-4	
	With 3.5 % rapeseed oil and niacin infused into the proximal duodenum	6 NA	17.7		2.4*	
Cervantes <i>et al.</i> (1996) <sup>(37)</sup>	Eight different forage:concentrate ratios; lucerne hay or haylage and maize silage were used as forage, maize and soyabean meal as concentrate	0	20.3		1·6 NAM	Whole blood
	With 12 g NAM	12 NAM	24.0		1.9 NAM*	
	With 400 g Ca salts of fatty acids and 12 g NAM	12 NAM	21.1		1.9 NAM*	

NA, nicotinic acid; NAM, nicotinamide

It must be kept in mind that after supplementation in the usual range for dairy cows, NAM seems to be the dominating form of niacin in blood. Apart from relatively low NEFA values in some surveys, this could also explain the absence of a niacin effect on NEFA in most studies, even in those where an effect on blood niacin concentrations was shown<sup>(37,38,42)</sup>. In two of those studies, the increase in blood niacin was an increase of NAM<sup>(37,38)</sup>, which would not be expected to act on lipolysis. Reduction of plasma NEFA was achieved in fasting cows after one single abomasal infusion of 6 mg NA/kg body weight (approximately 5 g/cow)<sup>(46)</sup>, but not after continuous duodenal infusion of 6 g NA/cow per d<sup>(53)</sup>. Maybe if higher amounts of NA were to reach the duodenum, concentrations of NA in blood would

be enhanced, possibly due to an increase in absorption via passive diffusion of NA at higher concentrations. Therefore, lipolysis would be affected, while physiological amounts due to an oral supplementation are converted in the liver into NAM and have therefore no effect.

In human subjects, it was often observed that after the effect of NA decays there was a major rebound of NEFA plasma concentrations<sup>(50)</sup>. The same result was achieved in dairy cows as well<sup>(46)</sup>. Pires & Grummer<sup>(46)</sup> concluded that the magnitude of the rebound depends on the dose of NA or duration of time with decreased NEFA. Karpe & Frayn (50) suggested that NA interferes with the ability of adipose tissue to normally regulate its lipolysis, but mechanisms are not known. Pires & Grummer (46) state that if NA is continuously delivered

<sup>\*</sup> Significant differences (P $\leq$ 0·05) between the control and niacin groups have been observed for these parameters.

<sup>†</sup> In these studies, the vitamer applied was not named. It was just stated that niacin was supplemented. But since the term niacin is occasionally also used as synonym for NA<sup>(45)</sup>, it is assumed that NA was fed in these surveys.

<sup>‡</sup>The vitamin content was determined via different assays without possibility to distinguish between the vitamers.

<sup>§</sup> Niacin was mixed in the concentrate; the goal was to reach an intake of 6 g niacin/cow per d.

There was no difference between control and treatment, but there was between NA and NAM for the NA concentration in blood (P≤0.05).

