Xylitol: production strategies with emphasis on biotechnological approach, scale up, and market trends

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Abstract

Xylitol, a sugar alcohol that is mostly derived from natural sources such as birch wood, corn cobs, and various plant materials like berries, oats, and mushrooms shows promising potential for use in various fields in the future like medicine, food, and pharmaceuticals. The current review paper focuses on a biotechnological approach that overcomes the limitations of traditional chemical methods for synthesizing xylitol, a sugar alcohol that is commonly used as a sugar substitute. The new methods can save time by utilizing waste byproducts such as lignocellulosic biomass, which can benefit from integrated management of hemicellulose with a high xylose content for xylitol extraction and its cost-effective structural reformulation into value-added products. Improved xylitol production from both wild and genetically modified strains is discussed in the paper. Increases in both xylitol production and its practical applications can be used to foretell the direction of the market. Suggestions were made for increasing xylitol output by altering both the substrate and the processing conditions. Out of the various approaches described in the article, the microbial/biotechnological method was found to be promising for future upscaling in the production of xylitol, which is then followed by fermentation and downstream processing. The future applications of xylitol in relation to market trends are also discussed further.
Keywords: Xylitol production; Biotechnological; Genetically Modified Strains; Upscale; Lignocellulosic Biomass.

1. Introduction

Xylitol is a pentose alcohol sugar with the chemical formula $C_5H_{12}O_5$, a member of the polyol family of compounds, which are characterized by their alcohol functional groups (-OH). It presents sweetness similar to regular sugar and has applications and potential in at least three types of industries viz., orthodontic, pharmaceuticals, and food (Prakasham et al., 2009). Xylitol prevents dental caries. It stabilizes salivary proteins and improves mouth odor thereby improving oral treatments. Xylitol increases saliva production, relieving xerostomia- a dry mouth condition (Nwinyi and Kalu, 2021). Xylitol cools and refreshes the mouth, masking the medicinal taste of certain drugs (Arcaño et al., 2020). Also, this sugar prevents and treats acute otitis media, a common ear infection, safely and effectively is believed to be related to its ability to inhibit the growth of bacteria that cause the infection. Xylitol is thought to interfere with the ability of bacteria to attach to the surface of the respiratory tract, thereby preventing colonization and infection (Lee and Park, 2014; Vernacchio et al., 2007).

The use of xylitol as a chemical building block in various industrial sectors to produce high-value products also contributes to commercialization and its massive production. The US Department of Energy (DOE) calculates the global market for xylitol at 200,000 metric tonnes per year (Ravella et al., 2022). This makes it one of the top 12 value-added compounds derived from biomass. As a food, xylitol has been used as a sweetener and table sugar/sucrose substitute. The alcohol sugars are slowly absorbed and metabolized in the body so they do not tend to increase the blood sugar levels, making themselves a low glycemic index product. In other words, its consumption results in minimal changes in insulin and it is tolerated well even in large servings (Vasilescu et al., 2011). Regardless, its low caloric content characteristic (2.4 cal g^{-1}) makes it frequently included in the diet of diabetics or consumers seeking a

healthier lifestyle and consequently, solutions to replace table sugar (Arcaño et al., 2020). Moreover, sugar alcohols' additional qualities, including their prebiotic effects, have helped to boost their popularity in the substitutes market by promoting the growth of beneficial gut bacteria and inhibiting the growth of harmful bacteria, such as E. coli and Salmonella. This is due to xylitol's resistance to digestion by human enzymes, allowing it to reach the colon intact and serve as a food source for beneficial bacteria (Kandelman et al., 2021). Since, 1963, the FDA has approved xylitol as GRAS (Generally Recognized as Safe), and therefore, it has been used as a food additive in the industry (Nwinyi and Kalu, 2021). Xylitol can be obtained from a xylose-rich substrate known as xylan. This is a polysaccharide complex constituted of D-xylose residues in the main chain, linked by β (1-4) glycosidic bonds. Its composition, as well as the degree of polymerization, depends on the origin and it varies from plants to L-arabinose, D- or L-galactose, and D-glucose is also present (Bajpai, 2014; Heinze and Liebert, 2012). Xylan is one of the main components of hemicellulose (a branched hetero-polysaccharide found in angiosperm cell walls) (Singh et al., 2013). Together with cellulose and lignin, hemicellulose composes lignocellulosic biomass, which is an important, renewable, cheap, and abundant source of fixed organic carbon in nature. Numerous agricultural by-products are sources of lignocellulosic biomass, including cornhusk, bagasse (approx. 20-26% hemicellulose and 11-16% xylose), and brewers' spent grain (20 – 30 % hemicellulose and 1.5 - 4% xylose) (Subroto and Hayati, 2020). The use of these residues as raw material for the production of xylitol has been gaining emphasis in the scientific community, especially in studies addressing the enzymatic or microbiological route for this purpose (Mardawati et al., 2018a, b), and the method is considered cost-effective.

The xylitol industry is expected to be worth $6.93 billion worldwide by 2027. The worldwide xylitol market is expected to expand at a CAGR of over 6.4% between 2021 and 2027, from its projected 2020 valuation of $4.49 billion (Market watch, 2022). Increases in the incidence of lifestyle disorders such as obesity, high cholesterol, and cardiovascular disease are spurring public interest in xylitol as a means of reducing calorie consumption around the world. The xylitol market is expanding because of the rising need for sugar substitutes that are better in terms of health, cost, and safety. Moreover, as people are becoming more health-aware, they are increasingly prepared to spend money on sweeteners like xylitol rather than refined sugar. A rise in industrialization and a movement in customer desire toward sugar-free products are other contributing factors. Due to its antibacterial, antifungal, antiviral, and antimicrobial properties, xylitol finds widespread application in pharmaceutical and nutraceutical products. Additionally, xylitol is slowly digested in the human body, thus it has a minimal impact on blood sugar levels and is popular among persons with diabetes and excessive body weight. In addition, xylitol sales have skyrocketed since numerous nations' governments are encouraging people to switch to low-calorie alternatives like xylitol. Xylitol's positive effects on health are not only limited to dentistry but immune function, digestion, lipid metabolism, and bone metabolism are also greatly aided by the xylitol. It assists in the regulation of blood glucose and body weight, in addition to deterring ear and respiratory infections. Antibiotics and surgery are not the only options to be depended upon for treating the ailments, xylitol also addresses the cure and at times better than it (Benahmed et al., 2020).

Traditionally, xylitol production takes place through chemical processes, in which pure xylose is reduced to derivatives like polyethylene glycol and ethylene glycol at high temperatures and pressures (López-Linares et al., 2020). However, the high energy costs involved in the process and the complexity of the system (e.g., low selectivity and formation of L-Arabinitol or other by-products) drive the search for alternative routes that are more environmentally friendly (Subroto and Hayati, 2020). The main objective of the present study is to provide a broad overview of the state of the field regarding the different routes of xylitol extraction through chemical or biotechnological aspects, with emphasis on the fermentation route using yeast culture which favorably has given the best yield so far. In addition, this review also discusses the substrates used so far or potential, and on the investigations about scale-up xylitol production.

2. Xylitol production: different extraction routes and substrates used

The manufacture of xylitol has been influenced by many generations referring to the historical development of the processes used to produce xylitol. Extraction of xylan from wood (first generation) was followed by catalytic reduction of xylose or xylose-rich hydrolysate using metal catalysts (second generation). From the third generation

onward, bioprocessing processes will predominate, with the employment of photoautotrophic bacteria to manufacture the xylitol (Ahuja et al., 2020).

2.1 Chemical route of obtaining xylitol

One of the ways to obtain xylitol is through chemical or thermo-chemical processes. The use of this approach on an industrial scale started in Finland in the 1970s, using vegetal materials (such as corncob, birch wood, and other rich flora) as a starting point (Xu et al., 2019). This procedure is performed in 4 steps, as summarized in Figure 1.

