Chapter

Hundred Years of Lactitol: From Hydrogenation to Food Ingredient

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Abstract

The first report on the synthesis of lactitol dates back to the early 1920s. Nearly 100 years have passed since then, and the applications of lactitol have exceeded its original purpose. Currently, lactitol is used in bakery, confectionery, chocolate, desserts, chewing gum, cryoprotectant, delivery agent, and stabilizer in biosensors. Lactitol is the main reaction product derived from the hydrogenation of lactose. This chapter is aimed at providing a succinct overview of the historical development of lactitol, a summary of its synthesis, and an overview of its properties and applications.

Keywords: lactitol, catalytic hydrogenation, sugar alcohols, low-calorie sweeteners, lactose utilization

1. Introduction

Lactitol, a sugar alcohol, is not found in nature, and its synthesis requires lactose in solution, hydrogen gas, and solid catalyst. The first attempts of lactitol synthesis were made about 100 years ago. Since then, the synthesis of lactitol has evolved into a highly efficient process with a projected production of 1.9 million metric tons by 2022 [1]. In a nutshell, the synthesis consists in the incorporation of a hydrogen ion into the carbonyl group of lactose. Such incorporation involves a set of multiple elementary reactions known as Langmuir-Hinshelwood-Hougen-Watson (LHHW) kinetics. The hydrogenation has consensually thought to occur by adsorption, reaction surface, and desorption of the reactants. A number of kinetics models suggest that the surface reaction is the predominant step [2]. Within the surface reaction, the reaction between two adsorbed species is catalyzed by a transition metal supported in an inert material. Over the years, several catalytic systems (metal and support) have been investigated in terms of their physical and chemical properties. An important feature of the catalytic hydrogenation is the multiphase nature of the reaction, where liquid, solid, and gas are brought into contact for a given time. Upon completion of the reaction, lactitol is separated from the slurry by centrifugation and crystallization. In crystalline form, lactitol can exist in four crystal forms, depending on the crystallization protocol [3]. Each type of crystal is characterized by its melting point and solubility. The most common structure of lactitol is the monohydrate form, and therefore it is the most studied one.

Lactitol is best known as a nutritive sweetener, whose relative sweetness is between 30 and 40% comparable with that of sucrose [4]. More importantly, regulatory agencies such as European labeling and FDA consider a caloric value of lactitol as 2.4 and 2.0 kcal g^{-1}, respectively, which correspond to a reduction of 48–40% with respect to sucrose [5]. The molecular structure of lactitol offers stability over a wide range of pH and temperature, making it a suitable candidate for the synthesis of biopolymers, hydrogels, and surfactants. Over the last past decades, lactitol has emerged into a multipurpose ingredient from low-caloric sweetness to coating material in chewing gums.

This chapter summarizes relevant advancements over the 100 years of lactitol history. Section 2 provides a historical overview of lactitol, highlighting some of the most significant milestones. Section 3 discusses an overview of the catalysts used for the hydrogenation of lactose. Section 4 addresses some chemical and physical properties of lactitol. Finally, a summary of current and potential applications of lactitol is discussed in Section 5.

2. Historical timeline

Figure 1 illustrates selected milestones of lactitol over the past 100 years. A comprehensive review of the technological advancements of lactitol can be found elsewhere [1]. Chemical catalysis was perhaps the first great contributor to the advancement of lactitol. In 1920, Senderens [6] hydrogenated lactose over activated nickel. Senderens' catalysis was very unstable, making unrealistic any kind of large-scale production. The stability of nickel-based catalysts became a reality with the invention of the sponge nickel by Raney in 1925 and 1926 [7]. Raney's invention consisted of crystalline particles of active nickel embedded within an inactive metal. In subsequent years, the reaction kinetics of hydrogenation was elucidated, which allowed the production of lactitol at high yields and selectively.

Early production of lactitol was aimed at research facilities, where potential applications were investigated throughout 1930–1970. In 1938, the crystalline structure of lactitol was elucidated by purification and crystallization of the hydrogenated slurry [8]. A second anhydrous crystalline form of lactitol, dihydrate, was discovered by 1952 [9]. In subsequent years, lactitol entered the fields of nutrition, material science, and biotechnology. Fortification of infant food, synthesis of lactitol-based polyethers, sweetening agent, and animal feed are examples of applications of lactitol.

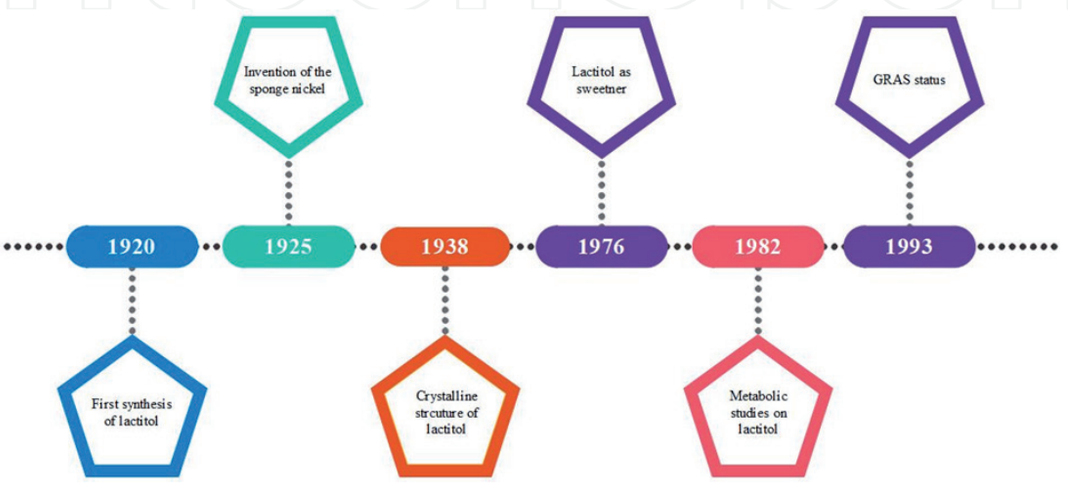

Figure 1.
Selected scientific and commercial milestones of lactitol over the past 100 years. Adapted from [1].

