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Recent advances in xylitol production in biorefineries from lignocellulosic biomass: a review study

Avanços recentes da produção de xilitol em biorrefinarias com base em biomassas lignocelulósicas: um estudo de revisão

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ABSTRACT

The progression of sustainable practices in biorefineries is pivotal in mitigating carbon emissions and optimizing the utilization of natural resources, thereby preserving the environment. Biorefineries, which convert lignocellulosic biomass into a variety of products, distinguish themselves by efficiently transforming waste into high-value products. Xylitol stands out among biorefinery products. Derived from the conversion of xylose present in lignocellulose, it not only offers health benefits but is also considered an intermediate molecule in the production of valuable chemical products. Microbiological methods for xylitol production are increasingly acknowledged as efficient and environmentally friendly alternatives. These are some of the main factors discussed in this review, which aims to demonstrate the biotechnological route for producing xylitol through lignocellulosic materials. Several studies were observed to characterize various lignocellulosic residues, and it was noted that *Eucalyptus globulus* and banana leaves exhibit high levels of xylose. By analyzing the most recent researches related to xylitol production, the possibility of co-production of bioethanol using the same biotechnological route of xylitol production was identified. For instance, studies have shown that a combination of bagasse and sugarcane straw, as well as rice straw residue, are capable of producing substantial levels of xylitol and ethanol. The yields reached 30.61 g/L of xylitol and 47.97 g/L of ethanol, and 34.21 g/L of xylitol and 2.12 g/L of ethanol, respectively. These innovations not only promote sustainability but also have the potential to generate positive impacts on the global economy.

Keywords: waste; lignocellulose; biotechnological route; xylose.

RESUMO

O avanço das práticas sustentáveis nas biorrefinarias desempenha um papel crucial na mitigação das emissões de carbono e na utilização eficiente dos recursos naturais, preservando o meio ambiente. As biorrefinarias, que convertem biomassa lignocelulósica em uma variedade de produtos, destacam-se pela capacidade de transformar resíduos em produtos de alto valor agregado. Entre os produtos da biorrefinaria, o xilitol destaca-se. Ele é obtido pela conversão da xilose presente na lignocelulose e oferece benefícios à saúde, sendo considerado uma molécula intermediária na produção de valiosos produtos químicos. Os métodos microbiológicos na produção de xilitol são cada vez mais reconhecidos como uma alternativa eficiente e ambientalmente amigável. Esses são alguns dos principais fatores discutidos nesta revisão, que visa demonstrar a rota biotecnológica de produção do xilitol com o uso de materiais lignocelulósicos. Vários estudos foram observados quanto à caracterização de diversos resíduos lignocelulósicos, e notou-se que o *Eucalyptus globulus* e a folha de bananeira apresentam altos teores de xilose. Ao se analisarem as pesquisas mais recentes relacionadas à produção de xilitol, foi identificada a possibilidade de coprodução de bioetanol na mesma rota biotecnológica de produção do xilitol. Por exemplo, estudos demonstraram que a mistura do bagaço e a palha da cana-de-açúcar, bem como o resíduo de palha de arroz, foram capazes de produzir níveis elevados de xilitol e etanol, atingindo 30,61 g/L de xilitol e 47,97 g/L de etanol e 34,21 g/L de xilitol e 2,12 g/L de etanol, respectivamente. Essas inovações não apenas promovem a sustentabilidade, mas também têm o potencial de gerar impactos positivos na economia global.

Palavras-chave: resíduos; rota biotecnológica; xilose.

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Introduction

The implementation of sustainable procedures in biorefineries is crucial for mitigating climate change by reducing carbon emissions, promoting efficient resource utilization, and fostering innovations that contribute to shaping a more ecological future. Furthermore, it constitutes an integral component of the global endeavor to attain environmental goals and secure the long-term health of our planet (Bhowmick et al., 2018; Usmani et al., 2021).

Biorefineries are processing facilities that transform raw biomass materials into a diverse array of bioproducts. By transforming waste and by-products into high-value-added products, biorefineries not only contribute to sustainability but also generate additional revenue, fostering recycling and circular economy practices (Velvizhi et al., 2022; Santos et al., 2023).

A lignocellulosic biomass constitutes the organic material present in plants, representing a promising source of raw material for various industries, as it is the most abundant sustainable carbon resource worldwide (Dharmaraja et al., 2023). The structure of lignocellulosic biomass may vary according to the type of material, but generally, it is composed of cellulose and hemicellulose polysaccharides, interconnected by the lignin polymer (Ning et al., 2021).

The valorization of vegetal biomass waste (i.e., residues of lignocellulosic biomass materials) presents a viable alternative for the production of bioproducts in biorefineries (Chen et al., 2023). Over 200 value-added compounds have already been developed from lignocellulosic biomass, employing numerous treatment techniques (Usmani et al., 2021).

The depolymerization of lignocellulosic biomass polysaccharides generates sugars, which are then used as platform molecules for the production of higher value-added products such as ethanol, methanol, biodiesel, hydrogen, furfurals, resins, xylitol, bioplastics, etc. (Ning et al., 2021; Velvizhi et al., 2022). These are a variety of products derived from biomass with industrial applications in the pharmaceutical, chemical, electrical, and petroleum sectors, offering the potential for diverse applications (Zhou and Wang, 2020).

A substantial portion of hemicellulose consists of xylose sugar fractions. A notable compound originating from xylose conversion is xylitol, a substance exclusively derived from plant biomass (Mohamad et al., 2015). Xylitol is of great relevance, with significant applications in the pharmaceutical, dental, and food industries, besides being a valuable intermediate in the synthesis of various chemical commodities (Hernández-Pérez et al., 2019).

Hence, there is a belief that xylitol, as a cost-effective substitute for petrochemical products in chemical processes, could have a significant positive impact on the global economy, contributing to its valorization (Hernández-Pérez et al., 2019; Queiroz et al., 2022). In this context, technologies inherent to biorefinery processes aimed at xylitol production, through the efficient use of waste, become more attractive, outlining themselves as highly sustainable production systems (Queiroz et al., 2022).