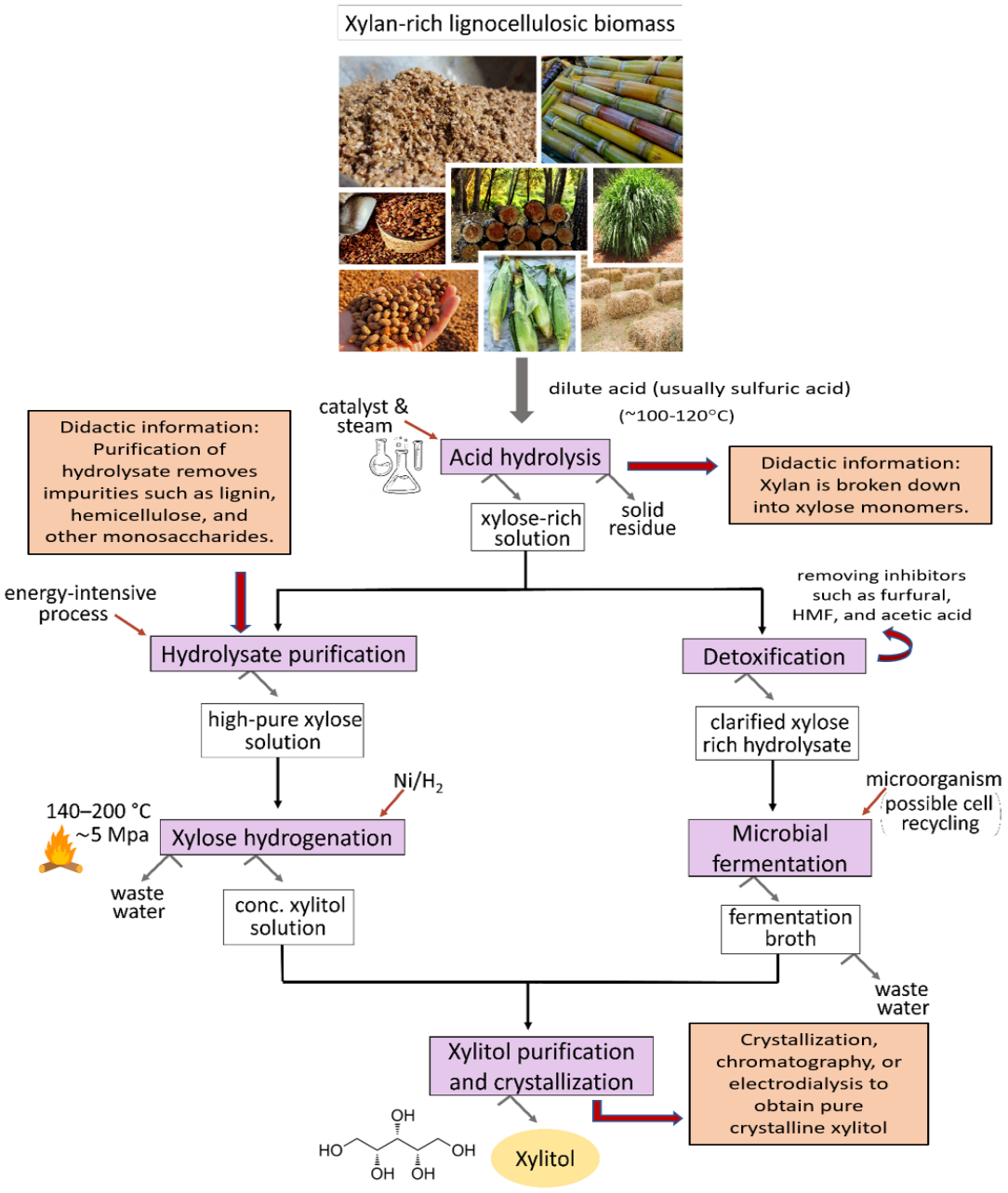

Figure 1. attached demonstrates on procedure of lignocellulosic biomass through chemical and biotechnological routes.

The first step is the acid hydrolysis of lignocellulosic biomass, aiming to break the rigid structure of this material (depolymerization) and thus produce a mix of monomeric sugars (hexose or pentose) that dissolve in the reaction medium (Kumar et al., 2009). Two fractions are obtained from this stage: the solid residue, composed mainly of lignin and cellulose precipitates, and the soluble portion (or hydrolysate) composed of glucose, xylose, and other sugars (galactose, arabinose, and mannose). Other desirable products of acid hydrolysis include amino acids, which are used in the production of food additives, and fatty acids, which are used in the manufacture of soaps and detergents (Naik et al., 2010). The yield of the soluble fraction depends on the type of biomass and the reaction conditions (Abril and Navarro, 2012; Hyvönen et al., 1982; Rafiqul and Sakinah, 2013; Yi and Zhang, 2012). The branched and amorphous arrangement of hemicellulose allows it to be readily hydrolyzed, with a recovery of 70–95% of its sugars. However, undesirable products may be formed during the acid hydrolysis from unwanted secondary reactions. They are classified into three groups: (i) components from sugar degradation, such as furfural and hydroxymethylfurfural (HMF); (ii) products released from the breakdown of hemicellulosic acetyl groups (acetic acid); and (iii) lignin degradation substances (polyaromatic and aromatic compounds) (Fehér et al., 2018). The simultaneous occurrence of these reactions results in maximum xylose yield when operating conditions (reaction time, acid concentration, pressure, temperature, and solid-to-liquid ratio) are optimized (Arcaño et al., 2020). The formation of both desirable and undesirable products during acid hydrolysis can have significant implications for subsequent processes such as purification and downstream processing. If unwanted byproducts or impurities are present, they can complicate the purification process and lead to lower yields and increased processing costs. Therefore, it is essential to exercise careful control over the conditions of acid hydrolysis to minimize the formation of undesired products and maximize the yield of desired ones. By doing so, the overall efficiency and cost-effectiveness of the process can be improved.

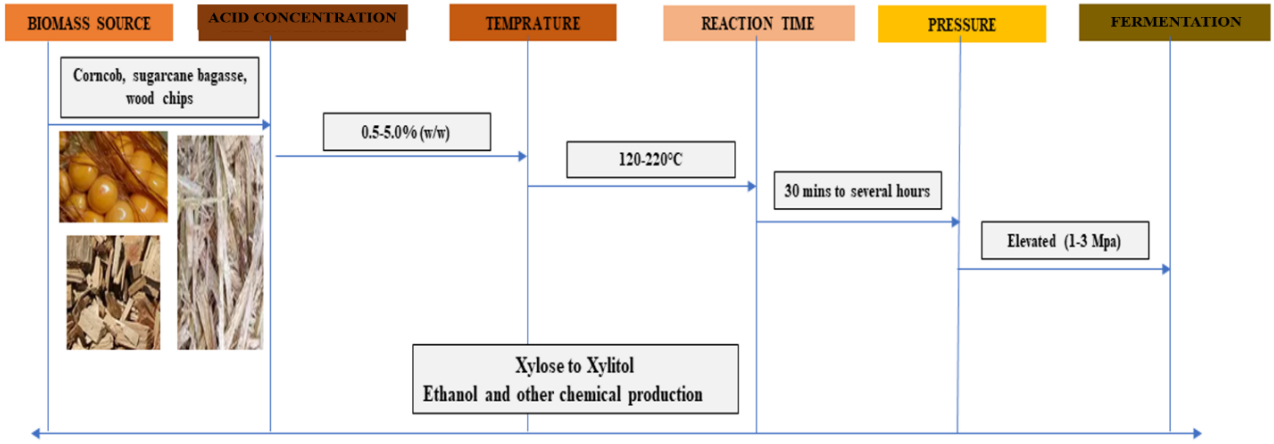

Figure 2. signifies general scheme of acid hydrolysis of biomass source carried out by chemical companies.

Traditionally, the extraction and hydrolysis of the hemicellulosic fraction are performed using acid pretreatment at concentrations ranging between 0.5, 1, and 1.5 % (m/m) and a temperature range from 120 to 160 °C (Gírio et al., 2012). Nevertheless, alternative methods have been utilized for instance, Jia et al. (2016) produced hemicellulosic hydrolysate by tetrabutylammonium hydroxide, and further carried out acid hydrolysis with a 7% sulfuric acid solution with a hydrolysis time of 2 h at 100 °C. Apart from H_2SO_4, other mineral acids such as hydrochloric acid (Gómora et al., 2020; Radillo et al., 2011; Zhang et al., 2021), nitric (Kashcheyeva et al., 2020; Zhang et al., 2011), and phosphoric (Cao et al., 2018; Gomora-Hernandez et al., 2020b) have also been tested. The utilization of organic acids such as trifluoroacetic acid (Dong et al., 2009), acetic acid, maleic acid, succinic acid, and citric acid has also been discussed (Gírio et al., 2012). Zhuang et al. (2011) also proposed a mixture of formic acid and hydrochloric acid to hydrolyze wheat straw.

