

Review Article

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## Xylitol: Production, Optimization and Industrial Application

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### ABSTRACT

The purpose of this review is to shed light on the metabolic profile of xylitol, xylitol production ability of yeast and significant application of xylitol in bioprocessing industry. Quite a lot of parameters influence Xylitol production. Optimized substrate concentration, carbon source, inoculum, aeration, temperature, pH and nitrogen supply are an essential concern. Chemical and enzymatic hydrolysis performs a crucial role in the creation of precursor xylose from agricultural biomass. And it is modified to xylitol predominantly by way of yeast stress. The most customarily used practices are Hydrolysis below acidic which are subjected to quite a lot of procedure parameters. A detoxing process is carried out as many fermentation approach inhibitors are produced for the duration of chemical hydrolysis that decreases xylitol creation. Hemicellulose, which is the second most plentiful polysaccharide in the atmosphere after cellulose, is degraded into xylitol via yeast. Hemicellulose has been successfully converted into fermentable ingredients by the continuous efforts by researchers in the last two decades. Hemicellulose has been efficiently changed into fermentable ingredients by way of the continuous efforts by using researchers in the last two decades. Hemicellulose is probably degraded into fermentable sugars and its conversion into price added products opens up a substantial area of purposes of xylitol in meals production.

### Keywords

Xylose, Xylitol,  
Hemicellulose,  
*Candida* sp,  
Factors,  
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### Introduction

Yeast is one in all the easiest industrial microorganisms, due to its principal position in production, winemaking, baking, and alcohol making. *Saccharomyces cerevisiae* is that the most intensively considered unicellular eukaryote and one of the main industrial microorganisms used in the production of biochemical (Kavsceek *et al.*, 2015). Yeast cells ordinarily come across a mixture of more than a few carbohydrates in industrial strategies. Glucose and sucrose are

probably spent first. The presence of these sugars outcome within the suppression of, the glyoxylate cycle, gluconeogenesis inhalation and the uptake of less preferred carbohydrates (Verstrepen *et al.*, 2004). There are notable differences between baker's yeast, brewer's yeast, wine yeast and distiller's yeast, and these as *S. Cerevisiae*, *S. Bayanus*, and *S. Pastorianus*, according to existing taxonomic classifications (Vaughan-Martini *et al.*, 1998; Cletus., 2003).

The metabolic process of *S. cerevisiae* is explicit for the consumption of glucose, fructose and its disaccharide sucrose. Within the emerging interval of bioeconomy, nevertheless, microbial cell factories ought to successfully eat more plausible, affordable and normally accessible carbon sources, mainly lignocellulose (Hong *et al.*, 2014; Liang *et al.*, 2014). *S. Cerevisiae* can't instantly consume cellulose and for this reason, pretreatment is required to unleash the glucose. The second most plethoric monosaccharide in plant biomass is xylose, however, the amount of xylose metabolism in currently used laboratory and industrial yeast traces are too slow to be of use in a biotechnological method, especially for this reason of too low xylitol dehydrogenase (XDH) activity (Van *et al.*, 1989; Richard *et al.*, 1999).

Xylitol entails the help as a sweetener for diabetic patients. Creation study of xylitol is warranted as xylitol is a worth-brought product with an increasing market point of view. Industrial scale sustainable production of xylitol is with the aid of chemical discount of D-xylose in the incidence of a nickel substance at excessive temperatures. However, this is found to be a costly affair as the excessive temperature and strain requirements, huge separation and purification approaches make the process complex and sophisticated (Meinander *et al.*, 1994). An additional direction for xylitol construction is microbial fermentation (Roberto *et al.*, 1995). The fungi equivalent to *Pachysolen caninophiles*, *Candida guilliermondii*, *Candida paraphimosi*, and *Candida tropicalis* produced xylitol by common xylose-assimilating yeasts (Dahiya *et al.*, 1991; Kim *et al.*, 1998, Morimoto *et al.*, 1986; Yahashi *et al.*, 1996). The microbiological method converts xylose present as xylan in hemicellulose feedstock into xylitol (Nigam and Singh, 1995).

Corncoobs, cottonseed, soybean stalks, popcorn shells, sugarcane bagasse (Horeckar, 1962) and birch wood are one of the crucial fundamental feedstocks used for xylitol creation (Jeffries., 1994). In yeast, D-xylose is diminished to xylitol by means of the enzyme xylose reductase in the presence of NADPH or NADH co-enzymes (Parajo *et al.*, 1998). In some facultative microorganism, xylose reduction to xylitol would be possible with the help of decreasing equivalents even underneath oxygen-free stipulations with the aid of warding off the NAD/NADH redox method imbalance through an NADH-elegant reductase approach.

