

Biotechnological production of xylitol from agricultural waste

Producción biotecnológica de xilitol a partir de residuos agrícolas

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ABSTRACT

Agricultural residues valorization has been an important issue over the last decades. Agricultural crop waste is an abundant, non-food, renewable, and low-cost feedstock to obtain attractive products for the food industry. The interest in replacing food ingredients such as artificial sweeteners with these obtained by biotechnological processes has grown in recent years, due to consumer's high demand for low-calories foods and beverages without sacrificing taste. Several types of low caloric sweeteners are being obtained from the biotransformation of agricultural residues, with xylitol above all, for environmental, economic, and nutritional reasons. In recent years, the conversion of hydrolyzed agricultural residues into xylitol using enzymes, yeasts, and fungi has shown significant advances, although there are still many problems to be solved. This review presents the main advances in the use of microorganisms, substrates, and process conditions for the biotransformation of agricultural residues to xylitol. Besides, the main advantages and disadvantages of xylitol obtained by biotechnological routes compared to traditional chemical routes are discussed.

Keywords: Xylitol, agricultural residues, biotechnological pathways, sweeteners, food additives

RESUMEN

La valorización de residuos agrícolas ha sido un tema importante en las últimas décadas. Los desechos de cultivos agrícolas son una materia prima abundante, no alimenticia, renovable y de bajo costo útil para obtener productos atractivos para la industria alimenticia. El interés por reemplazar ingredientes alimenticios de origen sintético por aquellos obtenidos por procesos biotecnológicos ha crecido en los últimos años debido a la gran demanda de los consumidores por los alimentos y bebidas con bajo contenido calórico sin sacrificar el sabor. Varios tipos de edulcorantes de bajo contenido calórico se han obteniendo a partir de la biotransformación de residuos agrícolas, destacando de todos ellos el xilitol por razones ecológicas, económicas y nutricionales. En los últimos años, la conversión de hidrolizados de residuos agrícolas en xilitol utilizando enzimas, levaduras y hongos ha mostrado avances importantes, aunque aún existen muchos problemas por resolver. En esta revisión se presentan los principales avances en el uso de microorganismos, sustratos y condiciones de proceso para la biotransformación de residuos agrícolas en xilitol. Además, se discuten las principales ventajas y desventajas del xilitol obtenido por rutas biotecnológicas comparado con las rutas químicas tradicionales.

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Palabras clave: residuos agrícolas, rutas biotecnológicas, xilitol, edulcorante, aditivos alimenticios

INTRODUCTION

Xylitol ($C_5H_{12}O_5$) is a five-carbon sugar alcohol with a similar sweetness to sucrose but with 40% less caloric content. Xylitol is mainly used in the pharmaceutical, cosmetic, dental, and food industry (Mohamad *et al.*, 2015). In the food industry, the importance and high demand are mainly due to its low caloric content, low glycemic index and its lack of interfere with the nutritional value of food (Elamin *et al.*, 2012).

At an industrial level, xylitol is mainly produced by the catalytic hydrogenation of birch wood (Prakasham *et al.*, 2009). The process is based on the reduction of D-xyloses to xylitol using dilute acids, high temperatures, metal catalysts, high pressure, and multiple purification steps (Sousa-Aguiar *et al.*, 2014). The hard operation conditions of the process have caused an increase in xylitol price, about 10 times higher than sucrose or sorbitol, which has made this method not profitable (Ur-Rehman *et al.*, 2015). Due to these problems, alternative routes to obtain xylitol are being explored. One of the most promising is the biotechnological route, which use microorganisms capable of converting D-xyloses from hemicelluloses into xylitol. The *Candida* genus yeasts (*C. boidinii*, *C. tropicalis*, *C. guilliermondii*, and *C. shehatae*) are the most used to produce xylitol (Cristobal-Sarramian and Atzmüller, 2018; Ur-Rehman *et al.*, 2015).

Agricultural residues are feedstock with great potential to produce xylitol due to their high xylans content present in the form of hemicelluloses (Ur-Rehman *et al.*, 2015). Several studies have explored the biotechnological production of xylitol from many agricultural wastes such as rice husk (Hickert *et al.*, 2013), soybean hull (Cortivo *et al.*, 2018), corn cobs (Wei *et al.*, 2010), sugar cane bagasse (Vaz de Arruda *et al.*, 2017), sorghum bagasse (Ledezma-Orozco *et al.*, 2018), and rapeseed straw hemicellulosic hydrolysate (López-Linares *et al.*, 2018) obtaining interesting data.

In this work, we present an analysis of recent and important investigations related to the production of xylitol by biotechnological ways, covering the main agricultural residues used as feedstock, the main microorganisms used for this purpose, and the possible applications of xylitol in the food industry. Additionally, we review some advantages and disadvantages of the production of xylitol by biotechnological routes.

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Agricultural residues

Agricultural residues are any material that remains in the field after harvest such as mixture of stems, leaves, and pods, commonly called straws (Sun, 2010). The processing of crops seeds also generates large amounts of waste, like cobs and husks. Agricultural waste is an abundant source of organic compounds such as cellulose, hemicellulose, lignin, minerals, lipids, proteins, and pectins (Saini *et al.*, 2015). The integral use of these residues can contribute to reduce the adverse effects in the environment; for example, the pollution generated during the open burning of these residues, and at the same time, their transformation into useful products for some industries would help to reduce the production cost of cosmetics, medicines, and food additives (Sun, 2010) among others.

Chemical composition of agricultural residues

Another name for agricultural residues is lignocellulosic materials, because of their cell walls composition, a network of polysaccharides and cross-linked aromatic polymers. The predominant component in cell walls is cellulose, followed by hemicellulose and finally lignin (Peng and She, 2014); cellulose is covalently bound to the hemicellulose, filling the spaces between polysaccharides (Figure 1). Cellulose is the most abundant organic material in nature and constitutes 30-50 % of agricultural waste. Chemically, cellulose is a linear homopolymer formed by the binding of β -D-glucose monomers through β -1,4-O-glucosidic bonds. Cellulose has a linear structure connected by multiple hydrogen bonds between different glucose chains hydroxyl groups (Lee *et al.*, 2014). Such alignment in its structure produces the formation of a fibrous structure with crystalline zones and amorphous zones.

