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Lactose and Lactose Derivatives[#]

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ABSTRACT

Milk is an important food substance and has a complex polydisperse system. The main components of milk consist of lactose, protein, and lipids. Mineral substances and vitamins are also present in milk as minor nutrients. Lactose known as milk sugar is the only carbohydrate in milk and it consists of glucose and galactose. The content of lactose in milk has varied according to milk types. Moreover, it is the most important energy source during the first years of human life, providing almost half of the total energy needed by newborns. Lactose is obtained industrially from the residues of cheese and casein production processes. Lactulose, lactitol, lactobionic acid, galactooligosaccharide, lactosucrose, epilactose, and tagatose are commonly known lactose derivatives. These derivates are produced from lactose using various methods such as epimerization, oxidation, and reduction. In this review, up-to-date information about lactose, lactose derivatives, and the production methods of lactose derivatives are given.

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Introduction

Milk is an important food substance that is secreted from the mammary glands to feed the offspring of mammal species after birth and contains almost all the nutrients that the offspring needs. The composition of milk is affected by many factors such as race, age, physiology, feeding status, stress, and especially the species of the mammal. While humans use milk obtained from a wide range of animals for their nutritional purposes, the most commonly consumed milk types are cattle, buffalo, goat, and sheep milk (Walstra et al., 2005).

Milk is a complex polydisperse system. While their exact amounts vary by species, the main components of milk consist of lactose, protein, and lipids. Mineral substances and vitamins are also present in milk as minor nutrients. Water, on the other hand, constitutes a large portion of the milk of all species (Park, 2009).

The only carbohydrate in milk is lactose. Lactose is a disaccharide found in nature only in mammalian milk in varying proportions, and it consists of glucose and galactose (Schaafsma, 2008). Lactose is the most important energy source during the first years of human life, providing almost half of the total energy needed by newborns (Silanikove et al., 2015).

The lactose content in milk types varies (Üçüncü, 2005). While human milk has the highest lactose content (~ 7 g/100 mL), the lactose content in cow's milk (~ 4.6 g/100 mL) is lower (Schaafsma, 2008). Lactose is present in milk in the form of a true solution. The lactose concentration in milk is inversely related to the number of fats and proteins contained in the milk. This is why the lactose content of human milk is higher than that of other milk types (Köse and Ölmez, 2016). The value of fat, protein, and lactose content in milk of different mammalian species is given in Table 1 (Fox et al., 2015; Fox et al., 2017).

Since the lactose in fermented milk products such as yoghurt, ayran, and kefir is fermented by lactic acid bacteria, the lactose content of these products is lower than in milk. During cheese production, most of the lactose in milk passes into the whey. Hard cheeses contain almost no lactose, especially compared to soft and semi-hard cheeses. The reason for this is that the lactose remaining in the structure of hard cheese is completely converted into lactic acid by the starter cultures (Schaafsma, 2008).

Table 1. Fat, protein, and lactose content of different mammalian milk

Species	Fat (g/100 g)	Protein (g/100 g)	Lactose (g/100g)
Human	3.8	1.0	7.0
Cow	3.7	3.4	4.8
Goat	4.5	2.9	4.1
Sheep	7.4	4.5	4.8
Horse	1.9	2.5	6.2
Donkey	1.4	2.0	7.4
Elephant	11.6	4.9	4.7
Reindeer	16.9	11.5	2.8
Buffalo	6.7	4.7	4.8

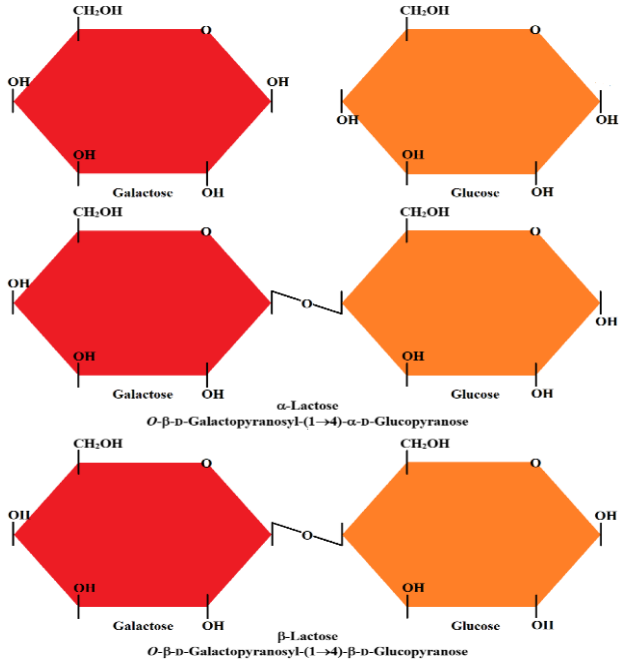

Figure 1. The configurations of the α- and β- lactose.