Depending on the raw material used, the hydrolysate rich in xylose is then subjected to a purification process (second stage), with the objective is to reduce or eliminating the undesirable by-products, phenolics, and volatile compounds. The mechanisms involved in this process using ion-exchange chromatography and activated carbon comprises the elimination of diluted salts, degradation of products, and discoloration of the hydrolysate (Heikkilä et

al., 1997; Vallejos and Area, 2017; Zamani, 2015). However, other physical, chemical, and biological methods have also been used for the purification of xylose. These treatments are mostly employed when the conversion of lignocellulosic biomass takes place via the biotechnological route. In this context, the purification process is referred to as detoxification, as it seeks to eliminate or reduce the concentration of fermentation inhibitors that can be toxic to microorganisms. It is worth noting, however, that not all detoxification methods are capable of completely removing all inhibitors. Instead, many of these processes aim to decrease the concentration of inhibitors to levels that do not negatively impact the fermentation process (Llano et al., 2017; Vallejos et al., 2016; Wang and Feng, 2010). Various other technologies examined include evaporation, solvent extraction, precipitation, neutralization, ultrafiltration, and encapsulation (Arcaño et al., 2020).

From purified xylose, xylitol is produced by catalytic hydrogenation (a Ni-H_2 alloy) (third step). The temperature is controlled in the range of 140–200 °C as it considerably influences the product selectivity and regulates the overall reaction kinetics. Together with the increase in temperature, the high pressure (around 5 Mpa) favors the hydrogen solubility and the achievement of a high hydrogenation velocity in bulk liquid (Rafiqul and Sakinah, 2013; Su et al., 2013). The kinetic model of the reaction is semi-competitive, with the pentose sugar occupying the catalytic active site. This interaction between the hydrogen and pentose monomer conducts the overall reaction rate and the dissociated hydrogen is adsorbed on interstitial sites available (Su et al., 2013). Thus, if the aqueous solution contains other carbohydrates besides xylose, they are hydrogenated until they reach their polyol form. A xylitol yield of approximately 80% is obtained in this stage (Baudel et al., 2005).

The last step of the process involves two distinct phases, xylitol purification and crystallization respectively. Xylitol solution is purified by separating the catalyst using filtration and ion exchange chromatography. Crystallization, on the other hand, involves passing the purified liquid phase to the solid phase, commonly applying cooling, evaporation, or precipitation. The mechanisms involved in crystallization include supersaturation, nucleation, and crystal growth. Organic solvents can be used to induce crystal growth, which affects their shape and Kim and Jeffrey (1969) found that ethanol promotes a prismatic structure, whereas tetrahydrofuran leads to the formation of elongated needles. Hexagonal or irregular shapes can be observed in the absence of solvents (Martínez et al., 2007, 2009). The purity achieved can be more than 98%, with a crystallization yield of greater than 75% (Pachapur et al., 2016).

Xu et al. (2019) reported that despite its effectiveness and widespread use, the chemical route is gradually being replaced by the xylose biosynthesis perspective. This is attributed to several characteristics inherent to chemical production, such as the use of toxic catalysts, expensive metals, and high pressures and temperatures, making the system environmentally unsafe and energy-intensive. Moreover, the high cost of the process is also linked to the chromatographic approach to separate and purify the D-xylose from the hemicellulose-xylan hydrolysate. Thus, the biotechnological route appears as an opportunity to produce xylitol in an environmentally friendly context and with advantages during operation.

2.2 Biotechnological production of xylitol

The hydrolysates generally contain other components in addition to hemicellulose sugars, based on the chemical complexity of hemicelluloses. These components include phenolic or aliphatic acids, other weak acids generated from sugar degradation, and furaldehydes, which can be potential inhibitors to the microorganisms employed in the subsequent steps of the process (Gírio et al., 2012). Ur-Rehman et al. (2015) reported that furfurals, by interfering with cellular respiration, inhibit microbial growth in the range of 25–99%, depending on their concentration in the medium (0.5–2 g/L) and cell mass yield per ATP. Therefore, detoxification, also called clarification, is an important step in the process. Contrary to the requirement of ultra-pure xylose sugar (chromatographic purification) for chemical conversion, bland detoxification of hydrolysates may fulfill the feed clarification principle. This can be achieved through adsorption by activated charcoal or over-liming. Manaf et al. (2022) developed a detoxification strategy based on coconut shell activated charcoal and controlled pH to reduce the quantities of furfural (79.9%) from an oil palm fronds hydrolysate and showed acetic acid concentration also decrease to 73.7%. Ahuja et al. (2022) proposed the reuse of activated charcoal to reduce operating costs by up to 38%. In a similar procedure, Sun et al. (2022) prepare chitosan-chitin nanofiber hybrid hydrogel beads in order to adsorb furfural and 5-HMF from a sugarcane bagasse hydrolysate. The methodology proved to be effective, as furfural and HMF were eliminated in the proportion of 68.4%

and 63.1%, respectively while retaining sugars (glucose and xylose). Furthermore, during microbial cultivation, an increase in the specific growth rate at least 4.1 times after adsorption was achieved. Romero-Garcia et al. (2022) used a microbial treatment to carry out the detoxification and used Saccharomyces cerevisiae as an interesting approach to detoxifying a liquid fraction from olive stones previously treated with sulfuric acid. As furfural, HMF, acetic acid, and glucose were consumed during the biological detoxification and the resultant solution was useful for subsequent inoculation with *Candida boidinii*. Different studies have been carried out to increase the tolerance of Saccharomyces cerevisiae against the inhibitors present in lignocellulosic hydrolysates (Costa et al., 2017; Sardi et al., 2016; Sousa et al., 2013; Mukherjee et al., 2022; Zhang et al., 2019). Cámara et al. (2022), performed a complete survey of engineered mutants of this fungus and found that the phenotype identified as beneficial for a specific inhibitor does not imply tolerance for a collection of inhibitors. In addition, the studied data indicated that it may not be worthwhile to optimize strains for each inhibitor independently. Finally, within the same context of biological detoxification, Jofre et al. (2021) proposed the recycling of residual biomass from xylitol production using *Candida tropicalis* as a fermenting agent. In other words, the authors employed residual yeast biomass to detoxify the hemicellulosic hydrolysate through biosorption and then utilized the hydrolysate for reproduction of the xylitol.

Once the xylose-rich hydrolysate is detoxified, the sugars can be used as a carbon source in the form of simple sugars such as xylose, glucose, and arabinose. It may also contain other carbon sources such as oligosaccharides, organic acids such as acetic acid, and lactic acid by different microorganisms using microbial fermentation. During microbial fermentation, microorganisms utilize the carbon source and undergo metabolic processes that result in the production of a variety of end products, such as organic acids, alcohol, and gases. The specific type and amount of end products generated are dependent on various factors, including the type of microorganism employed, the fermentation conditions, and the nature of the carbon source. As with any fermentation, several factors can affect microbial growth, such as aeration rate, pH, temperature, nutrients, inoculum concentration, and mode of reactor operation. Proper control of these variables is significant for obtaining high-quality products with high efficiency. There have been many investigations on the optimal environmental conditions for microbial growth aimed at biotechnological xylitol production (Abou Zeid et al., 2008; Ayubi et al., 2021; Hodaifa et al., 2022; Pappu & Gummadi, 2017; Salgado et al., 2012). Apart from acid hydrolysis, a recent study by Chen et al., 2022, liquid hot water (LHW) pretreatment has several distinct advantages over other existing pretreatment procedures, including little synthesis of monomeric sugars, considerable removal of hemicellulose, and good environmental consequences. Another recent study by Pant et al., 2022 reported on a novel technique comprising two-step fermentation of lignocellulosic hydrolysate for integrated generation of ethanol and xylitol utilizing a newly identified yeast strain, *Candida sojae* JCM 1644. When compared to the strategy involving simultaneous fermentation of glucose and xylose sugars, the two-step fermentation process increased the yield of xylitol and ethanol by 11.78% and 15.57%, respectively.