Table 5. Impact of niacin on several blood metabolites

Reference	Feeding ration	Niacin sup- plement (g/d)	NEFA (μmol/l)	BHBA (mg/l)	Glucose (mg/l)	Blood fraction	Lactation week†
Driver et al.	45 % forage (lucerne hay and silage), 55 %	0	69 mg/l	106	495	Plasma	- 1 until 15
$(1990)^{(38)}$ ‡	concentrate (ground corn, ground oats,	6	82 mg/l	97			
	heat-treated soyabean meal)						
	45% forage (lucerne hay and silage), 55%	0	97 mg/l	116	443		
	concentrate (ground corn, ground oats, heat-treated whole soyabeans	6	74 mg/l	108	457		
Jaster & Ward	50 % maize silage, 50 % concentrate	0	250	29	556	Plasma	2
$(1990)^{(47)}$	(ground shelled corn, soyabean meal)	6 NA	202	33	518		
Martinez <i>et al.</i>	40.9/ shanned lucerne how 60.9/ concentrate	6 NAM	223	22	560	Diasma	Average
(1991) <sup>(43)</sup> ‡	40 % chopped lucerne hay, 60 % concentrate (beet pulp, whole cottonseed and -meal,	0	367	n.d.	711	Plasma	Average 84 DIM
	corn, wheat, molasses), total 2 % fat	12	490*		727 701		
	40 % chopped lucerne hay, 60 % concentrate	0	468 546*		721 720		
	(beet pulp, whole cottonseed and -meal, corn, wheat, molasses, fat), total 4 % fat	12	546*		739		
Erickson <i>et al.</i> (1992) <sup>(55)</sup>	45 % forage (lucerne grass haylage, maize silage), 55 % concentrate (high-moisture	0	265	65	554	Plasma	2 until 14
	shelled corn, soyabean meal)	12 NA	238	52*	553		
	With 3 % Ca salts of long-chain fatty acids	0	303	78	532		
	With 3% Ca salts of long-chain fatty acids and niacin	12 NA	352	65*	521		
Chilliard & Ottou (1995) <sup>(53)</sup>	79% forage (corn silage, hay), 20% concentrate (beet pulp, wheat, barley, rapeseed meal, soyabean meal, molasses)	0	130	46	725	Plasma	Average 110 DIM
	With niacin infused into the proximal duodenum	6 NA	93	40	733		
	77 % forage (corn silage, hay), 18 % concentrate (rapeseed meal, soyabean meal)						
	With 3.5% rapeseed oil infused into the proximal duodenum	0	118	49	665		
	With 3.5% rapeseed oil and niacin infused into the proximal duodenum	6 NA	150	47	683		
Cervantes <i>et al.</i> (1996) <sup>(37)</sup>	Eight different forage:concentrate ratios; lucerne hay or haylage and maize silage were used	0	120	39	588	Plasma	Average 112 DIM
	as forage, maize and soyabean meal as concentrate	12 NAM	126	38	589		
	With 400 g Ca salts of fatty acids	0	157	40	600		
	With 400 g Ca salts of fatty acids and nicotinamide	12 NAM	151	33	592		
Christensen <i>et al.</i> (1996) <sup>(27)</sup>	40% forage (lucerne haylage, maize silage), 60% concentrate (corn, soyabean hulls and	0	157	64	607	Plasma	Average 30 DIM
	meal), total 2.8% fatty acids	12 NA	174	58	681		
	40 % forage (lucerne haylage, maize silage),	0	159	50	681		
	60% concentrate (corn, soyabean meal, whole raw soyabeans, tallow), total 5.9% fatty acids	12 NA	189	54	736		
Minor <i>et al.</i> (1998) <sup>(54)</sup> ‡§	49–60 % forage (lucerne and maize silage), 51–40 % concentrate (cracked corn,	0	378	114	594	Plasma	– 19 d until 40
(1000) 43	soyabean meal, roasted soyabeans, whole cottonseeds)	12	389	110	610		until 10
	40-50% forage (lucerne and maize silage),	0	293	80	622		
	60-40 % concentrate (ground corn, starch, soyabean meal, roasted soyabeans, whole cottonseed)	12	225	78	640		
Drackley <i>et al.</i> (1998) <sup>(48)</sup> §	40–50 % forage (lucerne haylage, maize silage), 60–50 % concentrate (soyabean meal and	0	98	50	692	Plasma	4 until 43
()	hulls, shelled corn)	12 NA	117	48	693		
	40-50 % forage (lucerne haylage, maize silage),	0	134	46	718		
	60-50% concentrate (soyabean meal and hulls, whole raw soyabeans, shelled corn, fat)	12 NA	122	53	694		

BHBA, β-hydroxybutyrate; NA, nicotinic acid; NAM, nicotinamide; n.d., not determined; DIM, days in milk.

\*Significant differences (P≤0·05) between the control and niacin groups have been observed for these parameters.

†Blood values given in this Table derive from that lactation week or are a mean of the given time span, where 0 is calving; therefore negative numbers are weeks prepartum and positive values post-partum.

<sup>‡</sup> In these studies, the vitamer applied was not named. It was just stated that niacin was supplemented. But since the term niacin is occasionally also used as a synonym for NA<sup>(45)</sup>, it is assumed that NA was fed in these surveys.

 $<sup>\</sup>S$  Several diets postpartum were given; therefore, the forage:concentrate ratio differs.

in sufficient quantities, it will limit lipolysis in adipose tissue and therefore reduce plasma NEFA.