Production and Importance of Lactose

Lactose, (β-D-galactopyranosyl-(1→4)-D-glucose), has been produced industrially for more than 100 years. Fat, protein, lactose, and mineral substances are present in whey that is released during cheese production. Whey contains approximately 4-5% lactose. For this reason, the first preferred substance in lactose production is whey (Tarakçı and Küçüköner, 2005; Yerlikaya et al., 2010).

Lactose is obtained by concentrating the remaining liquid after the separation of fat, protein, and mineral substances in whey and then crystallizing the concentrate. Separators and evaporators were used to obtain lactose in periods when membrane separation methods weren't yet available. In this method, the fat is separated by passing the whey through separators, and after the pH of the lean part is adjusted to 6.8, it is boiled to precipitate the whey proteins and calcium. The liquid containing lactose is taken into a vacuum evaporator to vaporize the excess water, and the resulting concentrated phase is then taken into the crystallization tank and crystallized. Following the crystallization, crystals are washed and dried in rotary dryers and then packaged (Durham, 2009; Paterson, 2009).

Due to the advances in membrane technology in the 1970s and the decrease in membrane costs as of the 1990s, filtration systems became the most prominent lactose production methods. In this method, protein-free lactose is produced by efficiently ensuring the recovery of whey proteins. Advances in lactose production, along with research and development focusing on calcium precipitation, nanofiltration, ion exchange, color removal, and chromatography, have taken purification as the key determinant of process efficiency (de Souza et al., 2010).

Edible and pharmaceutical-quality lactose has wide application areas in the food, feed, and pharmaceutical industries. It is especially used as a supplement for infant food formulations and as a drug additive (carrier) for pharmaceutical products. In addition, while it can contribute to the color and taste of bakery and pastry products, it can also be used in the production of glucose, galactose, and lactose derivatives through hydrolysis (de Souza et al., 2010; Seki and Saito, 2012; Bramhankar et al., 2018). Lactose is frequently included in diets due to its sweetening power, calorie value, and low glycemic index (Schaafsma, 2008). In addition, lactose taken with milk and dairy products regulates the absorption of various minerals (Ca and P) in the intestines. This is achieved through the lactic acid released in the intestines as a result of the fermentation of lactose. The resulting acidic environment increases the absorption of mineral substances (Anonymous, 2021).

Lactose Metabolism and Lactose Intolerance

Lactose is a disaccharide consisting of glucose and galactose monosaccharides. It is created through the β-1-4 glycosidic bonds between the 4th carbon atom of glucose and the 1st carbon atom of galactose. Lactose has two isomeric forms, known as the alpha (α-) and beta (β-) configurations (Figure 1). The difference between these isomers varies according to the hydroxyl group in the 1st position in the structure of glucose. The physical properties of these two isomers are different from each other and they exist in an aqueous solution as a mixture of alpha and beta lactose (Bramhankar et al., 2018).

Lactose in mammals is broken down into glucose and galactose, the monosaccharide components, by an enzyme known as β-galactosidase (lactase). This enzyme mostly binds to the mucosal membrane of the small intestine and prefers the beta form of lactose. After this breakdown process, monosaccharides are actively absorbed and transported to the liver via the portal vein. Both sugars share the same absorption pathway. Glucose and galactose, which are monosaccharides, are sugars that are actively absorbed through the intestine (Schaafsma, 2008). While the absorbed glucose is used as an energy source, galactose is used as a structural element of components such as glycolipids and glycoproteins (Di Rienzo et al., 2013; Köse and Ölmez, 2016).

