Review

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Lactose and type 2 diabetes: Nutritional and metabolic perspectives

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Abstract

Diabetes mellitus, particularly type 2 diabetes (T2D), is one of the most prevalent metabolic disorders worldwide, strongly influenced by lifestyle and nutritional factors. Current dietary recommendations emphasize the importance of carbohydrate quality and food matrix effects in modulating glycaemic control and insulin sensitivity. Lactose, the principal disaccharide in milk, is frequently overlooked in the context of diabetes research, as most attention has been focused on other dietary sugars such as glucose, sucrose, and fructose. However, lactose displays a relatively low glycaemic index compared to other carbohydrates and is hydrolysed into glucose and galactose, the latter showing potential antioxidative and anti-inflammatory effects. Moreover, a growing body of evidence suggests that dairy intake is associated with a reduced risk of type 2 diabetes, with fermented dairy products, such as yogurt and kefir, consistently showing the most protective associations. Recent studies have further highlighted the role of genetic variation in lactase persistence and non-persistence, pointing to the potential influence of gut microbiota and lactose fermentation products on glucose homeostasis. The aim of this review is to provide an overview of current evidence linking lactose metabolism and dairy consumption to the risk, regulation, and management of type 2 diabetes.

Keyword: lactose; milk; dairy products; type 2 diabetes

Introduction

Diabetes mellitus, particularly type 2 diabetes (T2D), represents one of the most significant public health challenges of the 21st century, with global prevalence steadily increasing in both developed and developing countries (IDF, 2025). According to the International Diabetes Federation, over 500 million adults worldwide were living with diabetes in 2021, and this number is projected to rise to more than 640 million by 2030 (IDF, 2021). Lifestyle and dietary factors are strongly implicated in the pathogenesis of T2D, and growing attention has been directed towards the role of carbohydrate quality and food matrix in glycaemic control and insulin sensitivity (Atkinson et al., 2021).

Lactose, the principal disaccharide in milk, is often overlooked in diabetes-related nutrition research. Compared with other dietary sugars such as glucose, sucrose, and fructose, lactose exhibits a relatively low glycaemic index and distinct metabolic fate. Upon hydrolysis by lactase, lactose yields glucose and galactose, the latter of which has been associated with antioxidative and anti-inflammatory properties (Jenkins et al., 1985; Shkembi and Huppertz, 2023). These characteristics suggest that lactose may influence glucose homeostasis differently than other simple carbohydrates.

Furthermore, accumulating epidemiological evidence indicates that dairy consumption, particularly fermented products such as yogurt and kefir, is associated with a reduced risk of T2D (Chen et al., 2014; Gijsbers et al., 2016; Zhang et al., 2022). Fermentation processes not only reduce the lactose content of dairy products but also generate bioactive metabolites, such as short-chain fatty acids and bioactive peptides, which may further contribute to improved insulin sensitivity and glycaemic regulation (Antony and Vijayan, 2021; Saleem et al., 2024; Park and Mannaa, 2025). Recent genetic and microbiome studies additionally suggest that lactase persistence or non-persistence may modulate the relationship between dairy intake and diabetes risk (Luo et al., 2024; Kakkoura et al., 2024).

The aim of this review is therefore to provide a comprehensive overview of current evidence linking lactose metabolism and dairy consumption to the risk, regulation, and management of type 2 diabetes. This narrative review integrates current biochemical, nutritional, epidemiological and clinical evidence to provide a structured understanding of the role of lactose and dairy consumption in type 2 diabetes.

Lactose

Lactose ($C_{12}H_{22}O_{11}$) is a major disaccharide of milk. It is composed of one unit of ß-D-galactose and one unit of ß-D-glucose linked by a ß(1→4) glycosidic bond (Figure 1). This linkage is specific and requires the enzyme lactase (lactase-phlorizin hydrolase, LPH) for hydrolysis. Structurally, lactose is a reducing sugar because the free anomeric group of glucose can participate in oxidation and condensation reactions, enabling diverse functional roles in food systems, including participation in Maillard reactions.

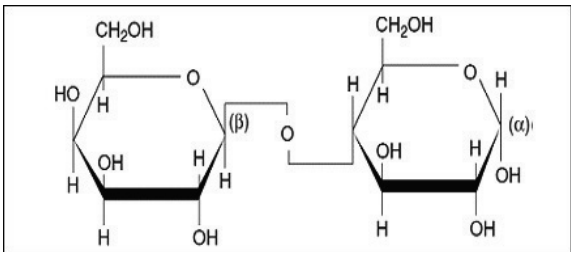

***Figure 1**. Chemical structure of lactose (Barać and Sarić, 2023)*

Lactose exists in two crystalline forms: α-lactose monohydrate and anhydrous ß-lactose (Jelen, 2022). The α-form is more stable in aqueous solution and commonly crystallizes during the drying of milk powders, whereas the ß-form exhibits higher solubility in water. These differences in crystalline form significantly influence the physicochemical properties of dairy powders and the stability of dairy products during storage.

Another important property of lactose is its relatively low sweetness (approximately 20-30 % of sucrose (Dominici et al., 2022), which contributes to the characteristic taste of milk but also allows its use as a carrier and stabilizer in food formulations. Upon enzymatic hydrolysis by lactase, lactose yields glucose and galactose, both of which are substantially sweeter. For this reason, enzymatic hydrolysis of lactose is commonly applied in the production of lactose-free milk and fermented dairy beverages with enhanced sensory properties.