This phenomenon might also be an explanation for the increase in NEFA in the work of Martinez *et al.* <sup>(43)</sup>, if blood measurements were done in the rebound phase, but authors only named the day of blood sampling, not time after feeding. The time of measurement might be another explanation for studies without a niacin effect on NEFA. NEFA returned to starting values 4–6h after one abomasal infusion of 6 mg NA/kg body weight (approximately 5 g/cow)<sup>(46)</sup>. This might take longer with an oral supplementation, since niacin has to pass the reticulo-rumen, but in some studies blood concentration of NEFA was measured before morning feeding<sup>(48,53,54)</sup>, where the effect might already have disappeared.

In conclusion, NEFA have been shown to be lowered by NA under certain conditions, but not by NAM. After the effect of NA disappears, a rebound above basal values occurs, which afterwards returns to normal. Apparently, to induce these effects, the amounts of niacin arriving at the duodenum have to be high, which might not be the case in feeding trials with an oral, not rumen-protected supplementation. However, there were effects after oral supplementation as well. Based on data available, it is not possible to conclude if the presence or absence of an effect after oral supplementation is based on sampling time or the amount of NA arriving in blood.

# **β-***Hydroxybutyrate*

The only significant effect of niacin on BHBA in Table 5 was found in the work of Erickson *et al.* <sup>(55)</sup>, where BHBA was lowered due to niacin feeding. Even in studies where niacin concentrations in blood have been enhanced <sup>(37,38,42)</sup> no effect was found. But an interaction between niacin, fat and week of lactation was detected once <sup>(48)</sup>, since niacin feeding enhanced ketones during fat supplementation and decreased ketones when no fat was added throughout the study. But in lactation weeks 1 to 3, almost the opposite was seen. Jaster & Ward <sup>(47)</sup> also observed a time effect towards a significant reduction of BHBA in both NA- and NAM-supplemented groups in week 4, but not in lactation weeks 2 and 6 to 12.

An absence of an effect of niacin on BHBA was attributed to the low level of BHBA<sup>(27)</sup>, because supplementation was started later in lactation, after the period with the highest incidence of ketonaemia<sup>(12,48,53)</sup>. Driver *et al.* <sup>(38)</sup> found more NAM in the blood of treatment groups, but assumed this is only beneficial if the cows are in state of abnormal carbohydrate or lipid metabolism. As was discussed above, the absence of an effect even if niacin concentrations in blood were enhanced, might also be due to the fact that NAM has almost no impact on lipolysis.

If an effect was seen, the mode of action of niacin on ketones was not clearly explained. Erickson *et al.* <sup>(25)</sup> postulated that changes in blood ketone-body levels following the administration of NA are mainly and perhaps entirely due to changes in plasma NEFA levels, which was also observed in other surveys<sup>(56)</sup>. But this is not obvious in several studies in Table 5. BHBA concentrations in the niacin-supplemented group were significantly lower in the study of Erickson *et al.* <sup>(55)</sup>. This could not be seen in the NEFA level, at least not in the fat-supplemented rations. Others also observed

differences in responses of NEFA and BHBA concentrations in blood to a niacin supplementation<sup>(48)</sup>. Erickson *et al.* <sup>(55)</sup> concluded that NA impeded ketogenesis, but had no influence on lipolysis. As another mechanism they mentioned that mobilised fatty acids are stored in the liver of niacin-supplemented cows. However, in general it was deduced that the mechanism by which niacin reduces ketones is not known<sup>(55)</sup>.

It was recently discovered that BHBA is an endogenous ligand of HM74A in humans<sup>(52)</sup>. The authors suggested that BHBA is therefore itself anti-lipolytic and regulates its own production with a negative feedback by decreasing serum level of fatty acid precursors for hepatic ketogenesis. If this also happens in ruminants, it seems to support the theory that an impact of NA on NEFA is responsible for the effect of niacin on BHBA. The lack of responses in most studies might be traced back to either the amount of NA reaching the blood or to a time effect.

