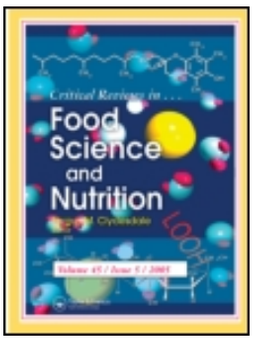

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Xylitol: A Review on Bioproduction, Application, Health Benefits, and Related Safety Issues

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Xylitol is a pentahydroxy sugar-alcohol which exists in a very low quantity in fruits and vegetables (plums, strawberries, cauliflower, and pumpkin). On commercial scale, xylitol can be produced by chemical and biotechnological processes. Chemical production is costly and extensive in purification steps. However, biotechnological method utilizes agricultural and forestry wastes which offer the possibilities of economic production of xylitol by reducing required energy. The precursor xylose is produced from agricultural biomass by chemical and enzymatic hydrolysis and can be converted to xylitol primarily by yeast strain. Hydrolysis under acidic condition is the more commonly used practice influenced by various process parameters. Various fermentation process inhibitors are produced during chemical hydrolysis that reduce xylitol production, a detoxification step is, therefore, necessary. Biotechnological xylitol production is an integral process of microbial species belonging to Candida genus which is influenced by various process parameters such as pH, temperature, time, nitrogen source, and yeast extract level. Xylitol has application and potential for food and pharmaceutical industries. It is a functional sweetener as it has prebiotic effects which can reduce blood glucose, triglyceride, and cholesterol level. This review describes recent research developments related to bioproduction of xylitol from agricultural wastes, application, health, and safety issues.

Keywords Xylitol, production, application, health effects, safety issues

INTRODUCTION

Xylitol is a naturally occurring sugar-alcohol having five carbon atoms and five hydroxyl groups and present in a very small quantity in fruits such as plums, strawberries, and raspberries and vegetables such as cauliflower, pumpkin, and spinach. Commercial production of xylitol is based on hydrogenation of xylose in a nickel-catalyzed process which is an energy and cost demanding. Therefore, some alternative biotechnological processes have been studied, especially those involving yeasts from *Candida* genus. Currently, xylitol market lies between 20,000 and 40,000 tons per year with an economic value ranging between 90 and 340 million dollars (Van Wyk, 2001; Granstrom et al., 2007a, b; Prakasham et al., 2009).

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Xylitol has applications for at least three types of industries, namely, food (for dietary especially in confectioneries and chewing gums), odontological (due to its anticariogenicity, tooth rehardening, and remineralization properties) and pharmaceutical (for its tooth friendly nature, capability of preventing otitis, ear and upper respiratory infections, and its possibility of being used as a sweetener in syrups, tonics, and vitamin formulations) (Prakasham et al., 2009). However, the foremost utilization is for the prevention of dental caries as it inhibits the growth of microorganisms responsible for tooth decay (Yoshitake et al., 1971; Hyvonen et al., 1982; Makinen, 2000a, b). Besides this, it is accepted for consumption for diabetics and helps in treatment of hyperglycemia as its metabolism is independent of insulin (Yoshitake et al., 1971). Furthermore, it is also considered to be a functional food due to its prebiotic nature (Leonhardt, 2005). Its market value is increasing day by day and is estimated to be \$340 million per year with a selling price of \$4–5 kg^{-1} (Prakasham et al., 2009).

It can be produced either by chemical hydrogenation of xylose or by biotechnological processes. The chemical process is difficult, costly, and energy intensive. One of the alternatives is bioconversion of renewable biomass sources which requires hydrolysis followed by bioconversion of xylose from crude hydrolysate to xylitol employing specific microbial strains for fermentation (Sreenivas et al., 2004, 2006). The precursor xylose is produced from agricultural wastes by enzymatic or chemical hydrolysis and can be converted to xylitol mostly by yeast strains which present the possibilities of economic production by reducing required energy when compared to chemical production. Biomass pretreatment under acidic conditions is the most commonly used practice and is influenced by various process parameters. Various microbial growth inhibitors are produced during acid hydrolysis that decrease xylitol production from xylose, a detoxification step is, therefore, crucial. As a cheap raw material, agricultural wastes are considered as potential sources for its bioproduction.

This review describes the conversion of hemicellulosic biomass toward production of xylitol and its utilization in various food and medicines. Furthermore, the xylitol health effects and safety issues are discussed.

NATURE AND OCCURRENCE OF XYLITOL

Xylitol ($C_5H_{12}O_5$) is a naturally occurring pentose sugar alcohol used as sweetener. It was first synthesized in 1891 by German and French scientists. During the next five decades, it got very little attention, however sugar shortage during World War II prompted the search for new sweetener. Its chemical structure is shown in Fig. 1. Sweetening power of xylitol is equivalent to sucrose; however, other polyols possess less sweetness than sucrose. It has one-third caloric content than conventional sugar and thus has potential to replace sucrose in low caloric products. The physical and chemical properties of xylitol are listed in the Table 1. The special properties of xylitol find use in food and pharmaceutical industries. It occurs as an intermediary product of carbohydrate metabolism in humans and animals. About 5–15 g xylitol is produced per day in human adults (Pepper and Olinger, 1988). It is present in some fruits and vegetables in a very low quantity (Table 2) (Emodi, 1978; Wang and Van Eyes, 1981; Parajo et al., 1998).