Product recovery and downstream are the ultimate goal and define the feasibility and effectiveness of any process. The recovery of highly pure xylitol from fermentation broth presents certain challenges, as the broth contains many impurities, complex nutrients and other chemicals from biomass, microbial cells and cellular debris, leftover unreacted sugar (arabinose, xylose, and glucose), and unspent nutrients mixing of sugar alcohols such as sorbitol, arabinitol (which are very difficult to separate from the xylitol fraction), together with xylitol. This mixing demands various purification steps before crystallization, which may increase the cost of the process. Insoluble fractions and cell debris can be cleared by centrifugation, while again, activated charcoal could be used for the decolorization of broth. However, Dasgupta et al. (2017) reported that the initial concentration of sugar is the principal concern, as it only does not determine the yield, but also requires adequate strains for good fermentation. Thus, there has been interested on the part of researchers concerning the development of strategies aimed at the xylitol recovery from several fermentation broths, including membrane technologies (Cardoso and Forte, 2021; Alves et al., 2021; Kresnowati et al., 2019; Wei et al., 2010).

The biosynthesis of xylitol involves the conversion of lignocellulosic hydrolysate into xylitol through enzymatic systems or the use of whole-cell biocatalysts (Dasgupta et al., 2017) Apart from xylitol even ethanol is produced byproduct. Scale-up studies have shown that the ethanol yield increases with increasing concentrations of xylose in the fermentation broth. Ethanol can be separated from the fermentation broth using various methods, including distillation, adsorption, and membrane separation. The addition of ethanol production as a co-product can significantly improve the economics of xylitol production, making it a more attractive and profitable process (Hua et al., 2019).

Xylose, which is obtained by treating lignocellulosic material, serves as the starting material for xylitol production. Xylose fermentation is carried out by different microorganisms, including fungi, bacteria, and yeast, through various pathways. The first step is carried out similarly as in the chemical route, with the prior treatment of the lignocellulosic material in order to obtain a xylose-rich solution (Figure 1). In this case, different hydrolytic technologies were developed mostly addressing the chemical processes (acid dilution) (Manaf et al., 2022; Goli & Hameeda, 2021; Narisetty et al., 2021; Romero-García et al., 2022). While enzymatic cellulose hydrolysis is common, hemicellulose breakdown for xylitol production has not yet been extensively studied. Therefore, a chemical or physical-chemical pretreatment is necessary to increase the accessible area and break the crystalline structure of cellulose to facilitate enzyme access to hemicellulose. Additionally, lignin, which provides rigidity to the cell wall, is naturally resistant to microbial activity (Brodeur et al., 2011; Zhai et al., 2018). Xylitol production through hemicellulose depolymerization can lead to the development of multi-product biorefineries, where biomass is fully utilized to produce xylitol, ethanol, and other chemicals together. Recovery of xylitol and other products is a crucial step, and various separation and purification techniques are available like chromatography, and crystallization. These techniques can be combined to achieve higher levels of purity and yield in the xylitol recovery process (Antunes et al., 2021a, b; Du et al., 2020; Pant et al., 2022; Raj & Krishnan, 2020).

2.3 Different types of substrates for the production of xylitol

Chemical procedure using Raney nickel as a catalyst to convert hemicellulosic xylose to xylitol is one method, while the other, biotechnological conversion of xylose to xylitol, is accomplished by microorganisms that produce enzymes for xylose metabolism. Xylose is sourced from the hemicellulose-rich fraction of lignocellulosic biomass, which involves products like wood and agricultural wastes. Different substrates that aid in xylitol production includes items abundant in hemicellulosic or xylan rich contents like plum, banana, strawberries, raspberry (Mussato, 2011; Washüttl et al., 1973). Other rich sources include corn cobs, sugarcane bagasse, brewer spent grain, rice and wheat straw. **Table 1**, shows the various types of substrates commonly used and xylitol yield capability.

TABLE 1, Different types of substrates used for the xylitol production

Substrate origin	**Name**	**Route used for xylitol production**	**Conditions**	**Xylitol Productivity (g/g)**	**Microorganism used**	**Reference**
Agriculture / livestock	Corn biomass (corn bran)	Chemical	Acid pretreatment (72% H_2SO_4, 30 ºC, 1.5 h)	0.79	--	Irmak et al., 2017
	Corn biomass (corn cob)	Biotechnological	Acid pretreatment [0.5% (w/w) H_2SO_4 and 1.5% (w/w) H_3PO_4, 128 ºC, 1 h]	0.82	*Kluyveromyces marxianus* CICC 1727-5	Du et al., 2020
	Corn cob and *Albizia* pod	Biotechnological	Acid pretreatment	0.90	*Candida tropicalis* K2	Singh et al., 2022
	Rice straw	Biotechnological	Alkali pretreatment	0.80	*Candida tropicalis*Y-27290	Swain and Krishnan, 2015

			(Aqueous ammonia, 120 ºC, 1 h)			
	Sugarcane straw	Biotechnological	NS (Aerobic condition, initial OD 0.5)	0.91	*S. cerevisiae* FMYX	de Mello et al., 2022
	Sugarcane bagasse	Biotechnological	Acid pretreatment (H_2SO_4, 121 ºC, 20 min)	1.50	*Candida tropicalis*	Cardoso and Forte, 2021
Food industry	Brewer's spent grain (BSG) and grape stalks	Biotechnological	Acid pretreatment [3% (w/w) H_2SO_4, 121 °C, 1 bar]	BSG hydrolysate = 0.56 Grape stalks = 0.25	*Komagataella pastoris* DSM 70877	Araújo et al., 2021
	Brewer's spent grain (BSG)	Biotechnological	Hydrothermal processing (120 °C, 15 min, 46 mg g^{-1} dry BSG)	0.81	--	Swart et al., 2021
	Brewer's spent grain (BSG)	Biotechnological	Acid pretreatment (liquid/solid ratio of 8 g, H_2SO_4,17 min)	0.70	*Candida guilliermondii*	Mussatto & Roberto, 2005
	Olive stones	Biotechnological	Aqueous extraction (to extract solids) (130 °C, 90 min)	0.38	*Candida boidinii*	Romero-García et al., 2022
	Chestnut shell	Biotechnological	Acid pretreatment (1.25, 2.5, 5 and 10 % H_2SO_4, 121 °C, 1 h)	0.83	*C. tropicalis* M2	Eryasar and Karasu-Yalcin, 2016
Others	*Brassica juncea*	Biotechnological	Alkali pretreatment (0.2 M NaOH, 160 ºC, 30 min)	0.62	*Candida sojae* JCM 1644	Pant et al., 2022
	Treated oil palm frond	Biotechnological	Acid pretreatment (4.0% (v/v) HNO_3)	0.43	*Kluyveromyces marxianus* ATCC 36907	Manaf et al., 2022

Glucose	Biotechnological	Modification expression of xpdh from *Clostridium difficile* (Shake-flask fermentation, 24 hours)	0.058	*E. coli*	Abdullah et al., 2022
Bagasse, Japanese cedar	Chemical	Acid pretreatment (H_2SO_4)	0.62	--	Yamaguchi et al., 2016

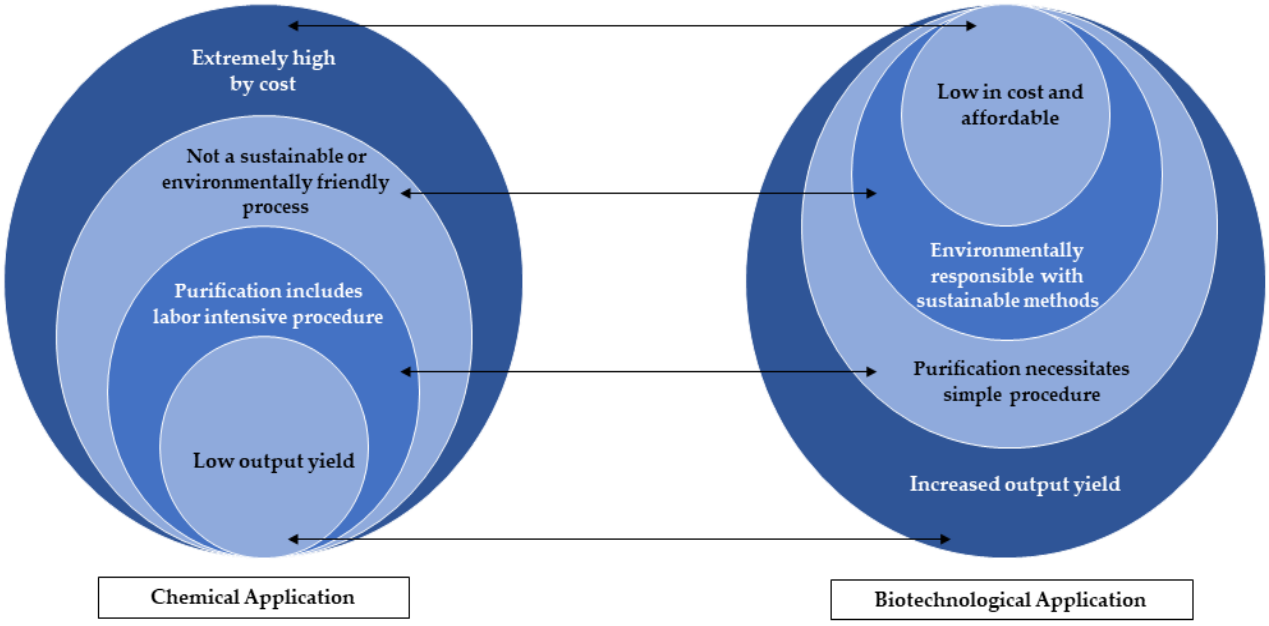

Figure 3. represents the comparison between chemical and biotechnological approaches, including information on which is superior choice for xylitol production.

