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Milk Fat Synthesis: Mechanisms and Influencing Factors

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Milk fat is one of the major components of milk and contributes significantly to its nutritional and economic value. Milk fat depression (MFD) is a condition where milk yield remains relatively normal but milk fat percentage drops significantly. It is mainly associated with nutritional and rumen fermentation imbalances. Understanding nutrition plays a crucial role in preventing and managing MFD. Excessive dietary unsaturated fatty acids, low fibre diets, and high levels of rapidly fermentable carbohydrates can alter rumen fermentation, leading to increased production of specific biohydrogenation intermediates (e.g., trans-10, cis-12 CLA) that inhibit de-novo milk fat synthesis in the mammary gland. Knowledge of proper forage-to-concentrate ratio (40:60 to 60:40), maintaining effective fibre (NDF≥28%; 31.2% peNDF from particles greater than 1.18mm or 18.5% peNDF from particles greater than 8mm), avoiding abrupt dietary changes, and balancing fatty acid sources helps minimize the risk. The synthesis of milk fat in dairy cows involves two main sources: *De novo fat synthesis within the mammary gland and Preformed fatty acids derived from dietary fat and mobilized body fat*. Both processes work together to determine the quantity and composition of milk fat.

1. *De Novo* Fat Synthesis in the Mammary Gland

De novo synthesis refers to the formation of fatty acids within the mammary epithelial cells from precursor molecules.

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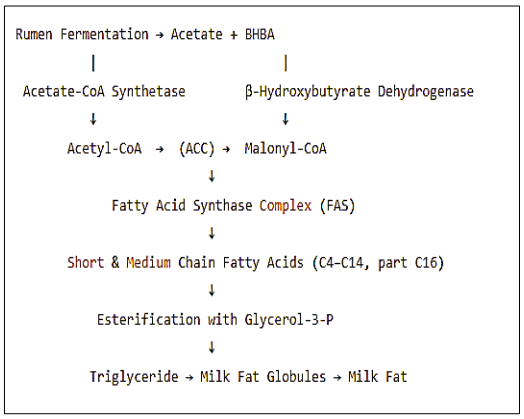
- ✓ VFAs from the rumen are the major substrates. Acetate and β-hydroxybutyrate (Butyric acid is absorbed and metabolized into BHBA by ruminal epithelium cells) are the key precursors absorbed from the rumen and transported to the mammary gland.
- ✓ *De Novo* Fat Synthesis increases linearly with increase in ruminal acetate: propionate ratio, being maximum when A/P ratio is ~2.2. While, high grains/ starch diets lower milk fat by suppressing fibre fermentation.
- ✓ *De novo* synthesis predominantly forms short- and medium-chain FA (C4–C14) and part of C16 (palmitic acid) which provides 30–50% of milk fat.

Figure 1. De Novo Mechanism of Milk Fat Synthesis



- ✓ These fatty acids contribute to the physical properties of milk fat, like melting point and texture.

✓ **Key Enzymes in de novo milk fat synthesis:**

- Acetyl-CoA Carboxylase (ACC): rate-limiting enzyme that catalyses acetyl-CoA into malonyl-CoA.
- Fatty Acid Synthase (FASN): primary enzyme responsible for synthesizing short- and medium-chain fatty acids.
- Glucose-6-Phosphate Dehydrogenase (G6PD): A rate-limiting enzyme in the pentose phosphate pathway, which supplies NADPH, a crucial reducing agent for de novo fatty acid synthesis directly linking G6PD activity to the production of milk fat.

✓ **Regulation:**

- SREBP-1: Sterol Regulatory Element Binding Protein 1, a transcriptional activator that promotes the expression of lipogenic genes like FASN and ACC, increasing fatty acid synthesis during lactation.
- AMPK: AMP-activated protein kinase. Activation of AMP-activated protein kinase (AMPK) inhibits SREBP-1, thereby suppressing de novo fatty acid synthesis.

✓ **Influence of dietary fat on de-novo fatty acid synthesis:** A high-fat diet (>6-7% DMB) decreases the expression of de-novo fatty acid synthesis enzymes (FASN) and reduces the proportion of short-chain fatty acids in milk.

2. Use of Dietary Fat and Preformed Fatty Acids

The other portion of milk fat originates directly from fatty acids in the cow's diet or mobilized from the adipose tissue. Dietary fat and mobilized body fat provides 50–70% of

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milk fat, mainly the long-chain fatty acids (C16–C18 and above). The profile depends on the type of fat in the diet (saturated vs unsaturated).

a) Dietary lipids provide mainly long-chain fatty acids (C16 and above).