In 1977, the sweetness intensity of lactitol was established by the development of the sweetness scale using sucrose as a reference [10]. Soon after, lactitol was incorporated in confectionary formulations and chewing gum. In the 1980s, lactitol found applications in the field of hygiene and medicine, where it was used to formulate toothpaste, mouthwashes, and aseptic products. Metabolic concerns related to the consumption of lactitol were studied in 1981 [11]. In years thereafter, lactitol was used for the treatment of liver disease [12]. In 1993, the Food and Drug Administration (FDA) granted the status of Generally Recognized as Safe (GRAS) [13]. The current literature on applications of lactitol reveals about 3000 patents, ranging from a low-calorie sweetener to a surfactant and stabilizer agent. Nowadays, lactitol and other sugar alcohols represent a significant global market with various applications, and its production is projected to reach 1.9 million metric tons by 2022.

3. Production of lactitol

3.1 Catalytic hydrogenation

Lactitol is not found in nature, and it can only be produced through catalytic hydrogenation of lactose. Thus, the transition state theory of catalytic surface reactions is the foundation of lactitol synthesis. The actual synthesis consists of a sequence of elementary reactions, namely adsorption, surface reaction, and desorption [14]. Collectively, all these reactions are known as the Langmuir-Hinshelwood-Hougen-Watson (LHHW) kinetics [2]. **Figure 2** illustrates the LHHW kinetics that is formulated from a presumed elementary step. Then, the rate is derived through the different elementary steps with the assumption of one of them is the rate-determining step, while the others are achieved the equilibrium. The overall reaction rate is strongly affected by temperature and pressure since these variables determine the equilibrium of the elementary reactions.

3.1.1 Adsorption

Lactose and hydrogen are adsorbed through chemisorption, where the exchange of electrons with surface sites leads to the formation of a chemical bond [15]. Lactose is adsorbed from the bulk solution, a process that overcame the interaction forces of the solvent. A molecular mechanism is responsible for adsorbing the

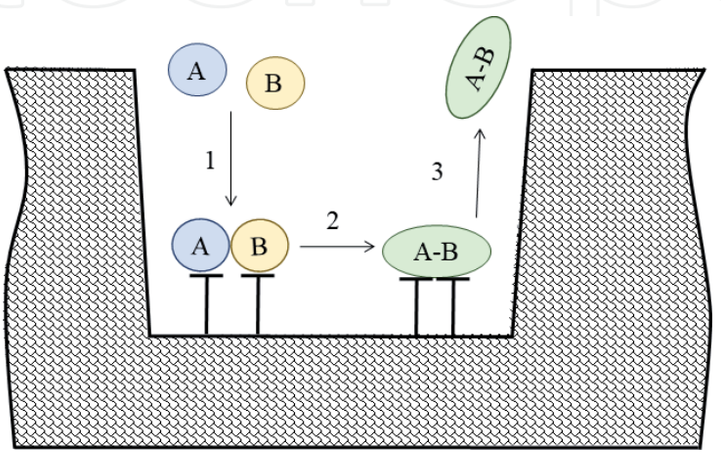

Figure 2.
Illustration of Langmuir-Hinshelwood-Hougen-Watson kinetic. Adapted from [2]. Numbers 1, 2, and 3 represent adsorption, surface reaction, and desorption, respectively.

lactose and hydrogen is followed a dissociative mechanism ($H_2 \leftrightarrow 2H^*$) due to the action of transition metals. Dissociative adsorption requires an adjacent vacant site, and the rate of attachment is proportional to the square of the vacant concentration [16]. The adsorption of reagents occurs within a very short timeframe. Once the adsorption is completed, the adsorbed molecules are in equilibrium with those molecules in the bulk phase.

3.1.2 Surface reaction

Examples of reaction mechanisms occurring at the surface include duel-site, single-site, two adsorbed species, and unabsorbed species [17]. Such mechanisms have been used for hydrogenation of a number of carbohydrates including, glucose, fructose, xylose, and lactose [18].

3.1.3 Desorption

The products of the surface reaction are subsequently desorbed into the reaction medium. Theoretically, the rate of desorption is exactly the opposite in sign to the rate of adsorption [19]. However, the desorption of reaction products is regarded as rapid and therefore neglected within the rate equation.