Currently, large-scale production of xylitol is predominantly carried out through chemical reduction reactions of D-xylose, occurring under high pressure and temperature conditions. This method is costly, complex, time-consuming, and environmentally harmful (Xu Yirong et al., 2019). In this regard, researchers have turned their attention to microbiological methods in xylitol synthesis, due to the advantages they offer, such as lower energy consumption and lower costs during the process. In this approach, xylitol production from xylose is based on the use of biomass hydrolysate, proving to be energetically efficient and ecologically justified (Xu Yirong et al., 2019).

This review provides a summary of recent advances in xylitol biosynthesis strategies. It begins with a brief introduction to the operation of biorefineries and the relevance of using lignocellulosic biomass. Next, the chemical properties of xylitol and its various applications are explored, with special emphasis on its role as an intermediate molecule in the production of high-value-added chemical products.

Furthermore, this review addresses the primary stages of xylitol bioproduction, encompassing pre-treatment techniques with emphasis on acid hydrolysis, methods for detoxifying the hydrolysate, bioconversion process from xylose to xylitol, and ultimately, purification, recovery, and crystallization techniques for xylitol. In the concluding remarks, the importance of choosing a lignocellulosic biomass raw material rich in xylose is highlighted, as well as the possibility of co-producing other fermentation products alongside xylitol.

Methodology Of Systematic Review

SciFinder was selected as the primary database for this study, covering the period from 2018 to 2023 (five years). Additionally, supplementary sources, including Google Scholar and ScienceDirect, were utilized to complement the research. The initial article selection was based on literature data related to the term "xylitol biomass." Subsequently, data refinement was conducted to identify significant advances in the field through keyword searches like "biomass waste", "biotechnological route", and "xylose". The outcome of this process emphasized the relevance of the literature, resulting in the identification of 53 articles that underwent a more in-depth analysis.

Biorefineries And The Use Of Lignocellulosic Biomass

Biorefineries are facilities that utilize biomass as their primary raw material source to achieve integrated production of energy, chemical platforms, and biomaterials, many of which are renewable. Through the comprehensive utilization of biomass, it is possible to extract various high-value bioproducts, thereby fostering accelerated growth in the bio-based circular economy (Velvizhi et al., 2022).

The primary sources of lignocellulosic biomass include forest residues, agricultural residues, energy crops, organic municipal solid waste, and industrial residues (wood, paper, cellulose) (Ashokkumar et al., 2022). Characterized as a sustainable organic source with low carbon emissions, low cost, and easy accessibility, it does not compromise the global food supply. Besides, lignocellulosic biomass has notable potential as a renewable energy source and provides a viable alternative to mitigate global climate change (Asim et al., 2019; Li et al., 2019).

The composition of lignocellulosic biomass is highly diverse, with a complex hierarchical structure consisting mainly of cellulose (35–50%), hemicellulose (20–35%), and lignin (5–30%), along with other minor components such as minerals, acetyl, and phenolic groups (Patel and Shah, 2021). During the conversion process, this biomass typically releases 5- and 6-carbon sugars, which can then be converted into biofuels (e.g., bioethanol, biohydrogen, among others) and valuable biochemical compounds (e.g., xylitol, furfural, organic acids, among others), as illustrated in Figure 1 (Suhartini et al., 2022).

Among the main components of lignocellulosic biomass, hemicellulose is the most accessible and susceptible to decomposition through enzymatic agents, owing to its random and amorphous structure. Hemicelluloses are built by heterogeneous, complex, and highly branched polymers, including a variety of sugars such as glucose, arabinose, xylose, galactose, and mannose, along with organic acids like acetic acid and glucuronic acid (Hoang et al., 2021).

About 90% of hemicellulose comprises xylose fractions. Apart from its potential application in ethanol production, the conversion of xylose from biomass facilitates the production of other high-value-added products. Xylitol, a prominent compound resulting from xylose conversion, is exclusively derived from biomass, with no available petrochemical alternative (Arcaño et al., 2020).

Being a platform molecule, xylitol possesses significant chemical properties for several industries and can undergo diverse transformation processes to yield numerous compounds (Irmak et al., 2017). In this context, studies have explored various biorefinery scenarios for xylitol production, utilizing different lignocellulosic biomass residues as raw materials.

Considering the presented context and underscoring the significance of this study, a literature review of the past 20 years was conducted to analyze the frequency of articles addressing the topic "xylitol" with a focus on residual biomass. Figure 2 illustrates the results of this work, revealing a notable exponential growth of 93% between 2000 and 2021, reflecting recent advancements in addressing this topic. This growth reinforces the relevance and purpose of this work.