Its sweetness level is equal to that of sucrose, and it can substitute sucrose on a weight-to-weight basis. When dissolved in water, xylitol has low viscosity and negative heat effects, and it does not require insulin for metabolic regulation. Owing to these benefits, the use of xylitol in the food industry is growing fast. Moreover, engineered *S. cerevisiae* expressing the *XYLI* gene from *P. stipitis* was reportable to supply xylitol (Hallborn *et al.*, 1991). There are two basic strategies for developing production host for a biotechnological process. In the first, a suitable host can be selected from a large number of species based on its performance regarding parameters such as product yield, productivity, and tolerance to the product or other environmental stressors (e.g. pH, temperature, saline). In many cases, targeted optimization of such a host is not possible because the tools for genetic analysis and engineering in that species are not available, leaving only evolutionary optimization or random mutagenesis to produce optimized strains. The second potential strategy is to begin with a widely known species appreciate *S. cerevisiae* and optimize it for product and vital bioprocess conditions. A

few examples of this approach exist, however species-specific traits usually hinder the event of hosts with high productivity and yields on the brink of theoretical limits. However, *S. Cerevisiae* is that the host of substitute in a few instances, when you consider that of the colossal array of tools for genetic engineering and to the enormous varies of expertise related to all options of yeast biology (Kavsceek *et al.*, 2015).

### **Chemical profile of xylitol**

Xylitol could be a without additives sugar alcohol of the five carbon type, i.e. the xylitol molecule consists of five carbon atoms and five hydroxyl groups (Chen *et al.*, 2010). But, then how can this be considered as sugar? The legitimacy for including polyols in the sugar field results from its biochemical relationships; polyols are formed from sugars and can be converted to sugars (i.e. aldoses and ketoses) (Mäkinen, 1989). Some chemical library outlines sugars as crystalline, sweet carbohydrates, so sugar alcohols too fall during this class (Figure 1).

### **Metabolic features of xylitol**

It is mandatory to briefly understand the metabolism of carbohydrate in human body for the better understanding of the oral safety of the xylitol. Xylitol is a natural intermediary product which quite often occurs in the glucose metabolism of human and other animals, and also within the metabolism of several plants and micro-organisms. In human, the normal blood xylitol level ranges between 0.03 and 0.06 mg per 100 ml. As an outcome of the benefit with that it is regenerate within the metabolism, xylitol accommodates a low regular-state attention in human blood (Gupta *et al.*, 2012; Syal and Vohra, 2013).

The rate of excretion of xylitol in the urine is approximately 0.3 mg per hour; there is no major difference between healthy and diabetic subjects in this sense (Mäkinen, 1978).

A major part of liver glycogen is supplied by xylitol or primarily D-glucose. Xylitol is oxidized to carbon dioxide and water by the normal, physiologic path of carbohydrate breakdown (Weissman, 1999). In liver takes place the 85% of the xylitol turnover in the body and about 10% is metabolized extra hepatically in the kidneys, and the small amount is used up by blood cells, the adrenal cortex, lung, testes, brain, fat tissue, etc. The difference between endogenous ("natural") xylitol and that which is supplied from outside should be mentioned: once a xylitol-containing diet is consumed, endogenous xylitol is that the physical intermediate product from D-xylulose and L-xylulose (these area unit the keto-sugars appreciate xylitol) (Mäkinen, 1978). This reaction takes place in the mitochondria catalyzed by enzymes which are specific for xylitol. On the other hand, exogenous (ingested) xylitol is slowly absorbed, and eventually enters the portal circulation and the liver where it is dehydrogenated in the cytoplasm of the liver cells by the non-specific polyol dehydrogenase enzyme which can also act on sorbitol. This enzyme plays a key role in xylitol metabolism and largely determines the metabolic rate of xylitol. Once xylitol is given for a number of days, AN adaptation takes place: the enzyme's levels area unit increased in order that the metabolic capability of a topic, UN agency is conversant in xylitol, is considerably increased.

The factors that contribute to the success of yeasts as probiotics are their robust size, diversity in morphology (budding, pseudomycelial), nutritional flexibility

(ability in utilizing a broad range of nitrogen, carbon, and phosphorous sources), ability to have stress tolerance (to low pH/oxygen/water activity, high osmotic pressure), enzyme secreting potency (secrete a broad range of enzymes such as lipase, peptidase, amylase, invertase, phytase, etc.) (Syal and Vohra, 2013), antioxidative / antitumor/ antimicrobial activity (effective against a wide range of pathogens), and ability to produce several other useful metabolites (Fredlund *et al.*, 2002).

