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Review

Effect of dietary energy source on energy balance, production, metabolic disorders and reproduction in lactating dairy cattle

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Abstract – The pathway for oxidation of energy involves a balanced oxidation of C2 and C3 compounds. During early lactation in dairy cattle this C2/C3 ratio is out of balance, due to a high availability of lipogenic (C2) products and a low availability of glycogenic (C3) products relative of the C2 and C3 products required for milk production. This review compares studies which manipulated dietary energy source and shows that dietary energy source can affect the balance of the C2/C3 ratio, as indicated by plasma NEFA, β-hydroxybutyrate (BHBA) and glucose levels. It is shown that glycogenic nutrients increase glucose and insulin concentrations and decrease NEFA and BHBA plasma levels. Extra lipogenic nutrients elevate NEFA and BHBA and decrease plasma glucose concentrations. Lipogenic nutrients generally increase milk fat percentage and decrease milk protein percentage, suggesting a surplus of C2 compounds. The inverse is the case for feeding extra glycogenic nutrients, implying reduced deamination and oxidation of glycogenic amino acids. Feeding extra glycogenic nutrients improved the energy balance (EB), in contrast to ambiguous results of lipogenic nutrients on EB. Moreover, glycogenic feed may reduce the severity of ketosis and fatty liver, but increased the incidence of (sub)clinical acidosis. Since studies are scarce, it seems difficult to draw conclusions on the effects of dietary energy source on reproduction. However, lipogenic nutrients decrease glucose and increase NEFA and BHBA plasma levels. High plasma NEFA and BHBA and low plasma glucose levels are associated with decreased reproductive performance, which might imply the C2/C3 compound balance to be important for reproductive function.

lipogenic nutrients / glycogenic nutrients / reproduction / energy metabolism

1. INTRODUCTION

1.1. Negative energy balance and related disorders

Over the last several decades, intense genetic selection, improved dairy nutrition and cow management have significantly increased the milk yield of dairy cattle, in particular in the Holstein Friesian cattle breed. It is now well known that these economically favorable developments are accompanied by some negative consequences, such as an increase in the incidence of metabolic

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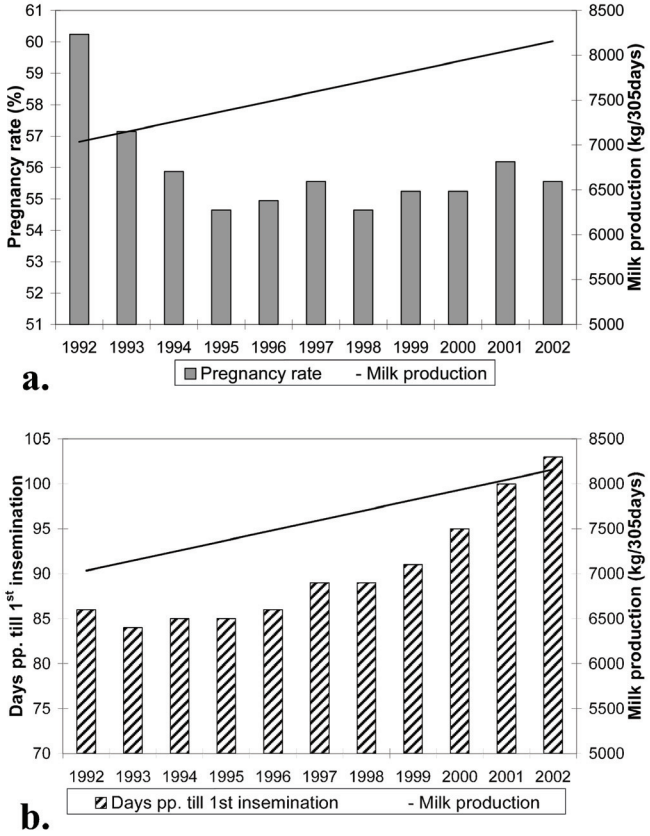

Figure 1. Pregnancy rate and annual milk production of dairy cows in The Netherlands from 1992–2002 (**a**); Interval pp till 1st insemination and annual milk production of dairy cows in The Netherlands from 1992–2002 (**b**). Data based on > 1 million calvings per year (adopted from [5]).

diseases and a reduction in reproductive performance [1–4], as illustrated for the pregnancy rate of dairy cattle in The Netherlands in Figure 1a (adopted from [5]). However, in The Netherlands, pregnancy rate has seemed to be stabilized from 1995 onwards. Dutch dairy farmers were able to consolidate the pregnancy rate by increasing the number of days postpartum (pp) till first artificial insemination (Fig. 1b; adopted from [5]), resulting in an increase in inter calving interval (from 393 days in 1992 to 417 days in 2002). Veerkamp et al. [6] indicated that the increase in genetic merit for feed intake did not parallel the increase in genetic merit for milk yield. They suggested that selection on high genetic merit for milk yield is only partially compensated for by an increase in feed intake resulting in an ongoing increase in negative energy balance (NEB) status during early lactation.

Energy balance (EB) can be defined as the difference of net energy intake minus net energy expenditure for maintenance and milk production. If energy expenditure is higher than intake, EB is negative [7] and cows lose body weight. Most studies on the effect of EB on reproductive performance in dairy cattle estimate the EB in the cattle from estimated dietary net energy intake

minus an estimation of energy requirement for maintenance and minus the energy produced in milk [8–18]. Other studies use the change in body weight or body condition score (BCS) as indicators for a cow's energy status [19–21].

Several reviews have been published concerning the effect of EB status in dairy cattle on reproductive efficiency [22–35]. A status of NEB decreases LH pulse frequency, growth rate and diameter of the dominant follicle, weight of the corpus luteum (CL), peri-estrous hormone concentrations like estradiol (E2) and progesterone (P4) [11, 24, 25, 36–39]. In addition, NEB has been related to more days till the first observed estrus postpartum (pp) [12, 16, 40], more days till first ovulation [8, 11, 22, 32], more days open pp [41], decreased conception rates following artificial insemination [14, 21, 25, 41] and lower pregnancy rates [15].

As recently reviewed [42], the early lactation period in dairy cattle have been clearly identified with an increased disease incidence. NEB has been indicated as an important factor involved. Epidemiological studies have related NEB directly or indirectly via milk yield to laminitis, leg problems, mastitis and metabolic disorders like ketosis, ruminal acidosis and displaced abomasum [43–45].