In aqueous solutions, lactose undergoes mutarotation, establishing equilibrium between α- and ß-anomers, with about 37 % α and 63 % ß at room temperature (Roos, 2009; Sánchez-García et al., 2021). This process is temperature- and pH-dependent and strongly influences solubility and crystallization (Portnoy and Barbano, 2021). During spray drying and other rapid dehydration processes, lactose is frequently present in an amorphous form, which is highly hygroscopic and prone to re-crystallization during storage, resulting in caking and undesirable changes in texture (Hupertz and Gazi, 2016; Janssen et al., 2023; Altamimi et al., 2017; Afrassiabian et al., 2019). These physicochemical characteristics have direct implications for the stability of dairy powders and infant formulas. Beyond its role in sweetness and Maillard reactions, lactose fulfills key technological functions as a bulking agent, flavor carrier, and stabilizer in various food systems (Hupertz and Gazi, 2016). Moreover, lactose derivatives such as lactulose and galactooligosaccharides are of increasing interest due to their applications in food, pharmaceutical, and nutraceutical industries, where they serve as prebiotic ingredients and excipients in solid formulations (Dominici et al., 2022; Hassan et al., 2022). These structural and functional properties of lactose, together with its derivatives, are of particular importance when considering its metabolic fate and potential implications in glucose homeostasis and type 2 diabetes.

Lactose in milk and dairy products

While the previous section addressed structural and physicochemical properties of lactose, this section focuses specifically on its occurrence and variability in milk and dairy products. The lactose content of milk and dairy products varies depending on animal species, processing technology, and degree of fermentation. The following table (Table 1) summarizes the average lactose concentrations reported in the literature and nutritional databases. Cow's milk contains about 4.6-4.8 g/100 mL lactose, which is considerably lower compared to human milk that contains 6.5-7 % of this disaccharide. Goat's milk (4.3-5.0 g/100 mL) and sheep's milk (~4.7 g/100 mL) have slightly lower but comparable values, whereas buffalo milk typically contains about 4.9 g/100 mL(Fox and McSweeney, 2015).

In addition to lactose, 15-18 % of the total carbohydrates in milk are lactose derivatives, mainly in the form of oligosaccharides with linear or branched structures (Barać and Sarić, 2023). They are usually composed of 3-8 monomers, mainly galactose, fucose, and sialic acid (Fukuda et al., 2010). The content of these oligosaccharides depends on the type of milk. Lactose and its derivatives provide approximately 50 % of the energy requirements of infants (Vesa et al., 2000). As previously mentioned, lactose is composed of glucose and galactose, which are the main sources of energy and, as components of galactocerebrosides, also play an important role in brain development, hypoglycaemic and prebiotic effects relevant to diabetes (Barać and Sarić, 2023).

The lactose content of dairy products varies considerably depending on the degree of fermentation, processing, and aging. Fermented products such as yogurt and kefir contain slightly less lactose (Table 1) than milk because lactic acid bacteria partially hydrolyze lactose during fermentation. Although about 20 % of the lactose from the initial amount in milk ferments (Walstra et al., 2006), after fermentation yogurt can still contain 4-5 % lactose. The reason for this is that in the yogurt production process. Actually, the milk is fortified to a content of 14-16 g of dry matter/100 g (i.e. up to about 8 g/100 g of lactose), so that the lactose content in the final product differs slightly from that of the initial milk. However, the effect that these apparently identical amounts of lactose can have on the lactose-intolerant population is different (Tamime and Robinson, 1999). It is interesting that this population can consume yogurt, and the fact that lactose in yogurt (unlike lactose initially present in milk) does not cause an intolerance reaction (Tamime and Robinson, 1999; Gilliland, 1991). The most obvious explanations for this curiosity are that either the microorganisms in yogurt continue to metabolize lactose even after ingestion or the organisms undergo lysis during digestion, and the lactase thus released ensures that the level of lactose reaching the colon is too low to cause an adverse reaction (Tamime and Robinson, 1999; Gallagher et al., 1974; Desmaison et al., 1990). The lactose content of cheese largely depends on the variety and type of cheese, as well as on technological factors such as fermentation, ripening, and starter culture activity, similar to how these processes also affect the levels of proteins, lipids, minerals, and other components of cheese (Barać et al, 2017, 2018; 2024; Zheng et al, 2021). Fresh cheeses, including cottage cheese and mozzarella, retain moderate concentrations (2.5-3.5 g/100 g) due to the presence of whey. In contrast, ripened cheeses such as Camembert and Brie contain only 1-2 g/100 g, while hard cheeses like Cheddar, Parmesan, and Gruyère are almost lactose-free (<0.1 g/100 g), making them suitable

Table 1. *The average content of lactose in milk and dairy products*

Milk type	**Lactose content (g/100 mL)**	**Reference**
Human milk	6.5-7.0	Fox and McSweeney, 2015
Cow's milk	4.6-4.8	USDA FoodData Central, 2024
Goat's milk	4.3-5.0	Silanikove et al., 2015
Sheep's milk	~4.7	Silanikove et al., 2015
Buffalo milk	~4.9	Silanikove et al., 2015
Camel	4.5	Jelen, 2022
Donkey	6.3	Guo et al., Jelen, 2022
Dairy product	**Lactose content (g/100 g or mL)**	
Natural yogurt	~4.7	USDA, 2024
Greek yogurt	2.7-3.2	USDA, 2024; Verywell Health,
Kefir	~3.1	Li et al., 2021
Fresh cottage cheese	2.7-2.9	USDA, 2024
Mozzarella	2.5	Lactolerance.fr
Camembert/Brie (soft cheese)	1.0-2.0	Lactolerance.fr
Hard cheeses (Parmesan, Cheddar, Gruyère)	traces (<0.01) or lower than margine of detection	Portnoi and Mac Donald, 2009; Facioni et al., 2021
Condensed milk	9.5-12.5	McSweeney et al., 2015
Ice cream	≥5.0	USDA, 2024
Butter	<0.1	USDA, 2024
Lactose-free milk	<0.1	USDA,2024

for lactose-intolerant individuals. Condensed milk and ice cream are among the richest sources of lactose (≥9.5 g/100 g and ≥5 g/100 g, respectively), whereas butter has very low levels (~0.6 g/100 g) because most lactose is removed with the buttermilk fraction. Lactose-free milk is produced by enzymatic hydrolysis of lactose into glucose and galactose, resulting in a residual content of less than 0.1 g/100 mL, while preserving the nutritional composition of regular milk and improving tolerability in lactose-intolerant individuals. Lactose content also significantly varies in different whey-based products. In the Table 2 is given composition of the main types of whey-based dried products.

