The Application of Lactose in Sports Nutrition

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Abstract (150 words):

Lactose is a disaccharide of glucose and galactose, found exclusively in milk. Carbohydrates represent an important fuel for endurance and prolonged exercise. Recommendations for athletes include high carbohydrate diets to maximise performance, especially before, during and after exercise. However, lactose does not feature in guidelines for carbohydrate intake for athletes, despite athletes likely consuming nutritionally relevant amounts. This review will explore possible applications for lactose in a sports nutrition context. These include lactose as a fuel source, for before and during exercise, where maximizing availability of readily oxidisable carbohydrate can optimise performance. Lactose could play a role in a post-exercise recovery setting, as a vehicle for the delivery of glucose and galactose, for the optimisation of muscle and liver glycogen. Lactose may also act as a prebiotic, possibly promoting beneficial changes to gut microbiota. A discussion of the possible risks associated with lactose over-consumption and intolerance will also be considered.

Keywords: sugar, carbohydrate, sports nutrition, exercise metabolism, milk sugar

1. Introduction

Lactose is a disaccharide originating in mammalian milk, and is comprised of the monosaccharides glucose and galactose, bound by a β 1-4 glycosidic linkage (Mattar, de Campos Mazo, & Carrilho, 2012). Lactose within milk-derived dairy products is an extrinsic sugar, meaning it is not bound into the cellular structure of food (unlike intrinsic sugars such as glucose as starch in vegetables), and is free in the foods it is found in (Edgar, 1993). Milk-derived dairy products – containing variable amounts of lactose – have been a constituent of the human diet for approximately 8 000 years and feature prominently in the nutritional recommendations of most countries (Rozenberg et al., 2016). Governmental dietary recommendations encourage dairy intake in healthy individuals in the preponderance of countries, notably for their high calcium content, along with other micronutrients (U.S. Department of Health and Human Services and U.S. Department of Agriculture, 2015; Wang, Lay, Yu, & Shen, 2016) demonstrating the extensive demand for milk and dairy products. Dietary sources of lactose are numerous, with bovine milk usually containing the greatest lactose content of common foods (See **Table 1**). Isolated lactose and whey permeate, (a high-lactose (76-85 %) dairy ingredient produced when proteins are removed from liquid whey in the manufacturing of whey protein isolate) are used extensively to improve technical aspects of product formulation in foodstuffs such as baked goods, confectionary and soups (U.S. Dairy Export Council, 2015). Such dairy ingredients are also widely used in non-specific roles, such as bulking agents, animal feed or as fillers in capsules. Thus, lactose may feature in the human diet from a variety of traditional dairy and non-dairy sources.

Table 1. Lactose content of a variety of dairy products

Food	Lactose content (g) per 100 g / 100 ml
Cow's Milk	5.0
Lactose-free milk	<1.0
Ice cream	3.3 - 6.0
Cottage cheese	0.3 - 2.4
Cream cheese	2.5 - 3.0
Hard cheeses	≤0.1
Yoghurt	4.5 – 6.0
Whey protein concentrate	3.5

(Dieticians of Canada, 2013; Misselwitz et al., 2013; Tetra Pak, 2018)

Despite the widespread potential presence of lactose, surprisingly limited information on the contribution of lactose to the total energy intake (EI) of different populations is available. Most investigations into the sugar content of individuals' diets have been primarily concerned with added sugars and therefore lactose predominantly originating from dairy-derived products has often been excluded, typically being classed as a non-added sugar. However, a limited number of more specific estimations of lactose intake have been made. In Swedish women average lactose intake was 12 ± 8 $g \cdot day^{-1}$, approximately 50 kcal or ~2% of EI (Larsson, Bergkvist, & Wolk, 2004). Habitual lactose consumption in Canadian adults was reported to be similar, with milk sugar comprising ~11% of total sugar intake, estimated at approximately ~12 $g \cdot day^{-1}$ (Brisbois, Marsden, Anderson, & Sievenpiper, 2014). Whilst lactose is present in the diet, it

represents a relatively small amount, particularly in comparison to the other major dietary disaccharide sucrose. By comparison, mean added sugar intake (predominantly sucrose) totals ~58 g·day^{-1}far exceeding lactose intake (Brisbois et al., 2014) . Nonetheless, it is important to note that the presence of lactose in the diet varies considerably, depending on lactose tolerance status, food preference, and numerous other factors (Keith, Nicholls, Reed, Kafer, & Miller, 2011).

Though it has not been directly investigated, it is possible that athletes and recreationally active individuals may have a higher lactose intake than the general population. Athletes have a high EI to permit high volumes and intensities of training, far exceeding the EI of non-athletic populations (Grandjean, 1997). Athletes also have specific macronutrient requirements to facilitate recovery (including carbohydrate and protein) which can be conveniently obtained from dairy foods such as milk (James, Stevenson, Rumbold, & Hulston, 2019), or dairy-derived products, such as whey or casein protein supplements, which can contain ~4% lactose (Tetra Pak, 2018). However, the specific role of lactose in the diets of athletes or recreationally active individuals has rarely been considered. Apart from guidance on the avoidance of lactose for those recommended low FODMAP (fermentable oligo-, di-, mono-saccharides and polyols) diets, in contrast to other carbohydrates lactose does not feature explicitly in sports nutrition guidelines, perhaps due to a paucity of research. Because athletes may be consuming nutritionally relevant quantities of lactose that exceed those consumed by the general population, it is important to elucidate its metabolic effects so that its specific application can be understood in the context of sports nutrition. Therefore, this review will briefly summarise lactose metabolism, critically review the literature relating to the utility of lactose for athletes, highlight potential risks of lactose consumption and suggest areas for future research.

2. Lactose digestion, absorption and metabolism

Lactose is digested exclusively by the disaccharidase lactase (lactase-phlorizin hydrolase), located on the brush border of the small intestine (See **Figure 1**). Lactose is hydrolysed at its β 1-4 glycosidic linkage, releasing the constituent monosaccharides; glucose and galactose (Mattar et al., 2012). Both glucose and galactose are then actively transported by sodium-glucose transporter proteins (SGLT1), followed by GLUT2 allowing entry to the hepatic portal vein (Thorens, 2014; Turk, Martingn, & Wright, 1994).