LIGNOCELLULOSIC BIOMASSES FOR BIOPRODUCTION

Lignocellulosic biomasses (LBs) are wide spread, abundant, renewable, cost-effective, and economical sources of polysaccharides which can be used for xylitol production. These sources include agricultural, agro-industrial, and forestry residues. These residues contain lignocellulose as organic matter which is mainly composed of cellulose (34–50%), hemicellulose (19–34%), lignin (11–30%), and smaller amounts of pectin, protein, extractive, and ashes. Composition of these components differs with the source of plant species, age, and growth conditions. Most abundant heterogeneous polymer of LBs is hemicellulose which comprises of pentoses (xylose and arabinose), hexoses (mannose, glucose, and galactose), and sugar acids. In contrast to cellulose, hemicellulose is not chemically homogeneous. Xylans are the most abundant hemicelluloses (Bobleter, 1994). Xylans of many plant materials are heteropolysaccharide with homogeneous backbone chain of 1, 4-linked β-D-xylopyranose units. In addition to xylose, xylan may contain arabinose, glucuronic acid, or its 4-O-methyl ether, and acetic acid, ferulic

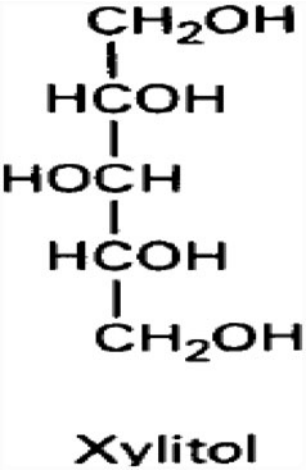

Figure 1 Xylitol chain structure.

Table 1 Chemical and physical properties of xylitol

Formula	$C_5H_{12}O_5$
Molecular weight	152.15
Appearance	White, crystalline powder
Odor	None
Solubility at 20°C	169 g/100 g H_2O
pH in water (1 g/10 mL)	5–7
Melting point (°C)	93–94.5
Boiling point (at 760 mmHg)	216°C
Density (bulk density) (15°C)	1.50 g/L
Caloric value 4.06 cal/g	(16.88 J/g)
Moisture absorption (%) (4 days, 20–22°C);	
at 60% relative humidity	0.05
at 92% relative humidity	90
Density (specific gravity) of aqueous solution (20°C);	
10%	1.03
60%	1.23
Heat of solution	Endothermic, 36.61 cal/g
Viscosity (CP) (20°C);	
10%	1.23
40%	4.18
50%	8.04
60%	20.63
Relative sweetness	Equal to sucrose, greater than sorbitol, and mannitol
Specific rotation	Optically inactive

acid, and p-coumaric acids. The composition of branches depend on the source arabinofuranosyl, A-1, 2, or 4 are glucuronic acid substituents (Eda et al., 1976). They can thus be positioned homoxylan as linear, arabinoxylan, and glucuronoxylan glucuronoarabinoxylan. Xylans from different sources, such as grasses, cereals, softwood, and hardwood differ in their composition. Birchwood xylan contains 89.3% xylose, arabinose, 1%, 1.4% glucose, and 8.3% anhydrouronic acid (Kormelink and Voragen, 1993). Rice bran xylan contains 46% xylose, arabinose 44.9%, galactose 6.1%, glucose 1.9%, and 1.1% anhydrouronic acid (Shibuya and Iwasaki, 1985). Wheat arabinoxylan contains 65.8% xylose, 33.5% arabinose, 0.1% mannose, galactose 0.1%, and 0.3% glucose (Gruppen et al., 1992).

Corn fiber xylan is one of the heteroxylans complex with linked β (1, 4)-xylose (Saha and Bothast, 1999). It contains 48–54% xylose, arabinose 33–35%, 5–11% galactose, and 3–6% glucuronic acid (Doner and Hicks, 1997). Almost 80% of the xylan backbone is highly substituted with monomeric side chains of arabinose or glucuronic acid linked to O-2 and/or O-3 of xylose residues, and also by oligomeric side chains containing arabinose, xylose, and galactose (Saulnier et al., 1995). The heteroxylans which are interconnected to form a network in which the cellulose microfibrils are embedded are strongly influenced by diferulic cross-bridges. Structural wall proteins might be cross-linked together by isodityrosine bridges and with feruloylated heteroxylans, thus forming an insoluble network (Hood et al., 1991).