3.2 Catalysts

The design and selection of catalyst systems have been a major research topic in organic synthesis and chemical engineering. Several factors should be considered for the adequate selection of a catalyst system including, the transition metal, supporting material, preparation methods, and solvent. For lactose hydrogenation, metals such as nickel (Ni), ruthenium (Ru), and palladium (Pd) within a range of 1–10% are commonly used due to their relatively high reactivity and selectivity toward aldehyde groups. The concentration of the metal is linearly related to its activity within a limited range of 1 to 10%. Outside the concentration range, the metal is not available for reaction. A number of metal-based catalysts have been developed for lactitol production, including nickel-based, ruthenium-based, and other metal-based catalysts.

3.2.1 Nickel-based

Raney in 1920s patented a protocol where active metal (Ni) was embedded within an inactive metal (Al) frame [7]. The activity of the Raney's catalyst results from the random distribution of nickel crystals within the inactive crystal lattices [20]. A number of metals have been added into the Raney-nickel catalysts to further increase the reactivity [21]. Chromium, molybdenum, and tungsten are examples of metals added. The use of metal promoters (Cr-, Mo-, and Fe-Ni) showed a five-fold rate enhancement over non-promoted Raney nickel in the hydrogenation of glucose [21]. Although nickel-based catalysts are an effective catalyst for lactose hydrogenation, it suffers from the deactivation problem due to the nickel leaching and catalyst sintering. This results in a loss of catalyst activity and high nickel content in the lactitol product solution.

3.2.2 Ruthenium-based

Ruthenium is another metal used as a catalyst supported in different materials, such as carbon, alumina, silica, and synthetic gel. The ruthenium catalyst was effective

for the hydrogenation of monosaccharides and disaccharides [22]. Ruthenium-based catalysts are supported in alumina (Ru/Al2O3), silica gel (Ru/gel), titanium dioxide (Ru/TiO2), crosslinked polystyrene (Ru/CP), and activated carbon (Ru/C). Ruthenium-based catalyst is more active than a nickel-based catalyst, and this leads to the higher catalyst selectivity [23]. Moreover, ruthenium-based catalyst was more stable than Ni based catalyst in the hydrogenation process; this leads to the extended lifetime of catalysts [23].

3.2.3 Other metal catalysts

Metals such as copper (Cu) and Pd have also been studied for the hydrogenation of lactose. For instance, Cu/SiO_2 was effective for the catalytic transformation of lactose to a high yield mixture (75–86%) of sorbitol and galactitol [24]. The boron nitride supported palladium (Pd/h-BN) was applied for the hydrogenation of lactose. The results indicated that the high lactose conversion ratio (up to 50%) was obtained with this catalyst.

3.3 Reaction pathways

Lactitol is the main product formed during the hydrogenation of lactose, followed by a considerable formation of lactulose, lactulitol, lactobionic acid, sorbitol, and galactitol [23]. All these compounds are formed through a combination of hydrogenation, isomerization, hydrolysis, and oxidation. **Figure 3** illustrates the reaction pathways occurring during the hydrogenation of lactose. A number of factors influence the occurrence and extent of a given reaction. Temperature, pressure, pH, agitation, type of catalysts, concentration, and catalyst load are examples of such factors [2].

3.3.1 Hydrogenation

Lactose is readily reduced to its corresponding alcohol, where the carbonyl group reacts with the hydrogen ion. This reaction is represented by scheme (1), and it is the main reaction occurring during the hydrogenation. Concomitantly, other reducing sugars (lactulose, galactose, and glucose) are also hydrogenated to form their respective alcohol (lactulitol, galactitol, and sorbitol). These reactions are exemplified in scheme (4), (10), and (9), respectively. Lactulose is formed through isomerization, while galactose and glucose are formed via hydrolysis of lactose.

3.3.2 Isomerization

The temperature used during hydrogenation may trigger the isomerization of lactose via enolization of the glucose molecule, scheme (4). Hypothetically, galactose, and glucose may undergo isomerization to form D-Tagatose and fructose, respectively. The yield corresponding to derives from isomerization is rather low. This is because the isomeric form of a reducing carbohydrate is prone to hydrogenation. Scheme (9) and (10) illustrate the hydrogenation of glucose and galactose, respectively.

3.3.3 Hydrolysis

Lactose may hydrolyze to some extent, leading to the formation of galactose and glucose, scheme (8). Lactulose and lactulitol may also hydrolyze, and their respective product can be hydrogenated. These sets of reactions are illustrated in