The lactose content in bovine milk can show minor variations depending on breed, stage of lactation, and seasonal feeding practices. However, these fluctuations are generally small, often within a few tenths of a percent. For example, multivariate analyses of Holstein and Jersey cows reported mean lactose concentrations of ~4.5 % with standard deviations around 0.2-0.3 % (Alessio et al., 2016), while its content progressively and rapidly decreases during lactation which is contrary to trends for lipids and protein concentration (Fox et al., 2015; Lim et al., 2020). Unlike fermentation and enzymatic hydrolysis, technological treatments such as pasteurization or UHT processing do not significantly alter lactose concentration but may influence protein–mineral interactions affecting its stability in the dairy matrix (Jelen, 2022). From a nutritional perspective, precise knowledge of lactose levels in different dairy matrices is essential for dietary management of lactose-intolerant individuals, for the formulation of infant nutrition products, and for the development of specialized sports supplements such as whey protein concentrates and isolates.

The variability of lactose content across different dairy matrices is not only important for nutritional labeling and lactose intolerance management, but also has implications for metabolic responses, which will be discussed in later sections.

Lactose digestion and metabolism

Lactose is the main carbohydrate in milk and consists of one molecule of glucose and one of galactose linked by a ß-1,4 glycosidic bond. Its digestion depends on the activity of

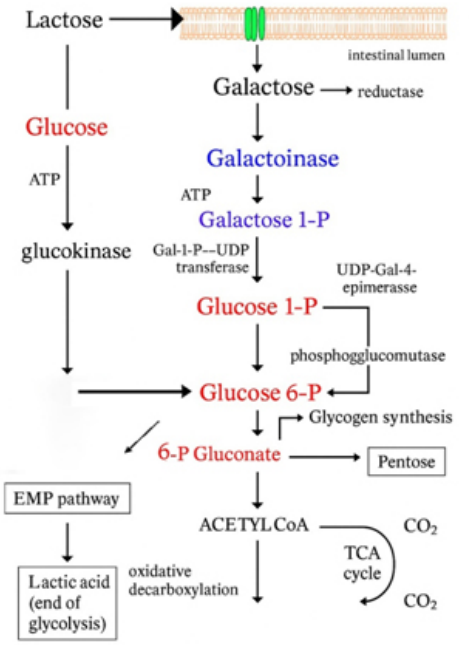

Figure 2. Schematic representation of the pathway of lactose metabolism

ß-galactosidase (3.2.1.23, ß-D-galactoside galactohydrolase) known as lactase-phlorizin hydrolase or simply lactase, an enzyme located in the brush border of the small intestine (Swallow, 2003). This enzyme catalyzes the hydrolytic breakdown of lactose into the monosaccharides, glucose and galactose (Figure 2). Lactase activity is highest in infancy but decreases after weaning in the majority of the global population, leading to the phenotype of lactase non-persistence (LNP). In contrast, in populations with a history of pastoralism and dairy consumption, genetic variants in the lactase (LCT) gene enable lactase persistence (LP), allowing continued lactose digestion into adulthood (Enattah et al., 2002; Ingram et al., 2009).

After hydrolysis, glucose is rapidly absorbed and directly contributes to circulating blood glucose, whereas galactose follows a distinct metabolic route through the Leloir pathway. In the liver, galactose is converted to glucose-1-phosphate and can enter glycolysis or glycogen synthesis

Table 2. Composition of the main whey-based dried products (%, w/w; Jelen, 2022)

Product	Lactose	Protein	Ash
	%		
Dried whey	71-73	12.5	8.5
Demineralized dried whey	83	15.0	1.0
Deproteinated whey[a]	75-83	2.0-6.8	8.4-11.0
WPC "34"[b]	50	34.0-35.0	7.0
WPC	4-21	65.0-80.0	3.0-5.0
WPI	<1	88.0-92.0	2.0-3.0
Edible ("crude") lactose	99.0	0.1	0.2
Refined (USP) lactose	99.85	0.01	0.03

WPC - Whey protein concentrate; WPI - Whey protein isolate; [a]USP - United States Pharmacopeia; [b]UF - permeate or ion exchange treatment

(Holden et al., 2004). This difference in metabolic fate implies that lactose does not behave identically to other disaccharides, such as sucrose, in terms of postprandial glycaemia and long-term metabolic effects (Jenkins et al., 1985). Furthermore, according to several investigations (Conte et al., 2021; Jumbo-Lucioni, 2013; de Lima et al, 2017; Nilsson et al., 2004), this distinct metabolic route enables galactose to exert modulatory effects on oxidative stress and inflammatory processes, which may influence diabetes-related pathophysiology.