#### Glucose

In the studies cited in Table 5, no significant effect of niacin on blood glucose can be seen, even in studies with enhanced blood niacin concentrations. An impact of time after parturition is possible, since Jaster & Ward<sup>(47)</sup> found no effect in lactation weeks 2 and 8 to 12; however, in lactation weeks 4 and 6, the NAM group exhibited enhanced glucose concentrations, while the NA group was not different from control.

In other studies not included in Table 5, glucose concentrations were equal in control and treatment groups<sup>(28,44,57,58)</sup> or there was an increase<sup>(59)</sup> in the niacin-supplemented group.

For dairy cows it was assumed that increased glucose and insulin concentrations occurred in blood after niacin supplementation due to greater gluconeogenic activity<sup>(59)</sup>. Others concluded that it is not clear if this is due to increased gluconeogenesis or decreased removal of glucose<sup>(47)</sup>. Chilliard & Ottou<sup>(53)</sup> observed a decreased slope of glucose elimination after an intravenous injection of glucose when niacin was infused into the duodenum of cows in mid-lactation. Furthermore, the decrease in plasma glucose following an insulin challenge was less in the niacin group. In humans, NA was assumed to lower insulin sensitivity, but this was not observed in 20 % of subjects studied<sup>(60)</sup>. Enhanced glucose elimination after an intravenous glucose tolerance test was found in cows in negative energy balance, despite lower insulin concentration, which suggests an increased response to endogenous insulin<sup>(61)</sup>. It was proposed that the decreasing impact of sufficient amounts of NA on NEFA is the cause for the observed results, rather than a direct effect of NA, since high NEFA concentrations have been shown to induce insulin resistance<sup>(61)</sup>. But results seem to be contradictory, which may in part be explained by different levels of energy supply and thus lipolysis. Other explanations cannot be given; it can only be concluded that insulin is involved in reactions of blood glucose to niacin.

# Milk

To our knowledge, only two research groups measured the niacin content of milk of dairy cows<sup>(14,62)</sup>. Values ranged from 0.46 to 0.87 mg/l<sup>(14,62)</sup>. Wagner *et al.* <sup>(62)</sup> found only

NAM, while Nilson *et al.* <sup>(14)</sup> did not distinguish between vitamers. NAM content of milk was enhanced after NA supplementation <sup>(62)</sup>, but the highest niacin intake resulted in the lowest milk niacin content in the other study <sup>(14)</sup>. Ruminal niacin concentrations have also been measured, and no relationship was apparent between ruminal and milk niacin concentrations <sup>(14)</sup>. But other information is lacking; therefore no statement for the carryover of niacin into milk can be made.

The influence of niacin supplementation on other milk parameters is shown in Table 6, where only studies measuring at least milk yield, fat and protein content are included.

# Milk yield

In two studies, milk yield was increased after niacin supplementation<sup>(37,48)</sup>, while it was not influenced in the others mentioned in Table 6. The absence of a niacin effect was explained in that cows were too far into lactation and thus not in a negative energy balance<sup>(42)</sup>. But this would not match with the work of Cervantes *et al.* <sup>(37)</sup> where an effect was seen even though cows were in mid-lactation and probably not in a negative energy balance. In other studies not presented in Table 6, milk yield was either not affected<sup>(62)</sup> or was increased due to niacin feeding<sup>(47)</sup>. But these authors did not observe differences until lactation week 9. In addition, values in the NA group did not differ from control; only the NAM group did<sup>(47)</sup>.

The increase in microbial protein production after niacin feeding was made responsible for enhanced milk production<sup>(47)</sup>. Furthermore, these authors suggested that the function of niacin in lipid and energy metabolism might play a role. Even if the niacin content of plasma was enhanced after niacin supplementation, this had no impact on milk yield<sup>(38,42)</sup>. But in one study NAM in plasma and milk yield were enhanced in supplemented animals<sup>(37)</sup>. Therefore, exact mechanisms remain unclear.