1.2. Energy metabolism in high-producing dairy cattle

Metabolism has been recognized to supply the intermediate signals in the relations between NEB and reproduction or health status in dairy cattle. Figure 2a (adopted from [46]) illustrates the pathway of substrates used for energy metabolism in non-lactating dairy cattle. The dietary ingredients fiber, carbohydrates and protein provide substrates for ruminal fermentation and result in the ruminal production of volatile fatty acids (VFA). The main VFA produced are acetate and butyrate, which are or can split up into fragments containing two carbon atoms (C2) (lipogenic), and propionate, which is a fragment containing three carbon atoms (C3) (glycogenic). Rumen resistant dietary ingredients and microbial matter can be digested and absorbed in the intestine and provide either C2 or C3 compounds. The final common pathway for oxidation involves the oxidation of a C2 (acetyl-coenzyme-A) and a C3 (oxaloacetate) fragment to form citrate in a molecular ratio 1:1. Citrate proceeds through a series of intermediate reactions of the Krebs cycle to make ATP, NADH and $FADH_2$ available. NADH and $FADH_2$ can react with oxygen to produce energy for the body as ATP (respiratory chain reaction). In addition, Figure 2b shows that dairy cattle in early lactation usually have a limited dry matter intake and are therefore in a negative energy balance. This results in the mobilization of body reserves. Mobilized body reserves are mostly body fat (mainly C2 compounds) and to a lesser extent body protein (partly C2, partly C3 compounds). Mobilization of body fat results in elevated blood NEFA levels, which can be oxidized to Acetyl-CoA or stored in the liver as tri-acyl glycerol (TAG), possibly causing fatty liver. The high milk production in early lactation requires a high lactose production (from C3 compounds) which results in decreased glucose and insulin levels. The production of Acetyl-CoA from acetate, butyrate and fatty acids from body reserves is high whilst at the same time C3 compounds from glucose and glucogenic precursors, including glucogenic amino acids, are driven towards lactose. Consequently, the ratio of oxaloacetate to acetyl-CoA is out of balance. The availability of citrate to form ATP in the Krebs cycle is decreased. Acetyl-CoA is diverted to the production of ketone bodies, acetone, acetoacetate and β-hydroxybutyrate (BHBA), resulting in a status of ketosis.

In summary, the metabolic effects of an NEB are an imbalance in C2/C3 nutrient ratio and low plasma glucose and insulin concentrations and high concentrations of plasma NEFA, BHBA, acetone, acetoacetate and liver TAG.

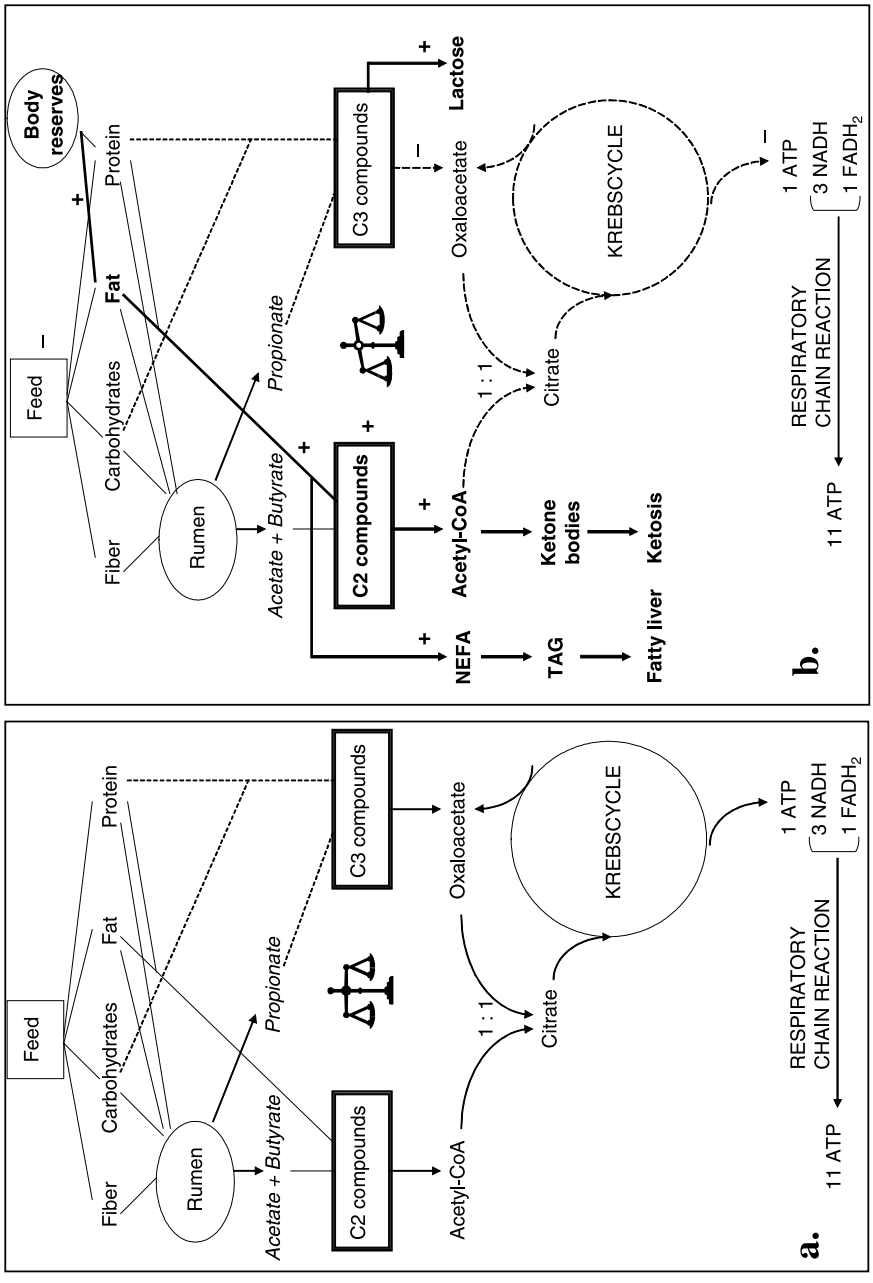

Figure 2. Energy metabolism of non-lactating dairy cattle (**a**); Energy metabolism of lactating dairy cattle in a negative energy balance (**b**) (adjusted from [46]).

Several reviews have indicated nutrition to be important in the prevention and treatment of NEB related disorders [25, 47–54]. The relation of NEB with protein metabolism has been reviewed [25, 47], just as the relation between dietary fat (C2 compounds or lipogenic) and metabolic and reproductive disorders [48, 51, 54–56]. However, the key problem that occurs in the metabolism of a dairy cow in early lactation seems to be the unbalanced availability of C3 (glycogenic) and C2 (lipogenic) compounds derived from nutrients and body reserves.

The C2/C3 compound ratio can be manipulated by ingredients in the diet. Lipogenic dietary ingredients, like dietary fat or forages that stimulate the ruminal production of acetate and butyrate, are expected to increase the C2/C3 compound ratio. Glycogenic nutrients are either ruminal fermented and result in the production of propionate or are intestinal digested and absorbed as glucose. Consequently, glycogenic nutrients like grain, nonfiber carbohydrates or propylene glycol are expected to decrease the C2/C3 compound ratio.

The scope of this review is to find evidence implying the possibilities to modify the C2/C3 ratio by dietary ingredients, measured by altered blood parameters that indicate the EB status and to find evidence that indicates that a more glycogenic or lipogenic diet affects metabolic disorders, milk production, energy balance and reproductive function.