Incomplete hydrolysis of lactose in LNP individuals results in delivery of lactose to the colon, where it undergoes microbial fermentation. This process produces gases and short-chain fatty acids (SCFAs), such as acetate, propionate and butyrate, which exert systemic effects on host metabolism. Among the fermentation products, butyrate serves as a primary energy source for colonocytes, while propionate can regulate hepatic gluconeogenesis and acetate contributes to lipogenesis, highlighting the systemic metabolic relevance of lactose-derived SCFAs (Roberfroid et al., 2010). SCFAs are increasingly recognized as modulators of insulin sensitivity, energy homeostasis and inflammatory responses, providing a possible explanation for epidemiological findings that link dairy consumption with reduced risk of type 2 diabetes (Luo et al., 2024). Furthermore, lactose fermentation may contribute to shaping the gut microbiota composition, favouring beneficial bacterial groups such as *Bifidobacterium* and *Lactobacillus*, which in turn influence metabolic health. The interplay between lactose digestion, gut microbiota and host genetics therefore represents a key area of research, particularly in the context of diabetes prevention and personalized nutrition strategies.

Understanding these genetic, enzymatic, and microbial determinants of lactose digestion is critical for tailoring dietary strategies aimed at improving glycaemic control and reducing type 2 diabetes risk.

Glycemic index and acute effects of lactose

Glycemic Index (GI) is defined as the incremental area under the blood glucose response curve (0–2 h) following ingestion of 50 g available carbohydrate from a test food, expressed as a percentage of the response to the same amount of carbohydrate from a reference food (usually pure glucose) (FAO,1997). It is widely used to classify carbohydrate-containing foods according to their effect on postprandial blood glucose. Foods are internationally classified according to their glycemic index (GI) as low (≤55), medium (56-69), and high (≥70), a categorization consistently applied in the International Tables of Glycemic Index and Glycemic Load Values (Foster-Powell et al., 2008; Atkinson et al., 2021). Lactose, with a GI of around 46 (glucose = 100), has consistently been shown to have a lower glycaemic impact than sucrose (~65) or many rapidly digestible starches (Atkinson et al., 2021; Shkembi and Huppertz, 2023). This lower glycaemic potential suggests that lactose may play a different role in glucose homeostasis compared to other simple carbohydrates commonly consumed in modern diets. Lactose-derived glucose contributes to postprandial glycaemia and should therefore be interpreted within the overall dietary glycaemic load and total energy intake.

Beyond glycaemic responses, the insulinotropic properties of dairy foods containing lactose are of particular interest.

Table 3. *Glycaemic index (GI) of sugars and dairy products*

Food / Carbohydrate	GI (Glucose=100)	Source
Glucose	100	Atkinson et al. (2021)
Sucrose	~65	Atkinson et al. (2021)
Fructose	~15-25	Atkinson et al. (2021)
Lactose	~46	Atkinson et al. (2021)
Dairy product		
Whole milk	44±2	Foster-Powell et al. (2002)
Milk 3 % fat	34±9	Foster-Powell et al. (2002)
Skim milk	32±5	Foster-Powell et al. (2002) Atkinson et al. (2021)
Pura Light Start milk (Australia)	30±5	Foster-Powell et al. (2002)
Regular plain milk (250 mL)	≈ 37	GIF (2024)
Yogurt, plain (unsweetened)	36±4	Foster-Powell et al. (2002) Atkinson et al. (2008)
Yogurt, fruit + sugar (low-fat)	33-47	Foster-Powell et al. (2002) Atkinson et al.(2008)
Sweetened, low-fat yogurt	47	Foster-Powell et al. (2002) Atkinson et al. (2008)
Diet yogurt (aspartame)	23-25	Foster-Powell et al. (2002) Atkinson et al. (2008)
Plain regular yogurt (200 g)	≈ 17	GIF (2024)
Yogurt, red fruit (UK)	42±12	Foster-Powell et al. (2002,2008)
Custard, low-fat vanilla (Nestlé, Australia)	36±3	Atkinson et al. (2021)
Custard, no-bake (prepared with milk)	35±2	Foster-Powell et al. (2002)
Custard, homemade (milk + starch + sugar)	43±10	Foster-Powell et al. (2002) Atkinson et al. (2021)
Custard, low-fat trifle flavor	30±3	Foster-Powell et al. (2002); Atkinson et al. (2008)

Recent evidence demonstrates that milk and lactose-equivalent meals elicit only modest increases in blood glucose but induce a disproportionately high insulin response (Nilson et al., 2004; Shkembi and Huppertz, 2023). This effect has been attributed to bioactive components of the dairy matrix, especially branched-chain amino acids, which can stimulate insulin secretion directly or through incretin hormones (Hoyt et al., 2005; Vanweert et al, 2022; Barać and Sarić, 2023; Bo et al., 2024; Vučić et al., 2020; Barać et al., 2021,2025; Gantner et al., 2024). Specifically, branched-chain amino acids such as leucine and isoleucine can directly stimulate insulin secretion by acting on pancreatic ß-cells, whereas bioactive peptides released from dairy proteins have been shown to enhance incretin hormone secretion, particularly glucagon-like peptide 1 (GLP-1), thereby amplifying the insulinaemic response to milk (Nilsson et al., 2004; Shkembi and Huppertz, 2023). In line with this, a randomized controlled trial in healthy adults showed that the ingestion of different types of milk produced only moderate rises in postprandial glucose, yet insulin levels increased more than three- to fourfold, accompanied by elevated circulating BCAAs and incretin responses (Tessari et al., 2022). These findings reinforce that lactose cannot be evaluated in isolation, as its physiological effects are strongly modulated by the surrounding food matrix.