A variety of other plant biomasses has also been evaluated as a source of raw materials such as corn (Sreenivas et al., 2006), sugarcane bagasse (Carvalho et al., 2005; Sreenivas et al., 2006; Branco et al., 2011), eucalyptus (Villarreal et al., 2006), spent brewing grain (Mussatto and Roberto, 2004; Carvalheiro et al., 2005), olive tree pruning (Romero et al., 2007), soyabean hull (Schirmer-Michel et al., 2008), palm oil empty fruit bunch fiber (Rahman et al., 2007), rice straw (Liaw et al., 2008), banana peel (Ahmad, 2010), mongbean hull, peanut hull, oat hull (Mushtaq, 2011), and coffee husks (Arrizon et al., 2011). These are organic in nature and are of great significance for sustainable development in contrast to renewable nonorganic materials and fossil carbohydrates (Van Wyk, 2001; Granstrom et al., 2007a, b; Prakasham et al., 2009).

PRETREATMENTS OF LIGNOCELLULOSIC BIOMASS

Biomass pretreatment plays a crucial role in a LB-based material for processing of three major output streams i.e. cellulose, hemicelluloses, and lignin (Carvalheiro et al., 2008). LBs exhibit a significant stability against chemical and biological attacks and cannot often be converted into simple sugars under normal conditions. Therefore, pretreatment is necessary in order to alter the structural integrity, remove the lignin, and increase the surface area to make LB available as fermentable sugars. However, performance of pretreatment depends on selected LB harvesting nature, lignin and other component composition, time, temperatures, and chemicals used (Iranmahboob et al., 2002).

A variety of pretreatments are available for LBs to fractionate, solubilize, and hydrolyze into cellulose, hemicellulose, and lignin components (Weil et al., 1994; Wyman, 1994). These treatments include application of concentrated acid (Goldstein and Easter, 1992), dilute acid (Saha and Bothast, 1999), alkaline (Koullas et al., 1993), SO2 (Clark and Mackie, 1987) hydrogen peroxide (Gould, 1984), steam explosion (autohydrolysis) (Fernandez-Bolanos et al., 2001), ammonia fiber explosion (AFEX) (Dale et al., 1996), wet-oxidation (Schmidt and Thomsen, 1998), lime (Kaar and Holtzaple, 2000), liquid hot water (Laser et al., 2002), CO_2 explosion (Saulnier et al., 1995), and organic solvent treatments. In each process, the LB is reduced in size which opens its physical structure (Chum et al., 1988).

Chemical hydrolysis is a simple and rapid method for hydrolysis of HB; however, treatment conditions vary with the biomass and with respect to chemical agent type, concentration, incubation temperature, and time (Sun and Cheng, 2002). For acid hydrolysis, different mineral acids such as sulfuric acid (Vinals-Verde et al., 2006), nitric acid, hydrochloric acid (Herrera et al., 2004), and phosphoric acid are used at high temperature and pressure. Pretreatment with dilute acid at high temperature fractionate hemicellulose to its component sugars (xylose, arabinose, and other sugars), which are soluble in water (Bungay, 1992). The hydrolysate also comprises of cellulose and lignin. The lignin can be separated with solvents such as formic acid or ethanol.

Enzymatic hydrolysis is another alternative hydrolysis method which offers conceptual edges like low chemical and energy use, but it depends on enzyme accessibility to the heterogeneous biomass structure. The rate of enzymatic hydrolysis of LBs is dependent on catalytic properties of enzymes, their loadings concentrations, the hydrolysis period, biomass type, pretreatment method employed, reaction parameters employed, and compounds produced during pretreatment process (Zhu et al., 2008).

COMPONENTS OF BIOMASS HYDROLYSATE

A range of products such as glucose (mainly from cellulose and hemicellulose), xylose, mannose, galactose and acetic acid (from hemicellolose), and phenolic compound (from lignin) are produced during the hydrolysis process. Moreover, other compounds are also produced during hydrolysis mainly, when chemical hydrolysis is employed. Without exception, all sugar liquors obtained by chemical hydrolysis contain furfural, hydroxymethyle furfural (HMF) phenolic compounds and aliphatic acids. Furfural and HMF are degradated products of pentoses and hexoses, respectively. Further degradation of furfurals leads to the production of formic acid. HMF is normally produced in less concentration as compared to furfural by hexoses degradation mainly due to the low quantities of hexose

in hemicellolose. This may be due to the conditions applied in the HB hydrolysis process that do not degrade hexoses in large quantities. Acetic acid is released by the breakage of hemicellulosic aceytle groups. Hydrolysis with dilute acid also degrades a minor part of lignin to a wide range of aromatic compounds (Palmqvist and Hahn-Hagerdal, 2000). In addition, other compounds such as acidic resins, tannic, terpene, palmitic acids, vanillic, syringic, caproic, caprylic, and pelargonic are produced during chemical hydrolysis (Mussatto and Roberto, 2004; Bower et al., 2008).

EFFECT OF INHIBITORS OF BH ON BIOCONVERSION OF XYLITOL

Hydrolysis of LBs is the first step in the bioproduction of xylitol. In the next step, it is purified from hydrolysate by various detoxification techniques. Furfurals, acetic acid, and phenolic compounds found in acid hydrolysates are removed when microorganisms are used in the subsequent steps (Du Preez, 1994). In the next step, hydrogenation of xylose by a chemical process with a Raney nickel catalyst or biological method using microorganisms is involved followed by purification (Jeffries and Sreenath, 1988; Parajo et al., 1998).