3. Types of microorganisms used by lignocellulosic biomass for xylitol production

Many agricultural lignocellulosic wastes produced every day around the world cause serious environmental pollution. One of most effective and efficient solution to these issues is to recycle these lignocellulosic wastes as main ingredients in nutritive compost preparations. It is commonly acknowledged that lignocellulosic wastes belong to category of second-generation feedstock. Wastes from bagasse, rice, corn, and other grains like barley beer, as well as wastes from a variety of other products, are some examples of potential substrates. Polysaccharides like cellulose, hemicelluloses, and pectin, as well as the phenolic polymer lignin, make up the majority of these substances. The descending order of microorganisms used in xylitol production sums up to be- Yeast > Fungi > Bacteria (Lugani et al., 2020).

3.1. In terms of xylose microbial metabolism

Xylose reductase is a key source of enzyme for xylitol production by various microorganisms; however, formate, glucose, gluconate, ethanol, and acetaldehyde have been observed to inhibit xylose reductase activity for optimal yield. The following future considerations are suggested for xylitol enzymatic production: (a) Since NADH is less expensive than NADPH, it should be used as xylose reductase; (b) retooling the xylose reductase to increase its life stage; and (c) investigating conversion processes using immobilised xylose reductase (Branco et al., 2012). In modern fermentation techniques, genetically modified strains of bacteria or yeast are used to improve xylitol production, resulting in an abundance of affordable, quality xylitol. The fundamental factors to consider scaling up of xylitol production are raw material high in xylan, and utilization of waste such as corn cobs, rice straw, sugarcane bass, and spent grain from breweries.

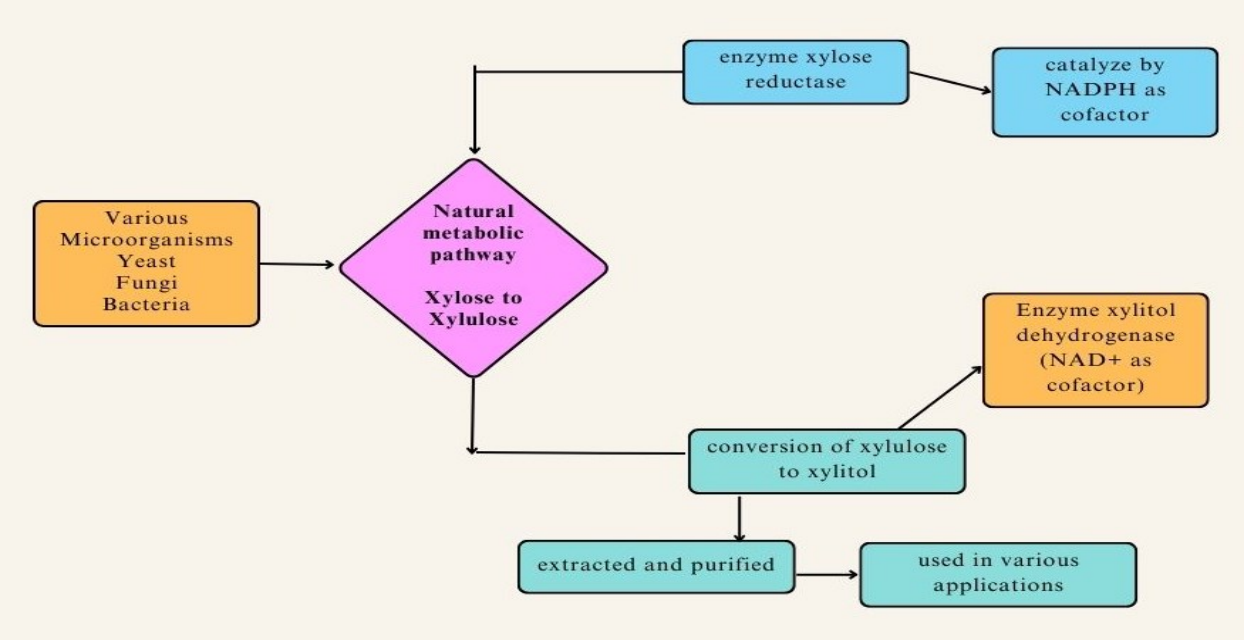

Figure 4. attached demonstrates metabolic pathways for natural synthesis of xylitol through microbial fermentation.

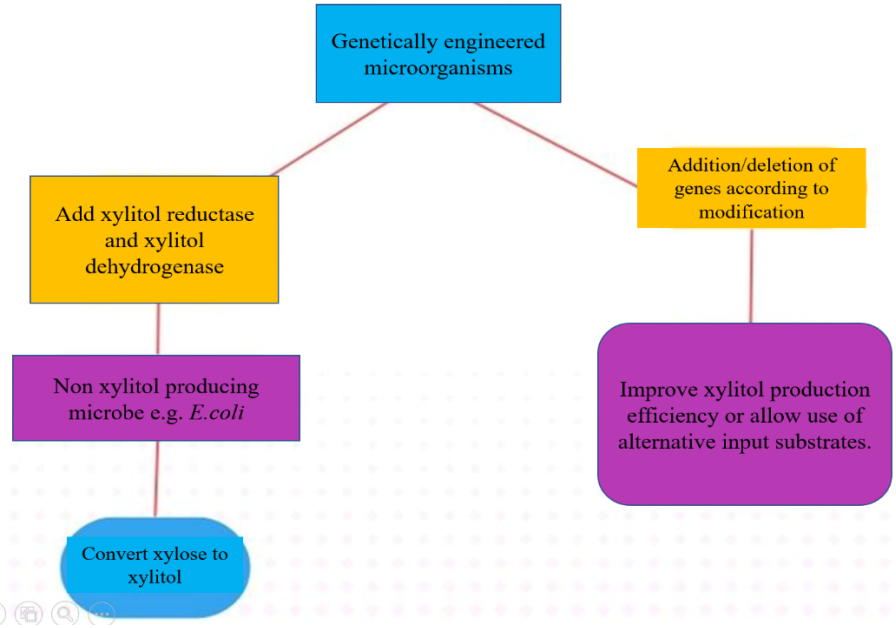

Figure 5. attached demonstrates metabolic pathways for engineered synthesis of xylitol through microbial fermentation.

3.2 GMO and wild strains used in xylitol production

Biotechnology has transformed the production of valuable products from agricultural waste, with genetically modified organisms (GMOs) leading the way. These organisms are engineered using advanced techniques such as gene deletion and overexpression to create high-efficiency and high-productivity strains. In contrast to conventional mutagenesis, genetic engineering offers a more precise and efficient method for altering microbial metabolic pathways and improving yield and productivity. Optimizing microorganisms is critical in the production of wine and beer through fermentation. While conventional methods involve using natural flora or commercialized pure strains, genetic modification is gaining popularity due to its ability to overcome limitations such as low alcohol sugar yield, slow fermentation rates, susceptibility to spoilage microbes and oxidation, and the possibility of off-flavors in the final product. By selecting desired traits such as alcohol tolerance, faster fermentation rates, and better resistance to spoilage, GMOs can be customized using inactivated or overexpressed genes and recombinant DNA technology (Yang et al., 2018). Wine/beer is produced through fermentation, in which microorganisms break down the complex sugars present in the natural form of seeds, skin, and stem into ethanol, alcohol-derived sugars, and carbon dioxide. Optimization of fermentation with yeast/fungi/bacteria can be done either by using a commercialized pure strain selected for its highly desired and consistent properties that involve gene regulation, or using natural flora of microorganism. Now technologies are improving leading to focus more on genetically modified organisms than conventional wild strains. As conventional strain method have low potential to increase yield of alcohol sugars. Also, wild strains exhibits some limitations as- (1) alcohol-resistant wild yeasts ferment steadily and leads to low speed in fermentation and excess residual sugar, (2) wild yeasts are less abundant than the cultivated yeast on grapes or any other fruit and fermentation is sluggish as natural flora is more susceptible to spoilage microbes and oxidation, (3) wild microorganisms can induce off-flavors in beverage. In conclusion, genetic engineering provides a more effective and precise way to optimize fermentation and increase yields of valuable products such as xylitol from agricultural waste. As technologies continue to advance, we can expect to see an increased focus on genetically modified organisms in biotechnology.