Lactose intolerance is a digestive system disease caused by the inability to digest lactose which is the main carbohydrate of milk. The reason for this disorder is lactase enzyme deficiency and/or insufficient enzyme activity in the individual. The lactose that is not absorbed in the small intestine and reaches the large intestine without being digested, where is fermented by the bacteria in the colon. As a result of this fermentation, people can be experienced symptoms such as diarrhea, abdominal pain, excessive gas, and bloating. To prevent lactose intolerance, approaches such as the consumption of fermented milk products, probiotics, and lactose-free products are recommended (Demircioğlu and Kaner, 2014; Szilagyi et al., 2019).

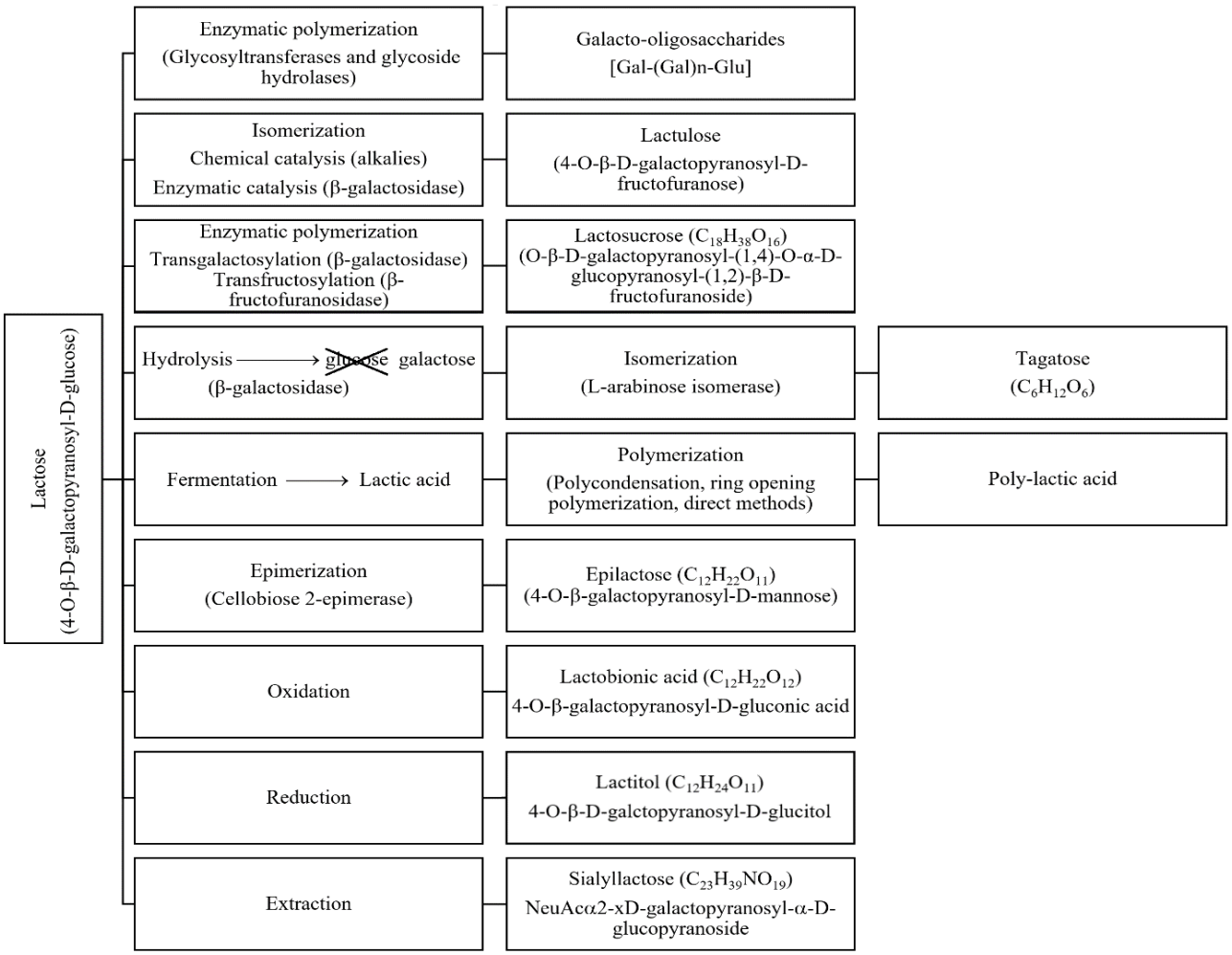

Figure 2. Lactose derivatives and production methods.