### **Factors affecting production of Xylitol**

There are a few explanations which might be in play in xylitol production in yeasts. There are carbon source, substrate concentration, aeration, inoculum, temperature, pH and nitrogen source.

### **Xylose Concentration**

One of the crucial parameters that impact substrate concentration (D-Xylose) is the yeast growth and the fermentation process. The initial concentration of xylose can affect the xylitol production. Taking this model, in the case of microorganisms that can grow in high osmotic pressure conditions or in the presence of elevated glucose concentrations, a high initial xylose concentration could presumably lead to a higher quantity of xylitol. As the initial concentration of xylose increases, oxygen level increases and thus avoiding the inhibition of the microbial growth. Ghindea *et al.*, (2010) showed that a significant cellular growth takes place in *C. tropicalis* at the beginning of the fermentation process, and the xylitol production found to be improving considerably.

### **Effect of Yeast Level**

Yeast extract is a key nutrient affecting the production of xylitol. Winkelhausen and

Kuzmanova (1996) stated that xylitol production rate increased when the medium contained 20 g/L yeast extract inoculated with *C. tropicalis* DSM 7524, while found xylitol production was inhibited at higher concentrations of yeast extract (>15 g/L). Barbosa *et al.*, (1988) found higher xylitol production at low yeast extract value but declined when the medium contained 5 g/L yeast extract.

### **Effect of Carbon Source**

When D-glucose is used as substrate in low concentration it leads to a growth in *C. tropicalis* and the production efficiency of xylitol. This effect can be explained by the fact that the D-glucose is used in cell growth, D-xylose being consumed only afterwards. The influence of carbon source also proved to be specific to certain species, since results varied in other cases, such as *C. guilliermondii* (Gurpilhares *et al.*, 2008).

### **Effect of Aeration**

Aeration is a key parameter for xylitol producing yeasts and determines whether D-xylose will be fermented or respired. It is found to be an effective process to determine the oxygen flux that will enable balanced utilization of carbon, both for growth and xylitol production. Prakasham *et al.*, (2009), reported xylitol production by yeasts is associated with microaerobic conditions. Several authors have reported effect of aeration and agitation rate on yeast growth and xylitol production (Branco *et al.*, 2007, Sreenivas Rao *et al.*, 2004, Walther *et al.*, 2001). But, Roseiro *et al.*, (1991) reported a combinatorial effect of substrate concentration and aeration rate on xylitol production in yeasts.

### **Effect of Temperature**

The suitable temperature for xylitol production by *C. tropicalis* is 30°C. The

xylitol production may be a temperature freelance method, if the yeast is genteel at a temperature between thirty and 37°C and it's found that the yield decreases dramatically higher than temperature (Silva *et al.*, 1994; Ghindea *et al.*, 2010). Sreenivas *et al.*, (2006) discovered that a variation of the 3°C affects (27%) the assembly of xylitol Iraqi National Congress. However, the conversion to xylitol by *Candida* sp B-22 has been discovered constant over the temperature vary of 35–40°C whereas at 45°C and better, the xylitol yield declined greatly (Cao *et al.*, 1994). This could ensue to the reduction within the activities of NADPH and NADH dependent sugar enzyme (Slininger *et al.*, 1987).

### **Effect of pH**

The ideal pH for *D. hansenii* is 5.5, though for *C. parapsilosis*, *C. guilliemondii* and *C. boidinii* the ranges are 4.5-5, 6.0, and 7.0 respectively. It has been observed that inhibition of microbial growth is due to undissociated form of acetate (Fond *et al.*, 1985). However, when pH is increased, the undissociated form of acetic acid may be decreased. The optimum pH for xylitol production in *Candida* species is 4.5–7 (Ghindea *et al.*, 2010). According to the observation of Cheng *et al.*, (2009) when the pH increases from 4.5 to 6.0 it leads to dramatic increase in xylitol and productivity.

However, the highest production of xylitol is found at pH 6.0. The finding of El-Batal and Khalaf (2004) shows that there is low xylitol production at pH 3.0, compared to pH 6.0 (Pfeifer *et al.*, 1996) and Rodrigues *et al.*, (1998) have observed that when pH is reduced in the medium, the toxic effect of acetic acid is increased because of the entry of acid into the cell in its undissociated form.