The glucose component of lactose reaches the liver, where first pass extraction occurs. Glucose is directed towards metabolic processes such as liver glycogen synthesis, or oxidised. However, much of the absorbed glucose will escape this fate and enter the systemic circulation. Divergence from blood glucose homeostasis results in insulin release (Koeslag, Saunders, & Terblanche, 2003). This leads to glucose uptake by tissues through GLUT4 transporter proteins, most notably in skeletal muscle leading to the formation of glycogen through the action of glycogen synthase (Boucher, Kleinridders, & Kahn, 2014). Plasma glucose that appears after ingestion can also be oxidised directly by peripheral tissues, including skeletal muscle and the brain (Kelley et al., 1988). This is the typical metabolism of ingested glucose, including free glucose and that derived after digestion of disaccharides or polysaccharides (such as sucrose or starch respectively) containing glucose. Ingested glucose is metabolised efficiently in healthy, insulin sensitive individuals, which minimises prolonged elevations in blood glucose to ~60 minutes, depending on the quantity of glucose and the form of ingestion (Abdul-Ghani, Lyssenko, Tuomi, Defronzo, & Groop, 2010). Glucose is the comparator carbohydrate used in the glycaemic index, an index of the 2-hr blood glucose response after carbohydrate ingestion *versus* the reference (100). Lactose has a lower glycaemic index of 46

due to the presence of a galactose molecule, and similarly the index of sucrose (61) is lowered by the presence of a fructose molecule (Wolever & Miller, 1995).

The metabolism of galactose is markedly different to glucose. Lactose is the primary dietary source of galactose, though it is also present in smaller amounts in legumes (e.g. garbanzo beans, lentils, soybean), and as bound galactose in other vegetables (Acosta & Gross, 1995). Like glucose, galactose is actively transported into the hepatic portal vein via SGLT1, and GLUT2 (Thorens, 2014; Turk et al., 1994). The hepatic portal vein transports galactose to the liver where first pass extraction occurs, and some galactose enters the Leloir pathway, the primary pathway for galactose metabolism in humans. The end-product of this pathway is glucose-1-phosphate, which is then available for glucose production or glycogen storage. However, the rate of gluconeogenesis from galactose is limited, which leads to the accumulation of galactose in the circulation in large amounts and in a sustained manner. Williams, Phillips, and Macdonald (1983) demonstrated that ingestion of 0.5 $g \cdot kg^{-1}$ body mass of galactose caused substantial accumulation of plasma galactose, increasing from <0.1 $mmol \cdot L^{-1}$ at baseline to 1.70 ± 0.42 $mmol \cdot L^{-1}$ after 60 min. By feeding subjects ~22 $g \cdot h^{-1}$ of galactose, Sunehag and Haymond (2002) estimated the maximal rate of splanchnic uptake to be ~10 $g \cdot h^{-1}$. Because the liver is the primary site for galactose metabolism, and there is little evidence for extra-hepatic metabolism, circulating galactose is ultimately removed via hepatic metabolism or renal losses.

It has been observed that glucose can augment the metabolism of galactose when the two free monosaccharides are co-ingested (Sunehag & Haymond, 2002). Co-ingestion of galactose and glucose more than doubles the first pass splanchnic clearance of ingested galactose compared to galactose alone and can eliminate or drastically reduce the rise in plasma galactose after

ingestion. Furthermore, glucose production was shown to be almost exclusively derived from galactose under these conditions, *via* the Leloir Pathway. However, the mechanisms explaining this increased splanchnic uptake have not been fully elucidated. It appears that intact lactose can exert a similar effect upon galactose metabolism to free glucose and galactose ingestion, both resulting in attenuated rises in plasma galactose (Williams et al., 1983). This occurs despite the requirement for digestion. In addition, Stellaard et al. (2000) demonstrated that the hydrolysis of lactose is not the rate-limiting step in its oxidation. Subjects ingested 40 g of naturally high ^{13}C lactose or pre-digested lactose (glucose and galactose) and showed that breath $^{13}CO_2$ recovery over 4 hours was not significantly different indicating that both conditions oxidised the constituent monosaccharides of lactose at the same rate, even when delivered as the disaccharide. This may suggest that lactose and its constituent monosaccharides exert similar metabolic effects, without much impact of the digestion stage, at least at this dose. This augmentation of galactose metabolism by glucose has only been directly investigated under resting conditions.

The metabolic fate of lactose described previously assumes that lactose hydrolysis has occurred. It has been demonstrated that small amounts of lactose (0.02 $mmol \cdot L^{-1}$) can appear in plasma following milk ingestion (~40g lactose; See **Figure 1**) in normal, non-pathological conditions (Pimentel et al., 2017). This was hypothesised to be due to passive diffusion through intercellular junctions in the intestinal cells at high lactose concentrations, which is subsequently excreted in the urine. If lactose is not digested in the small intestine (termed lactose maldigestion), it can pass from the small intestine into the colon (Misselwitz et al., 2013). Lactose may be fermented by a variety of local bacterial flora, which include *Bifidobacteria, Lactobacillus, Clostridium* and *Bacteroides* (Ito & Kimura, 2009). The fermentation of lactose by colonic bacteria can yield short-chain fatty acids (SCFA), lactic

acid, CH_4, H_2 and CO_2 in different quantities depending on the bacteria (Jiang & Savaiano, 1997a, 1997b; Rangel et al., 2016; Yazawa & Tamura, 1982). Some of these products of fermentation can trigger gastrointestinal (GI) symptoms, which is termed lactose intolerance, and can depend on the quantity of lactose ingested. Section 4.1 discusses in greater detail these pathologies related to lactose ingestion.

The majority of research on lactose ingestion and metabolism has been performed under resting conditions, with limited studies directly investigating lactose metabolism in an exercise context. Nonetheless, studies performed at rest, and those limited studies involving exercise will be used in this narrative review to explore the possible impact of lactose on salient aspects of sports nutrition, with a particular focus on lactose as an energy source for exercise, recovery from exercise and lactose as a prebiotic. There will also be a discussion of the possible considerations and risks of over-consumption of lactose, which must be considered before practical application in a sporting context.