After cellulose, hemicellulose is the second most abundant polymer in the chemical composition of agricultural waste (25 and 35 %) (Table 1). Unlike cellulose, hemicellulose

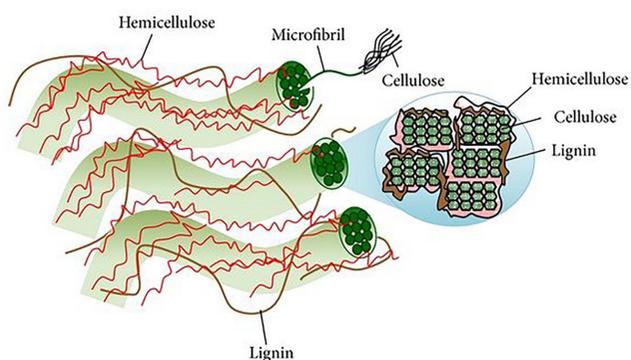


Figura 1. Estructura de la pared celular y sección transversal de las microfibras (cadenas de moléculas de celulosa incrustadas en un matriz de hemicelulosa y lignina). Adaptado de Lee *et al.*, 2014.

Figure 1. Plant cell wall structure and micro fibril cross-section (strands of cellulose molecules embedded in a matrix of hemicellulose and lignin). Adapted from Lee *et al.*, 2014.

lulose has a random, amorphous, branched structure with shorter chains composed of several heteropolymers such as xylans, glucomannans, arabinoxylans, galactomannans, and xyloglucans (Isikgor and Becer, 2015). The different heteropolymers that constitute hemicellulose are in turn, made up of 5- and 6-carbon monosaccharides (pentoses, hexoses, acetylated sugars, and uronic acid).

Table 1. Composición química de los principales residuos agrícolas.
Table 1. Chemical composition of the main agricultural wastes.

Agricultural waste	Cellulose (%)	Hemicelluloses (%)	Lignin (%)	References
Rice husk	31	22	22	(Kumar, 2010)
Wheat husk	36	18	16	(Bledzki <i>et al.</i> , 2010)
Barley husk	34	36	19	(Isikgor and Becer 2015)
Rice straw	43	34	22	(El-Tayeb <i>et al.</i> , 2012)
Wheat straw	40	34	17	(Jablonský <i>et al.</i> , 2015)
Barley straw	36	24	6	(Isikgor and Becer 2015)
Oat straw	31	20	10	(Isikgor and Becer 2015)
Corn stalks	35	19	6.9	(El-Tayeb <i>et al.</i> , 2012)
Sugarcane bagasse	47	27	21	(Rocha <i>et al.</i> , 2011)
Corn cob	41	13	35	(Cortivo <i>et al.</i> , 2018; Misra <i>et al.</i> , 2013)
Peanut shell	37	18	28	(Jaishankar <i>et al.</i> , 2014)
Almond shell	32	28	32	(Xie <i>et al.</i> , 2013)

Unlike cellulose and hemicellulose, lignin is a non-polysaccharide amorphous heteropolymer composed of multiple units of phenylpropane, which originate from three aromatic alcohols called monolignols: *p*-coumaryl alcohol, coniferyl alcohol, and sinapyl alcohol. During the lignification process, the connection of monolignols is through radical coupling reactions to form the lignin polymer. The aromatic constituents of the aromatic alcohols in the lignin polymer are known as *p*-hydroxyphenyl (H), guaiacyl (G) and syringyl (S) units. The proportion of these units varies according to the type of plant. The main bonds that make up the lignin polymer are carbon-oxygen and carbon-carbon type (β -O-4, α -O-4, 4-O-5, β -5, β -1, 5-5, β - β). The variability of bonds and monomeric units makes lignin a highly branched polymer, lacking regular order and repeatability. Also, lignin contains various functional groups, including aliphatic and aromatic hydroxyls, carbonyl, carboxyl, and methoxy groups (Buranov and Mazza, 2008).

BIOREFINERIES, BIOFUELS, AND SUB-PRODUCTS

A biorefinery is a structure capable of producing energy and products of commercial interest through the integral biomass processing (IEA bioenergy Task 42, 2008). The concept of biorefinery comprises a wide range of technologies capable of separating lignocellulosic biomass in its building blocks (carbohydrates, proteins, lipids, and aromatics compounds), where cellulose and lignin are used as precursors to obtain biofuels and chemical products; it is an analogous concept to oil refineries, which produce multiple fuels and petroleum-based products (Cherubini, 2010).

Studies predict that, due to global problems such as climate change and environmental pollution, associated with the increase in use fossil fuels, the constant increase in the prices of fossil resources and their uncertain availability, the viability of oil exploration will decrease soon. This makes the future of some chemical products and food additives, obtained through the chemical conversion of petroleum derivatives, uncertain. For these reasons, the conversion of lignocellulosic wastes into multiple products under the concept of the biorefinery is increasingly explored. Despite the significant advances achieved in this area, their focus is biofuel production (Cherubini, 2010). However, to obtain a significant advance and to get biorefineries commercialized, it is necessary to obtain multiple products besides biofuels. For this, the development of novel and efficient processes to generate valuable byproducts, as well as energy, is essential.

Under the objective of this review, the following sections describe and analyze recent research focused on the biotransformation of agricultural residues in sweeteners, specifically xylitol. Some of these investigations used a biorefinery scheme, taking advantage of the waste generated in the process of converting celluloses to biofuels. Other research focuses on exploring the feasibility of uncommon raw materials (abundant in hemicelluloses) to produce value-added compounds, the use of genetically improved microorganisms to achieve a higher conversion rate, and further research to evaluate the efficiency of fermentation processes to reduce costs and production times. Before reviewing the investigations related to obtaining xylitol using biotechnological routes, we include some essential aspects

of the sweeteners, xylitol, and the traditional chemical routes to obtain this sweetener.

SWEETENERS

Sweetener is any substance with the ability to impart a sweet taste to foods and beverages (Sharma *et al.*, 2016). The classification can depend on their origin, as natural or artificial, or depending on the caloric content, as high caloric content or low caloric content. There are around 40 different types of sweeteners (Table 2), although the most used in the food and beverage industry are of artificial origin, low caloric content, and high sweetening power. For example, the sweetening power of cyclamate is 24 to 40 times sweeter than sucrose; aspartame, and acesulfame are 100 to 200 times sweeter, while saccharin is 200 to 500 times sweeter. Xylitol has a sweetening power similar to sucrose, but with 40 % lower caloric content (Bellisle and Drewnowski, 2007). Some sweeteners can impart other attributes besides sweet taste, for example, mannitol, maltitol, xylitol, erythritol, and sorbitol add volume or texture to some foods.