The major drawback of chemical hydrolysis is the decline of available monosaccharide and production of their derivatives (furan, HMF and phenolic toxic compounds) which are microbial growth inhibitors and mired further biotransformation (Mussatto and Roberto, 2004). However, concentration of microbial fermentative inhibitory compounds is dependent on raw material as well as the operational conditions. Microbial toxicity can also be linked with fermentation variables like microbial physiological growth condition, pH of the medium and dissolved oxygen concentration. On the whole, biomass hydrolysate (BH) inhibitors can be categorized as lignin and sugar degradation products generated during hydrolysis and heavy metal ions.

For xylitol production furfurals derived from pentose sugars are the main microbial growth inhibitor compounds present in chemical hydrolysates. They inhibit the growth of microbes ranging from 25–99% relative to the furfural concentration (0.5–2 g/L) and cell mass yield per ATP by interfering with the respiration process. Martinez et al. (2001) reported that the growth of *Pichia stipitis* and *Sacchromyces cerivisiae* was reduced by 100% when the HMF in the concentration of 1.5 and 1 g/L was supplemented in the growth medium indicating the inhibitory effect variation with the type of microbial strain. Presence of low concentration of these compounds in the fermentation medium showed better microbial growth indicating the role of microbial strain properties during bioconversion of hydrolysates. In addition, the antagonistic effect of furfural and HMF along with acetate, formic, and leavulinic acid on microbial growth was also reported with *P. tannophilus* and *P. stipitus* during xylose fermentation (Vogel-Lowmeier et al., 1998).

A variety of lignin degradation products that include aromatic, polyaromatic, phenolic, and aldehydic compounds present in hydrolysate also cause inhibitory effects on microbial growth by integrating into biological membranes and affecting the membrane permeability. Phenolic compounds at more than 0.1 g/L concentration are reported to affect the xylose consumption, cell growth and xylitol production of *C. guilliermondii* (Villa et al., 1998). Acetic acid toxic effect is mainly associated with its pKa value as at this value acetic acid is liposoluble, diffuse across the plasma membrane and discharge protons resulting in cell death due to dropping the internal pH. However, presence of acetic acid at lower concentration (1.0 g/L) in the fermentation medium has been reported to improve the xylose to xylitol bioconversion (Felipe et al., 1995) probably due to more diffusion of internally pooled xylitol during xylose metabolism because of limited acetic acid effect at cell membrane. Heavy metals (iron, chromium, nickel, and copper) produced during hydrolysis mostly originate from corrosion of hydrolysis equipment cause cell toxicity by inhibiting metabolic pathway enzymes (Prakasham et al., 1999).

DETOXIFICATION STRATEGIES OF LB

Hydrolysis of LB is the first step in the process for the production of xylitol. In the next step, xylose is purified from hydrolysate by various detoxification methods. Furfurals, acetic acid and phenolic compounds found in acid hydrolysates are removed where as microorganisms are used in the subsequent steps (Du Preez, 1994). In the next step, hydrogenation of xylose by a chemical process in the presence of Raney nickel catalyst or biological method using microorganisms is involved followed by purification (Jeffries and Sreenath, 1988). With the aim to eliminate the microbial growth inhibitors and to enhance the fermentability of a hydrolysate, a number of detoxification strategies have been developed including physical, chemical, and biological techniques. However, the requirements for detoxification must be studied in each case, as it is dependent upon the strain employed and chemical composition of hydrolysate. Moreover, the effectiveness of detoxification process is also dependent on raw material, type of hydrolysis process, and microorganism employed (Sreenivas et al., 2006).

There are four different approaches to reduce the inhibitory effect of hydrolysate which include: (i) use of bioconversion friendly hydrolysis process; (ii) detoxification of hydrolysate before using for fermentation; (iii) use of microorganism who are resistant to inhibitor; and (iv) conversion of toxic compounds into nontoxic. In view of the fact, the detoxification may increase the cost of the production of the product, it is important to apply cost-effective and efficient ways to overcome detoxification. Another option to eliminate detoxification is to use metabolically engineered microbial strains which can tolerate inhibitors (Taherzadeh et al., 2000).

Physical detoxification method include vacuum evaporation which has limited scope and helps to minimize only volatile toxic compounds such as acetic acid, furfural, HMF, and vanillin. By employing a vacuum evaporation method, more than

90% of these compounds are removed from wood, rice straw, and sugarcane bagasse hemicellolosic hydrolysates (Mussatto and Roberto, 2004). However, this process enhances concentration of nonvolatile fermentation inhibitors and reduces volume of hydrolysate (Larsson et al., 1999). Activated charcoal, overliming, neutralization, sulfite treatment, treating with ion-exchange resins, and extraction with organic solvents reduce the ionization properties of inhibitory compounds. Among available treatments, pH adjustment is an effective and the most cost effective chemical detoxification method. Calcium hydroxide and sulfuric acid are commonly used for the treatment of hemicellulosic hydrolysates for removal of phenolic compounds, ketones, furfurals, and hydroxymethylefurfural (Nilvebrant et al., 2001; Sreenivas et al., 2006).