### **Nitrogen Sources and its effects**

Type and concentration of nitrogen source in the medium play a key role in influencing the xylitol production by microorganism. Lachke *et al.*, (1992) found that xylose consumption enhanced when media were supplemented with an organic nitrogen source. These organic nitrogen sources are found to be yeast extract and the urea by the yeasts for the production of xylitol (Tefaw and Assefa 2014). Lu *et al.*, (1995) reported the effect of glycine, asparagine, urea, yeast extract,  $(\text{NH}_4)_2\text{SO}_4$ ,  $\text{NH}_4\text{NO}_3$ ,  $\text{NaNO}_3$ ,  $\text{NH}_4\text{Cl}$ , and  $\text{NH}_4\text{H}_2\text{PO}_4$  as nitrogen sources for the production of xylitol by utilizing mutant *Candida* sp. L-102. A maximum (100 g/L) xylitol production was achieved by supplementing the medium with 114 g/Lxylose and incorporating 3 g/L urea.

### **Xylitol production using Hemicellulose from Agricultural Waste**

A few drawbacks associated with the chemical production of xylitol process are alteration proficiency, environment effect and energy input parameters; The new research has brought out alternative raw ingredients and production processes. Xylo-oligosaccharides and hemicellulose are the most common polysaccharides available in nature containing of heterogeneous polymers of hexoses (glucose, mannose and galactose) and pentose's like xylose and arabinose (Saha, 2003; Kuhad, 1993). In performance to commensurate with explain this data they sire be hydrolyzed into artless monomeric sugars either by chemical or enzymatic approaches for fermentation using microorganisms. Several studies on hydrolysis of xylose-rich hemi cellulose materials have been performed for utilization as substrates for biotechnological xylitol production. A variety of plant biomass materials were evaluated as source

of raw materials such as corn cobs (Sreenivas-Rao *et al.*, 2006), sugar cane bagasse (Carvalho *et al.*, 2005), eucalyptus (Villarreal *et al.*, 2016), and brewery's spent grain (Mussatto and Roberto 2004), olive tree pruning (Romero *et al.*, 2007), soybean hull (Santos *et al.*, 1995), palm oil empty fruit bunch fiber (Rahman *et al.*, 2007), and rice straw (Lu *et al.*, 1995). The utilization of these depends on the degradation of those polymeric substances to simple sugars, with hemicelluloses as predominant polysaccharide in the overall conversion method (Figure 2).

In turn chemical hydrolysis becomes a simple and rapid method for hemicellulosic material. The treatment circumstances vary with agro-industrial material and with respect to chemical agent type and concentration, incubation temperature and time (Sun *et al.*, 2002). The agricultural residues or hardwoods are used as raw materials; xylose is the most plentiful sugar in hydrolysates in addition to small fractions of other sugars. Integral or enzymatic hydrolysis has been proven as an in rotation hydrolysis method. This method offers the advantage of low chemical and energy use, but solely depends on enzyme accessibility to the diverse biomass structure. During the process of enzymatic hydrolysis, the enzymatic hydrolysis rate of lignocellulosic biomass depends on catalytic properties of enzymes, their loading concentrations, the hydrolysis period, reaction parameters employed biomass type, pretreatment method employed and compounds produced during pretreatment process (Zhu *et al.*, 2008). Reduction of hemicellulosic crystallinity improves the enzymatic hydrolysis rate and time in addition to the enzyme loading. Lignin is identified as a major limiting factor among all biomass components to enzyme attack on cellulose indicating the significance of reducing the

structural integrity caused by lignin before hydrolysis. Enzymatic hydrolysis results in high yields in bioconversion of sugars from pretreated photosynthetic biomass. However, the cost of enzymes is a major aspect and needs to be counted. Another alternative is the use of hemicellulosic hydrolytic enzyme blend; but, identification and optimization process of the specific enzyme blend for each material is required.

Traditional pathway engineering tactics have enabled figuring out xylose and arabinose catabolism in yeast, however for the excessive yield continued optimization of those strains are needed along with novel metabolic engineering tools and strategies (Young *et al.*, 2010). Specifically, novel methodologies should target and exploit additional cellular mechanisms influencing metabolic pathways, such as molecular transport, catabolite sensing and cellular tolerances.

The production of xylitol via the chemical procedure is pricey because of complex separation and purification steps. On the other hand, the fermentation process on an industrial scale is not feasible due to reduced productivity. As a result, it is most important to explore alternative ways for the amazing production of xylitol utilizing XR enzyme. The enzymatic technique probably able to overcome the disadvantages of the chemical approach that is largely being used at present and also the fermentation process that is under investigation (Figure 3).