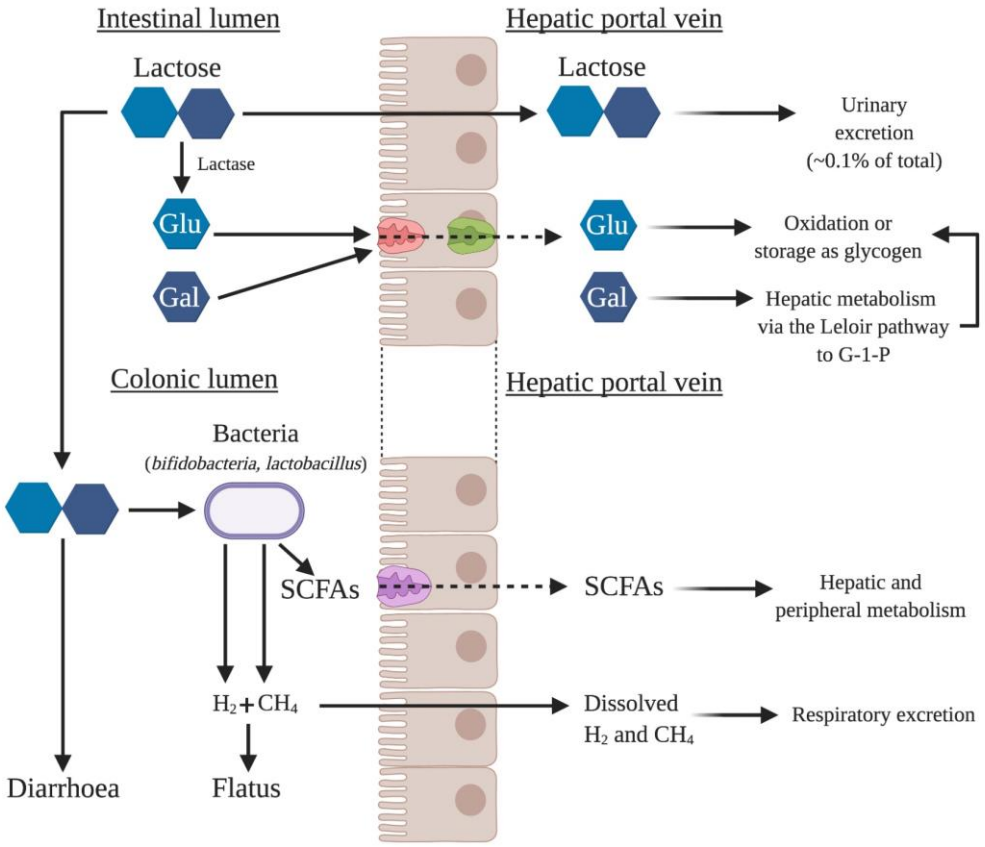

Figure 1. The digestion and absorption of lactose. Glu – glucose. Gal – galactose. SCFAs – short chain fatty acids. CH_4 – methane. H_2 – hydrogen. G-1-P – glucose-1-phosphate. Created with BioRender.com

3. The role of carbohydrate in sports nutrition

During exercise the availability of endogenous carbohydrate (as plasma glucose, liver & muscle glycogen) may be reduced to due to the high energy cost of training or competition. At moderate to high exercise intensities (≥60-70% $\dot{V}O_{2max}$) carbohydrate is the predominant energy source for ATP resynthesis (Bergman & Brooks, 1999; van Loon, Greenhaff, Constantin-Teodosiu, Saris, & Wagenmakers, 2001). Due to the limited quantities of stored carbohydrate, availability can limit performance in submaximal or intermittent high-intensity exercise of a duration >90 min, and is also required for short-lived, high intensity exercise performance (Burke, Hawley, Wong, & Jeukendrup, 2011). In addition to being an energy

substrate, glycogen can also regulate adaptive signalling pathways. Therefore, carbohydrate availability can be positive or negative with regards to adaptation. Although adaptations to resistance-type exercise may be impacted positively by high glycogen availability, the converse is true for endurance-type exercise (Mata et al., 2019). However, carbohydrate availability is pivotal to sustaining high exercise intensities, therefore high-intensity training sessions, and competitions should be performed with high carbohydrate availability.

Recommendations for maximising carbohydrate availability for exercise are typically divided into pre-exercise and during exercise. Carbohydrate intake in the hours preceding endurance, or extended exercise is important to ensure high endogenous carbohydrate availability, as both muscle and liver glycogen. This is imperative when multiple endurance exercise sessions are completed in one day, such as stage races, Ironman events, or in tournament settings. It is also necessary to ensure high carbohydrate availability following an overnight fast, during which liver glycogen may be reduced (Papin, König, Bulik, & Holzhütter, 2012). Ingesting carbohydrate during exercise (such as a drink or gel) is an effective strategy for improving performance in a variety of exercise scenarios, including endurance and intermittent exercise (Jeukendrup, 2011). Ingestion of additional carbohydrate provides an exogenous fuel source, which can reduce the reliance on stored carbohydrate, permit glycogen sparing, prevent hypoglycaemia, and positively impact the central nervous system (Burke et al., 2011).

3.1 Lactose as an energy source for exercise

Expert recommendations for pre-exercise carbohydrate intake suggest 1-4 $g \cdot kg^{-1}$ body mass in the preceding 1-4 hours (Burke et al., 2011). The meal should contain little fibre, fat and protein, which all delay gastric emptying and could contribute to GI distress or discomfort (Nuttall & Gannon, 1991). Lactose ingestion pre-exercise may be advantageous due to its low

glycaemic index of 46 (Wolever & Miller, 1995). Current guidelines recommend a low glycaemic index meal before exercise to prevent post-prandial hyperglycaemia, which may promote better maintenance of carbohydrate availability during exercise (Burke et al., 2011). However, there does not appear to be a benefit to exercise performance with low glycaemic index carbohydrate ingestion before exercise, compared to high glycaemic index carbohydrate ingestion (Burdon, Spronk, Cheng, & O'Connor, 2017). Some athletes may avoid lactose-containing dairy foods in the meal before exercise due to concerns around GI discomfort. However, Haakonssen et al. (2014) demonstrated that a pre-exercise high carbohydrate dairy meal containing ~40g of lactose resulted in no differences in gut discomfort or performance during a cycling time-trial compared to a high carbohydrate dairy-free meal. Although there has been no direct investigation into lactose ingestion pre-exercise *per se*, there are no reasons to indicate that lactose could not form part of a pre-exercise carbohydrate ingestion regime.