2. DIETARY ENERGY SOURCE RELATED TO BLOOD METABOLITES, METABOLIC HORMONES AND METABOLIC DISORDERS

2.1. Effect of lipogenic and glycogenic nutrients on blood metabolites and metabolic hormones

Plasma NEFA and BHBA levels are recognized as indicators for body fat mobilization and NEB in dairy cattle in early lactation [22, 48, 55, 57]. Decreased plasma glucose and insulin levels have been associated with NEB [12, 13, 57, 58] and increase as cows progress towards a more positive EB [59]. Table I shows reported effects of feeding either extra glycogenic or lipogenic nutrients on plasma NEFA, BHBA, glucose, insulin and growth hormone (GH) levels. Concerning plasma NEFA levels, 13 [9, 60–68] out of 15 studies found an increase after feeding extra lipogenic nutrients. In contrast to studies where extra glycogenic nutrients were fed, 13 [60, 61, 66, 68–73] out of 14 reported studies found a decrease in plasma NEFA levels. Plasma BHBA levels increased after feeding extra lipogenic nutrients in five out of eight studies [68, 69, 74, 75]. Extra glycogenic nutrients were related to a decrease in plasma BHBA levels in eight out of nine reported studies [61, 69, 70, 72, 74, 76]. Plasma glucose (10 out of 13 studies) and insulin (6 out of 9 studies) concentrations were decreased after feeding extra lipogenic nutrients and in almost all cases increased after feeding extra glycogenic nutrients (glucose 13 out of 14 studies; insulin 7 out of 8 studies) [8, 9, 60, 61, 64, 66–68, 70–72, 74, 76, 77]. Plasma GH concentration was increased in most studies (4 out of 6 studies) after feeding extra lipogenic nutrients [8, 9, 61, 64]. In contrast to a decrease after feeding extra glycogenic nutrients in 5 out of 6 studies [61, 70, 71].

In addition, liver triglyceride [78], and plasma triglyceride [66] concentrations were elevated after feeding extra lipogenic nutrients, in contrast to a study that found a decrease in liver triglyceride after feeding more non-fermentable carbohydrates [72] and studies that reported a decrease in plasma triglyceride levels after abomasal glucose infusion [66, 73]. Two studies found a positive effect of feeding extra glycogenic nutrients on liver glycogen content [70, 72], as a representative of stored carbohydrates.

Apart from an increase due to higher dietary fat content [69, 74, 75], plasma BHBA

Table I. Responses in metabolites and metabolic hormones to either extra lipogenic[a] or glycogenic[b] nutrients in dairy cattle based on means per treatment group.

Category	Responses (based on means per treatment group)			Total No. of animals compared
	Rise	No response	Decline	
NEFA				
Lipogenic nutrients	12	0	3	394
Glycogenic nutrients	1	0	13	165
BHBA				
Lipogenic nutrients	5	2	1	144
Glycogenic nutrients	0	5	5	106
Glucose				
Lipogenic nutrients	3	0	10	229
Glycogenic nutrients	13	0	1	167
Insulin				
Lipogenic nutrients	3	0	6	194
Glycogenic nutrients	9	0	1	167
GH				
Lipogenic nutrients	4	1	1	156
Glycogenic nutrients	0	1	5	44

[a] Lipogenic nutrients: prilled fat, CaLCFA, tallow.
[b] Glycogenic nutrients: grain, concentrates, starch, nonfiber carbohydrates, propylene glycol, glucose infusion.
Based on lipogenic nutrients: [8, 9, 60–67, 69, 74, 75]; glycogenic nutrients: [60, 61, 66, 68–74, 76, 77].

were also elevated with increasing dietary forage level [75]. Ruppert et al. [68] found no increase in BHBA, as an indicator of NEB, when fat was added to a corn silage diet, in contrast to an alfalfa silage diet. Since corn silage is mainly glycogenic (a high proportion of C3 nutrients) and alfalfa silage is mainly lipogenic (a high proportion of C2 nutrients), it seems logical that BHBA levels on a corn silage diet, are less increased than BHBA levels in cows on an alfalfa silage diet upon fat addition. In the corn silage diet the extra C2 nutrients of the fat addition are easier to metabolize because of the higher availability of C3 nutrients, compared to the alfalfa silage diet. It seems that the effect of dietary fat addition depends on the nature of other nutrients in the diet, suggesting the C2/C3 balance to be a factor in the concentration of plasma BHBA.

The considerable variation in effects of fat supplementation on metabolites and metabolic hormones may be explained by saturation of the fat source, as indicated by Thomas et al. [79]. In this study, a positive effect on insulin and IGF-1 levels was found for poly-unsaturated fat with mainly 16- and 18-carbon fatty acids (soybean oil) compared to the control, saturated (animal tallow) and highly polyunsaturated fat with considerable > 20-carbon fatty acids (fish oil). This was possibly caused by a difference in ruminal fermentation patterns between the fat sources since the poly-unsaturated fat treatment was expected to modify the rumen fermentation pattern in favor of propionic acid production. Moreover, digestibility of fat in the intestine depends on chain length and saturation. In general, fatty acids with more than 18-carbon atoms have a reduced digestibility whilst digestibility appears to be higher for unsaturated than saturated fatty acids [80]. Thus, a variation in the type of fat source added may increase

variation in the effects on metabolites because of a variation in the amount of extra metabolizable energy obtained.

Santos et al. [81] reported lower NEFA concentrations and higher glucose and insulin levels in cows fed steam-flaked sorghum compared to steam-rolled corn. This can be explained by a higher ruminal starch digestibility, and resulting higher ruminal propionate secretion, of steam-flaked sorghum compared to steam-rolled corn. This is in line with Simas et al. [82] who found elevated blood glucose levels in cows fed steam-flaked sorghum, compared to dry-rolled sorghum, which has a lower ruminal starch degradability. A study on starch infusion reported a difference in effect on plasma metabolite levels between infusion sites. Abomasal starch infusion tended to decrease plasma NEFA levels more than ruminal infusion. This is probably caused by the production of the VFA propionate, butyrate and acetate from ruminally infused starch, while infused abomasal starch is intestinally digested and absorbed as glucose [70].

In addition, several studies presented a diurnal rhythm for glucose, insulin, NEFA and BHBA in ruminants [83–85]. Especially, plasma NEFA levels seem to be more sensitive and variable before feeding compared to after feeding. This implies a time-of-day or a time-after-feeding effect when interpreting dietary effects on blood metabolites and metabolic hormones.

In conclusion, feeding extra lipogenic nutrients generally increases NEFA, BHBA and GH levels and decreases plasma glucose and insulin levels. Increased availability of glycogenic nutrients, e.g. dietary corn, starch infusion or propylene glycol increases plasma glucose and insulin levels, and decreases plasma GH, NEFA and BHBA concentrations. This shows that indicators for an imbalance in the C2/C3 ratio can be effectively manipulated by dietary energy source. The effect of the manipulation seems to be dependent on the availability of the energy source as a metabolic C2 or C3 compound. Secondly, the effect of manipulation also seems to depend on the balance between C2 and C3 compounds, in the rest of the diet.

2.2. Effect of lipogenic and glycogenic nutrients on metabolic disorders

As reviewed earlier [86, 87], increasing the availability of glycogenic nutrients, in particular of readily fermentable carbohydrates in the rumen, results in an increased incidence of both clinical (pH < 5.0) and subclinical (pH < 5.5) acidosis. This observation is confirmed by later studies on replacing alfalfa silage with corn silage [68] or replacing a high-fat concentrate with a high-starch concentrate [88], where in both cases the ruminal pH decreased with increasing availability of glycogenic nutrients compared to lipogenic nutrients. With subclinical or clinical acidosis, the ruminal tissue wall may become damaged and reduced intake, digestion, laminitis and liver anomalies can occur. Thus, the level as well as the type of glucogenic nutrients (rapidly versus slowly fermentable carbohydrates) influence the occurrence of (sub)clinical acidosis and this contributes to the observed variability in the effect of glucogenic supplements on production, energy balance and reproductive characteristics.