¿Why sweeteners are being consumed?

Weight loss, dental care, diabetes mellitus, and hypoglycemia are among the reasons for consuming sweeteners or sugar substitutes (Sharma *et al.*, 2016). Sugar substitutes provide a pleasant taste on the palate but contain less caloric content, for this is possible to consume foods and beverages prepared with sugar substitutes without gaining weight (Bellisle and Drewnowski, 2007). Although the use of some artificial sweeteners for this purpose has been questioned (Tandel, 2011; Ur-Rehman *et al.*, 2015), sugar substitutes do not damage the teeth since the microflora of the dental plaque cannot ferment them, consequently, they do not promote the appearance of dental caries (Janakiram *et al.*, 2017; Nayak *et al.*, 2014). Patients with diseases such as diabetes can eat a varied diet when consuming foods prepared with low-calorie sugar substitutes (Kishore *et al.*, 2012). Finally, in patients with reactive hypoglycemia, eating a diet that includes foods that contain sweeteners instead of sugar can control insulin levels produced by the rapid absorption of glucose from the blood stream (Islam, 2011; Islam and Indrajit, 2012).

Tabla 2. Tipos de edulcorantes.

Table 2. Types of sweeteners.

Sweeteners					
Nutritive Sweeteners			Non-Sugar Sweeteners		
Sugars	Natural	Modified Sugars	Sugar Alcohols	Natural	Artificial
Sucrose			Sorbitol		
Dextrose			Xylitol	Stevia	Aspartame
Glucose	Honey		Mannitol	Thaumatococca	Saccharin
Fructose	Maple syrup	High-fructose corn syrup	Erythritol	Pentadin	Sucralose
Lactose	Palm sugar	Invert sugar	Maltitol	Monelina	Acesulfame
Maltose	Coconut sugar		Isomaltulose	Brazzein	Cyclamate
Galactose			Lactitol		Neohesperidin
Trehalose					

Today, people pay more attention to the calories they eat and ingredients in the food they ingest. Besides, they demand natural and ecologically friendly products that contain fewer calories, but without sacrificing attributes such as taste or texture of food. This has led to the investigation of new routes to obtain safer sweeteners for consumers, maintaining or even improving the characteristics of artificial sweeteners. An example of this is the biotechnological production of xylitol. Currently, xylitol is the only sweetener produced through the transformation of agricultural waste through biotechnological routes.

XYLITOL

Xylitol ($C_5H_{12}O_5$) is a five-carbon sugar alcohol with a similar sweetness relative to sucrose, but with lower caloric content. Xylitol contains 2.4 calories per gram, 40 % fewer calories than sugar (Zhang *et al.*, 2014). Naturally, xylitol is present in fruits, vegetables, and some fungi, although in such small amounts that it could not be used for commercial purposes (Ping *et al.*, 2013). On a large scale, xylitol is produced by the catalytic hydrogenation of D-xylose (Prakasham *et al.*, 2009). Xylitol is mainly used in the pharmaceutical, nutraceutical, dental, and food industries (Mohamad *et al.*, 2015). Its importance and high demand in food industry lies mainly in its low caloric content, low glycemic index and it does not interfere with the nutritional value of foods (Elamin *et al.*, 2012). Due to these attributes, the food market demands more and more xylitol production every year. Studies estimate that the demand for xylitol will increase from 190 million metric tons in 2016 to 250 million metric tons for the year 2022 (<http://industry-experts.com/verticals/food-and-beverage/xylitol-a-global-market-overview>). The growth of the alternative market for sweeteners and the increase in the search for low-calorie sweeteners are two critical factors that have contributed to the increase in demand for xylitol (Dasgupta *et al.*, 2017).

Production of xylitol by chemical routes

The industrial production of xylitol involves the chemical conversion of xyloses derived from hemicellulose hydrolysates rich in xylans from wood residues. In the chemical conversion process, highly pure xyloses are converted to xylitol by hydrogenation, in the presence of a metal catalyst (Ni, Ru, Rh), followed by several purification steps to remove toxic compounds (Figure 2). At the end of the process, xylitol is concentrated and recovered by crystallization, with a purity higher than 98% (Delgado Arcaño *et al.*, 2018).

The severe conditions of the chemical production process of xylitol (80-140 °C, 31-40 atm, 3-5 hours of reaction), the rigorous purification processes, the high energy demand and the moderate xylitol yield (between 50 and 60 % of xylitol with respect to total xylose) are leading to the search for new alternatives for its production. The use of biotechnological routes to obtain xylitol using lignocellulosic biomass has been reported as an interesting alternative (Vallejos and Area, 2017).

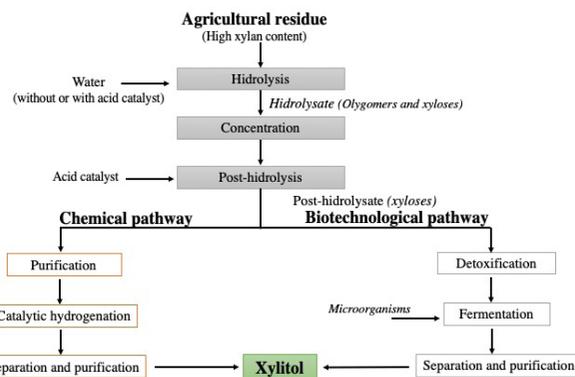


Figure 2. Producción de xilitol por ruta química y biotecnológica (Adaptado de Vallejos y Area, 2017).

Figure 2. Scheme of xylitol production by chemical or biotechnological pathways (Adapted from Vallejos and Area, 2017).