# Milk protein

In contrast to most studies in Table 6, Erickson *et al.* <sup>(55)</sup> observed a significant increase, and Drackley *et al.* <sup>(48)</sup> a significant decrease in milk protein concentration, after niacin supplementation. Furthermore, an interaction between niacin and type of soyabean processing <sup>(38)</sup>, or niacin and fat supplementation <sup>(28)</sup>, was demonstrated. For protein yield, tendencies for an increase due to niacin supplementation have been detected <sup>(37,48,55)</sup>. There were also tendencies for interactions between niacin, fat and week of lactation <sup>(48)</sup>. In the other studies in Table 6, no effect of a niacin supplementation was seen. Even in surveys where niacin concentration in blood was significantly enhanced in the supplemented group, differences in the response of milk protein to niacin supplementation occurred <sup>(37,38,42)</sup>. In one study, no effect was observed <sup>(42)</sup>, while an increase in protein yield was found in another <sup>(37)</sup>. Furthermore, an interaction between niacin and type of soyabean processing was also observed for protein concentration of milk <sup>(38)</sup>.

Erickson *et al.* <sup>(55)</sup> assumed that amino acid uptake of the mammary gland might be enhanced due to the effect of niacin on insulin. Intravenous insulin has been shown to

increase milk protein and the percentage of casein in milk<sup>(63)</sup>. Several studies also measured casein concentrations in milk. No effects of niacin on casein content or yield in milk were observed<sup>(43)</sup>; there even was a tendency for lowered casein content and yield after niacin supplementation<sup>(48)</sup>. However, in another study<sup>(44)</sup>, the decrease in percentage casein-N of total N due to niacin feeding was significant for only one of two rations. It is therefore not possible to conclude if niacin acts via insulin on casein and/or protein synthesis.

Especially in the case of protein yield, changes in milk yield might also play a role or were probably the reason for observed differences<sup>(48)</sup>. A theory for occasionally observed effects of niacin on milk protein content was an increased microbial protein synthesis in the rumen<sup>(55)</sup>. Other authors stated that mechanisms of niacin to increase protein content of milk still need to be clarified<sup>(38)</sup>. Thus, it cannot be concluded if effects are rather systemic or ruminal.

# Milk fat

Except for Belibasakis & Tsirgogianni<sup>(57)</sup>, who observed increased milk fat concentrations and yield after niacin was given, there were no significant effects of niacin on milk fat in studies in Table 6. Cervantes *et al.* <sup>(37)</sup> observed a tendency for decreasing milk fat content in NAM groups. Nevertheless, there have been several interactions. Interactions were found between niacin and fat<sup>(28)</sup> as well as between niacin, fat and week of lactation<sup>(48)</sup>. Bernard *et al.* <sup>(64)</sup> showed an interaction for niacin and processing of soyabeans. In surveys not mentioned in Table 6 no effect was seen<sup>(62)</sup>, whereas other authors found increased milk fat content in lactation weeks 1 and 4 after NAM but not after NA supplementation<sup>(47)</sup>.

If only studies are considered where niacin supplementation had an impact on blood niacin content, then there was no effect on milk fat (38,42) or a trend towards lower milk fat contents in the niacin-supplemented groups<sup>(37)</sup>. Therefore, changes following niacin supplementation might rather lie at the ruminal level. But since most research on the effects of niacin in the rumen was focused only on the rumen, and no milk measurements were done, it is difficult to accept or to reject this thesis. Three studies measured ruminal and milk parameters in the same trial (12,27,28) and all came to different results. One observed no effect of niacin on ruminal VFA concentration, but an interaction between niacin and fat on milk fat content(28). Another detected a tendency toward a decreased molar proportion of acetate and an interaction between fat and niacin for molar proportion of butyrate, which did not lead to changes in milk fat content or yield<sup>(27)</sup>. Campbell *et al.* <sup>(12)</sup> found no effect on ruminal VFA concentrations or molar proportions, or on milk fat. Hence, other mechanisms might be involved as well.