Grummer and Carroll [56] have suggested in their review that long-term fat supplementation might cause fatty liver via chronic elevation of plasma NEFA levels. This theory is supported by firstly other studies that found a positive relationship between elevated NEFA, decreased glucose levels and the incidence of fatty liver [58, 59, 89]; secondly, evidence that indicates the relationship between liver triglyceride content and plasma NEFA concentrations [59]; and thirdly, associations between dietary fat supplementation and elevated plasma NEFA levels [9, 63].

Several studies have found a decreasing effect of glycogenic feed on plasma NEFA, BHBA and triglyceride levels [60, 72, 90], also suggesting that glycogenic feed may

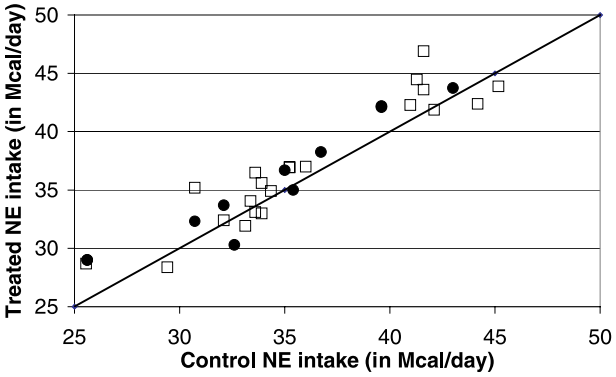

Figure 3. Effect of feeding supplemental lipogenic (□) or glycogenic (●) nutrients on net energy (NE) intake in Mcal per day. Points are based on means per treatment group. Points below the diagonal line represent studies with a negative effect of diet treatment, points above the diagonal line represent studies with a positive effect of diet treatment. Based on [15, 60, 61, 64, 65, 69–72, 75, 78, 99–101, 103, 104, 107, 112, 139].

reduce the incidence and severity of ketosis and fatty liver. Grummer et al. [91] supposed propionate, as a product of rumen degradable glycogenic feed, to be anti-ketogenic and advised to maximize hepatic glycogen stores to decrease the triglyceride/glycogen ratio in the liver, which has been indicated as a risk factor for fatty liver and ketosis.

In ketosis-induced cattle, by feed restriction plus 1,3-butanediol, Veenhuizen et al. [58] reported that triglyceride infiltration in the liver increases and liver glycogen content decreases as cows progress towards clinical ketosis. Kronfeld [92] reviewed that the supply of lipogenic precursors for milk production relative to glycogenic precursors in the diet determines the susceptibility of cows to spontaneous ketosis; liver triglyceride to glycogen ratio indicates the relative supply of these nutrients [55]. In addition, both Grummer [55] and Drackley [93] suggest in their reviews that the occurrence of fatty liver may also have a direct effect on carbohydrate metabolism by an impaired gluconeogenesis in the liver, resulting in an increased susceptibility to ketosis.

In vitro, high levels of ketone bodies have a negative effect on the chemotactic [94] and proliferative [95, 96] capacity of lymphocytes and the secretion of immunoglobulins by lymphocytes [94–97] has been identified. In vivo, BHBA levels have been positively related to the severity of mastitis as indicated by bacterial counts [98]. Such data indicate that ketosis may negatively affect some aspects of the immune system.

High plasma NEFA and BHBA levels and low glucose levels have been related to fatty liver and a status of ketosis [55, 91]. Lipogenic and glycogenic nutrients have an effect on ruminal pH and the NEFA, BHBA, glucose and liver triglyceride metabolite contents. As a result, it can be expected that the incidence and severity of fatty liver and ketosis as well as acidosis is affected by the lipogenic/glycogenic nutrient ratio. This indicates the C2/C3 nutrient balance to be an important element in the reduction of metabolic disorders in dairy cattle in early lactation, as shown in Figure 2.

3. DIETARY ENERGY SOURCE RELATED TO MILK PRODUCTION AND EB

The selection of the experiments presented in Figures 3, 4 and 5 is based on the criteria: dietary treatment (extra lipogenic