Activated charcoal is the other process receiving much attention because of low cost and high capacity to absorb free fatty acids, *n*-hexane, pigments, and other oxidation products (Ribeiro et al., 2001; Sreenivas et al., 2006; Misra et al., 2011). The efficacy of activated charcoal treatment is dependent on different process variables such as pH, temperature, contact time, and solid liquid ratio. Acidic pH favors the removal of neutral or nonionized phenolic molecules while alkaline pH favors the removal of organic bases during activated charcoal treatment. Increase of contact time is reported to influence the clarification process. The absorption process increases at elevated temperatures during charcoal treatment basically due to rapid rate of diffusion of absorbate molecule from the solution to the absorbent and temperature induced orientation of charcoal surface (Moreira et al., 2000). Comparative evaluation of different chemical detoxification methods indicates that anion exchange resins can remove higher percentage of fermentation inhibitors such as furfural (73%), acetic acid (96%), HMF (70%), and phenolic compounds (91%) in addition to substantial amount of aldehydes and aliphatic acids from hydrolysate than the cation exchange resins (Mussatto and Roberto, 2004; Sreenivas et al., 2006).

Biological detoxification can be done either by using specific enzymes or microorganism. Laccases and peroxides are generally employed for detoxification (Mussatto and Roberto, 2004). Microbial detoxification of hydrolysate involves utilization of toxic compounds for microbial growth or adaptation of specific microbs for hemicellulosic hydrolysate (Sreenivas et al., 2006). Schneider (1996) reported that acetic acid in the hydrolysate can be removed more than 90% by *S. cerevisiae* mutant from wood hydrolysate. Silva and Roberto (2001) and Sreenivas et al. (2006) have demonstrated that adaptation of *C. tropicalis* has been proved to be an efficient and economical approach to reduce the inhibition of xylose utilization for xylitol production from rice straw and corn cob hydrolysates.

Sreenivas et al. (2006) has worked on xylitol production from sugarcane bagasse and corn cob hydrolysate and reported that combined detoxification methodologies, i.e., chemical and biological are more effective as compared to single treatment process. The researchers reported that pH adjustment followed by activated charcoal and resin has tremendously helped up to certain level and adaptation of microbial strain would be the better option for effective and efficient use of sugary compounds.

BIOPRODUCTION OF XYLITOL

Detoxified hemicellulosic hydrolysate can be employed for producing xylitol where by hydrogenation of the xylose at 80–140°C and hydrogen pressures up to 50 atm in the presence of Raney nickel catalyst. The hydrogenated solution produced requires further processing (chromatographic fractionation, concentration, and crystallization) to attain pure xylitol (Melaja and Hamalainen, 1977; Hyvonen et al., 1982). About 50–60% of xylose is converted into xylitol, the refining and separation steps are the most cost effective (Nigam and Singh, 1995).

Yeast has been studied for xylitol bioproduction as an alternate to chemical reduction process (Granstrom et al., 2001). The first step in the process of xylose metabolism is transportation of sugars from the cell membrane into the cell by passive diffusion or facilitated diffusion. Passive diffusion is carried out by the gradient created in the concentration of the substrate and molecular parameters. Although, facilitated diffusion also occurs down a concentration gradient, which utilize substrate-specific transport protein carriers and the process is affected by pH and temperature during fermentation (Nicklin et al., 1999). D-xylose is used for cell respiration and biomass growth in aerobic conditions, but under oxygen limited conditions, xylitol is produced by yeast. It is due to a reason that under these conditions the intracellular amount of NADH is high due to lower rate of respiration. As a result, NADH acts as an inhibitor of xylitol dehydrogenase, redirecting xylose flux into xylitol (Granstrom et al., 2001, 2002). The pathway for xylose utilization by microorganisms is shown in Fig. 2. A number of yeasts and filamentous fungi possess the enzyme xylose reductase which can produce xylitol. Some xylitol producing yeasts

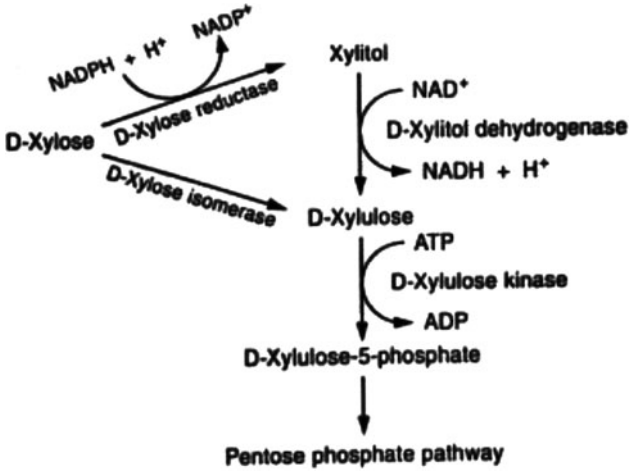

Figure 2 Pentose phosphate pathway.

include *Candida pelliculosa, Candida boidinii, Candida guilliermondii*, and *Candida tropicalis* (Saha and Bothast, 1997).