# **Future research directions**

Considering the number of metabolic reactions where NAD(H) and NADP(H) are involved, the importance of niacin is obvious. However, animal trials with niacin supplementation did not lead to consistent results; therefore it is still not possible to determine the exact conditions or doses for niacin supplementation. But there are several

Table 6. Impact of niacin on several milk parameters

Reference	Feeding ration	Niacin supplement (g/d)	Milk (kg/d)	Protein (%)	Protein (kg/d)	Fat (%)	Fat (kg/d)	Lactation week†
Driver et al.	45 % forage (lucerne hay and silage), 55 % concentrate	0	38.5	2.84	1.09	3.53	1.34	- 1 till +15
(1990) <sup>(38)</sup> ‡	(ground maize and oats, heat-treated soyabean meal)	6	37.8	2.83	1.07	3.44	1.28	
	45 % forage (lucerne hay and silage), 55 % concentrate	0	38.5	2.66	1.01	3.38	1.29	
	(ground corn, and oats, heat-treated whole soyabeans)	6	36.8	2.81	1.03	3.45	1.25	
Erickson et al.	60 % forage (corn silage, lucerne-grass silage), 40 % concentrate	0	24.2	3.16	0.77	3.19		Mid-lactation
(1990) <sup>(25)</sup>	(shelled corn, soyabean meal)	12 NA	24.6	3⋅18	0.78	3.22		
		12 NAM	24.5	3.15	0.77	3.18		
Martinez et al.	40 % chopped lucerne hay, 60 % concentrate (beet pulp, whole	0	30.8	2.99		3.29	1.01	On average
(1991) <sup>(43)</sup> ‡	cottonseed and -meal, corn, wheat, molasses), total 2 % fat	12	30-8	2.97		3.28	1.01	84 DIM
	40 % chopped lucerne hay, 60 % concentrate (beet pulp, whole	0	31.7	2.94		3.43	1.09	
	cottonseed and -meal, corn, wheat, molasses, fat), total 4% fat	12	31.2	2.94		3.41	1.06	
Lanham <i>et al.</i> (1992) <sup>(44)</sup> ‡	40 % forage (corn silage, Bermuda grass hay), 60 % concentrate (corn, soyabean meal)	0	19-3	3.61	0.70	4.08	0.80	On average 256 DIM
		Approximately 6§	19-1	3.52	0.67	3.88	0.74	
	40 % forage (corn silage, Bermuda grass hay), 60 % concentrate	0	19.8	3.50	0.67	4.02	0.76	
	(corn, soyabean meal, whole cottonseed)	Approximately 6§	18-1	3.55	0.63	3.81	0.69	
Erickson et al.	45 % forage (lucerne grass haylage, maize silage), 55 % concentrate	0	36.2	2.71	0.97	3.32	1.20	2 till 14
$(1992)^{(55)}$	(high-moisture shelled corn, soyabean meal)	12 NA	36.4	2.84*	1.03	3.32	1.21	
	With 3 % Ca salts of long-chain fatty acids	0	38-2	2.55	0.98	3.36	1.27	
		12 NA	39.3	2.68*	1.06	3.35	1.31	
Campbell et al.	60 % forage (lucerne haylage, maize silage), 40 % concentrate corn,	0	26.0	3.22		3.79		On average
$(1994)^{(12)}$	soyabean hulls and meal)	12 NA		3⋅19		3.77		200 DIM
		12 NAM		3.22		3.74		
		6  NA + 6  NAM		3.22		3.82		
Bernard <i>et al.</i> (1995) <sup>(64)</sup> ¶	54 % forage (corn silage, lucerne hay), 46 % concentrate (whole soyabeans, soyabean meal and hulls, corn, wheat middlings)							Whole lacta- tion
	Untreated soyabeans	0	25.5	4.90		3.78		
	Heat-treated soyabeans	0	25.9	4.69		3.72		
	Niacin	0	25.9	4.77		3.75		
		6 NA	25.5	4.82		3.75		
Ottou <i>et al.</i> (1995) <sup>(42)</sup>	79 % forage (corn silage, hay), 21 % concentrate (beet pulp, wheat, barley, rapeseed meal, soyabean meal, molasses)	0	22.5	3.11	0.70	4.34	0.98	On average 110 DIM
, ,	With niacin infused into the proximal duodenum	6 NA	24.1	3.15	0.76	4.26	1.03	
	77 % forage (corn silage, hay) 19 % concentrate (rapeseed meal, soyabean meal)							
	With 3.5 % rapeseed oil infused into the proximal duodenum	0	23.7	2.93	0.70	4.23	1.00	
	With 3.5% rapeseed oil and niacin infused into the proximal duodenum	6 NA	23.8	2.96	0.70	4.22	1.01	
Cervantes <i>et al.</i> (1996) <sup>(37)</sup>	Eight different forage:concentrate ratios; lucerne hay or haylage and maize silage were used as forage, maize and soyabean meal as concentrate	0	30.7	3.21	0.98	3.45	1.07	On average 112 DIM
(1000)		12 NAM	33.5*	3.31	1.11*	3.26	1.09	
	With 400 g Ca salts of fatty acids	0	31.8	3.17	1.00	3.57	1.14	
	That look out out of land	12 NAM	33.2*	3.14	1.04*	3.46	1.15	
Christensen et al.	40 % forage (lucerne haylage, maize silage), 60 % concentrate(corn,	0	36-1	3.04	1.09	3.89	1.39	On average
(1996) <sup>(27)</sup>	soyabean hulls and meal), total 2-8% fatty acids	12 NA	36.3	3.04	1.09	3.67	1.32	30 DIM
(,	40 % forage (lucerne haylage, maize silage), 60 % concentrate (corn,	0	37.4	3.02	1.10	3.50	1.27	55 Z.III
	soyabean meal, whole raw soyabeans, tallow), total 5-9 % fatty acids	12 NA	36.9	2.95	1.08	3.64	1.34	
Belibasakis &	50 % forage (corn silage), 50 % concentrate (corn, soyabean meal, wheat bran)	0	23.3	3.23	0.75	3.46	0.81	On average
Tsirgogianni (1996) <sup>(57)</sup> ‡	22 12 12 12 13 13 15 16 16 16 16 16 16 16 16 16 16 16 16 16	10	24.4	3.24	0.79	3.89*	0.95*	90 DIM