Production of xylitol for biotechnology routes

The basis for biotechnological production of xylitol from lignocellulosic materials resides on xyloses hydrogenation to form hemicelluloses, using several microorganisms such as yeast, bacteria, and fungi, of which, yeasts are best to produce xylitol (Figure 3). Yeasts of the genus *Candida* (*C. boidinii*, *C. tropicalis*, *C. guilliermondii* and *C. shehatae*) (López-Linares *et al.*, 2018), are the most used for the production of xylitol; in addition, the yeasts *Pachysolen tannophilus*, *Hansenula polymorpha*, *Debaryomyces hansenii* (Ledezma-Orozco *et al.*, 2018), and *Pichia guilliermondii* have also been used for this purpose, although to a lesser extent (Table 3). The preference for the genus *Candida* is due to the high yield of xylitol production, and for being efficient even under limited oxygen conditions. These microorganisms can produce xylitol as an intermediate metabolite of xylulose. For example, *Candida guilliermondii*, one of the most commonly used yeasts to obtain xylitol has two key enzymes in xylitol metabolism: (1) NADPH-dependent xylose reductase and (2) NADP⁺ dependent xylose dehydrogenase. The former reduces xylose to xylitol, and the latter oxidizes xylitol to xylulose, and both are induced by xylose (Silva *et al.*, 2004).

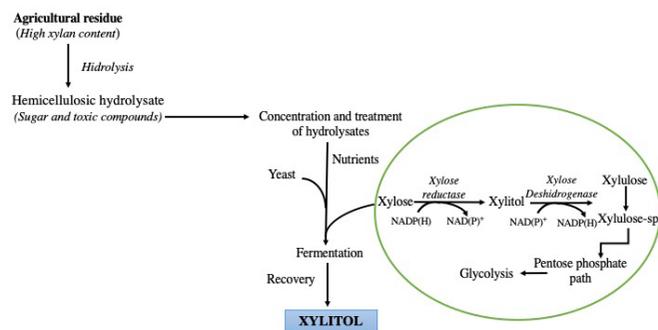


Figure 3. Producción biotecnológica de xilitol (Silva *et al.* 2004).

Figure 3. Biotechnological production of xylitol (Silva *et al.* 2004).

Research into xylitol production intensified not only because of the peculiarities of its flavor, but also for the possibility that fermentative processes becomes a viable alternative to current chemical routes. However, the toxic compounds obtained in the hydrolysates of agricultural residues have hampered the production of xylitol through fermentative processes of hydrolysates rich in xyloses. The most reported substrates for the microbial production of xylitol are acid hydrolysates of corn cob (Ping *et al.*, 2013), sugar cane bagasse (Unrean and Ketsub, 2018), oat husk (Cortivo *et al.*, 2018), rice and soybean husk (Cunha-Pereira *et al.*, 2017; Sehnem *et al.*, 2017) (Table 3).

These hydrolysates produce small amounts of toxic compounds such as furfural, acetic acid, and hydroxymethylfurfural (HMF), which can inhibit fermentation and adversely affect the yield of xylitol production. Acetic acid, for example, is a potent inhibitor of yeasts metabolism that convert xylose into xylitol and its effect depends on the concentration and fermentation time. To mitigate this problem, a frequent strategy prior to the hydrolysates fermentation is the use of detoxification processes using, for example, activated carbon (Delgado Arcaño *et al.*, 2018), saturation with lime (Mohagheghi *et al.*, 2006) or ion exchange resins (Kumar *et al.*, 2018). However, detoxification usually reduces the

efficiency of fermentation and requires additional facilities that increase xylitol production costs (Fehér *et al.*, 2018). The most feasible way to remove impurities and obtain xylitol while maintaining the biotechnological approach is the use of microorganisms that tolerate inhibitor compounds. These microorganisms can produce xylitol in adequate quantities in the presence of inhibitory compounds (Ledezma-Orozco *et al.*, 2018), high osmotic pressure, limited oxygen conditions even in combination with yeasts such as *S. cerevisiae* (Ping *et al.*, 2013). For example, Ledezma-Orozco *et al.* (2018) demonstrated that *D. hansenii* metabolizes xylose in the presence of acetic acid and furfural.

On the other hand, the combination of yeasts, such as *S. cerevisiae* and *C. tropicalis*, are used for the production of cellulosic ethanol (Sehnem *et al.*, 2017). Here, *S. cerevisiae* can ferment hexoses and *C. tropicalis* xyloses in a single step, obtaining ethanol from cellulose and xylitol from xyloses (Cheng *et al.*, 2014; Huang *et al.*, 2011; Mateo *et al.*, 2015).

In addition to the use of microorganisms tolerant to inhibitory compounds, there are reports on the use of ultrasonic waves that can improve the production of xylitol. Short intervals of ultrasonic waves applied during the fermentation of sugarcane bagasse hydrolysates can produce an increase of 17 to 20 % in the final yield of xylitol. This increase was attributed to the fact that sonication promotes the uptake

Tabla 3. Producción de xilitol por diferentes levaduras y condiciones de fermentación utilizando residuos lignocelulósicos como materias primas.

Table 3. Xylitol production by different yeasts and fermentation conditions using lignocellulosic waste as feedstock.

Microorganisms	Hydrolyzed feedstock	Fermentation conditions	Conversion yield of xylose to xylitol (g g ⁻¹)	References
<i>C. shehatae</i> HM 52.2	Rice husk	Reaction time 228 h Agitation 180 rpm Temperature 30 °C Aeration speed 0.33 vvm	0.11	(Hickert <i>et al.</i> , 2013)
<i>C. tropicalis</i> CCTCC M2012462	Corn cobs	Reaction time 100 h, Agitation 200 rpm Temperature 35°C, Aeration speed 0.4 vvm	0.71	(Ping <i>et al.</i> , 2013)
<i>C. tropicalis</i>	Corn cobs	Reaction time 66 h, Agitation 200 rpm, Temperature 30°C, pH 4.5	0.58	(Misra <i>et al.</i> , 2013)
<i>C. tropicalis</i> CICC1779	Corn cobs	Reaction time 24 h, Agitation 210 rpm, pH 6	0.77	(Jia <i>et al.</i> , 2016)
<i>C. guilliermondii</i> FTI 20037	Sugarcane bagasse	Reaction time 144 h, Agitation 450 rpm, Temperature 30°C, Aeration speed 0.7 vvm	0.69	(Vaz de Arruda <i>et al.</i> , 2017)
<i>W. anomalus</i> WA-HF5.5	Rice and soja husk	Reaction time 72 h, Agitation 180 rpm, Temperature 30°C, Aeration speed 0.33 vvm	0.86	(Sehnem <i>et al.</i> , 2017)
<i>Debaryomyces hansenii</i> and <i>C. guilliermondii</i>	Canola straw	Reaction time 72 h, Agitation 200 rpm Temperature 30°C	0.45 - 0.55	(López-Linares <i>et al.</i> , 2018)
<i>C. guilliermondii</i> BL 13	Soja husk	Reaction time 72 h, Agitation 180 rpm Temperature 23-33°C	0.46	(Cunha-Pereira <i>et al.</i> , 2017)
<i>S. cerevisiae</i> YRH 396 and <i>S. cerevisiae</i> YRH 400	Soja husk	Agitation 180-300 rpm, Temperature 28°C, Aeration speed 1 vvm, pH 5.5	0.45	(Cortivo <i>et al.</i> , 2018)

of xyloses, reduces the inhibitory effects of the substrate, improves the permeability of the cell membrane causing a rapid diffusion of nutrients from the substrate, which improves fermentation kinetics (Tizazu *et al.*, 2018a).