ROLE OF CANDIDA SPECIES AS MODEL ORGANISMS FOR XYLOSE METABOLISM

Candida species are utilized for xylitol production as they have well-developed pentose phosphate pathway (PPP) and can grow on xylose only which is a single substrate and energy source. The oxidative phase of PPP produces pentose phosphates from hexose phosphates provides NADPH which is required for its biosynthesis. The non-oxidative phase produces hexose phosphates and triglycerides from pentose phosphates. *Candida tropicalis* is one of the most successful organisms for xylitol production. Its industrial importance is due to its high uptake of xylose, xylitol production capability, and alkane and fatty acids degradation in its peroxisomes (Granstrom et al., 2001; Sreenivas et al., 2006).

Cheng et al. (2009) optimized pH and acetic acid concentration for bioconversion of hemicellulose from corncobs to xylitol by *Candida tropicalis*. It was produced by *Candida tropicalis* W103 from corncobs subsequently by acid hydrolysis, detoxification by boiling, overliming, and solvent extraction. It was observed that glucose in hydrolysate enhanced the growth of *Candida tropicalis* while acetic acid at high concentration had inhibitory effect. The inhibition by acetate can be eliminated by adjusting pH to 6 prior to fermentation. Under these optimal conditions, a maximum xylitol concentration of 68.4 g L^{-1} was achieved after 72 h of fermentation, giving a yield of 0.7 g xylitol g L^{-1} xylose and a productivity of 0.95 g L^{-1} h^{-1}.

The fermentation of mixtures of D-glucose and D-xylose by the *Candida tropicalis* NBRC 0618 has been studied by Sanches et al. (2008) under the most probable conditions. Synthetic culture medium was used in all the experiments, with an initial substrate concentration of 25 g L^{-1}, a constant pH of 5.0 and a temperature of 30°C. From the experiments, it was concluded that the highest yield in xylitol production was obtained from the mixtures with higher percentage of D-xylose, with an overall xylitol yield of 0.28 g g^{-1}. Arrizon et al. (2011) produced xylitol and bioethanol from sugarcane bagasse, coffee husks, and agava tequilana bagasse by utilizing *s. ceriavisae, C. magnolia, and C. tropicalis*. Among them *C. tropiclis* was found to be best for xylitol production.

FACTORS AFFECTING BIOPRODUCTION OF XYLITOL

Effect of pH on Bioproduction of Xylitol

It has been observed that inhibition of growth of microorganisms is happened due to undissociated form of acetate (Fond et al., 1985). However, increase in pH, the undissociated form of acetic acid may be decreased. The optimum pH for xylitol production for *Candida* species is 4.5–7 (Ghindea et al., 2010). It has been observed by Cheng et al. (2009) that ascending in the pH from 4.5 to 6.0 leads to dramatic increase in xylitol and productivity. However, the highest yield of xylitol is found at pH 6.0. The findings of El-Batal and Khalaf (2004) show that xylitol production is observed low at pH 3.0 as compared to pH 6.0. Pfeifer et al. (1996) and Rodrigues et al. (1998) have observed that the toxic effect of acetic acid increased due to low pH of the medium because of the entry of acid into the cell in its undissociated form. Acetic acid leads to cytoplasmic acidification inside the cells.

Effect of Temperature on the Bioproduction of Xylitol by Yeasts

The most appropriate temperature for xylitol production by *C. tropicalis* is 30°C. However, the yield for xylitol production is temperature independent, if the yeast is cultured at a temperature of between 30 and 37°C while temperature above 37°C, the yield decreases dramatically (Silva and Afshar, 1994; Ghindea et al., 2010). Sreenivas et al. (2004) observed that a change of the 3°C influences (27%) the production of xylitol in the presence of *C. tropicalis*. However, the conversion to xylitol by *Candida* sp B-22 has been observed constant over the temperature range of 35–40°C while at 45°C and higher, the yield declined greatly (Cao et al., 1994). This may be due to the loss of activities of NADPH and NADH dependent xylose reductase linked with temperature increase (Slininger et al., 1987).

Effect of Nitrogenous Sources on Bioproduction of Xylitol

Type and concentration of nitrogen source in the medium influence the xylitol production by microorganism. Palnitkar and Lachke (1992) found that xylose consumption enhanced when an organic nitrogen source was present in the media. Among nitrogen sources, the yeast extract and the urea are the nutrients preferred by the yeasts producing xylitol (Ghindea et al., 2010). Lu et al. (1995) reported the effect of glycine, aspargine, urea, yeast extract, $(NH_4)_2SO_4$, NH_4NO_3, $NaNO_3$, NH_4Cl, and $NH_4H_2PO_4$ 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 utilizing 114 g/L xylose and incorporating 3 g/L urea as the nitrogen source.

Effect of Yeast Level on the Bioproduction of Xylitol

Yeast extract is a vital nutrient for the production of xylitol, which provides all the required vitamins for the growth of microorganism. Winkelhausen and Kuzmanova (1998) stated that xylitol production rate increased when the medium contained 20 g/L yeast extract inoculated with C. *tropicalis* DSM 7524, while Da Silva and Afshar (1994) found inhibition effect at higher concentrations than 15 g/L. Barbosa et al. (1990)

also found higher xylitol production which declined when the medium contained 5 g/L yeast extract.