Saccharomyces cerevisiae is the most widely recognized example of a "domesticated" yeast, reviewed for the potential to extract alcohol sugars like xylitol due to its association with anthropogenic processes, often used to make bread, beer, and fermented beverages. There are two types of *S. cerevisiae*: wild and domesticated species. The domestication process that led to grape wine yeasts probably occurred some 2,700 years ago (Tofalo et al., 2011; Fay and Benavides, 2005; Mortimer and Polsinelli, 1999). Looking at the drawbacks of the wild strain, solutions were highly oriented towards GMOs (Genetically Modified Organisms). GMOs benefit the survival of fitness theory as one is selective about the addition and deletion of desired DNA to change the yield for alcohol sugars. Collectively, environmental parameters and processing conditions over time, rather than location, have driven the domestication process, resulting in specialized strains in highly diverse species. As a result, it appears that genetic engineering, directed evolution, or even the creation of entirely synthetic genomes could serve to circumvent and speed up the series of mutagenic events that are usually driven by the environment to create biodiversity. The goal of this strategy is maximum efficiency via design iteration (Suzzi, 2011).

Genetic tools are commonly utilized in biotechnology to engineer microorganisms for efficient production of xylitol from lignocellulosic materials. These tools include gene deletion, gene overexpression, and recombinant DNA technology. Gene deletion involves removing genes that prevent or slow down the production of xylitol, or that divert metabolic pathways away from xylitol production. An example of this is the deletion of the aldose reductase gene in *Candida tropicalis*, which resulted in a 30% increase in xylitol yield (Jeon et al., 2009). Gene overexpression involves introducing extra copies of genes involved in the xylitol biosynthetic pathway to increase xylitol production. An example of this is the overexpression of the xylitol dehydrogenase gene in *Candida parapsilosis*, which led to a 35% increase in xylitol yield (Kim et al., 2004). Recombinant DNA technology enables the insertion of foreign DNA into microorganisms to introduce or enhance desired metabolic pathways for xylitol production. This technology is widely used in the production of xylitol and other bioproducts. For example, the insertion of the xylose reductase gene into the yeast *Saccharomyces cerevisiae* enabled the production of xylitol from xylose (van Maris et al., 2006). Genetic engineering offers greater precision and efficiency in altering microbial metabolic pathways for improved xylitol production. While mutagenesis using physical or chemical mutagens can also enhance xylitol production in microorganisms.

Table 2, shows different types of GMO and wild strain used in xylitol production.

TABLE 2 Difference in wild strain and genetically modified strain for xylitol production.

Strain type	Microorganism with genetic modification	Substrate	Xylitol Production (g/L)	Fermentation condition	References
Yeast					
Wild strain	*Pichia pastoris*	Xylose	--	Aerobic	Louie et al., 2021
GMO strain	*Pichia pastoris* XYL1 and gdh		70 % higher		
Wild strain	*S. cerevisiae* NRRL-Y12632	Red carrot residue	4	Aerobic	Feng et al., 2018
GMO strain	*S. cerevisiae* NRRL Y-50463		6		
Wild strain	*S. cerevisiae* XP	Glycerol	23.3	Aerobic	Kogje and Ghosalkar, 2017
GMO strain	*S. cerevisiae* XP-RTK		47		
Wild strain	*Kluyveromyces marxianus* YZB001	Xylose	0.23	Aerobic	Zhang et al., 2014
GMO strain	*Kluyveromyces marxianus*YZJ015		34.71		
Wild strain	*Saccharomyces cerevisiae*	Xylose + Cellobiose	0	Anaerobic	Oh et al., 2013
GMO strain	*Saccharomyces cerevisiae* D-10-BT		19		
Bacteria					
Wild strain	*Escherichia coli*	Xylose	--	Aerobic	Jin et al., 2019
GMO strain	*Escherichia coli* BL21(DE3)		48.7		
Wild strain	*Corynebacterium glutamicum*	Xylose	0.6	Anaerobic	Sasaki et al., 2010
GMO strain	*Corynebacterium glutamicum* CtXR7		166		

Fungi					
Wild strain	*Aspergillus niger*	wheat bran and cotton seed hulls	--	Aerobic	Meng et al., 2022
GMO strain	*Aspergillus niger* disruption of ΔladAΔxdhAΔsdhA		40 times higher		
Wild strain	*Trichoderma reesei* Δxdh1 strain	Barley Straw	6.1	Aerobic	Dashtban et al., 2013
GMO strain	*Trichoderma reesei* Δxdh1Δlad1 strain		13.22		
Wild strain	*Aspergillus oryzae* KBN616	Xylose	4.2	Aerobic	Mahmud et al., 2013
GMO strain	*Aspergillus oryzae* P4		12.4		

4. Scale up studies for xylitol production

Some of the emerging strategies and technologies with potential to enhance xylitol bioproduction include the adaptive evolution of microbial strains to increase their tolerance to inhibitors and xylose uptake rate during the fermentation step, the development of engineered microorganisms to result in higher xylose-to-xylitol bioconversion yields, and xylitol purification techniques to increase the recovery yields (Louie et al., 2021). To find out if the process can be executed on a large scale and what steps in the production chain need to be improved, a techno-economic analysis- upstream, down streaming process of the entire production chain is necessary (Queiroz et al., 2022). Koppram et al. (2012) showed evolutionary engineering strategies utilizing *Saccharomyces cerevisiae* strain, TMB3400 to reduce the lag phase from 48 hour to 24 hour with higher xylitol yield (0.74 g/g) than the wild-type strain (0.61 g/g) in upscaling. An intriguing possibility to enhance yeasts' xylose assimilation is to use co-substrate fermentation. NADPH regeneration, a cofactor vital for the translation of xylose to xylitol in yeasts, has been examined in conjunction with co-substrates such as glucose. The ratio of these substrates' enzyme activities is a crucial factor in maximizing xylitol output and yield (Ko et al., 2006; Granström et al., 2007; Queiroz et al., 2022).

The large-scale bioproduction of xylitol also depends on the types of feedstocks used for biotechnological routes. For example, brewer spent grain feedstock input is 100 ton/hour, and its primary product is xylitol with a processing yield of 103.79 kg xylitol/ton BSG (Mussatto et al., 2013). (1) Feedstock supply for commercial production plants; (2) Industrial biomass pretreatment; and (3) Lessons learned from industrial operations are highlighted as three of the most important obstacles and workable issues for fermentative xylitol synthesis at commercial scale. To construct a state-of-the-art xylitol industrial production facility to reduce the facility's impact on the environment due to climate change, a strategy has been developed to determine the technological gap to overcome it through scaling-up (Ravella et al., 2022). Most of the published research based on lab-scale fermentation over the past two decades have either used pure xylose or a mixture of xylose and glucose, and have shown low titers, productivity rates, and/or yield. It is important to assess how these research findings can be scaled up to create a fermentative xylitol technology that can compete with the currently employed chemically catalyzed hydrogenation commercial process (Ravella et al., 2022). Numerous investigations on the use of agricultural wastes for xylitol synthesis have been undertaken. For example, a process scale-up of an efficient acid-catalyzed steam pretreatment of rice straw for xylitol production by *C. Tropicalis* MTCC 6192, followed by scale-up from lab to bench scale, resulted in a 60% xylitol yield in a 14 L fermenter (Singh et al., 2021).