Recent work resumed the use of immobilized yeasts to produce xylitol, in combination with ultrasound. Tizazu *et al.* (2018b) reported the use of ultrasound to improve xylitol production from sugarcane bagasse using *C. tropicalis* MCC 184 immobilized in polyurethane foam. The results of their studies showed that the application of sonication and immobilized yeasts could double the yield of xylitol, and reduce the fermentation time (Tizazu *et al.*, 2018b). The advantages of the use of immobilized yeasts compared to the use of suspended yeasts are higher cell density within the bioreactor, greater productivity and stability, reuse of the yeasts, easy separation of the yeasts from the substrate and reduction of toxic products at the end of the process (Wang *et al.*, 2012).

Several scientific research reviewed the molecular strategies, challenges, progress and perspectives to improve biotechnological production of xylitol using lignocellulosic residues (Dasgupta *et al.*, 2017; Delgado Arcaño *et al.*, 2018; Naidu *et al.*, 2018; Pal *et al.*, 2016; Venkateswar Rao *et al.*, 2016). All of these investigations provide a clear idea of the advantages and disadvantages of xylitol production using biotechnological routes (Table 4). These investigations reported that more research is necessary related to the economic viability of the production of xylitol from lignocellulosic waste, the recovery and separation of xylitol from the fermentation media, the crystallization processes of xylitol, as well as parameters for scale the production of xylitol.

Tabla 4. Ventajas y desventajas de la producción de xilitol mediante rutas biotecnológicas.

Table 4. Advantages and disadvantages of xylitol production through biotechnological pathways.

Xylitol production through biotechnological pathways	
Advantages	Disadvantages
Use of renewable raw materials	Difficult recovery
Use of multiple microorganisms	Multiple steps of purification
Eco-friendly processes	Relatively long production times
Moderate production conditions	High production cost
Less generation of toxic effluents	Difficult to scale at industrial level
Lower price of xylitol	
Non-caloric sweetener	

Potential applications of xylitol in the food industry

Current uses of xylitol includes sweetener in jams, jellies, desserts, confectionery, chewing gum, and baked goods. The most important use has been as a substitute for sugar in confectionery products and baked goods (Ur-Rehman *et al.*, 2015). In confectionery products such as candy or chewing gum, the use of xylitol is important because it provides a quick source of sweetness, flavor, and a refreshing effect. In general, xylitol is used exclusively or in combination with other sugar substitutes of sugar-free chocolate, hard candies, and water fillings (Ur-Rehman *et al.*, 2015).

In baked products, xylitol reduces the caramelization of sugars, which produce a darkening of the product due to the Millard reactions that occur between sugars and proteins. These reactions do not occur by the addition of xylitol, since it does not contain aldehyde or ketone groups. Investigations on the potential application of xylitol include baked goods such as bread and biscuits. It has been shown that biscuits prepared by replacing sucrose with xylitol up to 50% are sensory acceptable, microbiologically safe and has a longer shelf life (Mushtaq *et al.*, 2010; Winkelhausen *et al.*, 2007).

The replacement of sucrose by xylitol (obtained from the biotechnological processing of banana peels) has been reported in the preparation of rusks (Rehman *et al.*, 2013). The addition of more than 50% of xylitol in this type of bread decreased color and increased hardness of the product (Muhammad *et al.*, 2012). The addition of xylitol affects the rheological properties of the dough; mainly, the addition of high percentages of xylitol produced a discontinuous matrix of gluten, which do not entirely covers the starch granules. Consequently, this affects the sensory quality of bread (Sun *et al.*, 2014). There are reports indicating that the optimum amount of xylitol to impart positive sensory attributes in baked wheat bread (volume, hardness, texture, crumb color, and flavor) is between 5% and 10%. Outside this range, xylitol deteriorates dough properties and consequently of the bread (Sun *et al.*, 2014). In addition, xylitol has great potential as humectant ingredient in foods because it is highly hygroscopic in nature, absorbs water in food (Mushtaq *et al.*, 2010), and it has low glass transition temperature T_g (20°C lower than sorbitol) (Young and O'Sullivan, 2011).

In general, although there is little information regarding the use of xylitol in bakery products, research shows that xylitol can be used to replace sugars in different products such as cookies, bread, rusk, and confectionary products without affecting their physicochemical characteristics and shelf stability.

CONCLUSIONS

The production of xylitol is growing continuously due to the high demand for the manufacture of products for oral hygiene, pharmaceuticals, cosmetics and food sweeteners (baked goods, jams, gelatins, chewing gum, ice cream, etc.). Besides, the consumption of xylitol has shown positive effects in the prevention or treatment of diseases such as diabetes and obesity. The production of xylitol using various agricultural residues and alternative routes to chemical routes is widely investigated. The development of biotechnological processes using improved microorganisms (yeast, fungi, bacteria, and microbial consortia), the use of ultrasonic waves, systems with immobilized microorganisms, among other strategies are helping to obtain xylitol and xylitol-based products safer for consumers, although for now with a price above those obtained by chemical synthesis. The xylitol cost production by biotechnological routes on an industrial scale depend on the technologies used to obtain and purify xylose, convert xylose to xylitol and recover/purify xylitol.

Research on the use of low-cost substrates, the development of multipurpose microorganisms capable of tolerating extreme working conditions and the regulation of processes may make it possible to produce xylitol economically feasible.