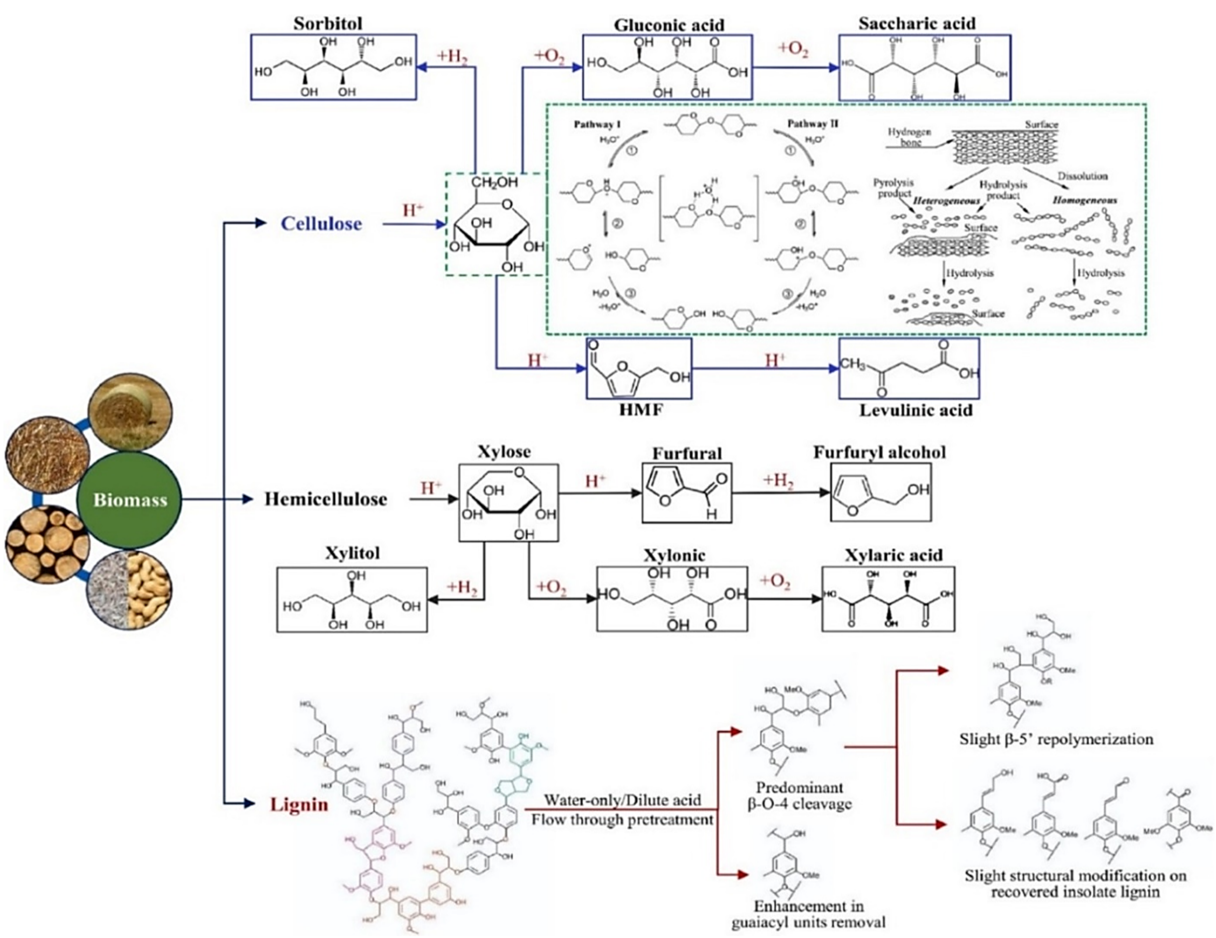

Figure 1 – Conversion of cellulose, hemicellulose, and lignin into their potential products.
Source: Hoang et al. (2021).

Xylitol

Xylitol is a five-carbon sugar alcohol with numerous advantageous properties. It exists as a white crystalline powder with the empirical formula $C_5H_{12}O_5$ and a molecular weight of 152.15 g/mol, being highly soluble in water (Xu Linlin et al., 2019; Saravanan et al., 2023). Discovered in the late 19th century, xylitol is naturally extracted in low concentrations from various foods, including fruits, vegetables, and mushrooms (Benahmed et al., 2020).

In the food industry, its use is beneficial as it does not contribute to food browning reactions (Arcaño et al., 2020). In the dietary industry, it is used as an artificial sweetener due to its sweet taste and low caloric value. It undergoes metabolism through an insulin-independent pathway, making it a suitable substitute for glucose in individuals with diabetes (Peterson, 2013; Kaur et al., 2022). In the pharmaceutical and medical fields, xylitol exhibits anticariogenic properties and is also employed in the treatment of diabetes, osteoporosis, ear infections, and respiratory infections (Benahmed et al., 2020; Umai et al., 2022).

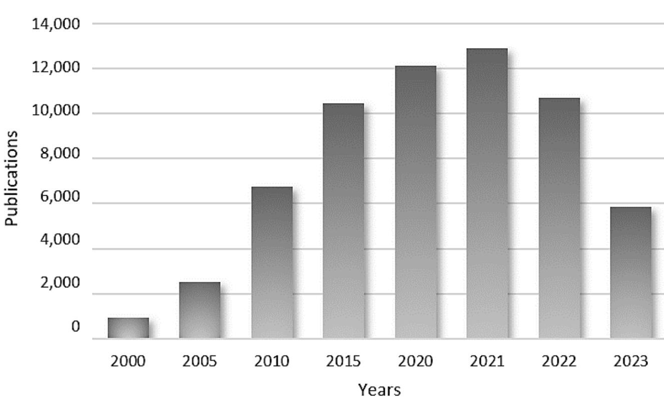

Figure 2 – Number of publications involving xylitol per year according to the SciFinder database, using the search term "xylitol biomass".

Numerous lignocellulosic residues have the potential for use in biorefineries due to their composition, which is rich in hemicellulose and, consequently, contains a significant amount of xylose, the precursor sugar of xylitol (Table 1).

Observations derived from the lignocellulosic composition of residues indicate the feasibility of obtaining substantial amounts of sugars, thus opening perspectives for the production of bioproducts in biorefineries. Igreja et al. (2023) emphasized a substantial percentage of hemicellulose, reaching 58.00% in açai seeds, indicating notable potential for production in biorefineries. Similarly, both babassu mesocarp and banana leaf revealed high percentages of hemicellulose and cellulose, registering 34.11% hemicellulose and 33.55% cellulose, and 32.59% hemicellulose and 29.39% cellulose, respectively (Brito Junior et al., 2020; Shankar et al., 2020).

Eucalyptus globulus and banana leaf exhibit high levels of xylose, reaching 36.01 g/L and 18.32 g/L, respectively (Shankar et al., 2020; Bonfiglio et al., 2021). This phenomenon is attributed to the high proportions of polysaccharides in lignocellulosic biomasses, resulting in the formation of substantial sugar yields.

Figure 3 illustrates that, in addition to xylitol, a variety of compounds can be obtained from xylose, including succinic, acetic, lactic, and butyric acids, butanol, 2,3-butanediol, acetoin, acetone, propanol, furfural, and xylitol. Xylitol was classified in 2004 by the United States Department of Energy (DOE) as one of the twelve key compounds for forming chemical platforms (Xu Yirong et al., 2019).