Recommendations for carbohydrate intake during exercise, including type and amount, depend on intensity and duration. Endurance exercise lasting <30 min does not require carbohydrate intake, whilst exercise lasting 30-75 min may require small amounts of carbohydrate (Jeukendrup, 2011). Exercise lasting 60-120 min requires greater intake of 30-60 $g \cdot h^{-1}$ of most carbohydrate forms, whilst durations of 120-180 min require up to 60 $g \cdot h^{-1}$ of rapidly oxidizable carbohydrate (glucose, glucose polymers). Exercise lasting >150 min may require up to 90 $g \cdot h^{-1}$ and necessitates the use of multiple transportable carbohydrates (glucose and fructose). Carbohydrate may be consumed in a liquid, gel or solid form, as all are oxidised at comparable rates (B. Pfeiffer, Stellingwerff, Zaltas, Hodgson, & Jeukendrup, 2010; B Pfeiffer, Stellingwerff, Zaltas, & Jeukendrup, 2010). The guidelines on carbohydrate ingestion during exercise do not mention lactose, and focus on ingestion of glucose, glucose polymers, sucrose

and fructose. This is likely due to a paucity of research into lactose and the limited data on its metabolism in an exercise context.

There are limited data on the metabolism of lactose and its monosaccharide constituents during exercise. However, pre- and during-exercise ingestion of free glucose and galactose in a 1:1 ratio has been investigated as a method to improve time trial (TT) performance (Stannard, Hawke, & Schnell, 2009). Subjects consumed galactose, galactose/glucose (1:1 ratio) or glucose/fructose (4:1 ratio) 45 min before beginning cycling for 120 min, while consuming 1 $g \cdot min^{-1}$, followed by a TT. TT performance was poorest in the galactose-only condition, and the glucose/galactose and glucose/fructose conditions were not different. Ingested galactose is oxidised ~50-60 % slower than glucose, due to the requirement for hepatic metabolism (Burelle, Lamoureux, Peronnet, Massicotte, & Lavoie, 2006; Leijssen, Saris, Jeukendrup, & Wagenmakers, 1995), which may explain the poorer TT performance with galactose ingestion. This demonstrates the potential for a blend of the free monosaccharides constituting lactose, both for improving TT performance, and for the maintenance of blood glucose concentration during exercise. Glucose production is almost exclusively derived from galactose when it is co-ingested with glucose at rest (Sunehag & Haymond, 2002), though it is not clear whether this is the case under exercise conditions when hepatic and GI metabolism are altered.

Lee, Maughan, Shirreffs, and Watson (2008) investigated the effects of ingestion of low-fat milk during exercise. Subjects exercised at 70% $\dot{V}O_{2peak}$ to exhaustion, whilst ingesting water, a glucose drink (~36 $g \cdot h^{-1}$ of carbohydrate), low-fat milk (~30 $g \cdot h^{-1}$ of carbohydrate) or low-fat milk with added glucose (~36 $g \cdot h^{-1}$ of carbohydrate). Whilst time to exhaustion (TTE) was not different between any conditions, when considered as percentage change *versus* water, the carbohydrate drink and milk ingestion resulted in an extended TTE. Although milk ingestion

does not isolate the lactose component and the confounding effects of other macronutrients in milk are not accounted for, this suggests that lactose could be a viable exogenous energy source during exercise. Additionally, Stellaard et al. (2000) compared ingestion of naturally high abundance ^{13}C glucose and lactose before 4 hours of light physical activity, and showed $^{13}CO_2$ recovery was comparable between carbohydrates. This implies that the oxidation of lactose may be equal to glucose alone and also suggests that oxidation of galactose is likely to have been augmented by the presence of glucose. However, interpretation of this study is hampered by its small sample size (n=5) and low exercise intensity (50 W).

Recently, Odell, Podlogar, and Wallis (2020) directly investigated the metabolic impact of lactose ingestion during endurance exercise. Subjects ingested 0.8 g·min^{-1} of lactose or sucrose, or water during 150 min of steady-state cycling at 50% W_{max}. Ingested lactose and sucrose were oxidised at comparable rates (0.56 ± 0.19 g·min^{-1} and 0.61 ± 0.10 g·min^{-1} respectively) during exercise. Despite the presence of galactose in the lactose condition, the exogenous carbohydrate oxidation rates were similar to sucrose, suggesting that the presence of glucose may have influenced the oxidation of galactose, which is known to occur at rest (Sunehag & Haymond, 2002). Exogenous lactose oxidation may have been slower than sucrose in the first ~30 minutes of the exercise bout, which may represent a delay in digestion, or possibly the slow metabolism of galactose via the Leloir pathway. However, this difference was non-significant, and lactose showed near-identical exogenous carbohydrate oxidation rates in the later stages of exercise. In addition, lactose ingestion promoted greater fat oxidation than sucrose, though not as high as that observed when water only was consumed. This may be due to lactose being less insulinemic than glucose at rest (Ercan, Nuttall, Gannon, Redmon, & Sheridan, 1993). Concurrently, oxidation of endogenous carbohydrate was lower with lactose ingestion than sucrose ingestion, which may represent the sparing of glycogen. Furthermore,

lactose ingestion was also effective at maintaining stable blood glucose during exercise, much like sucrose, unlike when water was consumed.

Lactose clearly has the potential to act as a viable exogenous energy source during, and potentially before exercise. It performs comparably to other carbohydrates in isolation and within milk, in terms of positive metabolic outcomes for exercise. Consideration of individual differences and lactose tolerance status should be made (see Section 4.1). Future investigations should seek to determine the source of the observed glycogen sparing that occurs with lactose ingestion (Odell et al., 2020), as well as its impact upon exercise performance or capacity *versus* other carbohydrates.