REFERENCES

- Bellisle, F. and Drewnowski, A. 2007. Intense sweeteners, energy intake and the control of body weight. *Eur J Clin Nutr*, 61(6), 691-700. 10.1038/sj.ejcn.1602649
- Bledzki, A.K., Mamun, A.A. and Volk, J. 2010. Physical, chemical and surface properties of wheat husk, rye husk and soft wood and their polypropylene composites. *Composites Part A: Applied Science and Manufacturing*, 41(4), 480-488. <https://doi.org/10.1016/j.compositesa.2009.12.004>
- Buranov, A.U. and Mazza, G. 2008. Lignin in straw of herbaceous crops. *Industrial Crops and Products*, 28(3), 237-259. <https://doi.org/10.1016/j.indcrop.2008.03.008>
- Cheng, K.-K., Wu, J., Lin, Z.-N. and Zhang, J.-A. 2014. Aerobic and sequential anaerobic fermentation to produce xylitol and ethanol using non-detoxified acid pretreated corncob. *Biotechnology for Biofuels*, 7(1), 166. 10.1186/s13068-014-0166-y
- Cherubini, F. 2010. The biorefinery concept: Using biomass instead of oil for producing energy and chemicals. *Energy Conversion and Management*, 51(7), 1412-1421. <https://doi.org/10.1016/j.enconman.2010.01.015>
- Cortivo, P.R.D., Hickert, L.R., Hector, R. and Ayub, M.A.Z. 2018. Fermentation of oat and soybean hull hydrolysates into ethanol and xylitol by recombinant industrial strains of *Saccharomyces cerevisiae* under diverse oxygen environments. *Industrial Crops and Products*, 113, 10-18. <https://doi.org/10.1016/j.indcrop.2018.01.010>
- Cristobal-Sarramian, A. and Atzmüller, D. 2018. Yeast as a production platform in biorefineries: conversion of agricultural residues into value-added products. *Agronomy Research*, 16(2), 377-388. <https://doi.org/10.15159/AR.18.066>
- Cunha-Pereira, F.d., Hickert, L.R., Rech, R., Dillon, A.P. and Ayub, M.A.Z. 2017. Fermentation of hexoses and pentoses from hydrolyzed soybean hull into ethanol and xylitol by *Candida guilliermondii* BL 13. *Brazilian Journal of Chemical Engineering*, 34 (4), 927-936.
- Dasgupta, D., Bandhu, S., Adhikari, D.K. and Ghosh, D. 2017. Challenges and prospects of xylitol production with whole cell bio-catalysis: A review. *Microbiological Research*, 197, 9-21. <https://doi.org/10.1016/j.micres.2016.12.012>
- Delgado Arcaño, Y., Valmaña García, O.D., Mandelli, D., Carvalho, W.A. and Magalhães Pontes, L.A. 2018. Xylitol: A review on the progress and challenges of its production by chemical route. *Catalysis Today*. <https://doi.org/10.1016/j.cattod.2018.07.060>
- El-Tayeb, T.S., Abdelhafez, A.A., Ali, S.H. and Ramadan, E.M. 2012. Effect of acid hydrolysis and fungal biotreatment on agro-industrial wastes for obtainment of free sugars for bioethanol production. *Brazilian journal of microbiology : [publication of the Brazilian Society for Microbiology]*, 43(4), 1523-1535. 10.1590/S1517-838220120004000037
- Elamin, K., Sjöström, J., Jansson, H. and Swenson, J. 2012. Calorimetric and relaxation properties of xylitol-water mixtures. *The Journal of Chemical Physics*, 136(10), 104508. 10.1063/1.3692609
- Fehér, A., Fehér, C., Rozbach, M., Rác, G., Fekete, M., Hegedűs, L. and Barta, Z. 2018. Treatments of Lignocellulosic Hydrolysates and Continuous-Flow Hydrogenation of Xylose to Xylitol. *Chemical Engineering & Technology*, 41(3), 496-503. 10.1002/ceat.201700103
- Hickert, L.R., da Cunha-Pereira, F., de Souza-Cruz, P.B., Rosa, C.A. and Ayub, M.A.Z. 2013. Ethanogenic fermentation of co-cultures of *Candida shehatae* HM 52.2 and *Saccharomyces cerevisiae* ICV D254 in synthetic medium and rice hull hydrolysate. *Bioresource Technology*, 131, 508-514. <https://doi.org/10.1016/j.biortech.2012.12.135>
- Huang, C.-F., Jiang, Y.-F., Guo, G.-L. and Hwang, W.-S. 2011. Development of a yeast strain for xylitol production without hydrolysate detoxification as part of the integration of co-product generation within the lignocellulosic ethanol process. *Bioresource Technology*, 102(3), 3322-3329. <https://doi.org/10.1016/j.biortech.2010.10.111>
- Isikgor, F.H. and Becer, C.R. 2015. Lignocellulosic biomass: a sustainable platform for the production of bio-based chemicals and polymers. *Polymer Chemistry*, 6(25), 4497-4559. 10.1039/C5PY00263J
- Islam, M.S. 2011. Effects of xylitol as a sugar substitute on diabetes-related parameters in nondiabetic rats. *J Med Food*, 14(5), 505-511. 10.1089/jmf.2010.0015
- Islam, M.S. and Indrajit, M. 2012. Effects of xylitol on blood glucose, glucose tolerance, serum insulin and lipid profile in a type 2 diabetes model of rats. *Ann Nutr Metab*, 61(1), 57-64. 10.1159/000338440
- Jablonský, M., Škulcová, A., Kamenská, L., Vrška, M. and Šíma, J. 2015. *Deep Eutectic Solvents: Fractionation of Wheat Straw* (Vol. 10).
- Jaishankar, M., Mathew, B.B., Shah, M.S., Murthy, K. and Gowda, K. 2014. Biosorption of few heavy metal ions using agricultural wastes. *Journal of Environment Pollution and Human Health*, 2(1), 1-6.
- Janakiram, C., Deepan Kumar, C.V. and Joseph, J. 2017. Xylitol in preventing dental caries: A systematic review and meta-analyses. *Journal of natural science, biology, and medicine*, 8(1), 16-21. 10.4103/0976-9668.198344
- Jia, H., Shao, T., Zhong, C., Li, H., Jiang, M., Zhou, H. and Wei, P. 2016. Evaluation of xylitol production using corncob hemicellulosic hydrolysate by combining tetrabutylammonium hydroxide extraction with dilute acid hydrolysis. *Carbohydrate Polymers*, 151, 676-683. <https://doi.org/10.1016/j.carbpol.2016.06.013>
- Kishore, P., Kehlenbrink, S., Hu, M., Zhang, K., Gutierrez-Juarez, R., Koppaka, S., . . . Hawkins, M. 2012. Xylitol prevents NEFA-induced insulin resistance in rats. *Diabetologia*, 55(6), 1808-1812. 10.1007/s00125-012-2527-z
- Kumar, P.S., Ramakrishnan, K., Kirupha, S. Dinesh, and Sivanesan, S. 2010. Thermodynamic and kinetic studies of cadmium adsorption from aqueous solution onto rice husk. *Brazilian Journal of Chemical Engineering*, 27(2), 347-355. <https://dx.doi.org/10.1590/S0104-66322010000200013>
- Kumar, V., Krishania, M., Preet Sandhu, P., Ahluwalia, V., Gnansounou, E. and Sangwan, R.S. 2018. Efficient detoxification of corn cob hydrolysate with ion-exchange resins for enhanced xylitol production by *Candida tropicalis* MTCC 6192. *Bioresource Technology*, 251, 416-419. <https://doi.org/10.1016/j.biortech.2017.11.039>
- Ledezma-Orozco, E., Ruíz-Salazar, R., Bustos-Vázquez, G., Montes-