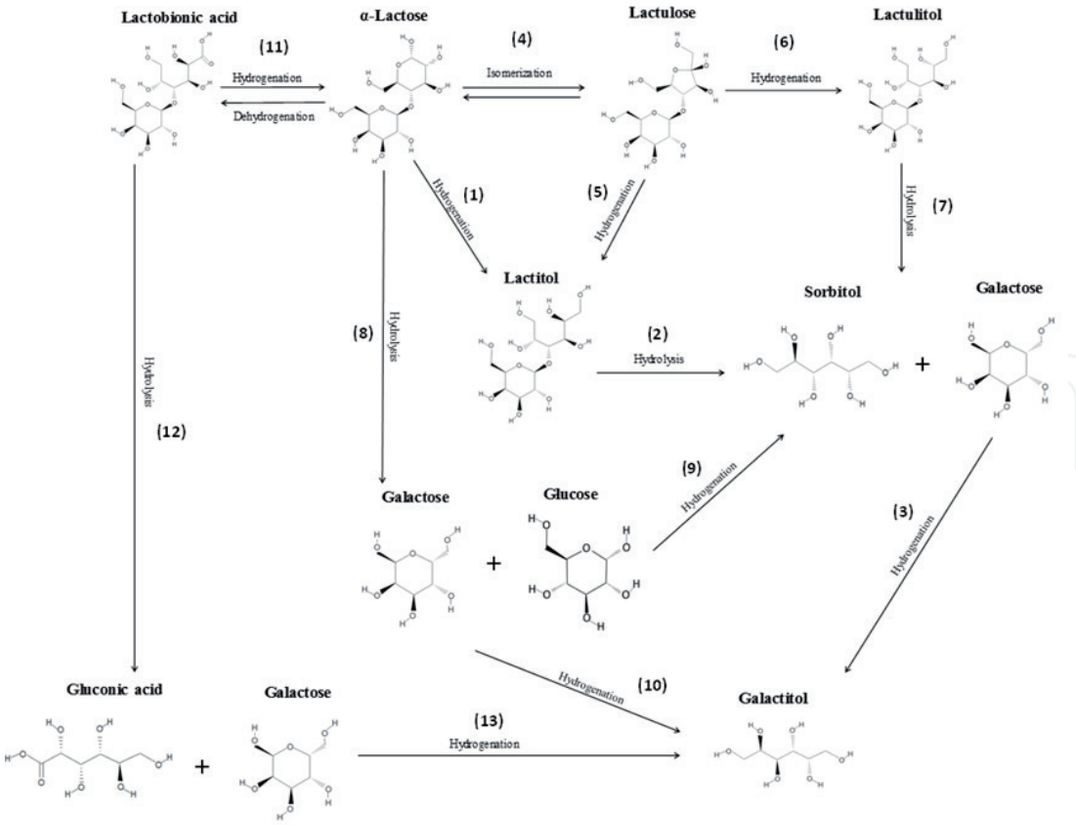

Figure 3.
Reaction scheme during catalytic hydrogenation of lactose.

scheme (5). Prolong reaction time and high temperature can induce the hydrolysis of lactitol, which leads to the formation of sorbitol and galactose, scheme (2).

3.3.4 Oxidation

Lactose can undergo dehydrogenation forming lactobionic acid, scheme (11). This situation would occur under a limited concentration of hydrogen. Subsequently, the lactobionic acid may undergo hydrolysis (scheme (13)) to form gluconic acid and galactose.

3.4 Production of lactitol

The industrial hydrogenation of lactose is commonly done in a batch mode using sponge nickel as a catalyst. In the hydrogenation of lactose, the reaction temperature ranged from 130 to 180°C, while the pressure of hydrogen gas varied between 50 and 170 bars. **Figure 4** exemplifies a hydrogenation batch reactor. The batch reactor is charged at the top of the tank. This type of reactor is based upon the movement of hydrogen from the gas phase to a liquid phase and across a liquid-solid interface to the surface of the supported catalyst, where the hydrogen gas is adsorbed. During the reaction, hydrogen gas is consumed by the catalytic reaction creating concentration gradients across the reactor. Such gradients control the net movement of hydrogen gas to the catalyst and, therefore, the speed of the reaction. Temperature, pressure, and agitation are the main variables controlling the reaction rate and final yield. Batch reactors offer the advantage of not having large temperature gradients, and the development of velocity profiles is negligible, which simplifies the operation. The performance of a batch reactor for catalytic hydrogenation depends on the hydrogen movement across the reactor. This feature

is the principal disadvantage of the batch reactor since they are designed to control the mass transfer only through agitation.

Alternatively, catalytic hydrogenation can be performed by a continuous flow of reactants. Conceptually, the continuous operation has been exemplified in a trickle-bed reactor using structured catalysis [19]. A simplified diagram of the continuous hydrogenation of lactose is presented in **Figure 5**. The process mainly consists of feed streams, heat exchangers, reactor units, and separator. Kasehagen [25] exemplified the production of lactitol under continuous mode using a lactose solution (50% wt/wt) in water with sponge nickel (1.8%) at 160°C and 130 bar. Under such conditions, about 98% of lactose was converted into lactitol.

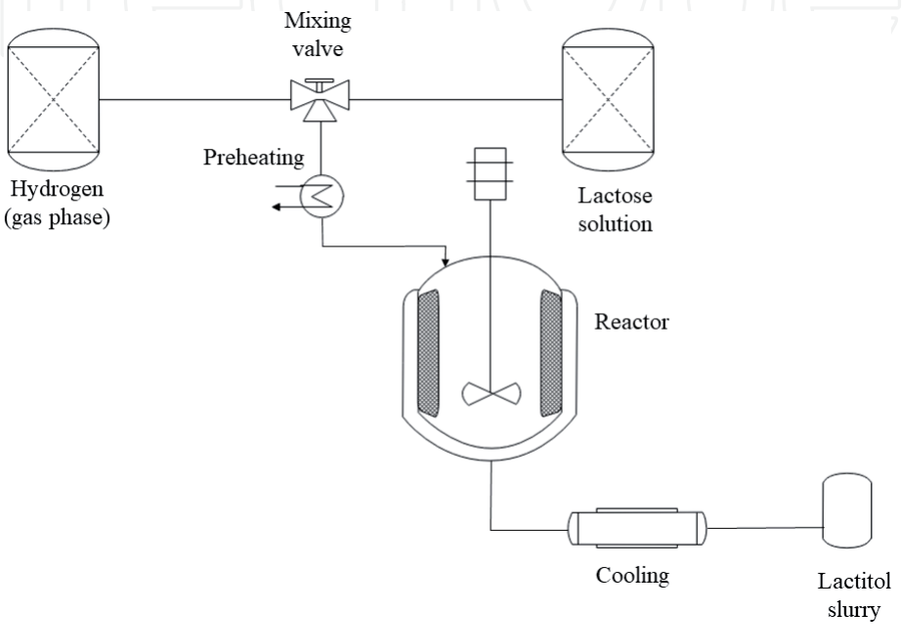

Figure 4.
Continuous-stirred tank reactor for batch hydrogenation of lactose.