3.2 Lactose in a post-exercise setting

Prolonged endurance or intermittent exercise can deplete or reduce glycogen, stored in the liver and the muscle. Whilst muscle glycogen is hydrolysed and oxidised locally by the muscle, liver glycogen is utilised in the maintenance of blood glucose homeostasis (Taylor et al., 1996). The impact of pre-exercise muscle glycogen content on exercise performance is well established. Low muscle glycogen content causes reduced endurance performance and capacity, whilst high muscle glycogen content predicts better performance and capacity (Bergström, Hermansen, Hultman, & Saltin, 1967; Widrick et al., 1993). Therefore, post-exercise replenishment of muscle and liver glycogen is a priority to ensure adequate endogenous carbohydrate for later exercise. This is particularly relevant for athletes in sports with multiple events in a day, such as in tournaments, events over multiple days or stage races such as the Tour de France, or even when multiple training sessions per day are performed.

Current recommendations for post-exercise nutrition advocate carbohydrate ingestion as soon as is practical to maximise preparedness for the next exercise bout. Current guidelines recommend ingestion of carbohydrate at a rate of 1.2 $g \cdot kg^{-1} \cdot h^{-1}$ in the initial hours after exercise, which is sufficient to maximise muscle glycogen replenishment in a post-exercise state (Burke et al., 2011). It has been extensively demonstrated that if sufficient quantities of carbohydrates of moderate to high glycaemic index are provided in the post-exercise period, muscle glycogen can be replenished optimally, though it has been observed that some carbohydrates perform poorly in the restoration of muscle glycogen, such as fructose (Blom, Høstmark, Vaage, Kardel, & Maehlum, 1987). However, more recently there has been an interest in carbohydrates with divergent paths for endogenous storage, namely fructose and galactose.

It has been observed that post-exercise glucose ingestion is a relatively poor strategy for optimising the resynthesis of liver glycogen, despite its positive effects on muscle glycogen replenishment (Décombaz et al., 2011). Both fructose and galactose have been demonstrated to be superior substrates for liver glycogen replenishment when co-ingested with glucose, which is likely due to their requirement for hepatic metabolism. Décombaz et al. (2011) compared combined maltodextrin and galactose, fructose or glucose ingestion, in total doses of 450 g (~69 $g \cdot h^{-1}$) after glycogen depleting exercise. Liver glycogen content was assessed via ^{13}C magnetic resonance imaging (MRI) over a 6.5h recovery period. Both galactose (8.6 ± 0.9 $g \cdot h^{-1}$) and fructose (8.1 ± 0.6 $g \cdot h^{-1}$) ingestion effectively doubled the liver glycogen deposition compared with glucose-only (3.7 ± 0.5 $g \cdot h^{-1}$). This increase in liver glycogen resynthesis can also be observed with sucrose ingestion compared to glucose (Fuchs et al., 2016). This demonstrates the requirement for carbohydrate types that require hepatic metabolism, in addition to glucose. To the author's knowledge, Décombaz et al. (2011)

performed the only investigation into liver glycogen replenishment post-exercise comparing galactose to other carbohydrates.

To promote optimal combined liver and muscle glycogen replenishment post-exercise, it is likely that glucose must be combined with a carbohydrate source that undergoes predominant hepatic metabolism (i.e. galactose, fructose). It is possible that lactose, as a disaccharide of glucose and galactose, may be sufficient to promote combined muscle and liver glycogen resynthesis, effectively acting as a blend of glucose and galactose. However, it remains to be investigated whether combined glucose and galactose feeding is as effective at replenishing muscle glycogen as glucose alone, which has been demonstrated for combined glucose and fructose ingestion (Fuchs et al., 2016; Trommelen et al., 2016; Wallis et al., 2008). This is an important factor determining whether glucose and galactose or lactose may be advantageous compared to glucose alone in the restoration of glycogen stores.

Whilst no studies have investigated muscle or liver glycogen replenishment and/or recovery of exercise performance or capacity with lactose ingestion, milk and chocolate milk have been extensively studied in recovery from exercise (Alcantara, Sanchez-Delgado, Martinez-Tellez, Labayen, & Ruiz, 2019; Amiri, Ghiasvand, Kaviani, Forbes, & Salehi-Abargouei, 2018). Milk ingestion has been shown to be equally effective at improving exercise capacity after an initial bout of exercise as carbohydrate-electrolyte beverages delivering similar amounts of carbohydrate in a number of investigations (Lee et al., 2008; Watson, Love, Maughan, & Shirreffs, 2008). Indeed, Loureiro, de Melo Teixeira, Pereira, Reis, and da Costa (2020) in a systematic review concluded that milk-based beverages result in similar effects on glycogen resynthesis and restoration of exercise performance to carbohydrate beverages. Chocolate milk has also been investigated for post-exercise recovery, as a convenient, carbohydrate and protein

rich recovery beverage. A systematic review and meta-analysis by Amiri et al. (2018) showed that chocolate milk ingestion after a variety of exercise types (including running and cycling) increased time-to-exhaustion (TTE) in a subsequent exercise bout, compared to placebos and mixed macronutrient beverages (containing carbohydrate, fat and protein). Furthermore, an investigation into chocolate milk ingestion and glycogen replenishment demonstrated that chocolate milk resulted in higher muscle glycogen restoration than an isocaloric carbohydrate beverage after an exercise bout, despite lower total carbohydrate content (0.84 $g \cdot kg^{-1} \cdot h^{-1}$ *versus* 1.2 $g \cdot kg^{-1} \cdot h^{-1}$) in the chocolate milk condition, which may be attributable to its protein content (Karfonta, Lunn, Colletto, Anderson, & Rodriguez, 2010). Ferguson-Stegall et al. (2011) showed that after an intense cycling exercise bout, chocolate milk was equally effective at replenishing muscle glycogen as an isocaloric carbohydrate beverage but resulted in improved TT performance.