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Table 6. Continued

Reference	Feeding ration	Niacin supplement (g/d)	Milk (kg/d)	Protein (%)	Protein (kg/d)	Fat (%)	Fat (kg/d)	Lactation week†
DiCostanzo et al.	50% forage (lucerne haylage, maize silage, earlage), 50% concentrate	0	28.0	2.90		3.40		On average
(1997) <sup>(59)</sup> **	(cracked corn, whole cottonseed and meal, soyabean meal and hulls,	12 NA	29.0	2.91		3.33		90 DIM
	blood meal, wheat middlings)	24 NA	25.9	2.91		3.38		
		36 NA	28.7	3.17		3.35		
Madison-Anderson et al. (1997) <sup>(28)</sup>	50% forage (lucerne hay, maize silage), 50% concentrate (rolled maize and barley, soyabean meal, molasses)	0	31.9	3.03	0.96	3.11	0.99	On average 53 DIM
		12 NA	32.2	3.11	1.00	3.32	1.05	
	50 % forage (lucerne hay, maize silage), 50 % concentrate	0	35.1	2.96	1.04	3.33	1.15	
	(rolled maize and barley, extruded soyabeans, molasses)	12 NA	35.5	2.92	1.04	3.22	1.14	
Minor et al.	49-60 % forage (lucerne and maize silage), 51-40 % concentrate	0	32.0	3.01	0.94	3.65	1.13	0 till 40
(1998) <sup>(54)</sup> ࠠ	(cracked corn, soyabean meal, roasted soyabeans, whole cottonseeds)	12	31.3	3.01	0.95	3.73	1.18	
, , , , , , , , , , , , , , , , , , , ,	40-50 % forage (lucerne and maize silage), 60-40 % concentrate	0	34.8	3.17	1.06	3.43	1.14	
	(ground corn, starch, soyabean meal, roasted soyabeans, whole cottonseeds)	12	33.1	3.19	1.03	3.55	1.20	
Drackley <i>et al.</i> (1998) <sup>(48)</sup> ††	40-50 % forage (lucerne haylage, maize silage), 60-50 % concentrate	0	30.5	3.29	0.99	3.56	1.06	4 till 43
	(soyabean meal and hulls, shelled corn)	12 NA	33.2*	3.16*	1.04	3.50	1.15	
	40-50 % forage (lucerne haylage, maize silage), 60-50 % concentrate	0	31.8	3.16	0.98	3.68	1.16	
	(soyabean meal and hulls, whole raw soyabeans, shelled corn, fat)	12 NA	33.6*	3.13*	1.05	3.60	1.21	

NA, nicotinic acid; NAM, nicotinamide; DIM, days in milk.