Hence, studies demonstrate that xylitol serves as a promising chemical molecule, acting as a building block for high-value compounds in biorefineries. Products derivable from xylitol through hydrogenolysis include ethylene glycol, propylene glycol, lactic acid, and glycerol. Xylitol oxidation allows for the formation of xylaric and xylonic acids. Additionally, a mixture of furans can be obtained through

Table 1 – Chemical composition of different lignocellulosic residues.

Biomass	Hemicellulose	Cellulose	Lignin	Glucose	Xylose	Reference
Açaí seeds	58.00%	3.60%	11.60%	1.30 g/L	1.90 g/L	Igreja et al. (2023)
Butia odorata seed husk	17.71%	11.71%	8.40%	0.98 $g/100g_{biomass}$	1.62 $g/100g_{biomass}$	Gallon et al. (2023)
Rice straw	22.68%	35.80%	22.41%	2.97 g/L	15.45 g/L	Kaur et al. (2022)
Cupuassu peel	10.13%	49.43%	11.36%	25.00%	6.16%	Marasca et al. (2022)
Almond endocarp	26.82%	33.47%	25.54%	0.13 g/L	11.43 g/L	Malayil et al. (2022)
Barley husk	14.30%	11.80%	12.00%	2.37 g/L	1.26 g/L	Soares et al. (2022)
Soybean husk and straw	9.70%	24.30%	15.00%	2.01 g/L	1.99 g/L	
Wheat straw	15.30%	33.00%	17.40%	2.32 g/L	4.52 g/L	
Eucalyptus globulus	25.00%	31.80%	31.20%	7.82 g/L	36.01 g/L	Bonfiglio et al. (2021)
Banana peel	7.30%	21.10%	14.10%	8.20 g/L	1.20 g/L	Araújo et al. (2021)
Banana leaf	32.59%	29.39%	15.35%	3.21 g/L	18.32 g/L	Shankar et al. (2020)
Apple pomace	23.60%	32.62%	25.38%	6.93 g/L	11.10 g/L	Leonel et al. (2020)
Coconut mesocarp	30.61%	30.50%	26.64%	22.47%	11.63%	Brito Junior et al. (2020)
Brazil nut endocarp	23.12%	23.33%	50.25%	14.14%	11.24%	
Babassu mesocarp	34.11%	33.55%	29.97%	16.70%	28.30%	

the hydrodeoxygenation of xylitol. Direct polymerization can result in the formation of polyesters and nylons (Figure 3) (Arcaño et al., 2020).

The increasing demand for xylitol in recent years has propelled significant growth in the global xylitol industry, as depicted in Figure 4. From 2016 to 2020, the global xylitol market witnessed substantial growth. Projections for the period 2020 to 2028 indicate continuous growth, with an estimated compound annual growth rate (CAGR) of 2.59%. This means that the market value, which was \$0.90 billion in 2020, is expected to reach \$1.10 billion by 2028 (Kaur et al., 2022; VMR, 2022).

This trend is expected to grow, given the diverse resources of lignocellulosic biomass available, providing xylose for xylitol production. This is confirmed when one observes that a relevant portion of the hemicellulose in lignocellulosic biomass consists of xylose. Consequently, the use of biomass in xylitol production demonstrates considerable potential, revealing its significant importance from both economic and social perspectives (Benahmed et al., 2020).

Bioproduction of Xylitol

Industrially, xylitol is produced via the catalytic hydrogenation of xylose in a three-phase process, employing a metallic catalyst. However, certain factors negatively impact the economic viability of xylitol, including the use of high-value reagents, severe reaction conditions involving high energy consumption due to elevated temperatures and pressures, and the necessity for additional steps in xylitol purification. These factors contribute to making xylitol a high-cost product compared to other sugar and alcohol options currently available in the market (Queiroz et al., 2022).

Recent advances have highlighted the biotechnological route as a potential alternative to the chemical route for xylitol production (Araújo et al., 2022; Vardhan et al., 2022; Bhavana et al., 2023). This technique relies on the use of microorganisms, such as bacteria, fungi, and yeasts, to carry out xylose fermentation. In this process, xylitol is generated as a byproduct of fermentation, particularly when microorganisms are unable to oxidize it into xylulose (Suhartini et al., 2022). This method consumes less energy and is environmentally friendly, avoiding high costs throughout the process (Xu Yirong et al., 2019). Besides, this route may provide another energy advantage by promoting the co-production of energy in a biorefinery through the burning of generated solid waste (Queiroz et al., 2022).

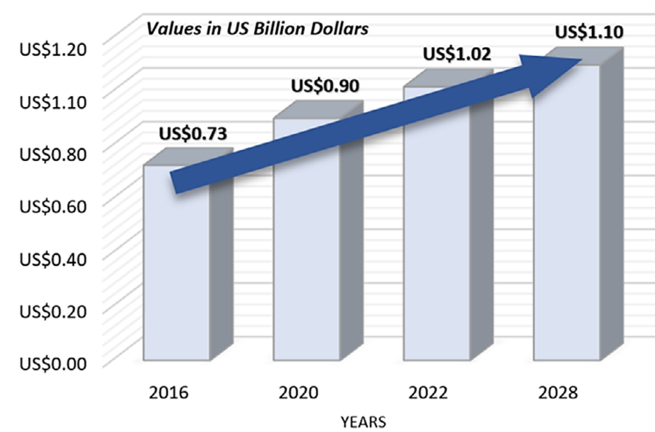

Figure 4 – Global xylitol market projections.
Source: Kaur et al. (2022) and VMR (2022).