Lactose intolerance is divided into two categories as primary and secondary lactose intolerance. In primary lactose intolerance, the lactase enzyme is congenitally absent or is too rare. In secondary lactose intolerance, absorption in the small intestine is reduced due to various reasons or absorption cannot occur due to diseases such as infections in the intestine, or celiac disease. To remedy secondary lactose tolerance, the underlying cause must first be identified and treated (Silanikove et al., 2015; Köse and Ölmez, 2016). In addition, lactose intolerance can often be confused with lactose malabsorption (insufficient absorption of lactose in the intestines) (Akal and Yetişemeyen, 2020; Gbadamonsi et al., 2020).

Lactose Derivatives and Their Health Effects

Lactose is an industrial by-product obtained by utilizing the residues of cheese and casein production processes (Bramhankar et al., 2018; Xiao et al., 2019). Lactose derivatives such as lactulose, lactitol, lactobionic acid, galactooligosaccharide, lactosucrose, epilactose, and tagatose are produced from lactose using various methods such as epimerization, oxidation, and reduction. Lactose derivatives and production methods are shown in Figure 2. These lactose derivatives exhibit several important physiological properties and effects such as having prebiotic properties, being indigestible, or having anti-obesity features. Investigation of the potential health benefits of lactose derivatives has led to the emergence of a wide range of application areas for them in the food, pharmaceutical, and chemical industries (Seki and Saito, 2012; Bramhankar et al., 2018; Xiao et al., 2019). Lactulose, galactooligosaccharide, and lactitol, in particular, are widely used in foods and pharmaceuticals. New lactose derivatives such as epilactose and tagatose have also recently gained attention (Seki and Saito, 2012).

Lactulose

Lactulose, (4-0-β-D-galactopyranosyl-D-fructofuranose), was first produced from lactose by a chemical reaction in 1930. It was formed by isomerizing the glucose present in the structure of lactose into fructose. For this reason, it is a semi-synthetic disaccharide containing galactose and fructose in its structure, and it doesn't exist naturally. The closed formula of lactulose is the same as that of lactose ($C_{12}H_{22}O_{11}$) and it has a molecular weight of 342.30 g/mol. In lactulose, galactose, and fructose molecules are connected with a β-1-4 glycosidic bond (Özden, 2005; Panesar and Kumari, 2011; Bramhankar et al., 2018).

Lactulose is widely used in pharmaceutical, nutraceutical (infant formulations, baby food), and food (confectionery, drinks, dairy products) industries due to its positive effects on human health. It is widely used in the pharmaceutical industry as it is an effective therapeutic against various disorders such as acute and chronic

constipation. It is included as a sweetener in diabetic products as it has less sweetness than sucrose (Aider and Halleux, 2007).

There is no natural lactulose in raw milk. During the heat treatment, some lactulose is formed in the milk and this lactulose is then taken into the body with the consumption of milk. Industrial production of lactulose is carried out by alkaline catalyst isomerization or enzymatic isomerization methods. Since the 1960s, lactulose has been chemically synthesized, but this method is not environmentally friendly. Nowadays, economical enzymatic methods are widely used instead of traditional chemosynthesis (Seki and Saito, 2012; Xiao et al., 2019).

Simple bases such as sodium hydroxide and calcium hydroxide were used as catalysts in the early years of lactulose production. Subsequently, other catalysts were discovered, including the following:

- Complexing agents such as aluminates and borates,
- Reagent-free methods (such as sepiolite anion exchange resin, electrode, and membrane combined electro activation system)
- Enzyme; isomerization and transgalactosylation (Panesar and Kumari, 2011; Sitanggang et al., 2016).

There are no enzymes to digest lactulose in the stomach or the small intestine. Therefore, it passes into the large intestine undigested. They are decomposed by fermentation by *Bifidobacterium* and other flora in the large intestine. Lactulose is also called the "Bifidus factor" because it can be used by most of the *Bifidobacterium* with probiotic properties and it promotes the growth of these bacteria. For this reason, lactulose is preferred in the preparation of baby foods. At the same time, it has also been reported to have prebiotic effects due to its functional properties (Akalın, 2002; Saarela et al., 2003; Şanlıdere Aloğlu and Uran, 2017). As a result of fermentation by the intestinal flora of lactulose which comes to the colon without being digested, short-chain fatty acids and various gases (H_2, CO_2, CH_4) are released. These substances reduce the pH of the intestinal environment and thus prevent the growth of pathogenic bacteria. Also, the absorption of calcium and magnesium minerals increases with reducing pH (Özden, 2005; Olano and Corzo, 2009).