- García, N., Roa-Cordero, V. and Rodríguez-Castillejos, G. 2018. Producción de xilitol a partir de hidrolizados ácidos no detoxificados de bagazo de sorgo por *Debaryomyces hansenii*. *Agrociencia*, 52, 1095-1106.
- Lee, H.V., Hamid, S.B.A. and Zain, S.K. 2014. Conversion of Lignocellulosic Biomass to Nanocellulose: Structure and Chemical Process. *The Scientific World Journal*, 2014, 20. 10.1155/2014/631013
- López-Linares, J.C., Romero, I., Cara, C., Castro, E. and Mussatto, S.I. 2018. Xylitol production by *Debaryomyces hansenii* and *Candida guilliermondii* from rapeseed straw hemicellulosic hydrolysate. *Bioresource Technology*, 247, 736-743. <https://doi.org/10.1016/j.biortech.2017.09.139>
- Mateo, S., Puentes, J.G., Moya, A.J. and Sanchez, S. 2015. Ethanol and xylitol production by fermentation of acid hydrolysate from olive pruning with *Candida tropicalis* NBRC 0618. *Bioresour Technol*, 190, 1-6. 10.1016/j.biortech.2015.04.045
- Misra, S., Raghuvanshi, S. and Saxena, R.K. 2013. Evaluation of corncob hemicellulosic hydrolysate for xylitol production by adapted strain of *Candida tropicalis*. *Carbohydrate Polymers*, 92(2), 1596-1601. <https://doi.org/10.1016/j.carbpol.2012.11.033>
- Mohagheghi, A., Ruth, M. and Schell, D.J. 2006. Conditioning hemicellulose hydrolysates for fermentation: Effects of overliming pH on sugar and ethanol yields. *Process Biochemistry*, 41(8), 1806-1811. <https://doi.org/10.1016/j.procbio.2006.03.028>
- Mohamad, N.L., Mustapa Kamal, S.M. and Mokhtar, M.N. 2015. Xylitol Biological Production: A Review of Recent Studies. *Food Reviews International*, 31(1), 74-89. 10.1080/87559129.2014.961077
- Muhammad, N., Salim ur, R., Fiaz, A. and Zarina, M. 2012. Biotechnological production of xylitol from dried banana peel hydrolysate and its impact on physicochemical properties of rusks. *Electronic Journal of Environmental, Agricultural and Food Chemistry*, 11(1), 2-14.
- Mushtaq, Z., Rehman, S.-u.-., Zahoor, T. and Jamil, A. 2010. Impact of Xylitol Replacement on Physicochemical, Sensory and Microbial Quality of Cookies. *Pakistan Journal of Nutrition*, 9(6), 605-610.
- Naidu, D.S., Hlangothi, S.P. and John, M.J. 2018. Bio-based products from xylan: A review. *Carbohydrate Polymers*, 179, 28-41. <https://doi.org/10.1016/j.carbpol.2017.09.064>
- Nayak, P.A., Nayak, U.A. and Khandelwal, V. 2014. The effect of xylitol on dental caries and oral flora. *Clinical, cosmetic and investigational dentistry*, 6, 89-94. 10.2147/CCIDE.S55761
- Pal, S., Mondal, A.K. and Sahoo, D.K. 2016. Molecular strategies for enhancing microbial production of xylitol. *Process Biochemistry*, 51(7), 809-819. <https://doi.org/10.1016/j.procbio.2016.03.017>
- Peng, P. and She, D. 2014. Isolation, structural characterization, and potential applications of hemicelluloses from bamboo: A review. *Carbohydrate Polymers*, 112, 701-720. <https://doi.org/10.1016/j.carbpol.2014.06.068>
- Ping, Y., Ling, H.-Z., Song, G. and Ge, J.-P. 2013. Xylitol production from non-detoxified corncob hemicellulose acid hydrolysate by *Candida tropicalis*. *Biochemical Engineering Journal*, 75, 86-91. <https://doi.org/10.1016/j.bej.2013.03.022>
- Prakasham, R.S., Rao, R.S. and Hobbs, P.J. 2009. Current trends in Biotechnological Production of Xylitol and Future Prospects. *Current Trends Biotechnology Pharmacy*, 3(1), 8-36.
- Rehman, S., Nadeem, M., Ahmad, F. and Mushtaq, Z. 2013. Biotechnological Production of Xylitol from Banana Peel and Its Impact on Physicochemical Properties of Rusks. *Journal of Agricultural Science and Technology*, 15(4), 747-756.
- Rocha, G.J.d.M., Martin, C., Soares, I.B., Maior, A.M.S., Baudel, H.M. and Abreu, C.A.M.d. 2011. Dilute mixed-acid pretreatment of sugarcane bagasse for ethanol production. *Biomass and Bioenergy*, 35(1), 663-670. 10.1016/j.biombioe.2010.10.018
- Saini, J.K., Saini, R. and Tewari, L. 2015. Lignocellulosic agriculture wastes as biomass feedstocks for second-generation bioethanol production: concepts and recent developments. *3 Biotech*, 5(4), 337-353. 10.1007/s13205-014-0246-5
- Sehnm, N.T., Hickert, L.R., da Cunha-Pereira, F., de Moraes, M.A. and Ayub, M.A.Z. 2017. Bioconversion of soybean and rice hull hydrolysates into ethanol and xylitol by furaldehyde-tolerant strains of *Saccharomyces cerevisiae*, *Wickerhamomyces anomalus*, and their cofermentations. *Biomass Conversion and Biorefinery*, 7(2), 199-206. 10.1007/s13399-016-0224-8
- Sharma, V.K., Ingle, N.A., Kaur, N., Yadav, P., Ingle, E. and Charania, Z. 2016. Sugar Substitutes and Health: A Review. *Journal of Advanced Oral Research*, 7(2), 7-11.
- Silva, D.D.V., Felipe, M.G.A., Mancilha, I.M., Luchese III, R.H. and Silva, S.S. 2004. Inhibitory effect of acetic acid on bioconversion of xylose in xylitol by *Candida guilliermondii* in sugarcane bagasse hydrolysate. *Brazilian Journal of Microbiology*, 35(3), 248-254. <https://dx.doi.org/10.1590/S1517-83822004000200014>
- Sousa-Aguiar, E.F., Appel, L.G., Zonetti, P.C., Fraga, A.d.C., Bicudo, A.A. and Fonseca, I. 2014. Some important catalytic challenges in the bioethanol integrated biorefinery. *Catalysis Today*, 234, 13-23. <https://doi.org/10.1016/j.cattod.2014.02.016>
- Sun, Q., Xing, Y. and Xiong, L. 2014. Effect of xylitol on wheat dough properties and bread characteristics. *International Journal of Food Science & Technology*, 49(4), 1159-1167. doi:10.1111/ijfs.12412
- Sun, R.C. (2010). *Cereal Straw as a Resource for Sustainable Biomaterials and Biofuels*.
- Tandel, K.R. 2011. Sugar substitutes: Health controversy over perceived benefits. *Journal of pharmacology & pharmacotherapeutics*, 2(4), 236-243. 10.4103/0976-500X.85936
- Tizazu, B.Z., Roy, K. and Moholkar, V.S. 2018a. Mechanistic investigations in ultrasound-assisted xylitol fermentation. *Ultrasonics Sonochemistry*, 48, 321-328. <https://doi.org/10.1016/j.ultsonch.2018.06.014>
- Tizazu, B.Z., Roy, K. and Moholkar, V.S. 2018b. Ultrasonic enhancement of xylitol production from sugarcane bagasse using immobilized *Candida tropicalis* MTCC 184. *Bioresource Technology*, 268, 247-258. <https://doi.org/10.1016/j.biortech.2018.07.141>
- Unrean, P. and Ketsub, N. 2018. Integrated lignocellulosic bioprocess for co-production of ethanol and xylitol from sugarcane bagasse. *Industrial Crops and Products*, 123, 238-246. <https://doi.org/10.1016/j.indcrop.2018.06.071>
- Ur-Rehman, S., Mushtaq, Z., Zahoor, T., Jamil, A. and Murtaza, M.A. 2015. Xylitol: A Review on Bioproduction, Application, Health Benefits, and Related Safety Issues. *Critical Reviews in Food Science and Nutrition*, 55(11), 1514-1528. 10.1080/10408398.2012.702288