Xylitol production involves the use of various types of reactors, such as batch reactors, fed-batch reactors, continuous stirred tank reactors (CSTR), and packed-bed reactors (PBR). Each reactor type has its own strengths and limitations, depending on specific process requirements and operating conditions. Batch reactors are uncomplicated and user-friendly, but their productivity is low, making them unsuitable for large-scale production. Conversely, CSTRs and PBRs have higher yields and productivity, but are more complex and require more maintenance (Koutinas et al., 2014). The production of xylitol often involves the use of immobilized enzymes or whole cells, which can offer several advantages over free enzymes or cells. Immobilization techniques can increase enzyme stability, enable reusability, and allow for easier separation from the reaction mixture (Zhang et al., 2019). Several immobilization techniques have been developed, including entrapment, adsorption, covalent binding, and cross-linking. Of these, entrapment and adsorption are the most commonly used techniques in xylitol production. Entrapment involves physically trapping enzymes or cells within a polymer matrix, while adsorption involves attaching enzymes or cells onto a solid support material. These techniques have been successfully used to improve the efficiency and sustainability of xylitol production processes (Nigam & Singh, 2011; Patel et al., 2017; Wang et al., 2018).

While immobilized systems offer several advantages for xylitol production, there are also some concerns that must be addressed. One issue is the cost of the immobilization materials, such as gel beads, which can be high and increase the overall production cost. Another concern is the stability of the immobilized enzymes or cells, which can be influenced by various factors such as temperature, pH, and substrate concentration. Thus, it is important to optimize the immobilization conditions and choose the most suitable immobilization technique to achieve high productivity and stability. Apart from the immobilization process, the choice of reactor type and operating conditions can also significantly impact the final product yield and quality. For instance, the use of batch reactors may result in low productivity, while continuous systems such as CSTR or PBR may offer higher yields and productivity, but require more maintenance. Other factors such as reactor design, feed flow rate, and nutrient availability also play an important role in the success of xylitol production on a large scale. Therefore, it is crucial to carefully consider all these factors to optimize the process and achieve optimal xylitol production.

Some examples of reactor types and process conditions used in bioreactors and immobilized systems for xylitol production include- Batch reactors which are simple and easy to operate, however, batch reactors have low productivity and are not suitable for large-scale production of xylitol. They are commonly used in small-scale research eras. Fed-batch reactors are commonly employed in industrial xylitol production as an extension of batch reactors. In a fed-batch reactor, the substrate (typically xylose) is added incrementally throughout the process to sustain a high concentration of the limiting nutrient. This gradual addition helps overcome substrate inhibition and enhances xylitol yield, resulting in improved productivity (Bouassida et al., 2023). CSTRs are commonly used in industrial xylitol production. They allow for continuous stirring, continuous nutrient supply, and simultaneous product removal, ensuring optimal conditions for microbial growth and maximizing xylitol production. CSTRs offer higher productivity and yield compared to batch reactor, but require complex design and maintenance for effective mixing and control (Jain and Gosh, 2021). To produce xylitol another type of reactor employed are packed-bed reactors (PBRs). They entail immobilizing enzymes or cells in a fixed bed where the substrate circulates and is transformed into xylitol. High productivity, precise reaction control, and simple scalability are all features of PBRs. To achieve effective mass transfer and avoid cell or enzyme leakage, careful design is required (Singh et al.,2014; Umai et al., 2022). When it comes to immobilization techniques for xylitol production, there are numerous techniques to follow from entrapment, adsorption, covalent, and cross linkage to many more. Crosslinking agents or matrix materials are frequently used in the immobilization process to fix enzymes or cells. To create a stable and functional immobilization system, it is essential to choose the right crosslinking agent type, concentration, and matrix material. For the immobilization process to be optimized and desired results to be achieved, several aspects must be carefully taken into account (Kaur et al., 2020). Apart from this, high productivity requires effective mass transfer of the substrate and product within the immobilization system. The xylitol production process can be improved by designing the immobilization system to enable optimal mass transfer (Rao et al., 2016; Jain et al., 2023).

TABLE 3, the table provides an overview of studies conducted on xylitol production, encompassing various microorganisms utilized, immobilization techniques, substrate types, bioreactor types, and xylitol production.

Microorganisms	Immobilization complimented technique	Substrate	Bioreactor type used	Xylitol Production g/l/h	References
Candida guilliermondii	Calcium-alginate	Sugarcane bagasse	Bubble column bioreactor	0.21	Branco et al., 2007
Candida subtropicalis WF79	Entrapment	Rice straw	--	0.73	Liaw et al., 2008
Candida sp. ZU04	Ca-alginate beads	Corn cob hydrolysate	Fluidized-bed bioreactor	0.84	Ding, 2011
Candida tropicalis	Polyurethane foam	Corn cob hydrolysate	Multi batch reactor	1.90	Wang et al., 2012
Saccharomyces cerevisiae, Candida shehatae, Spathaspora arborariae	Acid–enzymatic	Soybean hull hydrolysate	Cell bioreactors	Low	Hickert et al., 2014
Debaryomyces hansenii	Alginate beads	Xylose	Fed batch, Airlift bioreactor	0.43	Pérez et al., 2014
E. coli (rE. coli)	Adsorption	Carbon nanotubes	Batch reactor	0.22	Rahman et al., 2020

In the context of xylitol production, the utilization of bioreactors is a logical step toward scaling up the process. However, there exist several unique and lesser-known concepts that can be explored to effectively achieve scale-up, alongside potential bottlenecks and challenges that must be addressed when implementing biological xylitol production on a large scale. These concepts encompass- 1) Advanced bioreactor designs: the exploration of novel bioreactor designs, such as membrane bioreactors, fluidized bed reactors, or airlift reactors, can optimize mass transfer, enhance productivity, and improve xylitol yield. 2) Genetic engineering: the application of genetic engineering techniques to enhance the metabolic pathways of microorganisms involved in xylitol production can result in increased conversion efficiency and higher xylitol yields. 3) Co-utilization of lignocellulosic biomass: the development of strategies to effectively utilize lignocellulosic biomass as a feedstock for xylitol production can improve resource efficiency and reduce costs. 4) Process integration: the integration of xylitol production with other processes, such as lignocellulosic ethanol production or biorefinery concepts, can enhance overall process economics and maximize the utilization of raw materials (Zhang et al., 2015). Nonetheless, there are several bottlenecks and challenges in large-scale biological xylitol production, including- substrate inhibition, product recovery, and purification, oxygen transfer

which could affect microbial growth and xylitol production. To achieve the goal of large-scale xylitol production, it is essential to overcome these issues and consider the novel ways mentioned above (Zhang et al., 2015).

Large-scale biological xylitol production has several obstacles and difficulties. However, there are ways to deal with these issues, including through the use of bioreactors and immobilization strategies. Some of the main obstructions and potential remedies are listed as- 1) Low productivity: enhancing xylitol productivity to meet the needs of large-scale production is one of the major issues. Continuous bioreactor systems, like CSTRs or PBRs, which offer steady-state operation, appropriate nutrient supply, and increased productivity compared to batch reactors, can be used to address this. 2) Xylose, the primary substrate for the synthesis of xylitol, can have an inhibiting effect on the bacteria or enzymes involved. By progressively providing the substrate, maintaining a high concentration of the limiting nutrient, and increasing xylitol output, fed-batch techniques in bioreactors can assist overcome substrate inhibition. 3) Effective mass transfer: productivity may be impacted by bioreactor mass transfer restrictions. By providing a stable bed through which the substrate flows, immobilization systems like packed-bed reactors increase mass transfer, assuring effective contact with immobilized cells or enzymes and increasing productivity. 4) Stability and reusability: enzymes and cells must remain stable when used repeatedly for large-scale production to be cost-effective. By providing a supporting matrix or structure to keep the enzymes or cells inside the bioreactor system, immobilization techniques have the advantage of increased stability and reusability. 5) Cost and scalability: the cost of the immobilization ingredients and the process's scalability are crucial factors. The main goals of research and development are to improve immobilization methods, look into affordable materials, and streamline the immobilization procedure for widespread application (Koutinas et al., 2014).

Figure 6. critical points to upscale the xylitol production using biotechnological methods.