Early nutrition research suggested that lactose may lead to more stable postprandial glycaemia compared to sucrose or glucose, thereby supporting its potential as a preferable carbohydrate source in diabetic diets. More recent controlled trials comparing milk with carbohydrate-rich beverages have confirmed favourable glycaemic responses, despite the higher insulinaemic effect (Li et al., 2017; Dhaver et al., 2025). For example, in investigation of Dhaver et al. (2025), a crossover trial in individuals with type 2 diabetes showed that 2 % cow's milk, when matched for carbohydrates or calories with almond milk and served with oatmeal, produced similar postprandial glucose responses but significantly higher insulin secretion. Li et al. (2017) likewise reported that milk consumed with meals in overweight or obese adults led to lower glucose AUC (total postprandial glucose exposure over time) compared to sugar-sweetened beverages, yet with a greater insulin area under the curve. This paradox raises questions: while enhanced insulin secretion may aid glucose clearance in the short term, its long-term implications for individuals at risk of insulin resistance require further clarification. While these acute effects are relatively well documented, their translation into long-term outcomes such as insulin sensitivity and type 2 diabetes risk remains an area of active debate.

Current evidence points to the dual nature of lactose in short-term metabolic regulation. It tends to cause relatively modest rises in blood glucose, which could support diabetes management, but its ability to stimulate insulin release calls for cautious interpretation. Understanding these complex interactions is essential when evaluating the role of lactose and dairy foods in the dietary strategies for prevention and management of type 2 diabetes.

Dairy intake and risk of type 2 diabetes

The relationship between dairy consumption and the risk of type 2 diabetes (T2D) has been extensively studied in epidemiological research over the past two decades. Large prospective cohort studies and meta-analyses consistently indicate that higher consumption of dairy products, particularly fermented varieties, is associated with a reduced incidence of T2D (Chen et al., 2014; Gijsbers et al., 2016; Zhang et al., 2022). Among different dairy subtypes, yogurt has emerged as the most consistently protective food, with several analyses reporting a dose-dependent reduction in T2D risk with increasing yogurt intake.

For instance, a dose-response meta-analysis (Gijsbers et al., 2016) reported approximately a 14 % lower risk of type 2 diabetes when comparing the highest versus lowest categories of yogurt consumption. The protective effects of fermented dairy are thought to be linked to several mechanisms. Fermentation modifies the lactose content and produces bioactive peptides and metabolites, which may influence glucose metabolism, insulin sensitivity, and gut microbiota composition (Sochol et al., 2019). Moreover, probiotic bacteria present in yogurt and kefir may contribute to improved insulin action and reduced inflammation, thereby lowering diabetes risk (Toshimitsu et al., 2024). Certain probiotic strains, particularly *Lactobacillus acidophilus* and *Bifidobacterium lactis*, have been shown to improve insulin sensitivity and reduce markers of systemic inflammation, providing a plausible mechanism by which fermented dairy products may lower type 2 diabetes risk (Ejtahed et al., 2012; Tonucci et al., 2017). These effects are supported by randomized controlled trials demonstrating improved glycaemic control in prediabetic individuals consuming probiotic-enriched yogurt. Additional trials with kefir and other fermented milks have reported reductions in fasting glucose and serum insulin, although effects on HbA1c remain heterogeneous, suggesting that both product type and microbial strain composition are important determinants of clinical outcomes (Ostadrahimi et al., 2015; Tonucci et al., 2017; Zhong et al., 2024).

In contrast, the associations between non-fermented milk and T2D risk remain less consistent. Some studies suggest neutral effects, while others indicate a potential increase in risk when milk is consumed in high quantities, particularly in certain populations (Kakkoura et al., 2024). Similarly, findings regarding cheese are mixed, with some analyses showing protective effects while others report no association. These discrepancies may reflect differences in study design, dietary assessment, population genetics, and background diet.

Recent regulatory recognition by the U.S. Food and Drug Administration (FDA, 2024) has acknowledged the evidence supporting yogurt consumption and reduced T2D risk, granting a qualified health claim. This milestone underscores the growing consensus that not all dairy products exert uniform effects on metabolic health, and that product type, fat content, and fermentation status are critical determinants of health outcomes.

Current evidence suggests that dairy products, particularly fermented varieties, may play a beneficial role in reducing

the risk of T2D. However, heterogeneity in study findings highlights the need for further research, especially randomized controlled trials, to clarify the long-term impact of different dairy subtypes on diabetes prevention. These findings highlight the complexity of the dairy-diabetes relationship, emphasizing that the health effects of lactose-containing foods depend not only on the sugar itself but also on the broader dairy matrix.

Lactose intolerance, gut microbiota and diabetes

Lactose intolerance is a common condition resulting from reduced activity of lactase-phlorizin hydrolase in the small intestine. In individuals with lactase non-persistence (LNP), undigested lactose reaches the colon, where it is fermented by the gut microbiota, producing gases and short-chain fatty acids (SCFAs). This process underlies the gastrointestinal symptoms of lactose intolerance, but it may also have systemic metabolic consequences (Swallow, 2003; Roberfroid et al., 2010).

SCFAs, particularly acetate, propionate and butyrate, exert multiple effects on host physiology. They serve as an energy source for colonocytes, regulate gut barrier integrity, and act as signalling molecules that influence insulin sensitivity, lipid metabolism, and inflammatory pathways (Barać et al, 2025; Roberfroid et al., 2010). Butyrate serves as a primary energy source for colonocytes, propionate can inhibit hepatic gluconeogenesis and modulate lipogenesis, while acetate has been implicated in appetite regulation and lipid metabolism, together linking colonic lactose fermentation with systemic effects on glucose homeostasis (Canfora et al., 2015). Consequently, the fermentation of lactose in LNP individuals, although symptomatic, may contribute indirectly to metabolic benefits.

Recent genetic studies suggest that the relationship between lactose digestion and diabetes is more complex than previously thought. Evidence from large cohorts indicates that individuals with LNP who consume milk may have a lower risk of developing type 2 diabetes, compared to lactase persistent (LP) individuals with similar intake levels (Luo et al., 2024; Kakkoura et al., 2024). Although lactase non-persistent individuals typically consume less milk due to intolerance symptoms, emerging evidence suggests that the metabolic consequences of colonic lactose fermentation may offset this lower intake, potentially explaining the paradoxical association between LNP and reduced type 2 diabetes risk (Luo et al., 2024; Kakkoura et al., 2024). This counterintuitive finding may be explained by differences in microbiota composition and the metabolic effects of colonic fermentation products.