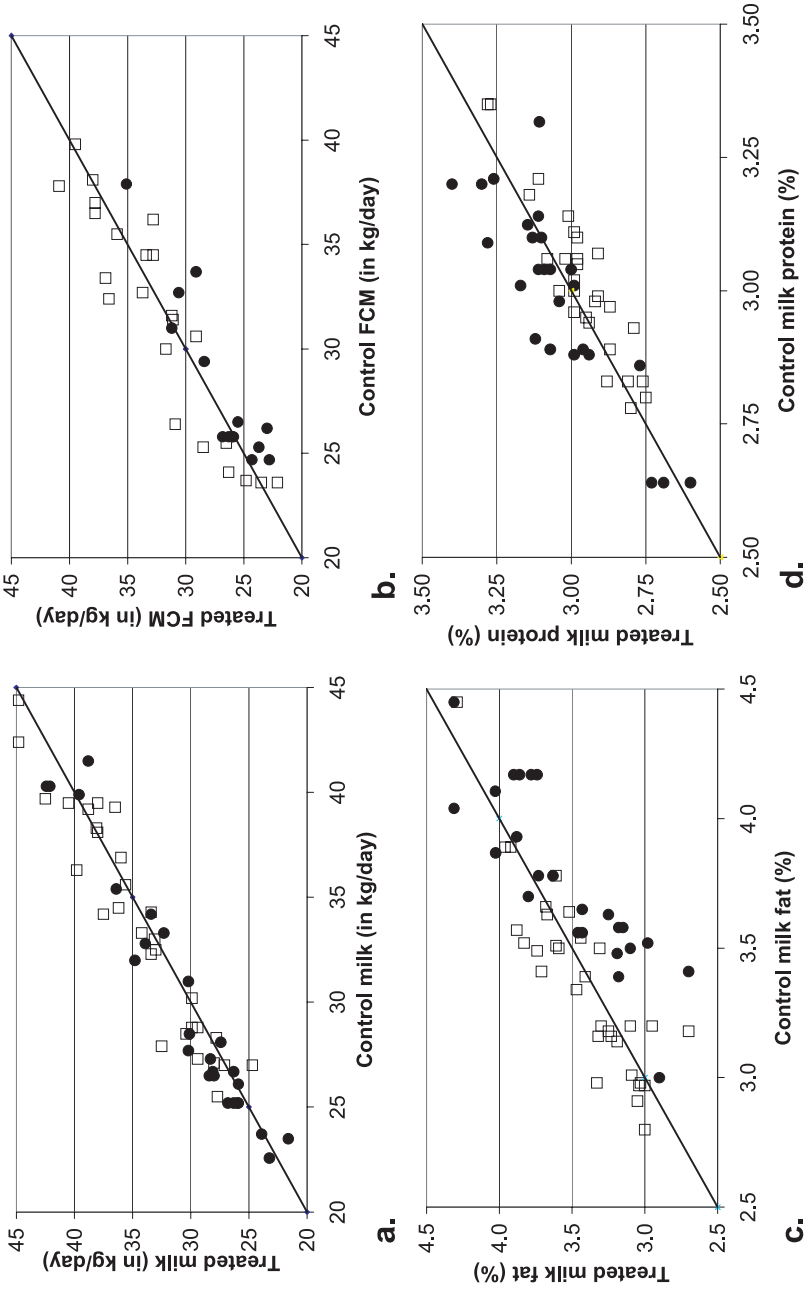

Figure 4. Effect of feeding supplemental lipogenic (□) or glycogenic (●) nutrients on daily milk production in kg (**a**), daily milk production in fat corrected milk (FCM) (**b**), milk fat % (**c**) and milk protein % (**d**). Points are based on means per treatment group. Points below the diagonal line represent studies with a negative effect of diet treatment, points above the diagonal line represent studies with a positive effect of diet treatment. Based on [8, 15, 60–72, 75, 77, 78, 82, 99–104, 106, 107, 110, 111, 115–122].

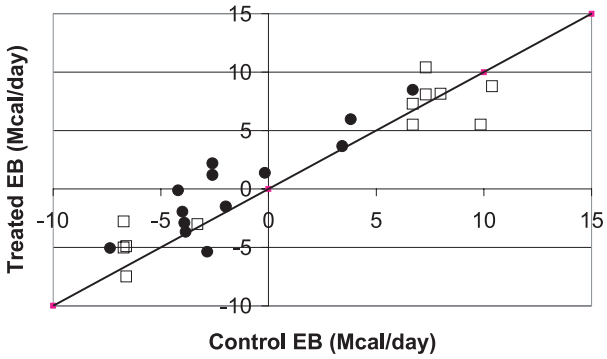

Figure 5. Effect of feeding supplemental lipogenic (□) or glycogenic (●) nutrients on EB. Points are based on means per treatment group. Points below the diagonal line represent studies with a negative effect of diet treatment, points above the diagonal line represent studies with a positive effect of diet treatment. Based on [8, 9, 15, 64, 66, 69, 71, 72, 77, 99, 106–108, 110, 112, 116, 120].

and/or glycogenic nutrients fed in the treatment group) and presence of mainly multiparous lactating dairy cattle. Table II in the appendix shows the dietary treatment, No. of cows, parity and DMI of the experiments presented in Figures 3 to 6.

3.1. Effect of lipogenic and glycogenic nutrients on energy intake

As shown in Appendix, most studies on altering the glycogenic/lipogenic nutrient ratio, also alter the energy content of the experimental diets. On the contrary, 22 out of 31 studies [8, 9, 15, 60, 61, 63–65, 67, 68, 78, 82, 99–107] reported a decrease in DMI after feeding extra lipogenic nutrients compared to 7 out of 14 studies [60, 61, 68, 72, 77, 78, 108–116] on extra glycogenic nutrients which showed a decrease in DMI in the treatment group. In general, the negative effect of extra lipogenic sources on dry matter intake is higher when the degree of saturation of fatty acids is lower, probably because of the more pronounced negative effects of unsaturated fatty acids on rumen carbohydrate fermentation. As a result, 73% of the studies on feeding extra lipogenic nutrients [15, 61, 63, 65, 75, 100, 101, 104, 106] and also 73% of the studies on increasing dietary glycogenic nutrients [61, 69–72, 117] obtained a higher net energy (NE) intake in the treatment group compared to the control group, illustrated by Figure 3.

3.2. Effect of lipogenic and glycogenic nutrients on milk production

Figure 4 shows an overview of studies that reported milk yield and composition after feeding either more glycogenic nutrients or lipogenic nutrients. Both feeding extra lipogenic nutrients or glycogenic nutrients had similar effects on kg of milk produced per day [8, 15, 60–72, 75, 77, 78, 82, 99–104, 106, 107, 110, 111, 115–122]. Milk fat percentage was usually elevated after feeding extra lipogenic nutrients (24 out of 32 studies) [15, 60–65, 67, 68, 75, 82, 99–104, 106, 121, 122], but it decreased after the addition of glycogenic nutrients to the diet (23 out of 26 studies) [60, 61, 66, 68–72, 78, 107, 110–113, 115–117, 120]. In most cases, milk protein percentage decreased after feeding extra lipogenic nutrients (23 out of 28 studies) [15, 60–63, 65, 67, 68, 75, 82, 99–104, 121]. However, extra glycogenic nutrients increased milk protein percentage in 18 out of 25 studies [60, 61, 66, 68–72, 77, 78, 107, 110, 112, 115–117, 120]. Concerning fat corrected milk (FCM),