Lactitol

Lactitol, (4-0-β-D-galactopyranosyl-D-sorbitol), was first reported by Senderes in 1920. It is a sugar-alcohol consisting of galactose and sorbitol by catalytic hydrogenation of lactose under high temperature and high pressure (Seki and Saito, 2012). Lactitol does not occur in nature and is produced only by the hydrogenation of lactose. Catalytic hydrogenation refers to a series of chemical reactions in which hydrogen is added to a reactive functional group. Hydrogen is added to the carbonyl group of the lactose molecule in lactitol production (Cheng and Martínez-Monteagudo, 2019). While lactitol is a synthetic disaccharide and is the primary product in the hydrogenation of lactose, very small amounts of lactulitol may also be produced in the medium (Zhang et al., 2020).

Lactitol has syrup and crystal forms. Crystal forms are in the form of monohydrate, dehydrate, or anhydride nature. Lactitol monohydrate is the most widely used commercial form of lactitol in Japan. Lactitol has a low calorific value and its taste is similar to that of sucrose. Due to this property, lactitol is used as a sweetener (Seki and Saito, 2012; Güneş et al., 2018). It is also a versatile ingredient that can be used by product developers in food formulations not only to provide low-calorie sweetness but also as a bulking agent, moisturizer, cryoprotectant, and prebiotic source (Cheng and Martínez-Monteagudo, 2019).

Lactitol cannot be digested in the small intestine since no enzyme can break down lactitol in the mucous structure of the small intestine. As it reaches the large intestine without being digested, lactitol can act as a prebiotic for the colon flora. The prebiotic effect encourages beneficial bacteria such as lactobacilli and bifidobacteria to multiply and dominate the environment while creating unfavorable conditions for potentially harmful intestinal coliforms, clostridia, and enterococci (Kontula et al., 1999; Bramhankar et al., 2018). Due to their prebiotic effect, they reduce the formation of ammonia in the intestinal flora. Also, it is frequently used in the treatment of patients with liver encephalopathy and the treatment of patients with chronic constipation (Schaafsma, 2008).

Lactobionic Acid

Lactobionic acid (LBA), (4-O-β-D-galactopyranosyl-D-gluconic acid), is the oxidation product of lactose and belongs to the aldobionic acid family (Bramhankar et al., 2018). It was synthesized for the first time in 1889 by Fischer and Meyer from lactose oxidized with bromine. It contains a part of galactose that is chemically attached to a gluconic acid molecule via an ether-like bond (Cardoso et al., 2019). Thus, it acts as a metal ion chelator and can retain calcium (Okur, 2015). While it is highly soluble in water, it is poorly soluble in organic solvents such as ethanol, glacial acetic acid, and methanol (Cardoso et al., 2019).

Due to the increasing use of LBA day by day, various alternative methods have been tried instead of the chemical production method that requires high cost and intense energy. Although methods such as the enzymatic method, catalytic hydrogenation, and heterogeneous catalytic oxidation have been tried, considering the cost and benefit factors, the production of LBA with biotechnological methods has recently been focused on (Sarenkova and Ciprovica, 2018; Cardoso et al., 2019).

LBA has excellent properties such as antioxidant, pharmaceutical, chelating power, bio-solubility, and amphiphilic. It does not show toxic properties. For this reason, LBA is considered a high-value-added compound and is widely used in the medicine, pharmaceutical, food, chemistry, and cosmetics industries (Sarenkova and Ciprovica, 2018).

LBA is used as an active ingredient in some cosmetics and skincare products due to its antiaging and regenerating properties. It has been reported to provide many benefits for the treatment of dermatological pathologies such as atopic dermatitis and rosacea as a cosmetic ingredient. In addition, it is used in detergent production in the chemical industry due to its sugar-based surfactant and biodegradability capabilities (Cheng and Martínez-Monteagudo, 2019). It is used a versatile in the food industry to tighten the gel structure in foods, carry calcium in functional beverages, reduce the ripening and ripening

time in cheese and yoghurt production, improve the taste of bitter and sour foods, preserve aroma freshness, and prepare dairy products with reduced lactose content (Gutiérrez et al., 2012; Yılmaz-Ersan et al., 2016).