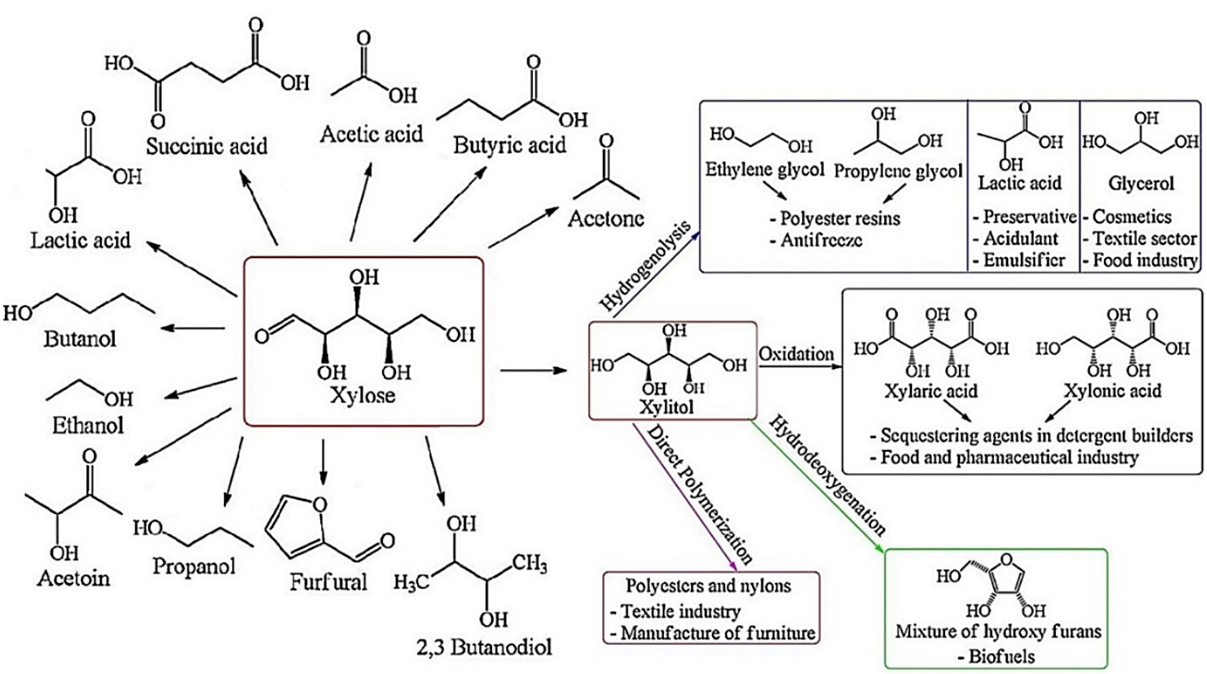

Figure 3 – Compounds obtained from xylose.
Source: adapted from Arcaño et al. (2020).

Since certain inhibitors (acetic acid, hydroxymethylfurfural, furfural, total phenolic acid, formic acid, levulinic acid) may form during xylose conversion, negatively impacting xylitol production, this process has its limitations (Suhartini et al., 2022). These compounds can negatively impact cell growth and microbial fermentation, reducing the sugar absorption rate, leading to a subsequent decrease in the production of the target product, necessitating detoxification before fermentation.

The key steps in the biotechnological production of xylitol include: 1. Pretreatment of lignocellulosic biomass; 2. Hydrolysis; 3. Concentration and detoxification of hemicellulosic hydrolysate; 4. Bioconversion of xylose to xylitol; and 5. Purification, recovery, and crystallization of xylitol (Figure 5).

Lignocellulosic biomass pretreatment

Biomass pretreatment is the initial step in the process designed to break down the recalcitrant structure, increasing the surface area for xylose recovery, which will be used as a precursor for xylitol production (Queiroz et al., 2022). This stage is economically viable as it enhances the conversion efficiency, subsequently improving the overall process efficiency (Santos et al., 2023).

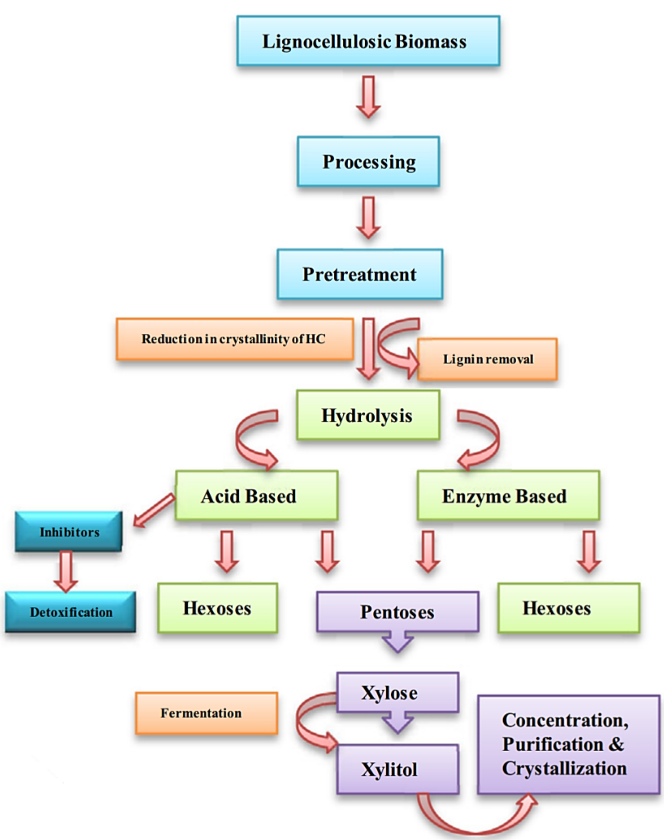

Figure 5 – Biotechnological production steps of xylitol.
Source: adapted from Rao et al. (2016).

Methods for pretreating lignocellulosic biomass can be categorized into: physical (microwaves and ultrasound), chemical (dilute acid, alkaline, among others), physicochemical (hydrothermal, ammonia-based), and biological (microorganisms). The choice of pretreatment is determined by the biomass crystallinity, degree of polymerization, and surface area, facilitating degradation (Suhartini et al., 2022).

Physical pretreatment methods are often employed as a preliminary step to other procedures, enhancing the subsequent process effectiveness by increasing biomass biodegradability by 20%. Their goal is to reduce the degree of polymerization and expand the surface area (Ahmed et al., 2022). Techniques such as microwave irradiation and ultrasound enable biomass fragmentation with higher energy efficiency, reducing production costs and increasing material porosity. However, they exhibit limited sugar release (Dharmaraja et al., 2023).

Cell rupture using physical methods is efficient, protecting biomass cells from contamination and ensuring material functionality during this process (Onumaegbu et al., 2018). However, it does not promote lignin and hemicellulose removal, necessitating the use of other pretreatment methods for the decomposition of these components (Ning et al., 2021).