### **Current research in xylitol**

Certain fruits and vegetables such as raspberry, strawberry and yellow plum constitute xylitol. At present, the extraction process from such sources is not cost-effective, due to the presence of relatively low xylitol content, based on dry weight

basis (Grembecka *et al.*, 2014). Hence, xylitol is widely produced through a chemical process at industrial scale, which is based upon catalytic xylose dehydrogenation. The process is not only costly and energy intensive, but also environmental risky due to the use of a toxic catalyst and high-pressure hydrogen gas (Prakasham *et al.*, 2009). These disadvantages tend to seek another production process (Park *et al.*, 2014). Xylitol production from microorganisms have been considered a sustainable process for numerous industrial applications because, the process can be conducted under mild controlled conditions. In microbes, yeast is the proficiency xylitol hack, utilizing xylose as sole substrates. In particular, yeast strains such as *C. boidinii*, *C. guilliermondii*, *C. parapsilosis*, and *C. tropicalis* have been extensively exploited for xylitol production (Mohamad *et al.*, 2015).

Because of the quality demand from the pharmaceutical and food industries, few culture conditions such as temperature, pH, and oxygen transfer rate have been optimized (Feffries and Jin, 2004; Sampaio *et al.*, 2008; Silva *et al.*, 2006). Despite the tremendous information available on the effect of these parameters on xylitol production by *Candida* sp. (Horitsu *et al.*, 1992; Li *et al.*, 2015; Misra *et al.*, 2011), *C. tropicalis* is particularly used for various industrial applications (Silva *et al.*, 1994; Rehman *et al.*, 2013). Although many microorganisms are capable of natively utilizing xylose, the baker's yeast (*Saccharomyces cerevisiae*) is the main as a result of the genetic tractability, wide industrial applications and ethanol construction ability.

Plant biomass such as corn (Sreenivas-Rao *et al.*, 2006), sugarcane bagasse (Carvalho *et*

*al.*, 2015; Sreenivas-Rao *et al.*, 2006; Branco *et al.*, 2007), eucalyptus (Villarreal *et al.*, 2006), spent brewing grain (Mussatto *et al.*, 2004), palm oil empty fruit bunch fiber (Romero *et al.*, 2007), rice straw (Liaw *et al.*, 2008), banana peel (Ahmad., 2010), mungbean hull, peanut hull, oat hull (Mushtaq *et al.*, 2010), and coffee husks (Arrizon *et al.*, 2012) are used as a source of raw materials due to its great significance for sustainable development in contrast to renewable nonorganic materials (Van Wyck., 2001; Granstrom *et al.*, 2001; Granstrom *et al.*, 2002; Prakasham *et al.*, 2009) nature and chemicals used (Iranmahboob *et al.*, 2002). Chemical hydrolysis treatment method is a simple and rapid but vary with treatment conditions (Sun and Cheng, 2002). Different mineral acids such as sulfuric acid, nitric acid, hydrochloric acid (Herrera *et al.*, 2004), and phosphoric acid are used to high temperature and pressure for acid hydrolysis treatment. Pretreatment with dilute acid at high temperature fractionates into xylose, arabinose, and other sugars, which are water soluble (Bungay, 1992). The hydrolysate also comprises of cellulose and lignin. The lignin can be separated with solvents such as formic acid or ethanol. The chemical process is laborious, and cost- and energy-intensive. These biotechnological processes are highly attractive alternatives that are able to produce a high-quality and cost-effective product. Enzymatic hydrolysis is another alternative hydrolysis protocol with low chemical and energy use and depends upon catalytic properties of enzymes, loadings concentrations, and the hydrolysis period, type of biomass, method of pretreatment and reaction parameters (Zhu *et al.*, 2008). Recombinant *Saccharomyces cerevisiae* harboring the XR gene encoding xylose reductase from *Pichia stipites* was also reported to convert xylose into xylitol using glucose as co-substrate (Hallborn *et al.*,

1991). Kogji and Ghosalkar (2016) reported highest volumetric (0.28 gL<sup>-1</sup> h<sup>-1</sup>) and specific (34 mgg<sup>-1</sup> h<sup>-1</sup>) xylitol productivities were obtained by *Saccharomyces cerevisiae* strains overexpressing xylose reductase (XR) genes from *Candida tropicalis*, *Pichia stipitis*, *Neurospora crassa*, and an endogenous gene GRE3.