The gut microbiota plays a central role in mediating these effects. Colonic fermentation of lactose can selectively stimulate the growth of saccharolytic bacteria, contributing to a microbiota composition associated with improved glucose metabolism and reduced low-grade inflammation (Roberfroid et al., 2010). Such interactions highlight the importance of considering both host genetics and microbial ecology in evaluating the impact of dairy consumption on diabetes risk.

It seems that lactose intolerance should not be viewed solely as a limitation to dairy intake. Instead, it represents a complex interplay between genetics, digestion, and gut microbiota, with emerging evidence suggesting that the metabolic consequences of LNP may include protective effects against type 2 diabetes under certain dietary contexts. These insights illustrate how lactose intolerance, traditionally viewed as a clinical limitation, may in fact offer novel perspectives on the broader role of lactose and the dairy matrix in metabolic health and diabetes prevention.

Potential mechanisms linking lactose to diabetes

Several biological mechanisms have been proposed to explain the potential link between lactose consumption, dairy intake, and type 2 diabetes (T2D). First, the relatively low glycaemic index of lactose (Table 1) results in smaller postprandial glucose excursions compared to other simple sugars, which may reduce long-term glycaemic burden and delay the onset of insulin resistance (Atkinson et al., 2021; Shkembi and Huppertz, 2023).

In addition to its effect on glycaemia, galactose, a product of lactose hydrolysis, follows a distinct hepatic metabolic pathway that may contribute to modulation of oxidative stress and inflammation. Experimental studies suggest that galactose can act as a substrate for the synthesis of glycoproteins and glycolipids, thereby influencing cell signalling and metabolic homeostasis (Holden et al., 2004). Because galactose must first be converted through the Leloir pathway before entering glycolysis, its metabolism is slower than that of glucose, which may contribute to more stable postprandial glycaemic responses. In addition, excessive intake of lactose-containing foods may indirectly influence insulin resistance through positive energy balance, weight gain and adiposity.

Fermentation of lactose in the colon, particularly in lactase non-persistent individuals, results in the production of short-chain fatty acids (SCFAs). These metabolites, including acetate, propionate and butyrate, are increasingly recognised as regulators of energy metabolism, appetite, and insulin sensitivity (Roberfroid et al., 2010; Luo et al., 2024). SCFAs also influence the release of gut hormones such as glucagon-like peptide-1 (GLP-1), which improve glycaemic control (Facchin et al., 2024; Zhang et al., 2024; Chembers et al, 2015).

Another mechanism involves bioactive peptides generated during fermentation of dairy products. These peptides have been shown to exert insulin-sensitising, antioxidant, and anti-inflammatory effects, contributing to improved glucose homeostasis (Sochol et al., 2019, Barać et al., 2017). Furthermore, dairy proteins, particularly whey, stimulate insulin secretion and satiety hormones, which may reduce subsequent energy intake (Nilsson et al., 2004).

Finally, the “dairy matrix” concept (Figure 3) highlights that lactose is not an isolated nutrient but interacts with

proteins, fats, minerals, and probiotics in ways that shape its metabolic outcomes. Importantly, these effects are not merely the sum of individual nutrients but arise from their synergistic interactions within the complex dairy structure (Thorning et al., 2017). These interactions indicate that lactose should not be evaluated in isolation but within the context of the dairy matrix and overall dietary pattern. Calcium and vitamin D in dairy products have been associated with improved insulin action and glucose homeostasis, partly by modulating intracellular signaling pathways and enhancing ß-cell function. In parallel, bioactive peptides derived from milk proteins during digestion or fermentation can exert insulinotropic and incretin-stimulating effects, further supporting glycaemic control. Moreover, probiotic strains in fermented dairy contribute to a favorable gut microbial composition, leading to higher production of short-chain fatty acids (SCFAs) and increased release of glucagon-like peptide-1 (GLP-1), both of which improve insulin sensitivity and postprandial glucose handling (Toshimitsu et al., 2024; Facchin et al., 2024; Zeng et al., 2023).

Within this framework, cheeses represent a particularly dynamic dairy matrix, where proteolysis and lipolysis during fermentation and ripening release bioactive peptides with antioxidant and antidiabetic properties. In addition to peptides, lipolysis also generates a complex profile of free fatty acids, and recent evidence indicates that fatty acid composition and health-related indices of traditional cheeses vary substantially with milk type, ripening conditions and production technology (Barać et al., 2018, 2025). Epidemiological studies suggest that fermented dairy, including cheese, is associated with neutral or even favorable effects on type 2 diabetes risk compared with non-fermented dairy (Zhang et al., 2025; Gautam et al., 2024). Experimental research further demonstrates that the profile of antioxidant peptides is influenced by multiple factors, including the type of milk, cheese variety, ripening duration, and technological conditions (Santiago-López et al., 2018; Martini et al., 2021; Yang et al., 2024; Barać et al., 2019; 2024). In this regard, Barać et al. (2019) showed that during ripening of white-brined cheeses, αs-casein was rapidly degraded, releasing antioxidant peptides, while both water-soluble and insoluble protein fractions contributed to the increase in antioxidant activity, with the insoluble fraction reaching up to a threefold rise after extended ripening. Such findings provide a strong biological rationale for differences in antioxidant capacity among cheese types and support the potential role of fermented dairy matrices in modulating oxidative stress and glycaemic regulation.