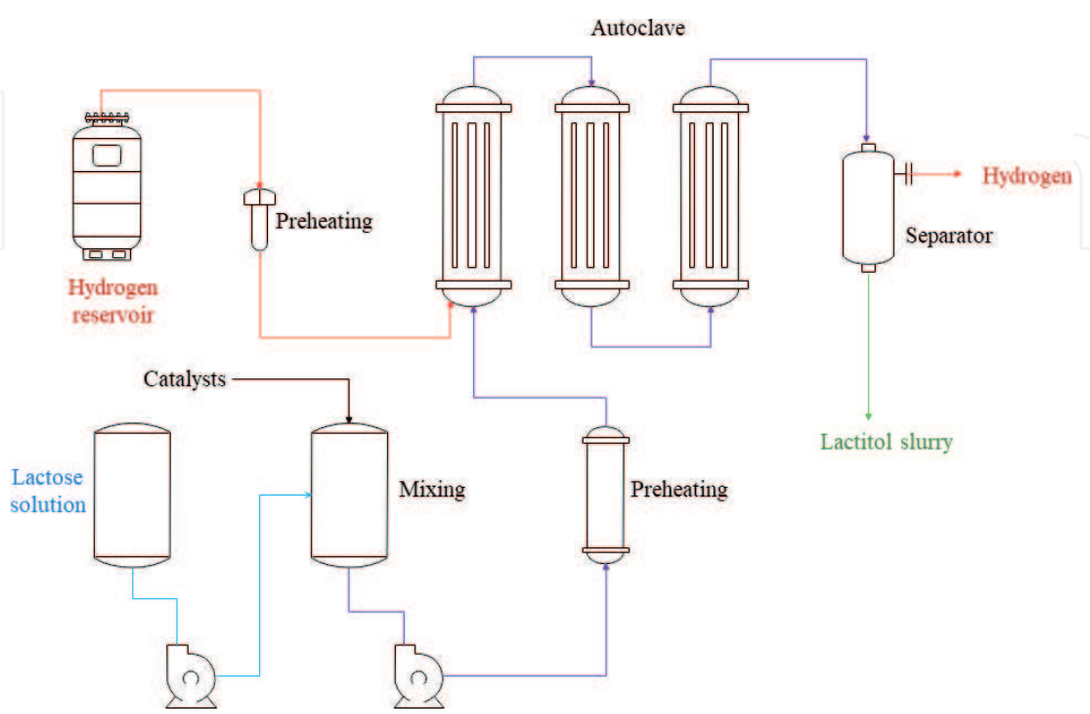

Figure 5.
Schematic representation of continuous hydrogenation of lactitol.

4. Properties of lactitol

4.1 Chemical and crystalline forms

In solid-state, lactitol can exist in different crystalline forms, having different melting points. Early observations showed the existence of two forms of anhydrous lactitol having different melting points [8, 9]. XRD and IR-spectra revealed three hydrate forms (mono-, di-, and tri-hydrate), two anhydrate (A and B), and one amorphous form [3, 26, 27]. The most common form of lactitol is monohydrate, which is obtained through slow crystallization of the lactitol slurry. Lactitol is a monoclinic polyol with one intra- and eight inter-molecular hydrogen bonds in its chemical structure [27]. All hydroxyl H-atoms form hydrogen bonds, which give rise to an eight-membered ring, chair conformation of the galactopyranosyl ring. The crystalline form of lactitol dihydrate is tetragonal with 3 intra- and 12 inter-molecular hydrogen bonds in its chemical structure [28]. Similar to lactitol monohydrate, all hydroxyl H-atoms form hydrogen bonds resulting in a chair configuration of the galactopyranosyl ring.

4.2 Solubility

Lactitol is found commercially as a crystalline powder. Interestingly, lactitol properties and therefore its potential application depend on the given crystalline form. Lactitol is recovered after hydrogenation, where the spent catalyst is removed via ion-exchange. Then, the slurry is evaporated under vacuum, and subsequently crystallized under prescribed protocol. Once the crystals are formed, the lactitol slurry is centrifugated and dried. Crystallization is the key step during the formation of a given crystal form. The crystallization of carbohydrates can be used as a general guideline of the crystallization of lactitol. Nurmi and Kaira [29] provided the most accurate guides in the literature for the crystallization of lactitol. Solubility curves of the lactitol crystals are illustrated in **Figure 6**. For simplicity, the solubility curve was divided into four regions.