### Xylitol Application

The shelf life, color, and taste of food products are enhanced by using xylitol. The sugar-free chocolate, chewing gum, hard candies, wafer fillings, chocolate, pastilles, and other sweets for diabetics are produced by utilizing xylitol along with other sugar substitutes (Bar, 1991). Chewing gums containing xylitol have been known to show medical applications (Uhari *et al.*, 1996; Featherstone *et al.*, 1982). Xylitol is slowly absorbed and metabolized inside the body. Consumption of xylitol is associated with several beneficial health effects such as significant reduction in tooth decay, increased bone density, weight loss and stabilization of blood sugar level (Vasilescu, 2011).

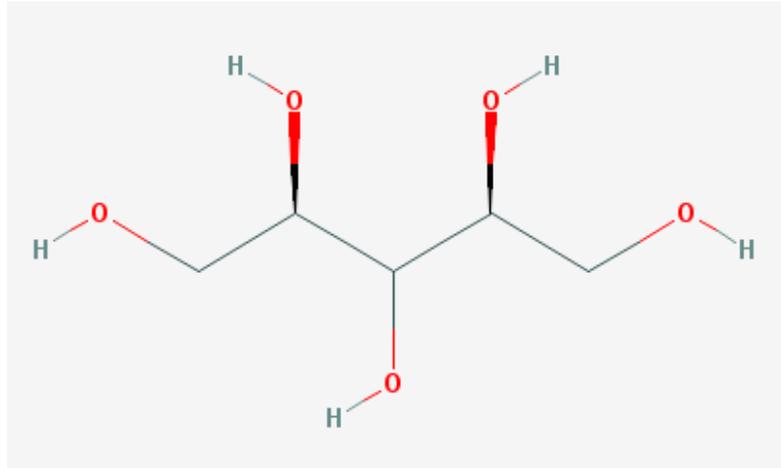
The addition of xylitol in bakery products provides the characteristic flavor and color to baked products and proved to be a good substitute in sugar cake. Sometimes, cookies prepared by adding xylitol have brown spotted due to the poor solubility of xylitol in cookie dough, which contained fat. Winkelhausen *et al.*, (1997) reported the potential application of xylitol as a low-energy sweetener in baked products.

Cookies were prepared with 100% xylitol and showed no significant effect on texture and flavor of cookies after long-term storage. However, the cookies containing xylitol showed good taste, color, flavor, and texture (Mushtaq *et al.*, 2010). Rusks were prepared by adding xylitol and concluded that texture of the rusks became hard (Ahmad, 2010). Xylitol are added in diets for its beneficial health effect to diabetic patients due to non-cariogenic properties, and non-fermentability. Cough syrups, tonics, and vitamin preparations made by addition of xylitol are non-fermentable and are harmless to the teeth (Feigal *et al.*, 1981).

**Table.1** Biotechnological Production of Xylitol from Agro-Industrial Wastes

| S. No | Wild Yeasts                              | Hemicellulose / Substrate                  | Yield g/ L <sup>-1</sup> /h | Reference                          |
|-------|--|--|-----------------------------|------------------------------------|
| 1     | <i>Candida guilliermondii</i> FTI 20037  | Sucrose supplementation of sugarcane straw | 0.57                        | Hernández <i>et al.</i> , 2015     |
| 2     | <i>Candida tropicalis</i> HDY-02         | Corn cob                                   | 58                          | Ling Het <i>et al.</i> , 2011      |
| 3     | <i>Candida athensensis</i> SB18          | Horticultural waste                        | 0.97                        | Zhang <i>et al.</i> , 2012         |
| 4     | <i>Candida magnolia</i>                  | Corn cob                                   | 18 g                        | Tada <i>et al.</i> , 2012          |
| 5     | <i>Pichia kudriavzevii</i> HOP-1         | Rice straw                                 |                             |                                    |
| 6     | <i>Pichia stiptis</i>                    | Sugarcane bagasse                          | 8.4                         | Buaban <i>et al.</i> , 2010        |
| 7     | <i>Debaromyces hansenii</i>              | Sugarcane bagasse                          | 0.28                        | Prakash <i>et al.</i> , 2015       |
| 8     | <i>Debaryomyces nepalensis</i> NCYC 3413 | Corn Cob                                   | 14.6                        | Paidimuddala <i>et al.</i> , 2014  |
| 9     | <i>Pachysolen tannophilus</i>            | Olive stones                               | 0.44                        | Saleh <i>et al.</i> , 2014         |
| 10    | <i>Kluyveromyces marxianus</i> NIRE-K3   | glucose and xylose                         | 0.88                        | Arora <i>et al.</i> , 2015         |
| 11    | <i>Kluyveromyces sp.</i> IIPE453         | Sugarcane bagasse                          | 0.61                        | Kumar <i>et al.</i> , 2015         |
| 12    | <i>Cyberlindnera galapagoensis</i>       | Sugarcane bagasse                          | 24                          | Guamán-Burneo <i>et al.</i> , 2015 |