Weight regulation and satiety may also be indirectly influenced by lactose-containing foods. The combined effects of lactose, dairy proteins, and fermentation-derived compounds may promote satiety, reduce energy intake, and thereby support weight management a critical factor in T2D prevention (Toshimitsu et al., 2024). In particular, dairy proteins such as whey stimulate postprandial secretion of satiety hormones including GLP-1, GIP and peptide YY, which slow gastric emptying and reduce appetite (Nilsson et al., 2004; Pal and Ellis, 2010). The presence of lactose further modulates these responses by contributing to a lower glycaemic load compared to other sugars, while fermentation generates bioactive peptides and SCFA that may enhance appetite regulation and energy balance (Chungchunlam et al., 2017). Epidemiological evidence also suggests that higher dairy intake is associated with reduced weight gain and lower risk of obesity, which indirectly translates into a lower risk of developing T2D (Chen et al., 2012).

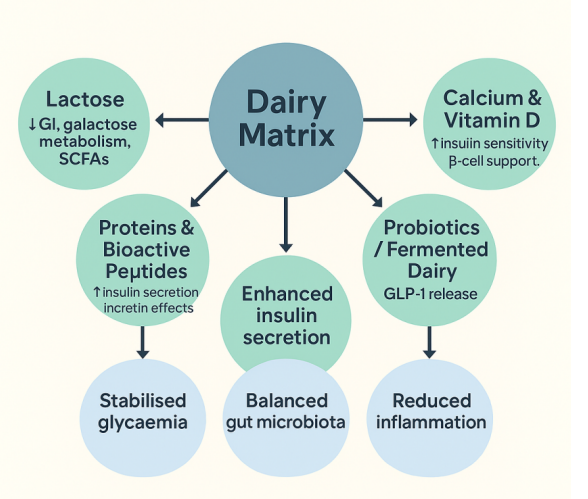

Figure 3. "Dairy matrix" concept

Taken together, these mechanisms suggest that the impact of lactose and dairy on diabetes risk is multifactorial, involving both direct metabolic effects and indirect modulation through gut microbiota and bioactive components. Understanding these pathways is essential for developing dietary recommendations that maximise the health benefits of dairy while minimising potential risks.

Clinical implication

The evidence linking lactose metabolism and dairy intake to type 2 diabetes (T2D) highlights several important clinical implications. First, the relatively low glycaemic index of lactose compared to other simple sugars suggests that lactose-containing foods may be suitable for individuals with diabetes when consumed in moderation (Atkinson et al., 2021; Shkembi and Huppertz, 2023). Clinical studies confirm that milk and yogurt elicit favourable postprandial glucose responses, although their insulinotropic effects should be considered in patients with impaired insulin sensitivity (Nilsson et al., 2004; Hoyt et al., 2005). Recent randomized trials further demonstrated that lactose-hydrolyzed milk supplemented with plant extracts (mulberry leaf and corn silk) attenuated postprandial glycaemic responses in adults with type 2 diabetes, suggesting that technological modifications of dairy products can enhance their metabolic benefits (Sun et al., 2025).

Fermented dairy products, particularly yogurt, appear to be the most beneficial in terms of diabetes prevention and management. Randomized controlled trials have demonstrated improved glycaemic control in prediabetic

individuals consuming probiotic-enriched yogurt (Toshimitsu et al., 2024). This aligns with epidemiological evidence supporting yogurt consumption as consistently associated with reduced risk of T2D (Chen et al., 2014; Gijsbers et al., 2016). Longitudinal evidence further indicates that higher dairy intake in prediabetic individuals is linked to a greater likelihood of regression to normoglycemia, while lower intake predicts progression to T2D (Bahadoran et al., 2024). Epidemiological studies consistently indicate that regular yogurt consumption is associated with a reduced risk of type 2 diabetes, with estimates suggesting that each additional 50 g of yogurt per day lowers the relative risk by approximately 7-9 % (Gijsbers et al., 2016; Díaz-López et al., 2019). These findings are corroborated by large cohort studies and meta-analyses, which suggest that higher consumption of dairy products, particularly milk and yogurt, is associated with a reduced risk of type 2 diabetes as well as obesity (Feng et al., 2022). Nevertheless, not all studies report significant associations; for example, Slurink et al. (2024) found that most dairy products were not strongly related to prediabetes risk or changes in glycaemic status, underscoring the importance of considering product type and population context. Moreover, randomized clinical trials with kefir and probiotic fermented milk have demonstrated reductions in fasting plasma glucose and serum insulin concentrations, while effects on HbA1c remain heterogeneous (Ostadrahimi et al., 2015; Tonucci et al., 2017; Zhong et al., 2024). Although outcomes depend on the type of product, microbial strains and intervention duration, yogurt and kefir can be recommended as part of a healthy dietary pattern for individuals at risk of or living with diabetes.

For individuals with lactose intolerance or lactase non-persistence (LNP), clinical recommendations should be more individualized. Lactose-free dairy alternatives and fermented dairy products, which contain lower amounts of lactose, are generally well tolerated and provide similar nutritional benefits. Notably, lactose hydrolysis preserves the nutritional composition of milk while increasing perceived sweetness, which can reduce the need for added sugars in lactose-free products.The emerging genetic studies suggest that LNP may not increase T2D risk and could even confer some protective effects mediated by colonic fermentation and the gut microbiota (Luo et al., 2024; Kakkoura et al., 2024). Therefore, intolerance should not automatically exclude patients from dairy consumption but should guide the selection of appropriate product types.

From a broader clinical and public health perspective, incorporating dairy into diabetes management plans should consider not only carbohydrate metabolism but also the contributions of proteins, fats, calcium, and bioactive components of the dairy matrix. Individual variability, shaped by genetics, microbiota, and metabolic health status, highlights the need for a personalised nutrition approach to maximize benefits while avoiding discomfort or metabolic complications. Taken together, clinical evidence supports the inclusion of appropriately selected dairy products as part of dietary strategies for prevention and management of type 2 diabetes.