Lactosucrose

Lactosucrose, (β-D-fructofuranosyl-4-O-β-D-galactopyranosyl-α-D-glucopyranoside), is a trisaccharide composed of galactose, glucose, and fructose. A lactosucrose molecule contains both lactose and sucrose structures. Lactosucrose is industrially produced using the β-fructosidase enzyme on a mixed solution of lactose and sucrose. Lactosucrose can also be produced using β-galactosidase (Seki and Saito, 2012). This sugar also shows prebiotic properties. Since it can reach the large intestine without being digested, it is broken down by the colon microflora. The pH of the environment decreases. As a consequence, beneficial bacteria are affected positively and it promotes the growth of bifidobacteria (Mu et al., 2013a; Xiao et al., 2019).

Galactooligosaccharides (GOS)

Galactooligosaccharide (GOS) is one of the most commonly produced oligosaccharides worldwide. Although they are naturally found in breast milk, they can also be obtained through synthesis (Demirci et al., 2017). Galacto-oligosaccharides are produced by It is produced by enzymatic transgalactosylation of lactose, which is composed of glucose and galactose molecules, using β -galactosidase. The transgalactosylation reaction is an intermediate step in which galactose units are polymerized into a glucose terminal unit to form GOS in varying degrees of polymerization. GOS usually consists of 3–8 units of galactose chains with a glucose molecule at their reducing end. GOSs formed as a result of enzymatic synthesis are a heterogeneous mixture with different chain lengths and connections, and are mostly obtained from concentrated lactose syrup. They are available in liquid and solid forms (Mehra and Kelly, 2006; Lamsal, 2012).

GOS is divided into two subgroups:

(i) GOS with excess galactose in C3, C4 or C6

(ii) GOS produced from lactose by enzymatic trans-glycosylation.

These oligosaccharides, called trans-galactooligosaccharides or TOS, are a mixture of trisaccharides and pentasaccharides linked by β- (1-6), β- (1-3), and β- (1-4) bonds in the final product (Davani-Davari et al., 2019).

The galactosidase enzyme is in the group of hydrolytic enzymes and has been used in the dairy industry for a long time to produce glucose and galactose from lactose. This hydrolytic activity increases the sweetness of dairy products. Since the lactose concentration in the product decreases as a result of enzyme activity, consumers with lactose intolerance can consume these products (Gosling et al., 2010).

GOSs are resistant to digestive enzymes. They reach the large intestine without being digested in the stomach and the small intestine. They prevent the growth of pathogenic microorganisms in the intestines while selectively promoting the growth of bacteria with probiotic properties such as *Bifidobacterium* and *Lactobacillus.* Thus, they also provide a certain degree of protection against colon cancer. They function as prebiotics since they act as a substrate for beneficial bacteria (Schaafsma, 2008; Park and Oh, 2010). As a result of their fermentation, energy is produced, the pH of the environment decreases, and short-chain fatty acids are formed. Due to these substances formed in the colon, the absorption of various minerals increases, and the blood lipid content decreases (Sangwan et al., 2011).

Dairy products processed by utilizing the GOS-forming activity of β-galactosidase may contain lower sugar content (e.g. lactose) and a higher volume of soluble fibers (e.g. GOS). The structure of GOS is less complex and less diverse than human milk oligosaccharides (HMO). GOSs is used in infant formulations to mimic the functions of HMO due to this feature (Gosling et al., 2010; Chen and Gänzle, 2017). GOSs are low in calories and are non-cariogenic. Their use is increasing day by day in confectionery, chewing gum, yoghurt, ice cream, and bakery sectors (Chen and Gänzle, 2017).

Tagatose

Tagatose, (D-lyxo-hex-2-ulo-pyranose), is a monosaccharide obtained by the isomerization of D-galactose present in the lactose structure (Kim, 2004). Tagatose, which is also called the ketose isomer of D-galactose, is rarely found in nature and is found in dairy products in small amounts (Seki and Saito, 2012). D-tagatose was discovered by Lobry de Bruyn and Van Ekenstein in 1897 while studying the effects of mild alkaline components on D-galactose. In 1939, Yvonne and her colleagues succeeded in transforming D-galactose into an alkaline crystalline product and named it α-D-tagatose (Roy et al., 2018).