**Fig.1** Xylitol 3D Structure.



**Fig.2** Xylose assimilation pathways using agricultural waste (Hemicellulose)

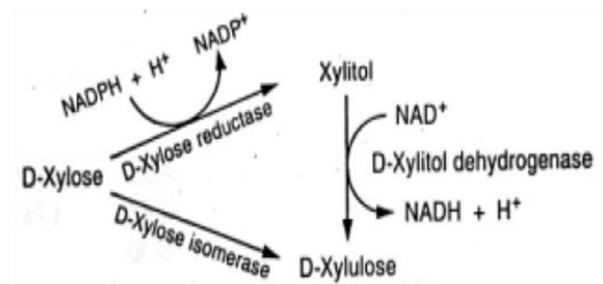
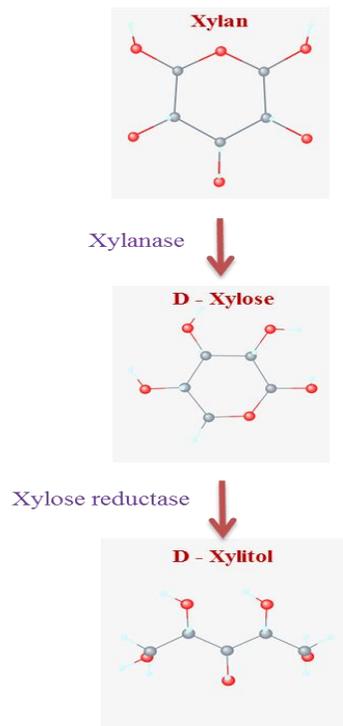
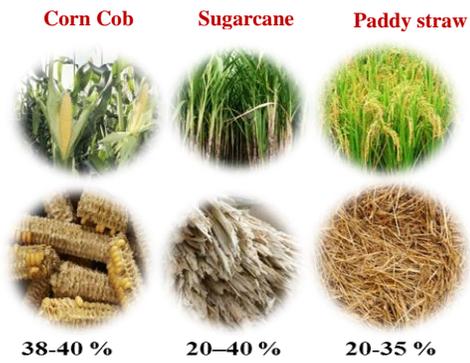
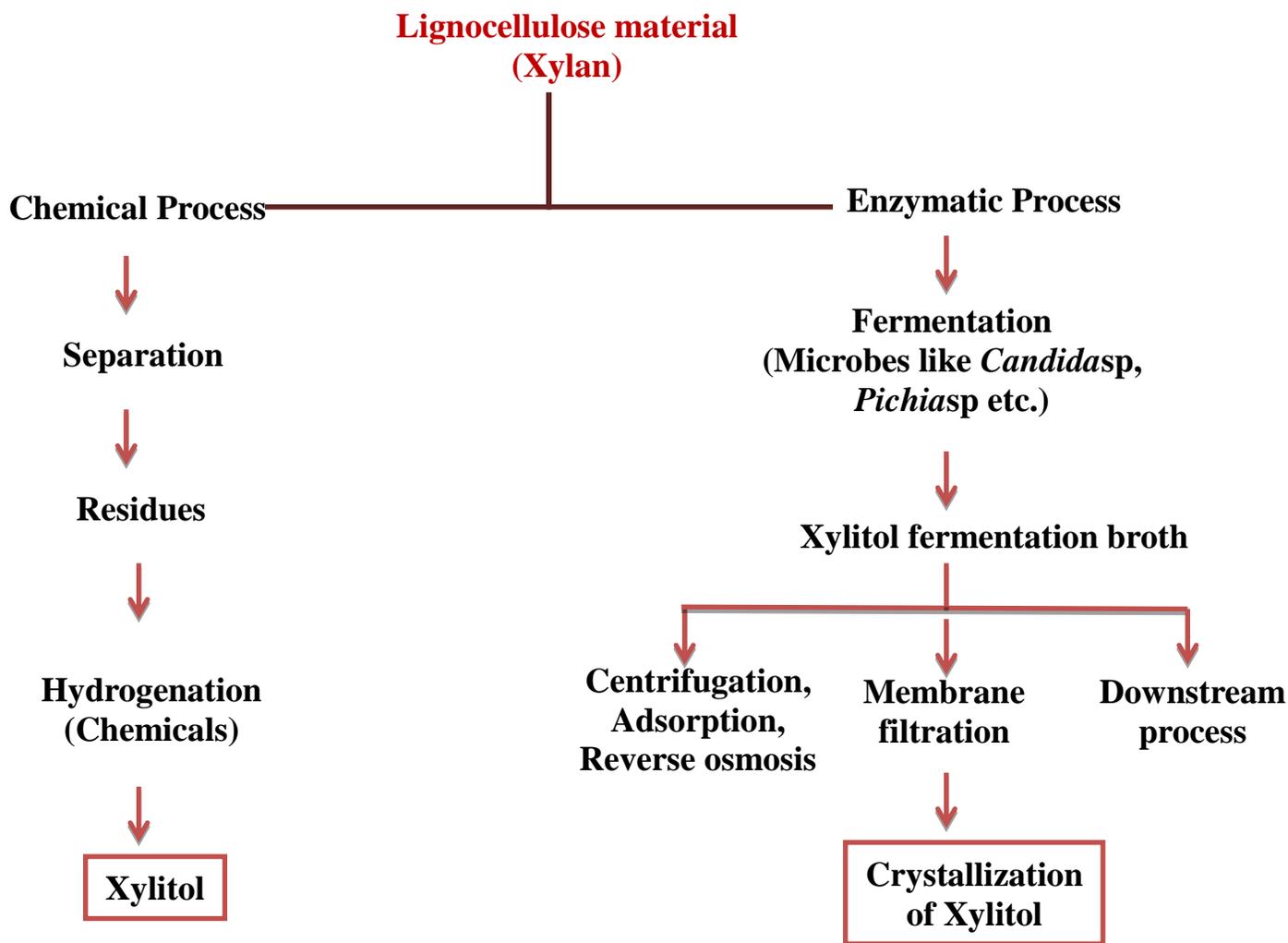