Gaps in knowledge and future

Although a growing body of evidence suggests that lactose and dairy products play a role in modulating the risk of type 2 diabetes (T2D), several important gaps in knowledge remain. One of the main limitations is the predominance of observational studies, which, despite large sample sizes and long follow-up periods, cannot establish causality. While meta-analyses support the protective role of dairy, particularly fermented products such as yogurt, these findings must be confirmed in long-term randomized controlled trials (RCTs) across diverse populations. Up to date, few RCTs have directly compared lactose-containing versus lactose-free dairy products in relation to glycaemic control or incident T2D, highlighting a critical gap in the evidence base. Another gap lies in the insufficient exploration of individual variability in response to lactose and dairy intake. Genetic studies have revealed that lactase persistence and non-persistence can modulate the association between milk consumption and diabetes risk (Luo et al., 2024; Kakkoura et al., 2024). However, heterogeneous findings suggest that future studies should integrate host genetics with detailed microbiome profiling to better explain interindividual variability in metabolic responses..

Mechanistic studies investigating how lactose and its metabolites affect oxidative stress, inflammation, and insulin sensitivity are still limited. Although SCFAs produced from lactose fermentation have been proposed as mediators of improved metabolic outcomes (Roberfroid et al., 2010; Luo et al., 2024), more experimental and clinical evidence is required to confirm these pathways. Similarly, the role of bioactive peptides from fermented dairy and their potential impact on diabetes prevention warrants further study (Sochol et al., 2019; Toshimitsu et al., 2024).

Future research should also employ advanced tools such as metabolomics, nutrigenomics, and microbiome profiling to unravel the complex interactions between lactose, the dairy matrix, and individual metabolic health. Incorporating precision nutrition approaches in clinical trials may help design targeted dietary strategies for individuals at different levels of genetic risk, metabolic status, or tolerance to lactose.

Taken together, current evidence increasingly supports a beneficial role of lactose and fermented dairy in diabetes prevention, yet further multidisciplinary research is essential to establish causality, identify underlying mechanisms, and develop personalised nutrition guidelines.

Conclusions

Lactose, the principal sugar in milk, plays a unique and complex role in metabolic health compared with other dietary carbohydrates. Its relatively low glycaemic index, distinct metabolic fate through galactose, and contribution to colonic fermentation products distinguish it from other simple sugars commonly consumed in the human diet.

Epidemiological and clinical evidence supports the view that dairy intake, particularly fermented products such as yogurt, is associated with a reduced risk of type 2 diabetes. Mechanistic insights further suggest that bioactive peptides, probiotics, short-chain fatty acids, and the broader dairy matrix contribute to beneficial effects on glucose metabolism, insulin sensitivity, and inflammatory status.

At the same time, the interplay between genetics and lactose digestion highlights the importance of individual variability. Lactase non-persistence, while often associated with intolerance symptoms, may also confer indirect metabolic benefits through colonic fermentation and modulation of the gut microbiota. These findings indicate that lactose intolerance should not be seen exclusively as a dietary limitation but rather as a factor shaping personalised responses to dairy intake.

Finally, the relationship between lactose, dairy consumption, and type 2 diabetes is multifaceted and context dependent. Recognizing the duality of lactose, as both a potential metabolic benefit and a source of intolerance, is essential for evidence-based nutritional guidance. Future research integrating genetics, microbiome science, and precision nutrition approaches will be crucial for tailoring dietary recommendations that maximise the health-promoting potential of dairy products while minimizing risks for vulnerable populations. Within this context, milk and dairy products should be considered nutrient-dense foods that can be incorporated into balanced dietary patterns aimed at the prevention and management of type 2 diabetes.

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Laktoza i dijabetes tipa 2: nutritivne i metaboličke perspektive

Sažetak

Šećerna bolest, osobito dijabetes tipa 2 (T2D), jedan je od najraširenijih metaboličkih poremećaja u svijetu, snažno uvjetovan životnim stilom i prehrambenim čimbenicima. Aktualne prehrambene preporuke naglašavaju važnost kvalitete ugljikohidrata i učinaka prehrambene matrice u regulaciji glikemijske kontrole i inzulinske osjetljivosti. U istraživanjima povezanima s dijabetesom, laktoza, glavni disaharid u mlijeku, često je zanemarena, budući da je većina pozornosti usmjerena na druge prehrambene šećere poput glukoze, saharoze i fruktoze. Međutim, laktoza ima relativno nizak glikemijski indeks u usporedbi s drugim ugljikohidratima te se hidrolizira na glukozu i galaktozu, pri čemu galaktoza pokazuje potencijalna antioksidativna i protuupalna svojstva. Sve veći broj dokaza upućuje na to da je unos mlijeka i mliječnih proizvoda povezan sa smanjenim rizikom od dijabetesa tipa 2, pri čemu fermentirani mliječni proizvodi, poput jogurta i kefira, pokazuju najizraženiji zaštitni učinak. Nedavna istraživanja dodatno ističu ulogu genetskih varijacija u perzistenciji i neperzistenciji laktaze, upućujući na mogući utjecaj crijevne mikrobiote i produkata fermentacije laktoze na homeostazu glukoze. Cilj ovoga preglednog rada je pružiti pregled aktualnih spoznaja koje povezuju metabolizam laktoze i konzumaciju mliječnih proizvoda s rizikom, regulacijom i upravljanjem dijabetesom tipa 2.

Ključne riječi: laktoza; mlijeko; mliječni proizvodi; dijabetes tipa 2

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