Although the chemical synthesis of tagatose began in the late 19th century, commercial production by chemical methods only had taken place in 1992. The first step in the chemical production of tagatose is the isomerization of D-galactose in the presence of an alkaline catalyst. The second step is the acid neutralization of the complex, which is stable in an alkaline environment. During the neutralization step, the acid reacts with D-tagatose to form an insoluble salt. The D-tagatose is then separated from the insoluble salt simply by filtration. However, D-tagatose production with the chemical method has several disadvantages such as complex purification steps, chemical waste, and by-product generation. For this reason, biological production research has accelerated (Roy et al., 2018).

It has been more economical and convenient to obtain galactose from lactose with the increased industrial production of the β-galactosidase enzyme. Therefore, galactose obtained from lactose has been used in the production of D-tagatose. The production of D-tagatose from lactose generally consists of two steps:

- To generate D-galactose by hydrolysis reaction of lactose using β-galactosidase, and chemical isomerization of D-galactose to D-tagatose with a calcium catalyst
- Reduction of D-galactose to D-tagatose as a result of enzymatic oxidation. All these methods involve a chemical process (Xiao et al., 2019).

Bacterial tagatose was first produced in 1984 by the Izumori group at the University of Kagawa Rare Sugar Research Center in Japan by the oxidation of galactitol by certain microorganisms. These microorganisms have galactitol dehydrogenase activity and are members of the *Arthrobacter*, *Mycobacterium*, and *Enterobacter* families. Although the efficiency of this method is approximately 92%, the production of D-tagatose from galactitol industrially is still not economical due to the high cost of galactitol production (Kim, 2004; Xiao et al., 2019).

Following the reports of Cheetham and Wootton in 1993 on the enzymatic production of D-tagatose from D-galactose by lactic acid bacteria, studies concentrated on this method. Bacteria with the L-arabinose isomerase (L-AI) enzyme mediate the conversion from D-galactose to D-tagatose (Oh, 2007). Some psychrotolerant, mesophilic, thermophilic, and hyperthermophilic bacteria are sources of L-AIs. During studies conducted in the last few decades, L-AIs obtained from bacteria were used in the biological production of D-tagatose. These bacteria are *Lactobacillus gayonii*, *Escherichia coli*, *Bacillus*, *Salmonella typhimurium*, *Geobacillus thermodenitrificans*, *Geobacillus sterothermophilus*, *Thermotoga neapolitana*, *Anoxybacillus flavithermus*, *Mycobacterium smegmatis*, *Lactobacillus fermentum* (Kim, 2004; Dalkıran, 2012; Xu et al., 2011). Microbial sourced L-arabinose isomerases have gained the attention of the industry, especially due to their feasibility in synthesizing D-tagatose (Oh, 2007). Enzymes of thermophilic bacteria are especially preferred for industrial use. Industrial enzymatic reactions taking place at high temperatures reduce the risk of contamination and substrate viscosity (Roy et al., 2018).

D-Tagatose has been recognized as safe (GRAS) in the USA and has received legal approval (Khuwijitjaru et al., 2018). Thus, it was allowed to be used as a sweetener in food and beverages (Levin, 2002; Xu et al., 2018). Although its sweetness is close to that of sucrose (~ 90%), it is a low-calorie (1.5 kcal/g) sugar. Because of this feature, it has attracted the attention of the industry and has been used as a sugar substitute (Xiao et al., 2019). It does not show the cooling effect seen in polyalcohol sugar substitutes (Kim, 2004). It is used in a wide variety of products, including dairy, beverages, confectionery, bakery products, health bars, chewing gum, and dietary supplements (Schaafsma, 2008). It has anti-caries and anti-diabetic properties (Xiao et al., 2019). Tagatose largely (80%) passes into the colon, undigested by the small intestine. Therefore, it has a prebiotic effect. It produces butyrate by fermenting in the colon and supports the growth of lactic acid bacteria (Schaafsma, 2008).