The region IV illustrates the required conditions to yield lactitol in anhydrous form. This has been illustrated by Nurmi and Kaira [29], who crystallized a 91%

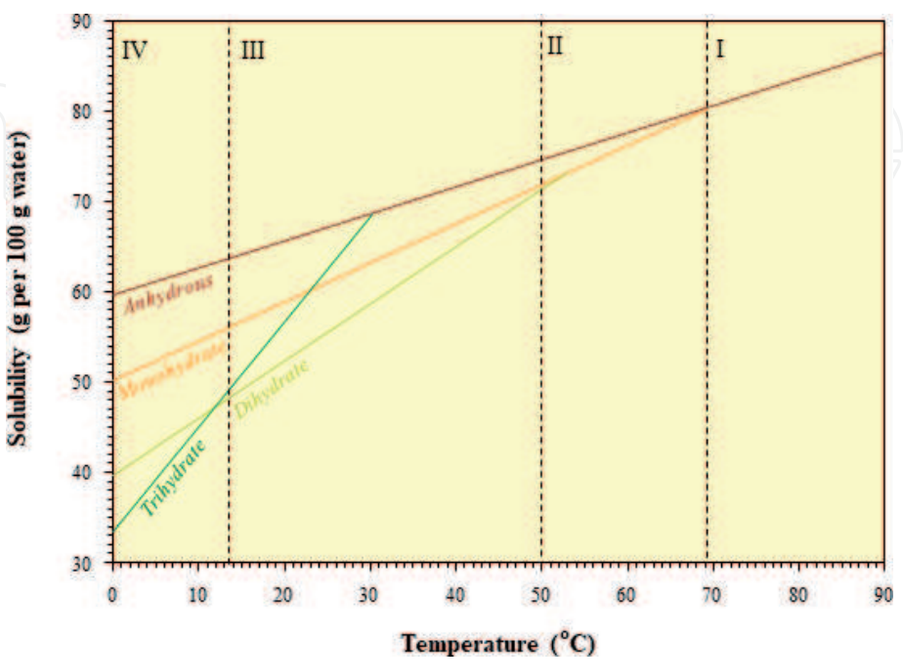

Figure 6.
Solubility curves of lactitol anhydrous, monohydrate, dihydrate, and trihydrate.

lactitol solution to obtain lactitol anhydrous. The solution was cooled from 95 to 75°C within 10 h, inducing the crystallization from solution. Similarly, Heikkila et al. [30] obtained lactitol anhydrous by cooling from 90 to 80°C a 90% lactitol solution. The working conditions for yielding lactitol monohydrate are exemplified in region II. Heikkilä et al. [30] obtained lactitol monohydrate using a four-step crystallization. Heikkilä's protocol involved the cooling of a 82% seeded lactitol solution from 70 to 40°C in 16 h. Wijnman et al. [31] obtained lactitol in the form of monohydrate by seeding a 80% solution of lactitol, and cooled it from 75 to 50°C in 18 h. The remaining mother liquid from this protocol was seeded and cooled down to 18–15°C to obtain lactitol dihydrate, indicated in region II. Wijnman et al. [31] followed a similar protocol to obtain 60% yield of lactitol dihyrate. Lactitol trihydrate, which is illustrated in region I, is obtained by further crystallization of the mother liquid at temperatures lower than 10°C [29].

4.3 Caloric value

Evidence of the reduced-calorie value of lactitol dates back to the 1930s, where the enzymatic hydrolysis of lactitol was found to be significantly slower than that of lactose [32]. This observation pointed out the possibility of a reduced calorie effect of lactitol. Indeed, Hayashibara and Sugimoto [33] measured the concentration of lactitol in the intestines of rabbits injected with a 20% solution of lactitol. After hours of injection, the lactitol concentration did not, while the concentration of glucose was reduced by 85%. Van Es et al. [34] analyzed the metabolized energy derived from lactitol and sucrose. They found that the energy contribution to the body was 60% less than for sucrose. European labeling considers a blanket caloric value of lactitol as 2.4 kcal g^{-1} [5]. At the same time, the Food and Drug Administration (FDA) establishes a general value of 2.0 kcal g^{-1}, a reduction of 48–40% with respect to sucrose.

4.4 Sweetness

Lactitol is known for its mild and clean sweet taste [4]. Relative sweetness is measured in relation to a reference value of 1, which corresponds to the sucrose sweetness at a given concentration [5]. Lactitol possess a relative sweetness from 0.3 to 0.42. Generally, lactitol sweetness is considered to be 30–35% of the sucrose sweetness. Thus, simply replacing sucrose with lactitol requires substantial amount of lactitol. Alternatively, lactitol is combined with other sweeteners to synergistically reduce the sucrose concentration.

4.5 Health claims

Lactitol is not considered as essential nutrient, but its consumption has been clinically linked to a number of health benefits. Health benefits and claims associated with the consumption of sugar alcohols have been reviewed elsewhere [35, 36]. Overall, sugar alcohols are a limited source of energy for oral bacteria that results in less production of acid. van der Hoeven [37] studied the cariogenicity of lactitol in fed rats, and observed that lactitol significantly reduced caries development when compared with sucrose. This observation was in agreement with the rate of fermentation by oral bacteria. Acid production from lactitol occurred at much lower rate than the acid production of sucrose. Clinical evidence demonstrated a reduction in the incidence of caries by the substitution of sucrose with sugar alcohols in chewing gum and candies. van Loveren [38] postulated that the preventive effects against caries in gums and candies formulated with sugar alcohols are due to a stimulation

of the salivary flow, providing a buffer capacity that washes away soluble carbohydrates. However, there is no consensus regarding the minimal dose required to reduce caries. Nevertheless, van Loveren [38] suggested that chewing of sugar-free chewing gum at least 3 times per day may reduce caries incidence.