Fig.3 Purification of xylitol in different method



Xylitol shows non-toxicity to the body via all routes of administration and Joint FAO/WHO skilled Committee on Food Additives (JECFA) and also the Scientific Committee for Food (SCF) of the EU have approved it as safe due to its low glycemic effect (Jain and Grover, 2015). There is a little or no outcome on blood glucose for the reason that of incomplete absorption (Schaefer *et al.*, 2009). Xylitol is regarded to be an advantage alternate sweetener for diabetic patients, since of controlling glucose stage of blood glucose, decreasing lipid stage, controlling weight and other

well-being advantages (Huttunen *et al.*, 1982).

In conclusion, xylitol to be economically viable and eco-friendly, alternative strategies of research was initiated. A focus should be maintained on a common platform of understanding of the hydrolysate material, hydrolysis procedure, microbial performance, bioconversion environment. Downstream processing is one of the essential aspects of development of an integrated technological solution for production of second-generation biorefinery

products like xylitol via biotechnological process at an economic industrial scale. Prospective of agricultural wastes for the production of xylitol; its utilization in various foods and pharmaceutical and health effects and safety issues have been reviewed. In food and pharmaceutical sectors xylitol is noted worldwide for its a low calorific value and various potential applications. Xylitol is produced by raw material of xylose as the substrate by chemical hydrogenation or bioconversion with certain microbial species. The chemical process is cost intensive and energy consuming manner. Hemicellulosic xylan can be converted to xylose either by chemical or enzymatic hydrolysis which depends on parameters related to biomass, hydrolysis, and enzyme. Chemical hydrolysis of agricultural biomass produces microbial growth inhibitors which need to be detoxified. Detoxification of hydrolysate can be carried out by physical, chemical, and biological methods. However, the combination of all these strategies is most suitable and cost effective approach. Much research has been carried out to find xylose-consuming species and has concluded that *Candida* species are the best xylitol producer. Microbial production of xylitol is influenced by various process parameters like pH and temperature. Several studies have investigated the optimization of xylitol production using free or immobilized cells in batch or in continuous fermentation conditions using different reactor configurations. Considering the limitation of microbial conversion of xylose to xylitol, especially with the use of the necessary high dilution rates and residence time, it is important to focus on the increase of xylose reductase-dependent enzymatic bioconversion of xylose from hemicellulosic hydrolysate. Xylitol is a promising sweetener that can be successfully utilized in the food industry for example confectionery,

dairy, bakery products and even for in cough syrups, for diabetics and health aware people.

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