Epilactose

Epilactose is a disaccharide containing galactose and mannose. It is obtained through the epimerization of lactose (Seki and Saito, 2012). Epilactose was first found in milk sterilized at high temperatures (Xiao et al., 2019). Heat-treated bovine milk contains traces of epilactose. It is difficult to synthesize epilactose chemically (Seki and Saito, 2012; Mu et al., 2013b). However, Japanese scientists isolated the sellebiosis-2-isomerase enzyme from *Ruminococcus albus*, which is an anaerobic ruminal bacterium and they succeeded in effectively transforming lactose into epilactose biologically (Seki and Saito, 2012; Xiao et al., 2019).

As a result of in vivo studies, it has been reported that epilactose is not digested in the stomach and shows prebiotic properties since it reaches the colon without breaking down. It has also been reported that the decrease of the pH in the colon increases the absorption of calcium and iron, increases the level of beneficial short-chain fatty acids, and reduces the risk of arteriosclerosis (Mu et al., 2013b; Chen et al., 2015; Xiao et al., 2019).

Cellobiose-2-epimerase, which is optimized for industrial epilactose production, should be resistant to weak acids and heat and should have a higher affinity for the lactose substrate. In addition, molecular studies should be conducted without delay to determine the three-dimensional structure of the enzyme and to obtain a more ideal enzyme for industrial epilactose production. More human trials are also needed (Mu et al., 2013b).

Sialyllactose

Sialyllactose is formed by the combination of sialic acid with lactose found in bovine and breast milk. Sialylactose is in the acidic oligosaccharide group since forms due to the binding of an acid to the lactose. Colostrum contains sialylactose, and its level decreases towards the end of the lactation period. Therefore, sialylactose is believed to primarily have defensive roles against early period infections (Seki and Saito, 2012; ten Bruggencate et al., 2014).

Sialic acid forms part of the sugar chain that binds to glycoconjugates and it has many important physiological roles. There are about 30 types of sialic acids known. The main sialic acids found in milk are N-acetylneuraminic acid and N-glycolylneuraminic acid. It has been reported that approximately 73% of sialic acid in human milk is bound to oligosaccharides (Seki and Saito, 2012; ten Bruggencate et al., 2014).

Oligosaccharides are highly resistant to hydrolysis in the gastrointestinal system. Only a small part of the oligosaccharides present in breast milk is absorbed in the neonatal small intestine. It is thought that sialylactose and sialylated oligosaccharides are beneficial to the intestinal flora, pathogens, and immune function, and can be added to baby foods (ten Bruggencate et al., 2014; Phipps et al., 2019).

Polylactic Aid (PLA)

Polylactic acid (PLA) is formed by the conversion of lactic acid, which is formed as a result of the fermentation of lactose, first to lactide and then to polylactic acid, by polymerization. Lactic acid is widely used in pharmaceutical, food, chemical, textile, and detergent industries due to its easy polymerization, low melting point, and good solubility. PLA, a biodegradable and biocompatible aliphatic polyester produced by polymerization of lactic acid, is an environmentally friendly thermoplastic. Biodegradability is the ability to hydrolyze at temperatures above 50° C in a period between a few months to a year. It is also important that it forms non-toxic decomposition products inapplicability. Its main advantages are environmental friendliness, biocompatibility, workability, and less energy requirement for its production (Rasal et al., 2010; Tektemur, 2011; Lasprilla et al., 2012).

Conclusion

Edible and pharmaceutical-grade lactose and its derivatives are frequently used in the food and pharmaceutical industries. Many studies have expressed that lactose has been found in many diets due to its sweetening power, caloric value, and low glycemic index, and also, lactose derivatives are used in many food products as prebiotics and sweeteners. The majority of lactose derivatives cannot be digested in the stomach and small intestine and pass directly to the large intestine. These derivatives are hydrolyzed by *Bifidobacterium* and other microflora in the large intestine and turn them into prebiotic components that are very beneficial for these bacteria. It is thought that lactose derivates will find more areas of usage in the production of many products in the field of food, medicine, and pharmacology due to the prebiotic properties of these components.

Authors' Contributions

Seval Andiç

Methodology, Investigation, Validation, Writing - original draft, Review, and editing.

Şehriban Oğuz

Investigation, Conceptualization, Validation, Review, and editing.

Conflict of Interest

The authors declare that they have no conflict of interest.

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