Xylitol Recovery from Fermentation Broth

The impurities present in fermentation broth contain nutrients remaining from fermentation that are yeast extract polypeptides, pigments, and inorganic salts. The recovery of dilute concentrations of xylitol from such a complex mixture is a major challenge. Yeast extract, an impurity in the broth is composed of amino acids, peptides, oligopeptides, and proteins. Methods for recovering xylitol are ion exchange resins, activated charcoal and chromatography. Gurgel et al. (1995) used both anion and cation exchange resins to purify xylitol from sugar cane bagasse hydrolysate fermentation broth. It has strong affinity for both cation exchange resin (Amberlite 200C) and anion exchange (Amberlite 94S), which resulted in 40–55% loss of product.

Xylitol was produced by *C. guilermondii* FTI 20037 from sugarcane bagasse hemicellulosic hydrolysate obtained by acid hydrolysis. Different assays were made in order to assess the best condition to clarify the fermented broth using activated charcoal. The clarified medium was subjected to ion-exchange resins after which xylitol crystallization was carried out. The optimum conditions for clarification were obtained by adding 25 g of charcoal to 100 mL of fermented broth at 80°C for 60 min with pH 6.0. The ion exchange resins were not found to be efficient for the current conditions. The crystallization technique showed better performance although the crystals were present in a viscous colored solution (Gurgel et al., 1995).

XYLITOL APPLICATIONS

Food and Confectionery

Food industry uses xylitol in the recipes of food products to improve shelf life, color, and taste of food products. It does not darken or reduce the nutritional value of proteins because it does not undergo Millard reaction. It is added in confectionery for infants and adults. It is used exclusively or in combination with other sugar substitutes in the production of sugar-free chocolate, chewing gum, hard candies, wafer fillings, chocolate, pastilles, and other sweets for diabetics (Bar, 1991). Sugarless pectin jellies can be produced with a combination of xylitol and hydrogenated starch hydrolysates. Crystalline xylitol is an excellent sanding material in combination with pectin jellies and other forms of confectionery. In each case, xylitol is added in crystalline phase in the production, the resulting fondants show pleasant cooling effect and a fine texture (Olinger and Pepper, 2001).

The world's leading application of xylitol is in sugar-free chewing gum. It is used to sweeten both stick and pellet forms of chewing gum because it provides rapid sweetness, flavor and quick cooling effect. Due to its rapid drying and crystallization properties, it is often used to coat pellet forms of sugar-free chewing gum. To ensure a satisfactory sweetness profile, sugar-free chewings are prepared with a mixture of polyol and intense sweetener However, a few brands added solely xylitol and most products contain less than 50% xylitol (Edgar, 1998). Moreover, it is used commercially in many countries, either individually or in combination with or without added sugar confectionery. Although, xylitol is used alone in the production of gum arabic pastilles, chocolate, candy, ice cream fillings, and other sweets; however, some sugar substitutes can be used in general to optimize sweetness, texture, and shelf life (Olinger and Pepper, 2001).

Bakery Products

The characteristic baking flavor is the result of a series of nonenzymatic browning reactions depending on the presence of keto groups or aldo groups. The xylitol addition in bakery products provides the characteristic flavor and color to baked goods. However, some browning can be expected from reducing sugar present in flour. In sugar cakes, xylitol proved to be a good substitute. The xylitol cake resembled closely to that of sucrose cake in respect of color and texture. Some time cookies prepared with xylitol have brown spotted, probably due to poor solubility of xylitol in cookie dough, which contained fat. However, mouth feel of xylitol cookies was more finely divided than sucrose cookies (Hyvonen and Espo, 1981).

Winkelhausen et al. (2007) studied the potential use of xylitol as a low-energy sweetener in baked goods. Cookies were prepared with 100% xylitol and their characteristics were compared with glucose and sucrose. The storage time of one to two weeks showed no significant effect on texture and flavor of cookies. However, three months storage showed a significant impact on texture and flavor of all the cookies. The cookies prepared with sucrose showed statistically significant affect after three months storage on crispness and tenderness. However, the cookies containing 50% of xylitol got maximum sensory scores including taste, color, flavor, and texture (Mushtaq et al., 2010). Rusks were prepared with different replacements of sucrose with xylitol and concluded that it could be replaced up to 50% in the product. Higher levels decreased the color development and the texture of the rusks became hard (Ahmad, 2010).

Pharmaceutical Industry

Xylitol can be used as an excipient or as a sweetener in many pharmaceutical preparations. As in foods, the advantages are suitability for diabetic patients, noncariogenic properties, and nonfermentability. Cough syrups, tonics, and vitamin preparations made with xylitol can neither ferment nor mold. Because xylitol is chemically inert, it does not undergo Maillard reactions or react with other excipients or active ingredients of pharmaceuticals. Xylitol-sweetened medications can be given

to children at night after tooth brushing without any harm to the teeth (Feigal et al., 1981).