- Vallejos, M.E. and Area, M.C. (2017). Chapter 12 - Xylitol as Bioproduct From the Agro and Forest Biorefinery. In Grumezescu , Holban (Eds.), *Food Bioconversion* (pp. 411-432): Academic Press.
- Vaz de Arruda, P., dos Santos, J.C., de Cássia Lacerda Brambilla Rodrigues, R., da Silva, D.D.V., Yamakawa, C.K., de Moraes Rocha, G.J., . . . das Graças de Almeida Felipe, M. 2017. Scale up of xylitol production from sugarcane bagasse hemicellulosic hydrolysate by *Candida guilliermondii* FTI 20037. *Journal of Industrial and Engineering Chemistry*, 47, 297-302. <https://doi.org/10.1016/j.jiec.2016.11.046>
- Venkateswar Rao, L., Goli, J.K., Gentela, J. and Koti, S. 2016. Bioconversion of lignocellulosic biomass to xylitol: An overview. *Bioresour Technol*, 213, 299-310. 10.1016/j.biortech.2016.04.092
- Wang, L., Wu, D., Tang, P., Fan, X. and Yuan, Q. 2012. Xylitol production from corncob hydrolysate using polyurethane foam with immobilized *Candida tropicalis*. *Carbohydrate Polymers*, 90(2), 1106-1113. <https://doi.org/10.1016/j.carbpol.2012.06.050>
- Wei, J., Yuan, Q., Wang, T. and Wang, L. 2010. Purification and crystallization of xylitol from fermentation broth of corncob hydrolysates. *Frontiers of Chemical Engineering in China*, 4(1), 57-64. 10.1007/s11705-009-0295-1
- Winkelhausen, E., Jovanovic-Malinovska, R., Velickova, E. and Kuzmanova, S. 2007. Sensory and Microbiological Quality of a Baked Product Containing Xylitol as an Alternative Sweetener. *International Journal of Food Properties*, 10(3), 639-649. 10.1080/10942910601098031
- Xie, R., Wang, H., Chen, Y. and Jiang, W. 2013. Walnut shell-based activated carbon with excellent copper (II) adsorption and lower chromium (VI) removal prepared by acid-base modification. *Environmental Progress & Sustainable Energy*, 32(3), 688-696. 10.1002/ep.11686
- Young, N.W.G. and O'Sullivan, G.R. (2011). 5 - The influence of ingredients on product stability and shelf life. In Kilcast , Subramaniam (Eds.), *Food and Beverage Stability and Shelf Life* (pp. 132-183): Woodhead Publishing.
- Zhang, J., Zhang, B., Wang, D., Gao, X. and Hong, J. 2014. Xylitol production at high temperature by engineered *Kluyveromyces marxianus*. *Bioresource Technology*, 152, 192-201. <https://doi.org/10.1016/j.biortech.2013.10.109>
- Research & Market. Xylitol – A Global Market Overview. [Consultado 12 noviembre 2018]. Disponible en: <http://industry-experts.com/verticals/food-and-beverage/xylitol-a-global-market-overview>