- Dietary fats are hydrolysed in the rumen to free fatty acids and glycerol. Some fatty acids undergo bio-hydrogenation by rumen microbes.
- Long-chain fatty acids escape rumen degradation (rumen bypass fat) and are absorbed in the small intestine.
- These fatty acids circulate in the blood as lipoproteins. They are directly incorporated into triglycerides without further chain elongation.

b) Body fat mobilization

- During early lactation, because of negative energy balance, stored fat is mobilized from the adipose tissue and provides non-esterified fatty acids (NEFAs) which are diverted towards either liver or mammary gland. NEFAs, that are taken up by mammary epithelial cells are incorporated into triglycerides.
- Mobilized body fat is especially important in early lactation when cows are in negative energy balance. Efficiency of dietary ME usage for milk production is ~60-64% while body tissue mobilization yields ~82% efficiency towards milk production.

Fat Mobilization and Liver Metabolism

The liver receives NEFA, which can either be oxidized for energy (ATP/ketone production), or be re-esterified into triglycerides (TAG). If TAG accumulates excessively in the liver, leads to fatty liver syndrome and impaired metabolism. To prevent this, the liver must package TAG into very-low-density lipoproteins (VLDL) for export.

Role of Methionine and Choline:

Methionine and Choline act as methyl donors, crucial in one-carbon metabolism and lipid transport/ mobilization from liver:

Methionine

- An essential amino acid and the first limiting AA in dairy cows.
- Through the S-adenosylmethionine (SAM) pathway, methionine donates methyl groups for synthesis of Phosphatidylcholine via the PEMT pathway. Phosphatidylcholine is a major phospholipid required for VLDL assembly and secretion.
- Adequate methionine → improved VLDL secretion → better removal of TAG from liver → less fatty liver, more efficient mobilization of fat for milk fat synthesis.

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Choline

- Can be obtained directly from the diet (rumen-protected choline because free choline is degraded in the rumen).
- Choline is a direct precursor of phosphatidylcholine via the CDP-choline pathway.
- Phosphatidylcholine is again critical for VLDL packaging and secretion.
- Without enough choline, fat accumulates in the liver, limiting NEFA mobilization → reducing substrate availability for milk fat synthesis.
- Mobilized NEFA (LCFA) transported via VLDL serve as preformed fatty acids that are directly incorporated into milk triglycerides.

Integration of De novo, preformed (dietary and adipose tissue) fat for milk fat synthesis:

- The mammary gland combines de novo synthesized fatty acids and preformed fatty acids into triglycerides.
- These triglycerides are packaged into milk fat globules coated with a membrane.
- Thus, the final composition of milk fat depends on:

✓ Rumen fermentation pattern (affecting acetate and BHBA supply).

✓ Dietary fat type and amount.

✓ Energy balance of the cow (mobilization of body fat).

Milk fat depression (MFD)

MFD in dairy cows is a multifactorial issue, usually nutritional but also influenced by management. Here's a structured list of its main causes:

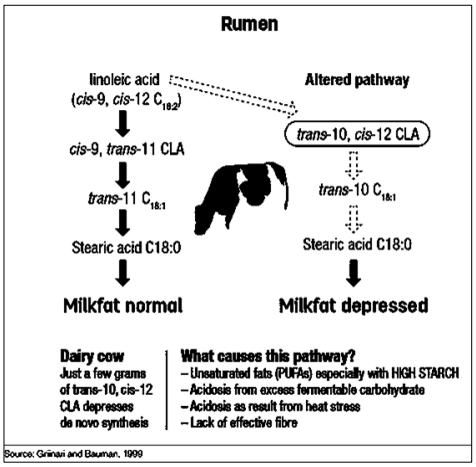

Figure 2. Altered bio-hydrogenation pathway and MFD

- High concentrate / low forage diets or excess rapidly fermentable carbohydrates (starch, sugars) → SARA: Low A:P ratio
- Low effective fiber (peNDF)
- High levels of unsaturated fatty acids (e.g., oils, oilseeds) → Altered biohydrogenation pathways: especially trans-10, cis-12 CLA → inhibit mammary fat synthesis.
- Inadequate rumen degradable protein (RDP)
- Inconsistent feed mixing → sorting of feed reduces fiber intake.

In conclusion, milk fat synthesis occurs in the mammary epithelial cells through a two-stage process: de novo synthesis and uptake of preformed fatty acids with a multi-regulatory mechanism through genetics, diet and reserved body fat mobilization.

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