Lactitol is frequently prescribed as a laxative agent for the treatment of chronic constipation [39]. As a laxative agent, lactitol is minimally absorbed in the small intestine, and when it reaches the large intestine, it creates an osmotic gradient that increases the water retention in the stool, enhancing its passage. Miller et al. [40] performed a meta-analysis on the efficacy and tolerance of lactitol for adult constipation. It was found that lactitol supplementation was not only well tolerated but also significantly improved symptoms of constipation.

5. Applications of lactitol

5.1 Cryoprotectant and dryoprotectant

Lactitol is a polyol having the ability of preventing physical and chemical degradation of protein preparations during frozen and drying. The effectiveness of lactitol as a cryoprotectant agent was demonstrated in fish muscle (rainbow trout), where lactitol preserved the structure of myofibrillar proteins [41]. Interestingly, lactitol influenced the kinetic of formation of hydrophobic residues in the surface of proteins. Similarly, Nopianti et al. [42] added lactitol to prevent protein denaturation of threadfin bream surimi during 6 months of frozen storage. A formulation made of 6% of lactitol resulted in protective effect comparable with that obtained for polydextrose and sorbitol. Ramadhan et al. [43] cryoprotected duck surimi by the addition of lactitol. More importantly, the studied by Ramadhan et al. [43] showed a protective effect after five cycles of freeze-thaw during 4-month of frozen storage.

Lactitol can form glassy matrices within the protein structure that immobilizes the system and preventing unfolding. Moreover, lactitol may form hydrogen bonds with the surrounding protein, helping the preservation the enzymes. Such mechanisms have been validated during the drying of protein preparations. Kadoya et al. [44] freeze-dried a solution of L-lactic deydrogenase and bovine serum albumin using lactitol monohydrate as a cryoprotective agent. Microscopic observation indicated the formation of hydrogen bonds that substitute water molecules, and maintaining the activity of L-lactic dehydrogenase. This is an important observation showing the protective effect of lactitol in pharmaceutical applications that helps to minimize product immunogenicity.

The preservation of archeological artifacts has benefited from the protective effect of lactitol. The stability of archeological wood was performed by the impregnation of lactitol prior to freeze-drying. It was showed that the impregnation of lactitol resulted in higher hygroscopicity compared with polyethylene glycol impregnation [45]. Babiński [46] treated waterlogged archeological oak with lactitol, and evaluated changes in dimensions and moisture content. Lactitol reduced the wood shrinkage after freeze-dried by replacing water molecules and fill the cell walls.

5.2 Surfactant and hydrogel

The structure of lactitol confers higher chemically stability than lactose and sucrose. Lactitol stability is due to the absence of the carbonyl group, resulting stability over a broad range of pH (3–9). Moreover, lactitol is not a reducing sugar (absence of carbonyl group) which does not participate in the Maillard reactions. Such properties of lactitol offer potential for non-conventional applications, such

as surfactants, emulsifiers, and hydrogels. Indeed, Van Velthuijsen [47] produced a non-ionic emulsifier made of lactitol via esterification of palmitic acid under alkaline conditions. Lactitol esters displayed relevant detergent activity by removing soil and stains from towels. Dupuy et al. [48] determined the micellization of lactitol-based surfactants in water. It was found that lactitol surfactants were barely dispersed at low concentrations, and the formation of micelles was due to their stearic hindrance. Drummond and Wells [49] produced mono-esters of lactitol with chain lengths from C8 to C16—octyl, dodecyl, and hexadecyl. The interfacial tension of such surfactants was determined by putting them in contact with hexadecane and triolein. The chain of the surfactant minimally reduced the interfacial tension than their shorter chain counterpart. Surfactants made of lactitol displayed the tendency to foaming over 30 min. This is an important observation indicating the great potential of lactitol based surfactants to be used as emulsifiers. It is worth to mention that surfactants made of lactitol have not been produced commercially.

Disaccharides from renewable sources can be used as building blocks for the synthesis of polymers and hydrogels. Wilson et al. [50] produced polyether polyols via lactitol propoxylation at alkaline environment. Lactitol polyether polyols showed similar viscosity and hygroscopicity than their counterpart sucrose-based polyols of the same hydroxyl number. Moreover, the decomposition of lactitol polyols was negligible. Wilson et al. [50] prepared rigid polyurethane foams from lactitol polyether polyols. Lactitol based foams showed physical properties comparable to that of the commercial foams. Hu et al. [51] hydrogenated sweet whey permeates and synthesized polyurethane foams by propoxylation of lactitol slurry. The lactitol foams were showed low-density, strong mechanical properties, and thermal stability. Lin et al. [52] controlled the propoxylation of lactitol to produce polyether polyols with nine polypropylene oxide branches. Such lactitol polyether polyols were used to prepare hydrogel via acylated polyethylene glycol bis carboxymethyl ether. Lactitol hydrogels absorbed water up to 1000% of their dry weight. Remarkably, these hydrogels expelled free water at a temperature above 30°C.