<sup>\*</sup> Significant differences (*P*≤0.05) between the control and niacin groups have been observed for these parameters.

<sup>†</sup> Values given in this Table derive from that lactation week or are a mean of the given time span, where 0 is calving; therefore negative numbers are weeks prepartum and positive values post-partum.

<sup>‡</sup> In these studies, the vitamer applied was not named. It was just stated that niacin was supplemented. But since the term niacin is occasionally also used as a synonym for NA<sup>(45)</sup>, it is assumed that NA was fed in these surveys.

<sup>§</sup> Niacin was mixed in the concentrate; the goal was to reach an intake of 6 g niacin/cow per d.

<sup>||</sup> In this study, there was no influence of niacin supplementation on milk yield; therefore, the authors gave only average milk yield for all groups.

<sup>¶</sup> In this study, 2 years were analysed, the mean of both years was taken; furthermore, values for each group have not been given, only for the main effects (processing of soyabeans, niacin supplementation), which are presented here.

<sup>\*\*</sup>This study was also designed to test the effect of different heat-stress-exposure; therefore different lines not only represent different niacin levels, but also different climatic conditions. Each niacin level had its own control group, but only values for the first one are presented here.

<sup>††</sup> Several diets post-partum were given; therefore the forage:concentrate ratio differs.

gaps of knowledge, which could, once resolved, answer this question. First, cognition of the effect of feeding on ruminal fermentation, niacin degradation and synthesis is insufficient. Furthermore, ruminal samples were taken at varying times after feeding and after niacin supplementation, which surely has an impact on the observed results. In addition, it is not known if absorption can occur in the abomasum or before the duodenal cannula and the mechanism of absorption is unspecified for ruminants. Niacin concentrations in blood also vary, which might be due to the different blood fractions analysed or vitamers examined. Different methods for niacin determination may lead to different results as well. It is also unknown whether some type of homeostatic system exists, as was suggested for man. NEFA concentrations in blood seem to be lowered by NA, but not by NAM, and it is uncertain if NA acts on ketone bodies via this effect on NEFA or if other mechanisms are involved. Furthermore, the effect on NEFA might also have an impact on glucose metabolism, which is mediated through insulin, even though mechanisms are not clear. The vitamin's mode of action on milk parameters is uncertain and might be systemic or ruminal or a combination of both. If effects are rather systemic, feeding trials with oral, not rumen-protected supplementations will have limits. This seems to be at least the case for blood parameters, since disappearance before the duodenum is high.

Considering these points, we would suggest the following directions for future research:

- (1) Different feeding regimens should be compared that characterise the impact of feed on niacin metabolism. Niacin content of the feed should be determined, as well as tryptophan, aspartate and quinolinate contents, since these are precursors of niacin synthesis.
- (2) Simultaneous determination of ruminal, duodenal, blood and milk parameters would be useful to detect potential conjunctions.
- (3) The time of sampling to investigate ruminal, duodenal and blood parameters should be standardised in relation to time of niacin feeding to avoid confusion between niacin and time effects.
- (4) Experiments should be conducted with niacin infused in the abomasum and simultaneous duodenal and blood niacin measurements to study absorption site and extent.
- (5) Studies on the mechanism of absorption for both vitamers would be useful.
- (6) Surveys on possible metabolic storage, for example, liver or tissues (such as ruminal or duodenal walls) seem to be favourable, where NAD(H) and NADP(H) concentrations are measured as well.
- (7) In general, research concerning niacin flow in the body is advisable.
- (8) To investigate if effects of niacin on milk parameters are rather systemic or ruminal, surveys with or without post-ruminal niacin infusion are desirable.
- (9) Studies on the influence of niacin on insulin in ruminants should be performed.
- (10) Distinctions should be made between both vitamers. In addition, the conditions and locations of conversion of one vitamer to another should be better investigated.

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