5. Future applications of xylitol

Xylitol sales temporarily slowed down due to the COVID-19 pandemic outbreak after a partial, ban on imports and exports, a shortage of workers, and so on. This has had a deleterious effect on the market's supply and demand for xylitol (Report Linker, 2021). The production of anhydro xylitol tripelargonate (AXP) is a novel application of xylitol and a sustainable plasticizer for poly (lactic acid)/poly (butylene succinate) (PLA/PBS) blends. Plasticizers play a useful role in toughening blends, as both toughness and elongation at break improve gradually with increasing plasticizer addition. Crystallization and ease of fabrication are enhanced, and the glass transition temperature is lowered, due to the addition of AXP (Hou et al., 2021). In the United States, xylitol is legally allowed to be added to food at the manufacturing stage in appropriate amounts for special dietary objectives. Its application also involves its use in nasal spray, sinus irrigation products, and syrups (www.xlear.com). It plays a huge role in Indian brands like The Himalya Drug Company and Bioxtra for manufacturing toothpaste and mouthwash (Hans et al., 2022). For the prevention of dental cavities, a daily intake of 6-10 g of xylitol is suggested and people with chewing

problems due to temporomandibular joint dysfunction are advised to use xylitol sweets instead of gum. Tolerance levels are also affected by factors such as an individual's weight and 40 gm per day of xylitol is often well tolerated by adults and children exposed to 45 g/d of xylitol and adults exposed to 100 g/d may develop diarrhea (Nayak et al., 2014). Metabolic follow-ups and loading assays form the basis for the present understanding of xylitol as a safe dietary food ingredient as the liver is primarily in charge of xylitol metabolism and the kidneys and other organs also play a role (Mäkinen, 2016). That is how xylitol's potential abilities roll down to the various mentioned industries and further applications will be seen shortly like its potential uses in medicine, cosmetics, and food processing. The medical industry has examined xylitol for its potential in treating diabetes, obesity, and cardiovascular disease, as well as for its anti-inflammatory and anti-cancer properties (Nayak et al., 2014; Mäkinen, 2016). The cosmetics industry has future versions embracing xylitol as a natural humectant and moisturizer for skincare products, due to its ability to improve skin hydration and elasticity (Kluczyk et al., 2021). The food industry has also started to incorporate xylitol as a sugar substitute in chewing gum, candies, and baked goods, as the demand for low-calorie sweeteners has increased among health-conscious consumers (Report Linker, 2021). Furthermore, xylitol has shown promise as a prebiotic, which can encourage the growth of beneficial gut bacteria (Benahmed et al., 2020). Researchers are also investigating xylitol's potential in other industries. For example, xylitol could be used as a feedstock for biofuel and chemical production, using lignocellulosic biomass as a renewable energy source (Zhang et al., 2021).

As research continues, the possible applications of xylitol are vast and exciting. This versatile compound has already shown great promise in various industries and will likely continue to offer even more potential uses in the future. There are currently 70 nations throughout the world that are involved in the supply and production chains of xylitol (Volza's Global Export Import data of xylitol, 2023). Xylitol is in great demand and supply, depending on the numerous industries it is utilized in. Market demand is distributed geographically for xylitol product which is mostly available in liquid and powder form. (Custom Market Insights, 2021). One unique aspect of the xylitol market is its potential use as a natural sweetener for pets, as there is an increasing demand for natural and healthy alternatives in pet foods and treats (Pet Business Staff, 2022). In addition, ongoing research is being conducted on the potential use of xylitol as a natural supplement for improving bone health and treating bone disorders like osteoporosis, due to its positive effects on bone metabolism (Mäkinen, 2016). Xylitol is a promising candidate for the production of bio-based and environmentally-friendly deicers. Its natural properties make it an effective and sustainable alternative to traditional deicing agents such as rock salt. The use of xylitol can help reduce the negative impact of deicers on the environment and infrastructure over time (The Municipal, 2021). Making antimicrobial textiles with xylitol is another fascinating use. It has been demonstrated that fabrics coated with xylitol have antibacterial qualities, which can aid in halting the development of dangerous germs and fungi. According to Niedzióka et al., 2017, this has potential applications in the healthcare sector where it may help lower the risk of healthcare-associated infections (HAIs). Another report-by-Report Linker, 2021 suggests the Asia-Pacific area will be the fastest-growing market for xylitol. In nations such as China, Japan, and India, rising disposable income and changing lifestyles are boosting demand for low-calorie sweeteners such as xylitol. According to the research, the food and beverage industry is the most important application segment for xylitol, followed by dental care items.

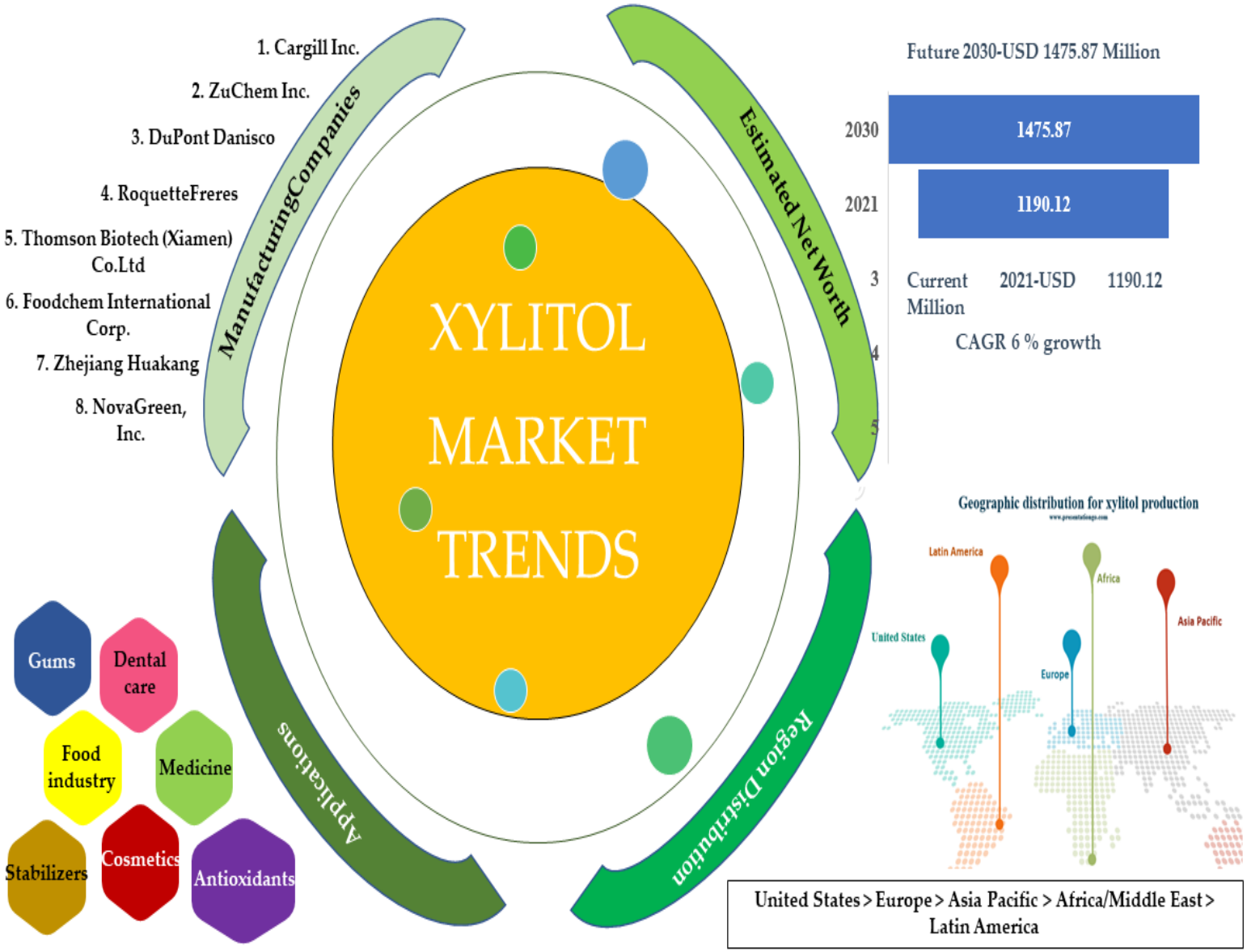

Figure 7. represents the ongoing market trend for the xylitol (Custom Market Insights, 2021).

6. Conclusion

This review provides a concise summary of the possible benefits that xylitol could have in a variety of industries, as well as new ways that could be taken in the future. In addition, the biotechnological method of producing xylitol proves to be more profitable than the chemical method in terms of cheaper costs with higher yields as compared to chemical methods. Therefore, it is high time for switching the current xylitol production with chemical execution by biotechnological approaches. Another element that must be taken into consideration is not to neglect the fact that the strains employed to extract xylose from hemicellulose to extract xylitol are most commonly genetically modified. Despite of prevailing detrimental pandemic effects, the current market trends indicate that xylitol will have favorable expansion and will become increasingly popular in the years to come.

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