One potential benefit to chocolate milk ingestion is that it contains a full spectrum of monosaccharides, including galactose (as lactose), fructose (as sucrose) and glucose from both disaccharides. Although it has not been directly investigated, the combination of two carbohydrates known to increase liver glycogen replenishment, as well as glucose, could have an additive effect over and above just one of these carbohydrates. This could explain the superior effects of chocolate milk ingestion compared to the carbohydrate (glucose) beverage on TT performance (Ferguson-Stegall et al., 2011). However, it is not possible to isolate the effects of the lactose component of milk or chocolate milk, compared to the other nutrients in milk such as protein, which can amplify insulin secretion and glycogen replenishment when carbohydrate intake is insufficient (Burke et al., 2011) as well as fat and electrolytes. A further benefit to chocolate milk in the post-exercise setting is its high protein content (~16 g per 500 ml), and high protein quality, containing whey and casein (Amiri et al., 2018). Indeed, Phillips,

Tang, and Moore (2009) note that milk proteins are superior to carbohydrate alone for post-exercise nutrition in the promotion of skeletal muscle hypertrophy. Therefore, chocolate milk and other flavoured dairy beverages can be considered multifunctional foods in a post-exercise setting.

3.3 Lactose as a prebiotic

There is potential for lactose, in some scenarios to act as a prebiotic, which represents an additional application in sports nutrition. Prebiotics are indigestible compounds, that are metabolised by gut microbiota, which affect the microbiota composition or activity (Bindels, Delzenne, Cani, & Walter, 2015) in a manner beneficial to the host (Carlson, Erickson, Lloyd, & Slavin, 2018). This potential aspect of lactose is supported by only limited research, and so the potential for lactose to act as a prebiotic requires more thorough investigation to further understand any possible benefits that could be conferred. Lactose can be considered a prebiotic, as in some individuals, undigested lactose may pass from the small intestine to the colon, where it is available for fermentation by local bacteria, much like established prebiotics such as galactooligosaccharides (GOS) and fructooligosaccharides (FOS) (Carlson et al., 2018). This is likely most common in individuals with a limited ability to digest lactose, though undigested lactose could also appear in the colon of individuals with a normal ability to digest lactose, thereby also conferring a prebiotic effect. However, in both groups this is likely dependent on the amount of lactose ingested and the individual's lactose digestion capacity.

The mechanisms explaining the positive impacts of prebiotics are not fully understood but may be linked to the cultivation of beneficial colonic bacteria, capable of producing short chain fatty acids (SCFAs) which are favourable for bowel health and immune function (Parada Venegas et al., 2019). Prebiotics could offer athletes and recreationally active individuals a performance

benefit through a number of indirect mechanisms, though to the authors knowledge, the impact of prebiotic supplementation on athletic performance has not been assessed. However, some benefits have been observed in healthy individuals, which may be applicable to athletes. Supplementation with GOS is associated with reduced GI illness, as well as reduced cold and flu symptom severity (Hughes et al., 2011). Preventing illness in athletes may reduce interruption to training or attenuate the direct impact of illness upon exercise performance in competition. Another potential benefit is the suppression of appetite by FOS supplementation that has been observed, which may benefit energy-restricted athletes (Cani et al., 2009). Although different prebiotics exert their effects through similar mechanisms, it is not known whether certain effects are linked to specific prebiotics. Therefore, the benefits of certain prebiotics should not be ascribed to others without direct investigation.

Whether lactose exerts a prebiotic effect has not been investigated, and it is not clear whether any prebiotic effect might occur alongside GI symptoms due to the presence of lactose in the colon. However, ingestion of any prebiotic can lead to GI symptoms, including flatulence and osmotic diarrhoea, which can be modulated by individual factors, as well as the total dose (Livesey, 2001). It is possible that regular consumption of dairy products containing lactose may confer some prebiotic effect in both lactose digesters and maldigesters, though the quantity of lactose required to achieve this is not known. Although not directly related to sports nutrition, prebiotics may also exert a number of health benefits which include a protective effect on colon cancer and the reduction of certain risk factors for cardiovascular disease (Slavin, 2013). These health benefits are thought to be conferred by SCFA production, of which butyrate is likely the most beneficial for colonic health.

4. Considerations for the application of lactose in sports nutrition

4.1 Relevant conditions and pathologies, relating to lactose

The application of lactose in sports nutrition may be confounded due to the presence of a variety of pathologies related to lactose digestion and absorption, including lactose maldigestion and subsequent intolerance. These conditions are a result of lactase non-persistence, the genetically determined, gradual decline in lactase activity to ~10 % of previous activity, after 2 – 3 years of age (Misselwitz et al., 2013). This condition is present in >90% of East Asians and ~70% of Mexicans and African Americans (Itan, Jones, Ingram, Swallow, & Thomas, 2010; Scrimshaw & Murray, 1988). However, in some individuals the activity of lactase does not reduce, remaining high into adulthood, which is termed lactase persistence, which is the normal condition in 80-95% of adults in Britain, Scandinavia and Germany (Itan et al., 2010). The development of lactase persistence is thought to be linked to the development of dairy farming over the past ~10 000 years (Ingram, Mulcare, Itan, Thomas, & Swallow, 2009).

Lactose maldigestion refers to the inefficient or incomplete digestion of lactose, generally due to lactase non-persistence (Misselwitz et al., 2013). Lactose maldigestion may also be referred to as lactose malabsorption. However, this term does not accurately describe the condition, as the absorption of lactose is not impaired, whereas the digestion stage is limited. Therefore, the term maldigestion should be used when referring to the ineffective digestion of lactose and use of the term malabsorption should be avoided unless specifically describing reduced absorption of lactose (or its constituent's glucose and galactose) into the splanchnic circulation.

Lactose intolerance (LI) refers to the GI symptoms that result from lactose maldigestion, which are a result of unhydrolyzed lactose passing from the small intestine into the colon (Misselwitz et al., 2013). These can include diarrhoea due to the lactose increasing the osmotic load, which

draws water into the intestines, and can lead to abdominal cramping or pain (Rangel et al., 2016). Flatulence and bloating can also result from the fermentation of the lactose by colonic bacteria which may produce gases including CH_4, H_2 and CO_2 (Jiang & Savaiano, 1997a, 1997b; Rangel et al., 2016; Yazawa & Tamura, 1982). Certain bacteria favour reduced gas production (such as *Bifidobacteria* and *Lactobacillus*) compared to other colonic bacteria (Tsukahara, Azuma, & Ushida, 2009).