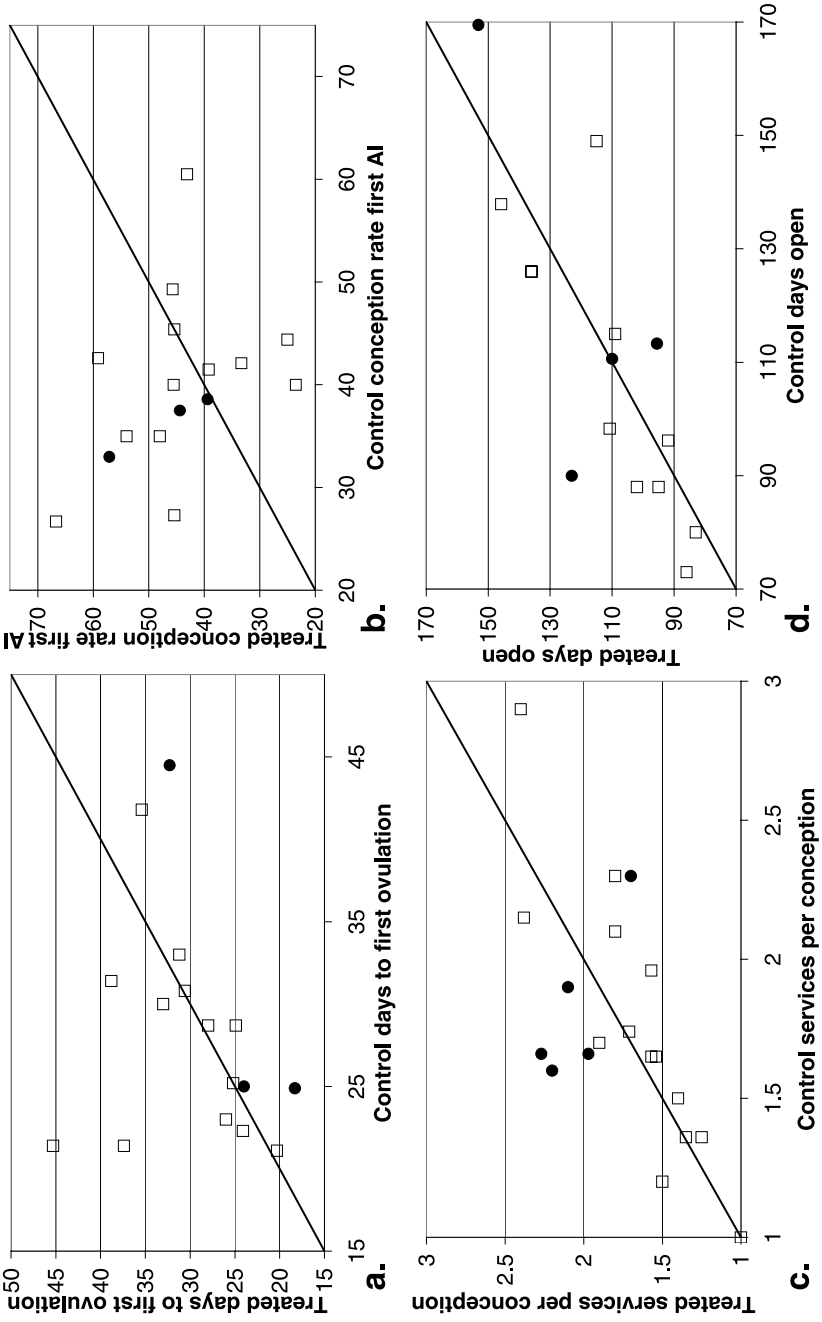

Figure 6. Effect of feeding supplemental lipogenic (□) or glycogenic (●) nutrients on days to first ovulation (a), conception rate following first artificial insemination (**b**), services per conception (**c**) and days open (**d**). Points are based on means per treatment group. Points below the diagonal line represent studies with a negative effect of diet treatment, points above the diagonal line represent studies with a positive effect of diet treatment. Based on [8, 9, 15, 62, 63, 65–67, 77, 81, 101, 102, 104–106, 109, 114, 118, 121, 122, 124–126].

lipogenic nutrients had a positive effect on FCM in 13 out of 23 studies [8, 15, 61–65, 68, 75, 82, 99–101, 104]. After feeding extra glycogenic nutrients, FCM decreased in nine of the 14 studies [61, 66, 68, 69, 71, 77, 78, 111, 115].

3.3. Effect of lipogenic and glycogenic nutrients on EB

The increased NE intake after feeding extra lipogenic nutrients, accompanied by an increase in milk fat percentage, suggests that the gained NE intake by feeding of lipogenic nutrients is probably beneficial to milk fat percentage and not to EB. This observation is supported by studies that found an increased body weight loss [9, 105] and body condition score loss [123] or a more negative EB [15] after dietary fat supplementation. Son et al. [15] even reported in a study on increased milk yield, an increased milk fat percentage, but lower NE intake after dietary fat supplementation. This suggests more body fat mobilization in the fat supplemented group than in the control group. Concerning milk composition, the inverse effect of feeding extra lipogenic nutrients is observed in a majority of the studies on feeding extra glycogenic nutrients. In a majority of the studies on feeding extra glycogenic nutrients, milk fat percentage is decreased and milk protein percentage increased. This can imply that proteins are saved from use as a glycogenic energy source after feeding extra glycogenic nutrients, indicated by the increased milk protein percentage. Figure 5 further supports these hypotheses, by presenting 18 studies on either feeding more lipogenic or glycogenic nutrients on the calculated EB. Eight of the 12 studies reported an increase in EB after feeding extra lipogenic nutrients [8, 9, 12, 15, 64, 66, 106]. In contrast to feeding extra glycogenic nutrients where 12 out of 13 studies were able to improve, not-significantly, the calculated EB [66, 69, 71, 72, 77, 107, 108, 110, 112, 116, 120].

In conclusion, extra lipogenic nutrients had variable results on EB and increased milk yield and milk fat percentage. This suggests a surplus of C2 compounds in the C2/C3 balance, resulting in elevated milk fat output. In contrast, glycogenic nutrients seem to increase the EB, decrease the milk fat percentage and increase the milk protein percentage, implying a more balanced C2/C3 ratio and therefore a protein-saving effect of glycogenic nutrients.

4. DIETARY ENERGY SOURCE RELATED TO REPRODUCTION

The selection of the experiments presented in Figure 6 is based on the following criteria: dietary treatment (extra lipogenic and/or glycogenic nutrients fed in the treatment group) and the presence of mainly multiparous lactating dairy cattle. Table II in the appendix shows the dietary treatment, No. of cows, parity and DMI of the experiments presented in Figure 6.

4.1. Effect of lipogenic and glycogenic nutrients on reproductive efficiency

Figure 6 illustrates the effects of feeding supplemental lipogenic or glycogenic nutrients on days to first ovulation, conception rate following first insemination, services per conception and number of days open. Increasing glycogenic nutrients was reached by supplying extra dietary starch [118], maize gluten [109, 124], ground shelled corn [109, 124], abomasal glucose infusion [66] or propylene glycol supplementation [77]. Days postpartum (pp) till first ovulation [66, 77, 109, 114] are reported to be reduced after feeding extra glycogenic nutrients in three out of four studies. Six out of 12 studies [8, 9, 15, 63, 66, 105, 106, 109, 125] on feeding extra lipogenic nutrients reported an increase, four a decrease [8, 15, 63, 66] and two found [15, 63] no effect on days pp. till first ovulation. Conception rate following first insemination is increased after supplemental glycogenic nutrients in both reported studies [77, 118]. Six out of

14 studies showed an increase in conception rate following first insemination by increasing the lipogenic nutrient proportion in the diet [15, 62, 63, 65, 104, 105, 121, 122, 125, 126]. Number of services per conception is increased in four [118, 124] out of five studies on feeding extra glycogenic nutrients. Only Miyoshi et al. [77, 118] found the number of services per conception to be reduced after propylene glycol supplementation. A majority of the studies (11 out of 15 studies) [62, 65, 101, 102, 105, 114, 121, 122, 125, 126] reported a decrease in services per conception after the addition of lipogenic nutrients. The number of days open are reported to be reduced by glycogenic nutrient supplementation in two out of three studies [77, 118]. A few studies (3 out of 10 studies) [62, 63, 65, 67, 101, 102, 105, 126] showed a decrease in the number of days open after fat addition to the diet.

In addition, several studies found increased pregnancy rates [15, 62, 63, 122, 127], elevated plasma progesterone (P4) level [15, 62, 63, 105], increased diameters of preovulatory follicles [64] and greater follicular populations [127–129] after dietary fat supplementation. However, other groups detected a negative relation between dietary fat addition and follicular development [9], pregnancy rates [65, 104, 125] or plasma P4 concentration [64].