Physical-chemical methods are employed in different lignocellulosic materials to produce simple fermentable sugar content. Hydrothermal pretreatment is an attractive option, using only high-temperature water without the addition of chemical solvents (Umai et al., 2022). However, the method requires a high amount of energy due to the use of large volumes of water (Dharmaraja et al., 2023).

Biological pretreatment methods offer several advantages, including low cost, minimal energy consumption, minimal inhibitor formation, and little dependence on chemicals, making them a more ecological alternative (Dharmaraja et al., 2023). However, the conversion into by-products is low, and lignin degradation is minimal, which is unfavorable for the next stage (Arcaño et al., 2020).

Chemical pretreatments are commonly used in lignocellulosic biomass pretreatment technologies. Alkaline pretreatment is highly efficient at delignifying lignocellulose, enabling greater enzymatic hydrolysis and resulting in fewer by-products. It can be considered a less harmful and corrosive chemical method, widely used as a safe solvent in hydrolysis or extraction processes. However, the hemicellulose conversion rate is low, which disadvantages this method (Arcaño et al., 2020; Suhartini et al., 2022).

Dilute acid pretreatment is widely recognized as the most effective method for hemicellulose solubilization (Ur-Rehman et al., 2015). This process facilitates cellulose fraction accessibility in subsequent steps. However, its disadvantage lies in the chemical residues generated, and acid use can lead to reactor corrosion, reducing equipment lifespan (Umai et al., 2022). Therefore, reaction conditions should be chosen to maximize xylose yield and minimize the formation of undesirable by-products.

Several studies have shown that a simple lignocellulosic biomass pretreatment method does not yield efficient results regarding its degradability. Combined pretreatment processes, integrating two or more technologies, are shown to be more effective in lignocellulosic biomass pretreatment when compared to the application of a single method (Dharmaraja et al., 2023; Santos et al., 2023). Due to the wide variety of available biomasses, determining the single most efficient method becomes challenging. The choice will primarily depend on the material characteristics and the intended use of biomass.

Hydrolysis

After pretreatment, the lignocellulosic material must be hydrolyzed into its monomeric sugar constituents. Acid hydrolysis is one of the oldest and most widely employed technologies to convert lignocellulose into fermentable sugars. Compared to other hydrolysis methods, acid hydrolysis excels at converting xylan into xylose due to its rapid hydrolysis rate, high reactivity and solubility of carbohydrates, and high delignification (Zhou et al., 2021). This makes xylose the most abundant sugar released in the hydrolysate (Rafiqul and Mimi Sakinah, 2013).

There are two main types of acid hydrolysis processes commonly adopted: diluted acid hydrolysis and concentrated acid hydrolysis. Concentrated acid hydrolysis has a significant advantage as it can be conducted at low temperatures, offering a higher sugar yield with minimal degradation. Sulfuric acid (H_2SO_4) is the most commonly used due to its accessibility and reduced cost. However, other acids such as hydrochloric, sulfurous, fluorhydric, and nitric acids can be used as alternatives (Zhou et al., 2021).

Concentration and detoxification of hemicellulosic hydrolysate

Nevertheless, hydrolysis can lead to the generation of contaminants, including furfural, a heterocyclic aldehyde derived from pentose degradation, and hydroxymethylfurfural (HMF), which results from hexose dehydration (Figure 6). In the biotechnological conversion route, the presence of furfural and HMF significantly and adversely affects the microorganism's specific growth rate and bioproduct formation. In essence, these compounds impact the entire fermentation process (Guo et al., 2022).

Consequently, following the acquisition of xylitol-rich hemicellulosic hydrolysate, a detoxification step is necessary to eliminate or reduce inhibitory compounds, thereby enhancing yeast fermentative performance during xylitol conversion. This process, often denoted as xylose purification or concentration in biotechnology, eliminates toxic compounds, resulting in purer and more concentrated xylose for biotechnological applications (Arcaño et al., 2020). This step plays a crucial role in improving the efficiency of the entire biological process (Queiroz et al., 2022).

Several approaches have been suggested to meet this challenge. Among the strategies employed are: adsorption on activated carbon and ion exchange resins, nanofiltration (i.e., membrane separation), reverse osmosis, vacuum membrane distillation, electrochemical processes, and biological approaches, such as the use of microorganisms, exemplified by *Coniochaeta ligniaria*, or enzymes like laccases and peroxidases (Suhartini et al., 2022).

Activated carbon is deemed a sustainable alternative that demands less infrastructure. Derived through pyrolysis, it exhibits high porosity, a large surface area, and various multifunctional groups. Additionally, it is a low-cost material (Qi et al., 2021). Thus, the use of activated carbon has been recognized as effective in eliminating inhibitory compounds present in hydrolysates. Klasson et al. (2011) and Li et al. (2014) observed significantly high removal rates of HMF and furfural with activated carbon, with efficiency reaching up to 100% in furfural removal.

Besides detoxification strategies, some researchers explore the utilization of microorganisms resistant to inhibitory compounds as a means to bypass the detoxification step in the xylitol biosynthesis route. Strains such as *Issatchenkia occidentalis* and *I. orientalis* demonstrate effectiveness in degrading inhibitory compounds present in hemicellulosic hydrolysates, resulting in substantial improvements in xylitol productivity and yield (Xu Yirong et al., 2019). However, further research is needed to prove the effectiveness of this method for large-scale industrial applications.

Bioconversion of xylose to xylitol

In the next step, the detoxified hydrolysate is used as a source of xylose in xylitol production. Compared to conventional methods, the biological route serves as an attractive alternative due to its relatively easy process, low chemical requirements, high product yield, high purity, and fewer downstream processing steps (Kaur et al., 2022).