The symptoms of LI, and their severity vary widely between individuals, depending on the individual's lactase activity and bacterial flora. There may also be variation between LI symptoms in the same individual in response to different foods or meals. For example, high fat or high osmolality foods can slow gastric emptying, which can reduce symptoms of intolerance (Jellema, Schellevis, Van Der Windt, Kneepkens, & Van Der Horst, 2010). Ingesting yoghurt can improve GI symptoms and breath H_2 response compared to milk, which is likely due to the presence of bacteria capable of hydrolyzing the lactose (Pelletier, Laure-Boussuge, & Donazzolo, 2001). Consideration of the dairy 'matrix' is important when discussing LI and other issues surrounding dairy and health, rather a reductionist single-ingredient approach (Szilagyi & Ishayek, 2018).

It is important to note that many individuals with lactose maldigestion can tolerate small amounts of lactose without GI symptoms. Indeed 0.4 g of lactose ingested as a pill did not alter GI symptoms significantly compared to a placebo, nor did it trigger a positive (>20 ppm) breath H_2 test (Montalto et al., 2008). Shaukat et al. (2010) reported that dairy products containing up to 12-15g of lactose are well tolerated by most adults with lactose maldigestion, equivalent to 250-300 mL of milk. Therefore, consumption of dairy products, as well as dietary supplements or medication capsules that use lactose as a filler should not necessarily be avoided by lactose

517 intolerant individuals, and the avoidance of all dairy products is no longer recommended
518 (Szilagyi & Ishayek, 2018).
519
520 **4.2 Diagnosis of lactase-related pathologies**
521 There are numerous tests to diagnose lactose maldigestion or intolerance, though none is
522 considered a 'gold standard' test. The lactose tolerance test involves ingesting a bolus of 25-
523 50g lactose, measuring blood glucose, and reporting acute GI symptoms (Hovde & Farup,
524 2009). If the lactose is hydrolysed, serum glucose is expected to rise, whilst no change, and/or
525 the presence of GI symptoms suggests LI. However, the test has very low sensitivity and
526 specificity (Misselwitz et al., 2013). The National Institute of Health requires the diagnosis of
527 LI to involve comparison to an inert placebo (Suchy et al., 2010), which can reduce the impact
528 of self-reported food intolerances which are often unsubstantiated (Misselwitz et al., 2013).
529
530 The H_2 breath test is widely used to assess lactose maldigestion, as GI symptoms after a lactose
531 challenge are better correlated with breath H_2 production than with changes in blood glucose
532 (Hermans, Brummer, Ruijgers, & Stockbrügger, 1997). Expired breath is collected before and
533 after ingestion of 25 g of lactose, and breath [H_2] >20 ppm implies that the lactose has not been
534 completely hydrolysed and has entered the colon where it is fermented by bacteria. The
535 measurement of CH_4 alongside H_2 has been shown to improve the prognostic capability of the
536 breath test (Hovde & Farup, 2009). However, false positives can be caused by small intestine
537 bacterial overgrowth, whilst false negatives may be caused by H_2 or CH_4 non-producing
538 subjects (between 2-43% of subjects; Gasbarrini et al. (2009)). A process known as 'full
539 colonic adaptation' can also occur, where repeated lactose intake selectively favours flora that
540 ferment lactose without the production of H_2 or CH_4 (Misselwitz et al., 2013). Inadequate
541 dietary control in the day(s) preceding the test may artificially inflate pre-test values, due to

presence of fermentable substrates such as fibre in the colon. Furthermore, the boundary of breath [H_2] of >20 ppm is arbitrary and does not relate to a threshold of lactase expression or the presence of GI discomfort.

Genetic testing can also be employed to diagnose of lactase non-persistence. Presence of the genetic polymorphism 13910C/C indicates lactase non-persistence. This test has a low false positive rate (<5 %) but generates false negatives if LI is caused by secondary factors. Testing for this polymorphism is only appropriate in Caucasian subjects (Misselwitz et al., 2013). Lactase activity in the jejunum can be assessed via biopsy, which is considered a 'reference standard' for the assessment of lactase deficiency. However, this method is extremely invasive and, lactase expression in enterocytes forms a 'mosaic' pattern meaning not all areas of the brush border express lactase strongly (Maiuri et al., 1991; Misselwitz et al., 2013). Therefore, biopsies can sample areas without lactase even in lactase persistent individuals, generating a false positive result.

It has been noted that it is possible for individuals to 'adapt' to lactose ingestion, showing decreased breath H_2 responses and GI symptoms in response to lactose feeding after chronic ingestion. Lactase activity does not increase in response to lactose exposure in humans (Gilat, Russo, Gelman-Malachi, & Aldor, 1972). However, adaptation of colonic bacteria in response to lactose ingestion is known to occur (for a review, see Szilagyi (2015)). 'Full colonic adaptation' is defined by Misselwitz et al. (2013) as a process in which "repeated intake of lactose selectively favours the growth of colonic flora that rapidly ferment lactose without producing hydrogen". Colonic bacterial adaptation may also occur in such a manner that hydrogen-producing bacteria remain, but that lactose that reaches the colon is still fermented, without the presence of symptoms (Di Stefano et al., 2007; Johnson, Semenya, Buchowski,

Enwonwu, & Scrimshaw, 1993b). Indeed, only approximately one third of individuals with positive H_2 breath tests experience GI symptoms (Di Stefano et al., 2007), highlighting the disconnect between breath H_2 responses and LI symptoms.

It has been demonstrated that lactose intolerant individuals can adapt to increasing lactose intake without intolerance symptoms. Johnson, Semenya, Buchowski, Enwonwu, and Scrimshaw (1993a) provided 22 lactose intolerant maldigesters with progressively increasing daily doses of lactose. All subjects increased the threshold at which symptoms were induced, to at least 7 g lactose, and 17 subjects increased to ≥12 g. Lactose maldigesters regularly consuming dairy foods may not suffer from LI, except at high doses where the ability of colonic bacteria (and limited lactase) to metabolise lactose is exceeded, whilst maldigesters with low lactose intake may suffer intolerance even at very low doses. Most individuals with lactose maldigestion can tolerate ingestion of ~12-15 g of lactose (~250-300 mL of milk) without symptoms (Shaukat et al., 2010).