Figure 6 confirms the conclusion of Staples et al. [54] that the effects of dietary prilled fat on reproductive performance are variable. In addition, Figure 6 shows that feeding extra glycogenic nutrients has variable effects on reproductive parameters as well. Several factors contribute to the diversity in effects of supplemental lipogenic and glycogenic nutrients on fertility in dairy cattle. First, as discussed before, the type of lipogenic nutrients (chain length and degree of saturation of long chain fatty acids) as well as the type of glycogenic nutrients (rate of fermentation in the rumen) affects the profile of nutrients absorbed from the gastro-intestinal tract which in turn may impact on reproductive parameters. For supplemental lipogenic nutrients, a possible role for fatty acid composition has been suggested and confirmed in several studies [79, 130]. Petit et al. [79, 130] found a difference in conception rate after first insemination and plasma P4 levels between cows fed extracted flaxseed meal (MEGALAC) or whole flaxseed (FLAX). They suggested, next to an increased DM intake, a lower daily milk production and a less negative NEB; also the increased concentration of linolenic acid in FLAX could be beneficial by increasing progesterone levels, decreasing prostaglandin levels and consequently increasing conception rate. They discussed the potential inhibition of prostaglandin secretion by absorbed linolenic acid, as supported by the increased milk progesterone concentration in cows fed FLAX. In addition, another study [79] found an enhancing effect of poly-unsaturated fatty acids on plasma insulin level and number of follicles compared to a control group and groups fed saturated or highly poly-unsaturated fatty acids. Similarly, the variation in type of glycogenic nutrients contributes to the observed variation in effects on reproduction. Santos et al. [81] observed a non-significant increase in luteal activity and P4 levels in cows on a diet high in rumen degradable starch (RDS), compared to a rumen resistant starch diet. The authors suggested the increased EB of the RDS group to be an explanation for this observation. Additionally, also the reported increase in insulin concentrations with the RDS treatment, probably resulting from an increased production of ruminal propionate, can be beneficial to ovarian function. Secondly, it is important to differentiate between isocaloric and non-isocaloric diets, since dietary energy density has been reported to have significant effects on reproductive performance [26, 131]. As illustrated in Figure 4, most studies increased the NE intake by adding more lipogenic or glycogenic nutrients to the diet. To study the effect of dietary energy source, it is highly favorable to offer isocaloric diets to prevent this interaction with dietary energy density. Thirdly, as shown in Figure 5, several authors

found an effect of glycogenic or lipogenic nutrients on the (calculated) EB [72, 77] which might interact with the effect of energy source on reproduction.

Concerning the above-mentioned explanations, they all also, have, besides an effect on reproductive performance, an effect on EB. This suggests that the effect of dietary energy source is not necessarily a direct effect of energy source availability, but might be an indirect effect via alterations of EB status by dietary energy source. This implies EB to be an intermediary in the effect of dietary energy source on reproductive performance.

A fourth consideration, concerning the interpretation of the effects of dietary energy source on reproductive parameters, is that parameters such as the number of services per conception or conception rate at first AI could largely depend on the protocol of the experiment. The minimum number of days until first AI seems particularly important in this aspect. A part of the presented studies in Figure 4b do not specify the determination of timing of AI [65, 118, 119, 121]. Most studies applied a waiting period till first AI ranging from 39 to 90 DIM [15, 62, 105, 126], other studies inseminated the cows after synchronization with a prostaglandin analogue [104, 132].

A fifth explanation can be that several authors suggested that optimum nutritional conditions for follicle growth are not necessarily recognized as optimum conditions for embryo-survival [52]. Exact knowledge about this hypothesis is lacking; however, it has been indicated that impaired body condition and prolonged low energy intake are detrimental to fertility. In contrast, short-term restrictions in dietary energy intake have been shown to increase subsequent pregnancy rates in heifers [133]. Explanations can probably be found in intermediate metabolic signals. Increased energy status is related to increased plasma insulin concentration [66, 77] which is beneficial to follicular development [50]. On the contrary, body fat mobilization, resulting from feed restrictions, is associated with increased plasma P4 levels [133, 134], probably caused by the steroid-storage function of fat tissues, which can be beneficial to pregnancy establishment and fertility.

In summary, it is difficult to draw conclusions on the effects of feeding either extra lipogenic or glycogenic nutrients on reproductive parameters. Firstly, reported effects seem to be variable due to the type of lipogenic or glycogenic nutrients and NE intake level effects on EB. Secondly, research on the relation between glycogenic nutrient addition and EB and reproductive parameters is desirable since studies on this subject are still scarce. Some suggestions can be made since glucose and insulin are increased after feeding extra glycogenic nutrients and are suggested as positive metabolic signals to the reproductive axis [11, 13, 19, 57, 118, 135]. Plasma NEFA and BHBA levels are increased after feeding extra lipogenic nutrients and associated with decreased reproductive performance and anestrous [9, 65, 136–138]. Both observations might imply that the C2/C3 compound balance is important for reproductive performance.

5. CONCLUSION

Dietary energy source affects the balance in C2 and C3 compound availability, as supplied by dietary ingredients and adipose tissue mobilization. Alterations in C2 and C3 compound availability result in modifications in blood metabolic profiles and production performance in lactating dairy cattle. These observations, together with the described effects of the C2/C3 compound ratio on energy balance and reproductive performance in dairy cattle, suggest a relationship between the availability of C2 and C3 compounds and EB and reproduction. However, since the described effects on reproduction are rather incoherent and studies on feeding extra C3 compounds and reproductive performance are scarce, further research could validate these suggestions.

Appendix

Table II. Studies presented in Figures 3 to 6. Dietary treatment, no of cows, parity and DMI.

	Dietary treatment	Isocaloric[a] Y/N	Extra nutrients (% DM)	Extra nutrients ($kg \cdot d^{-1}$)	Forage: concentrate (DM basis)	Cows (No.)	Treatment period (DMI)	Parity	DMI ($kg\ DM \cdot d^{-1}$)
Lipogenic studies									
[8]	Control				50:50	45	0–84	≥ 2	23.1
	Tallow + yellow grease	N	8.7	2.09					24.0
	Tallow + yellow grease	N	17.4	3.74					21.5
[9]	Control				45:55	42	0–100	≥ 2	17.3
	Prilled long chain satured fatty acids	N	2.5	0.39					15.5
[62]	Control, herd 1				52:48	95	0–150	≥ 2	
	Long chain fatty acids, herd 1	N		0.50					
	Control, herd 2					47			
	Long chain fatty acids, herd 2	N		0.50					
	Control, herd 3					47			
	Long chain fatty acids, herd 3	N		0.50					
[63, 132]	Control, low protein				48:52	45	1–120	≥ 2	19.6
	Megalac[b], low protein	N	2.2	0.42					19.0
	Control, high protein				47:53				19.4
	Megalac[b], high protein	N	2.2	0.44					19.8
[99]	Control				46:54	48	21–119		23.1
	Whole cotton seed (WCS)	N							23.9
	WCS + Megalac[b]	N	2.7	0.58					21.6
[125]	Control				45:55	90	0–75	≥ 1	
	Ca salts of long chain fatty acids	N	3						
[76]	Control				52:48	18	80	≥ 1	20.0
	Ca salts of long-chain fatty acids	Y	2.2		65:35				19.7
	Ca salts of long-chain fatty acids	N	2.2		52:48				20.5
[121]	Control				84:16	201	0–70	≥ 1	
	Megalac plus[d]	N	3	0.40					
	Megapro gold[e]	N	3	1.50					
[65]	Control				37:63	48	0–150	≥ 2	24.1
	Adolac[c]	N	2.2	0.50					24.3
[100]	Control				34:66	36	0–150	≥ 2	24.0
	Adolac[c]	N		0.55					23.3
[67]	Soybean meal					58	0–105	≥ 2	22.7
	Heat treated whole soybeans	N							22.4
[101]	Control				45:55	47	–14–35	≥ 1	15.3
	Partially hydrogenated tallow	N	2	0.40					15.5
[102]	Control				50:50	153	0–28		20.8
	Oilseeds (sunflower or soybean)	N							20.4
[122]	Control				44:56	108	14–135	≥ 1	

Table II. Continued.