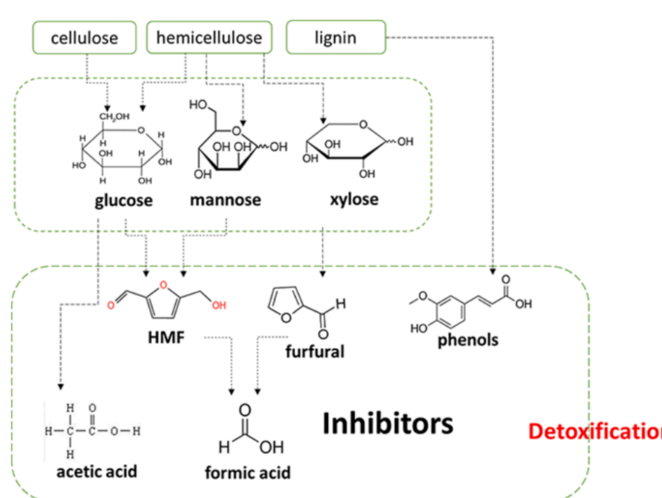

Figure 6 – Formation of furfural and hydroxymethylfurfural inhibitors.
Source: Guo et al. (2022).

To achieve this, various microorganisms possess the intrinsic ability to synthesize xylitol through xylose metabolism, naturally utilizing pentose sugars as a carbon source (Umai et al., 2022). Although bacteria, fungi, and yeasts have been mentioned in the literature for xylose to xylitol conversion, yeasts are widely recognized as the best in terms of xylitol production efficiency (Xu Yirong et al., 2019).

Yeast strains *Debaromyces* and *Candida* are widely acknowledged as highly effective for xylitol production. The species most frequently employed for this purpose include *Debaromyces hansenii* and *D. nepalensis*, and *Candida guilliermondii*, *C. boidinii*, *C. magnolia*, and *C. tropicalis* (Saravanan et al., 2023). As of *C. tropicali*s and *C. guilliermondii,* they are of great relevance in the industry due to their remarkable inhibitor tolerance, high xylitol yield, and ability to thrive in virtually all types of hemicellulosic hydrolysates (Kaur et al., 2022).

In general, the xylose fermentation process in yeasts consists of two stages: reduction and oxidation. Initially, xylose is reduced to xylitol by xylose reductase, with the coenzyme NAD(P)H (nicotinamide adenine dinucleotide phosphate) playing an essential role. Next, D-xylose is oxidized to xylulose by xylitol dehydrogenase before phosphorylation into xylulose-5-phosphate, catalyzed by xylulokinase (Mohamad et al., 2015). Among these two routes, the redox pathway is the main mechanism for xylose absorption and utilization by yeasts. To achieve a high xylitol yield with the best strain, optimizing fermentation conditions is crucial and has a direct impact on product manufacturing efficiency (Xu Linlin et al., 2019).

Overall, various fermentation techniques employ specific parameters to control the process. This includes regulating the pH of the fermentation medium, usually maintaining it in an acidic range. The optimal temperature range varies between 30 and 37°C, depending on the species of microorganism used. Additionally, the initial xylose concentration plays a crucial role, requiring optimization to ensure a high xylitol yield. This highlights the importance of the initial phases in xylose conversion (Umai et al., 2022).

Purification, recovery, and crystallization of xylitol

The purification, recovery, and crystallization of xylitol from fermentation broth constitute the final stage of the biotechnological route for xylitol production. At this stage, the fermentation broth containing xylitol needs to be separated from other compounds, including residual sugars, fermentation by-products, phenolic compounds, salts, proteins, among others (Queiroz et al., 2022).

Traditional methods for xylitol purification include ion exchange resins, activated carbon, chromatography, liquid-liquid extraction, and nanofiltration, providing a recovery yield of approximately 40 to 60%, obtaining a product with 98% purity (Queiroz et al., 2022). Research indicates that a combination of different techniques for purifying fermented broth containing xylitol is necessary to achieve significant impurity removal, as each method is more efficient for a specific purpose. Activated carbon, for example, is used for decolorization, while chromatography is effective for salt removal (Mohamad et al., 2015; Arcaño et al., 2020).

Vardhan et al. (2022) reported the purification of fermentation liquor from areca nut husk using cationic and anionic exchange resin employing a rotary evaporator, which subsequently needed to be crystallized through nucleation to form xylitol crystals.

In another study by Mohanasundaram et al. (2023), the purification of the fermentation broth began with a vacuum filtration process to separate the supernatant, which was then treated with activated carbon. The resulting clarified broth was concentrated in a vacuum rotary evaporator to increase the xylitol concentration, culminating in subsequent nucleation to promote crystallization.

Crystallization can occur through cooling, evaporation, precipitation, or a combination of these processes, resulting in the separation of liquid and solid phases, ultimately concluding the process. The use of organic solvents can influence the shape of xylitol crystals, and the absence of solvents can lead to the formation of irregular or hexagonal crystals. Solution purity, solvent concentration, temperature, cooling rate, and agitation are determining factors in the nucleation rate, growth, and purity of xylitol crystals (Arcaño et al., 2020).

The efficiency of these final stages, being the ultimate phase of the production chain, is influenced by the results achieved in the preceding stages. A fermentation broth with a high xylitol concentration and low impurity benefits from the purification stage. Thus, it is necessary to consider the composition of the fermentation medium and the performance of the microbial strain, which must be robust enough to produce xylitol with high yield, even in the presence of different compounds, as is the case with lignocellulosic hydrolysates.

Table 2 provides an overview of recent techniques used in xylitol production from lignocellulosic biomass as a raw material. Additionally, it is possible to note the co-production capacity of ethanol in the same biotechnological approach for xylitol acquisition.In general, the data presented in the table indicate that the effectiveness of the selected pretreatment stage, along with the fermentation conditions and mode of operation, can significantly impact the overall efficiency of xylitol production. Studies like that of Vardhan et al. (2022) clearly described all stages of pretreatment, hydrolysis, detoxification, fermentation, concentration, purification, and crystallization in the production process of 9.96 g/L of xylitol from areca nut husk (*Areca catechu*).

Several studies have demonstrated the viability of co-producing xylitol and ethanol using a biorefinery approach. Queiroz et al. (2023) revealed a potential sequential configuration producing 30.61 g/L of xylitol and 47.97 g/L of ethanol from sugarcane bagasse and straw. Another example is presented by Kaur et al. (2022), who observed the simultaneous production of 34.21 g/L of xylitol and 2.12 g/L of ethanol through fermentation using the yeast *C. tropicalis*, preceded by hydrolysis and detoxification processes.