Lactitol can be seeing as building block compound to design delivery systems for bioactive compounds. Already, Han et al. [53] prepared poly(ether polyol) hydrogel from lactitol, and it was showed ability of delivering acetylsalicylic acid over a pH range of 4–9. More importantly, the release was controlled by the amount crosslinking of the hydrogel. Han et al. [53] used lactitol cross-linked hydrogel to incorporate protein for controlled release of the protein into the surrounding fluid. It was found that the release of β-lactoglobulin, bovine serum albumin, and γ-globulin was constant over 2 h in a temperature range of 37–45°C. Constant release at such temperature range approaches the human body temperature, suggesting the use of lactitol based delivery system for clinical applications. Chacon et al. [54] prepared hydrogels of lactitol having swelling capacity up to 81-fold. The length of polypropylene oxide branches and the extent of crosslinking controlled the swelling capacity of the hydrogels. Chacon et al. [54] added a lipase within the lactitol hydrogel for temperature-controlled release. About 90% of the enzyme was released into the medium within the first 60 min at temperatures between 25 to 40°C. The development of drug delivery systems used lactitol as a target group [55], where the carrier is incorporated in liposomes for treatment of liver disease.

5.3 Bakery

Sugar reduction and replacing in bakery formulations has not been a trivial task in the past. This is because sugar not only provides a pleasant taste but also plays a critical role in the development of the quality characteristics of the batter or dough. Psimouli and Oreopoulou [56] replaced sugar with lactitol in equal amount for

cake formulations. The resulting batter was comparable in terms of flow index and the temperature of starch gelatinization. Sensory analysis indicated no significant difference between the batter formulated with lactitol and the one formulated with sugar. Frye and Setser [57] employed lactitol as a sweetener to optimize cake formulations having a reduction of 45% in the caloric content. Such formulations showed comparable attributes with a standard layer cake. Similarly, Zoulias et al. [58] evaluated the role of lactitol and other polyols as a sucrose replacement on the texture profile of cookie dough. The lactitol formulated dough resulted in medium values of hardness and consistency.

5.4 Chocolate and confectionary

The formulation of sugar-free chocolate represents a significant challenge because the entire sugar needs to be replaced, which in turns, affects the melting properties of the chocolate [59]. Mentink and Serpelloni [60] formulated a low-calorie chocolate having an equimolar blend of maltitol, lactitol, and isomaltulose. The formulation showed technical and organoleptic properties comparable to those of traditional formulation with sucrose. Synergistic effects have been reported when sugar alcohols are combined with other sweeteners. de Melo et al. [61] developed a sugar-free chocolate having acceptable sensory scores by the combination of high-intensity sweeteners and blends of sugar alcohols.

Sugar alcohols have also been used in the manufacture of hard-boiled sweets. Blends of lactitol, sorbitol, and mannitol provided sticky texture due to their hygroscopic nature. Such challenge is the principal limitation in the formulation of hard-boiled candies with sugar alcohols. Serpelloni and Ribadeau-Dumas [62] enhanced the process of hard coating by using a syrup of sugar alcohols. Another investigation on the role of replacing sugar in syrups demonstrated that about 40% of the total sugar can be replaced with lactitol without changes in the moisture content and density [63]. Lactitol addition produced a two-fold increase in the viscosity of the syrup. Blankers et al. [64] formulated a syrup sweetening suitable for soft confectionery applications. The syrup is made of lactitol and polydextrose, and it is combined with the lactitol slurry derived from lactose hydrogenation.

5.5 Chewing gum

Lactitol in combination with other sugar alcohols is used to formulate sugar-free chewing gum. The hygroscopicity of lactitol is relatively low, which facilities its incorporation into the gum. Huzinec et al. [65] incorporated lactitol within the microcrystalline cellulose carrier. With such blend, the release of flavor was extended in chewing gums. McGrew et al. [66] used active compounds in combination with mannitol, xylitol, maltitol, lactitol, and hydrogenated starch hydrolysates to control release of such active agent that are embedded in the gum base. Yatka et al. [67] formulated a generic gum base containing oligofructose and sorbitol, maltitol, xylitol, lactitol, and mannitol. Such a generic formulation was blended with glycerol. Subsequently evaporated to produce a low-moisture and sugar-free chewing gum. The combination of oligofructose and sugar alcohols improved quality properties, including texture, moisture adsorption. Reed et al. [68] formulated hard-coated chewing gum coated with a layer of lactitol, maltitol, and sorbitol.

5.6 Biosensor development

Lactitol can be used as an additive for biosensors because of the stabilizing effect on enzymes. Karamitros and Labrou [69] used lactitol to immobilize isoenzyme

glutathione transferase. About 5% of lactitol resulted in a prolonged stability of the enzymes. Gibson and Woodward [70] combined diethylaminoethyl-dextran hydrochloride (DEAE-Dextran) and lactitol for the stabilization of enzymes in a dry state. Such combination of DEAE-Dextran (10%) and lactitol (5%) preserved up to 95% of the activity after 16 d. Zhybak et al. [71] immobilized creatinine deaminase and urease in the presence of lactitol, and reported improvement in the stability of the biosensor. Remarkably, biosensor selectivity was not impacted by the addition of lactitol.

6. Conclusions

Over the past 100 years, lactitol has been evolving successfully finding new applications while its original purpose has expanded. Today, lactitol is added into a number of food formulations, such as bakery, confectionery, chocolate, desserts, chewing gum, and cryoprotectant. Research strategies for expanding the applicability of lactitol are needed including, solubility at different conditions, rheological behavior, heat stability, thermogravimetric analysis, stability toward heat and pH, particle size, bulk, and particle density, and crystallization kinetics.

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Conflict of interest

The authors declare no conflict of interest.

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