5. Potential limitations of lactose in sports nutrition

It is not entirely clear whether lactose can be a viable carbohydrate for exercise settings in light of the issues surrounding LI and maldigestion. A known or diagnosed intolerance generally precludes consumption of lactose, and although many maldigesters can tolerate small amounts of lactose without symptoms (Shaukat et al., 2010), these amounts are far below the quantities required for carbohydrate ingestion before (1-4 $g \cdot kg^{-1}$), during (30-90 $g \cdot h^{-1}$) or after (1.2 $g \cdot kg^{-1} \cdot h^{-1}$) exercise (Burke et al., 2011). Therefore, lactose should not form the major part of a carbohydrate ingestion regimen for exercise in individuals with diagnosed LI, except up to quantities of ~12-15 g, if tolerable. Furthermore, individuals following FODMAP exclusion diets should also avoid lactose as required.

Most lactose tolerant individuals can ingest large quantities of lactose without GI symptoms. During endurance exercise, ingestion of 48 $g \cdot h^{-1}$ of lactose did not result in worse mean GI symptoms than sucrose (Odell et al., 2020). However, one subject experienced mild LI symptoms in the hours post-exercise after lactose but not sucrose ingestion, despite being lactose tolerant and regularly ingesting dairy foods. It is not clear what the upper limit for lactose digestion is, though absorption of glucose and galactose via SGLT1 is limited to ~60 $g \cdot h^{-1}$, therefore lactose ingestion rates during exercise should not exceed this (Jeukendrup, 2010).

Individuals may have concerns about ingesting large quantities of lactose-containing dairy foods in the post-exercise period to achieve the required carbohydrate intake. It is unclear whether the hydrolysis of lactose in a post-exercise setting might limit the delivery of its constituent monosaccharides. However, investigations involving ingestion of large quantities of lactose (80-120 g) before and during exercise respectively, have not demonstrated any effects of maldigestion in the vast majority of lactose-tolerant subjects (Odell et al., 2020; Stellaard et al., 2000). Recommendations for post-exercise carbohydrate intake are higher than before or during exercise, but an investigation by Costa et al. (2020) involving participants ingesting 1.2 $g \cdot kg^{-1}$ of carbohydrate from chocolate milk showed that neither GI symptoms nor breath H_2 were elevated with a high carbohydrate post-exercise dairy meal compared to water ingestion. Therefore, lactose could be an appreciable contributor to post-exercise carbohydrate requirements. Dairy foods such as milk or yoghurt may offer an additional benefit over isolated lactose, as the dairy matrix (as seen in yoghurt) is known to improve GI comfort and deliver relevant nutrients such as protein and electrolytes (Pelletier et al., 2001; Szilagyi & Ishayek, 2018; Thorning et al., 2017). Individuals should determine which carbohydrates and foods, and

in what quantities, are appropriate for them to use pre-, during and post-exercise, based on their personal preference and responses. This is the case for all carbohydrates, including fructose in light of the presence of fructose malabsorption in some individuals (Putkonen, Yao, & Gibson, 2013).

An impediment to the application of lactose in sports nutrition is the unfavourable perception of dairy and lactose. Dairy products are commonly included in a description of healthy eating by children and adolescents, but to a lesser extent by adults (Paquette, 2005). The potential of milk to cause allergic symptoms is considered to be high (*versus* soy milk), and it is thought to cause serious disease (including heart disease, high cholesterol and obesity) to a greater extent than soy milk (Bus & Worsley, 2003). Self-diagnosis of LI is also common, with 11-16% of North Americans self-diagnosing LI, in most cases without clinical diagnosis of intolerance or maldigestion (Barr, 2013; Nicklas et al., 2011). This leads to inappropriate avoidance and reduced consumption of dairy foods (Barr, 2013; Keith et al., 2011).

Table 2. Summary of applications and considerations for lactose in sports nutrition

Potential application	Comments

Lactose as an energy source for exercise	• Ingested lactose can be readily oxidised during exercise, and results in higher fat oxidation and reduced reliance on endogenous carbohydrate oxidation • Lactose can form part of a pre- or during exercise carbohydrate feeding regimen
Lactose for glycogen restoration	• Lactose is the primary source of dietary galactose, which has been shown to increase post-exercise liver glycogen resynthesis • Studies on milk and chocolate milk suggest that lactose can be a substrate for muscle glycogen resynthesis, resulting in similar subsequent exercise performance to carbohydrate beverages
Lactose as a prebiotic	• Lactose can exert a prebiotic effect on the purportedly beneficial bacterial flora *Bifidobacteria* and *Lactobacilli* • It is not clear whether this may be concomitant with GI symptoms in lactose intolerant individuals
Considerations	
Lactose intolerance	• Lactose intolerant individuals should avoid large quantities of lactose, but 12-15 g is generally well tolerated
Amount of lactose required	• Nutritional recommendations for exercise settings involve large quantities of carbohydrate • Lactose and milk beverages do not trigger GI symptoms in most lactose tolerant individuals during, before or after exercise, even when ingested in large amounts.

GI - gastrointestinal

6. Summary and future directions

Although lactose does not feature in guidelines for carbohydrate intake for sports nutrition, it is becoming increasingly apparent that the dairy carbohydrate could play a role in the diets of athletes and recreationally active individuals. Lactose or its free monosaccharide constituents represents a viable fuel source for endurance exercise and can be incorporated into carbohydrate feeding regimens for during, and possibly pre- and post-exercise. Lactose may be a good choice for combined replenishment of muscle and liver glycogen after exercise due to its galactose component, though this remains to be directly investigated. It is also not clear whether a combination of glucose, galactose and fructose ingestion (as monosaccharides or

through use of lactose and sucrose as found in chocolate milk) might confer the optimal enhancement of post-exercise liver glycogen resynthesis, potentially explaining reported performance recovery benefits of chocolate milk. Lactose could also be considered a prebiotic in some scenarios, and future research should aim to determine whether it can engender similar benefits to established prebiotics. Although GI symptoms with lactose ingestion may occur, in most lactose tolerant individuals the carbohydrate can be ingested at rates conducive to recommendations for sports nutrition, though the ingestion of higher quantities of lactose should be investigated.

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