	Dietary treatment	Isocaloric[a] Y/N	Extra nutrients (% DM)	Extra nutrients (kg·d^{-1})	Forage: concentrate (DM basis)	Cows (No.)	Treatment period (DMI)	Parity	DMI (kg DM·d^{-1})
	Megalac[b]	N		0.50					
	Control					48	14–63		
	Adolac[c]	N		0.45					
[126]	Control				45:55	220	0–200	≥ 1	
	Megalac[b]	N		0.45					
[82]	Dry-rolled sorghum (DRS) 40%				34:66	36	5–96	≥ 1	21.6
	DRS + Megalac[b]	Y	2.5						17.8
	Steam-flaked sorghum (SFS) 40%								23.1
	SFS + Megalac[b]	Y	2.5						19.5
[103]	Dry-rolled sorghum (DRS)				38:62	40	85 ± 50	≥ 1	28.9
	DRS + Megalac[b]	N	2.5		37:63				30.8
	Steam-flaked sorghum (SFS)	Y			38:62				26.7
	SFS + Megalac[b]	N	2.5		37:63				26.1
	SFS + Megalac[b]	N	5		36:64				26.8
[105]	Control				25:75	126	0–120	≥ 2	20.3
	Ca soaps of fatty acids	N	2.6	0.53					20.2
[104]	Control				36:64	66	0–120	≥ 2	20.6
	Adolac[c]	N	2.5	0.51					20.3
[15]	Control, low protein				49:51	34	14–84		24.2
	Tallow, low protein	Y	3	0.72	65:35				22.8
	Control, high protein				49:51	34			25.1
	Tallow, high protein	N	3	0.68	65:35				24.1
[106]	Control				39:61	14	0–84	≥ 2	25.9
	Megalac[b]	N	1.8	0.36					24.4
Glycogenic/lipogenic studies									
[60]	Control				60:40	18	161	≥ 1	21.0
	High fat (white grease)	N	3						20.1
	High concentrate level (corn silage)	Y			40:60				21.3
[61]	Low ground shelled corn level (LC)				45:55	8	52	≥ 2	19.2
	LC + prilled long chain satured fatty acid	N	3	0.621					20.7
	High ground shelled corn level (HC)	N			70:30				20.2
	HC + prilled long chain satured fatty aci	N	3	0.582					19.4
[69]	Control				70:30	4	60		16.6
	VFA infusion (rumen)	N							16.4
	Propionate infusion (rumen)	N							16.6
	Glucose infusion (duodenum)	N							16.5
[66]	Control				26:74	4	111 ± 14	≥ 2	22.5

Table II. Continued.

	Dietary treatment	Isocaloric[a] Y/N	Extra nutrients (% DM)	Extra nutrients (kg·d^{-1})	Forage: concentrate (DM basis)	Cows (No.)	Treatment period (DMI)	Parity	DMI (kg DM·d^{-1})
	Glucose infusion (abomasal)	N		1.00					22.4
	Tallow infusion (abomasal)	N		0.45					22.7
	Yellow grease inf. (abomasal)	N		0.45					21.5
[68]	High alfalfa silage (HA)				50:50	6	31	≥ 2	24.8
	HA + tallow	N	4						22.9
	High corn silage (HC)	Y			50:50				22.6
	HC + tallow	N	4						21.4
[78]	High fat diet (tallow)				65:35	43	150 ± 3	≥ 2	21.6
	High grain diet (ground corn)	Y			50:50				22.5
[107]	Tapioca			2.00		32	0–100		20.9
	Ca salts of palm and soya oil	Y							20.2
Glycogenic studies									
[117]	Control				86:14	4	60–90	≥ 2	18.5
	Glucose infusion (intravenous)	N		0.34					18.8
	Glucose infusion (intravenous)	N		0.74					19.7
[124]	Low concentrate level			0.8		90	0–350	≥ 1	
	Medium concentrate level	N		4					
	High concentrate level	N		7.2					
[108]	Molassed sugar beet feed				30:70	21		≥ 2	16.3
	Barley	N							15.9
[75,109]	High forage:concentrate ratio				84:16	46	5–100	≥ 2	20.9
	Low forage:concentrate ratio	N			45:55				24.8
[50]	Control							2.8 ± 0.2	
	Extra starch	Y	16						
[110]	Fibre concentrate (sugarbeetpulp, Citruspulp, cottonseed)					6	32 ± 7	≥ 2	17.4
	Starch concentrate (barley, wheat, maize	N							17.0
[111]	Control				50:50	6	49–133	≥ 2	18.8
	High concentrate (74% groundshelled corn, 21% soyabean meal)				17:83				17.3
[119]	Control					234	–13–12	≥ 1	
	Propylene glycol	N		1					
[120]	Control				48:52	4			19.9
	Glucose infusion (duodenum)	Y		2.25					16.5
[112]	Low starch (0.5%)					52:48	50	46 ± 17	16.6
	High starch (38.4%) (wheat, barley, maize)	Y							16.4
[70]	Control					50:50	4 24 ± 2.1	≥ 2	22.5

Table II. Continued.

	Dietary treatment	Isocaloric[a] Y/N	Extra nutrients (% DM)	Extra nutrients (kg·d^{-1})	Forage: concentrate (DM basis)	Cows (No.)	Treatment period (DMI)	Parity	DMI (kg DM·d^{-1})
	Starch hydrolysate infusion (abomasum	N		1.5					21.8
	Starch hydrolysate infusion (rumen)	N		1.5					21.7
[71]	Control				46:54	10	15–41	≥ 2	19.2
	Glucose infusion (intravenous)	N							17.8
[72]	Control				40:60	75	–19–280	≥ 1	21.2
	High non-fiber carbohydrate (corn)	N							21.3
[77]	Control				50:50	35	0–42	≥ 1	15.7
	Propylene glycol	N		0.50					15.4
[113]	Megalac[b] + barley			0.41	61:39	24	0–350	≥ 2	13.6
	Megalac[b] + propionate + propylene glycol			0.41					16.1
[114]	Control				50:50	20	–42–0	≥ 2	15.7
	Extra barley	N		0.80					16.0
[115]	Control				55:45	5	53 ± 12		15.6
	Glucose infusion (duodenum)	Y		1.72[d]					16.6
	Glucose infusion (duodenum)	N		3.45[d]					16.7
	Propionate infusion (rumen)	Y		1.72[d]					16.0
	Propionate infusion (rumen)	N		3.45[d]					16.3
[116]	Molassed sugar beet feed + fishmeal				50:50	16	0–126	≥ 2	16.0
	Barley + fishmeal	N							15.5
	Molassed sugar beet feed + soyabean meal				48:52				15.5
	Barley + soyabean meal	N							16.0

[a] Treatment diet is isocaloric compared to control diet: Y(es)/N(o).
[b] Ca salts of palm fatty acids.
[c] Ca salts of long chain fatty acids.
[d] In Mcal·d^{-1}.
[e] Ca salts of palm fatty acids and extracted rapeseed meal and whey permeate.

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