Therefore, all research reporting the conversion of xylose to xylitol using microorganisms indicates that xylitol bioproduction is influenced by various operational variables.

Table 2 – Xylitol production by different techniques and operational conditions using lignocellulosic raw material.

Biomass	Procedure		Inhibitors	Xylitol	Other products	Reference
Corn cob	Pre-treatment Hydrolysis Fermentation Purification and Crystallization	NaOH 1.81%; 90min H_2SO_4 6%; 15min *Debaryomyces nepalensis* Vacuum filtration; Activated carbon; Vacuum rotary evaporator	0.09 g/L $_{(5\text{-HMF})}$ 0.05 g/L $_{(furfural)}$	21.15 g/L	—	Mohanasundaram et al. (2023)
Typha latifolia (aquatic weed)	Pre-treatment Hydrolysis Detoxification Fermentation	$NaHSO_3$ 2%; 18h; room temperature H_2SO_4 2%; 60min; 121°C Acid correction; Activated carbon *Candida tropicalis; Saccharomyces cerevisiae*	0.48–0.90 g/L $_{(phenolic)}$ 0.20–0.58 g/L $_{(furfural)}$	6.15 g/L	6.90 g/L EtOH	Goli e Hameeda (2023)
Sugarcane bagasse and straw	Hydrolysis Detoxification Fermentation	H_2SO_4 1%; 121°C; 20min pH adjustment; Activated carbon; 60°C; 100 rpm; 30min *Candida tropicalis*	0.36 g/L $_{(5\text{-HMF})}$ 0.04 g/L $_{(furfural)}$	30.61 g/L	47.97 g/L EtOH	Queiroz et al. (2023)
Areca nut husk (*Areca catechu*)	Pre-treatment Hydrolysis Detoxification Fermentation Xylitol concentration Purification and Crystallization	H_2SO_4 diluted H_2SO_4 121°C; autoclave; 30min pH adjustment; Activated carbon 30°C; 200 rpm; 1h *Candida tropicalis*; 227 rpm; pH 5.01; 31°C; 79h Centrifugation; pH adjustment; Ion exchange resin Nucleation; Ambient temperature drying; Filtration	0.037 g/L $_{(5\text{-HMF})}$ 0.011 g/L $_{(furfural)}$	9.96 g/L	—	Vardhan et al. (2022)
Rice straw	Hydrolysis Detoxification Fermentation	HNO_3 1%; 121°C; 30min Acidity correction; Activated carbon 1h; 30°C and 60°C; 170 rpm *Candida tropicalis*; 30°C; 150 rpm; pH 5.5; 96h	0.17 g/L $_{(5\text{-HMF})}$ 0.12 g/L $_{(furfural)}$ 1.07 g/L $_{(acetic\ acid)}$	34.21 g/L	2.12 g/L EtOH	Kaur et al. (2022)
Eucalyptus globulus	Pre-treatment Hydrolysis Detoxification Fermentation	Vapor explosion; 200°C; 10min H_2SO_4 4%; 121°C; 60min, Styrene resin membrane pH adjustment; Polystyrene resin divinylbenzene; $C_4H_8O_2$; 23°C; 250 rpm; 40h min *Kluyveromyces marxianus*; 300 rpm; 40°C	2.74 g/L $_{(5\text{-HMF})}$ 3.42 g/L $_{(furfural)}$	28.07 g/L	—	Bonfiglio et al. (2021)
Olive pomace	Pre-treatment Hydrolysis Detoxification Fermentation	Water extraction; 100°C; 30min H_2SO_4 2%; 170°C Ion exchange resin *Candida boidinii*	0.11 g/L $_{(5\text{-HMF})}$ 1.89 g/L $_{(furfural)}$ 5.59 g/L $_{(acetic\ acid)}$	5.97 g/L	2.00 g/L EtOH	López-Linares et al. (2020)
Apple pomace	Hydrolysis Detoxification Fermentation	H_2SO_4 121°C; autoclave; 20min pH adjustment; Activated carbon; 100 rpm; 30min; 60°C *Candida guilliermondii*; *Kluyveromyces marxianus;* 200 rpm; 30°C; 96h	0.15 g/L $_{(5\text{-HMF})}$ 0.30 g/L $_{(furfural)}$ 1.36 g/L $_{(acetic\ acid)}$	9.36 g/L $_{(C.\ guilliermondii)}$ 9.10 g/L $_{(K.\ marxianus)}$	10.47 g/L EtOH $_{(K.\ marxianus)}$	Leonel et al. (2020)
Banana leaf	Hydrolysis Detoxification Fermentation	H_2SO_4 2.5%; 121°C; 30min pH adjustment; Activated carbon; 200 rpm; 55°C; 60min *Candida tropicalis*; 30°C; 200 rpm; 60h	8.21 g/L $_{(phenolic)}$	11.20 g/L	8.10 g/L EtOH	Shankar et al. (2020)
Bamboo stem	Pre-treatment Hydrolysis Fermentation Purification	H_2O_2 30%; AcOH; 85°C; 2h Cellulase; 45°C; 200 rpm *Saccharomyces cerevisiae*; 30°C; 48h Pervaporation	—	12.3 mg/mL	21.5 mg/mL EtOH	Song et al. (2020)

EtOH: ethanol.

Investigating the effects of these variables is of particular interest as a prerequisite for achieving higher xylitol yield and productivity.

Moreover, the identification of an economically viable raw material containing a substantial proportion of xylose sugars in its structure can play a pivotal role in significantly augmenting xylitol yield.

Conclusions

Advancements in integrated biorefinery approaches involving lignocellulosic biomass, innovations in biomass pretreatment, enhanced acid hydrolysis techniques for increased xylose production, the implementation of detoxification processes to eliminate fermentation inhibitory compounds, and a deeper understanding of biotechnological conversion unveil new opportunities to surmount challenges in economically and environmentally sustainable xylitol production, meeting the escalating global demand.

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