Chewing gums containing xylitol have been shown to protect from ear infection in children (Uhari et al., 1996). Xylitol-coated pharmaceutical, confectionery products, and dietary complement preparations (Pepper and Olinger, 1988) cause a pleasant cooling in oral and nasal cavities similar to vaporization due to its negative heat of dissolution (Forester, 1988). It is utilized as a stabilizing agent in protein extractions to prevent denaturation of proteins (Maloney and Amburdkar, 1989). It has anticariogenic properties and reduces plaque formation because cariogenic bacteria cannot matabolize xylitol in its metabolism. Moreover, it has the capacity for moisture retention and hence is used in toothpastes (Pepper and Olinger, 1988).

In tablets, xylitol can be used as a carrier and/or as a sweetener (Laakso et al., 1982). In addition to sweetness, nonreactivity, and microbial stability, it offers the advantages of high solubility at body temperature and a pleasing, cooling effect. Coatings with xylitol or mixtures of xylitol and sorbitol (up to 20%) can be made by conventional pan coating and by sintering the surface of compressed tablets in a hot-air stream. In toothpaste, it may partially or completely replace sorbitol as a humectant. Because of its greater sweetness, xylitol improves the taste of the dentifrice and in the manufacture of transparent gels; it exhibits properties slightly superior to those of sorbitol (Pepper and Olinger, 1988).

An inhibitory effect on enamel demineralization has been postulated as well (Smits and Arends, 1988). There is also evidence that use of a xylitol-containing dentifice can result in a significant reduction of *Streptococcus mutans* in saliva (Svanberg and Birkhed, 1995). Because of its overall favorable effects on dental health, xylitol has also been applied in other oral care products, such as in mouth rinses and in artificial saliva (Featherstone et al., 1982).

HEALTH BENEFITS OF XYLITOL

Xylitol can be metabolized independent of insulin and can replace sugar on a weight to weight basis (Cao et al., 1994) making it a suitable sweetener for diabetic patients (Emodi, 1978). It is recommended for diabetic patients as it causes very little increase in glucose level and insulin in blood (Hassinger et al., 1981). Also, xylitol finds use in posttraumatic states or postoperative when efficient glucose utilization is inhibited (Forster, 1974). Catabolic disorders can also be corrected due to the anabolic effects produced by xylitol. When it is used regularly in diet, it limits obesity (Parajo et al., 1998). It is utilized for parenteral nutrition for infusion therapy (Beutler, 1984) as it is inert to amino acids. It is also used in the treatment of lipid metabolism disorders (Manz et al., 1973 and Aguirre-Zero et al., 1993). Several functional effects of xylitol being of low caloric sweetener and prebiotic nature are found to improve the health by researchers. Some of them are briefly listed in Table 3.

Table 2 Xylitol in fruits and vegetables (Jaffe, 1978)

Product	Xylitol (mg/100 g dry substance)
Brewer's Yeast	4.5
Carrot juice	12
Chestnut	14
Banana	21
Carrot	86.5
Onion	89
Fennel	92
Kohlrabi	94
Lettuce	96.5
Pumpkin	96.5
Spinach	107
White mushroom	128
Eggplant	180
Raspberry	268
Lamb's lettuce	273
Cauliflower	300
Strawberry	362
Yellow plum	935

Fate of Xylitol in the Gastrointestinal Tract

Much of the studies have been carried out on xylitol resistance to digestion by the oral bacteria leading to its anticariogenic properties. It has been concluded that the absorption of xylitol in the stomach and upper gastrointestinal tract is 20–30% of that of glucose and is not fully absorbed at all. The absorbed xylitol is thought to be nonactively transported through the intestinal tract (Wang and Van Eys, 1981). A study carried out by Asano Takashi et al. (1973) reported that absorption of xylitol could vary from 49 to 95% after three to four hours of ingestion, besides first time its use or chronic feeding. Still other researchers concluded that adaptation could occur over time, but it is considered to be due to the alteration of intestinal microflora (Wang and Van Eys, 1981). Another factor which affects the absorption of xylitol is gastric emptying. Salminen et al. (1984) reported the influence of xylitol on gastric emptying and observed that xylitol absorption is enhanced with more gastric emptying rate. Therefore, some modification may be possible, if xylitol is incorporated in diet.

Xylitol is not absorbed by active transport and does not require insulin for the uptake by liver, where it is converted into glucose, L-lactic acid, and glycogen under certain pathological conditions. After xylitol absorption in the blood stream, liver uptake of xylitol is insulin independent and causes very little increase in blood glucose, insulin, and glucagon level. The liver is the major organ for the removal of xylitol from the blood stream and metabolizes 50–80% of xylitol. The remaining 20% of xylitol can be metabolized by lungs, kidneys, fat stores, erythrocytes, and myocardium (Wang and Van Eys, 1981). These metabolized products can thus be converted into carbon dioxide and water by the normal physiologic conditions of carbohydrate metabolism (Makinen, 2004).

Table 3 Health benefits of xylitol

Xylitol dose (g)	Positive effect	Negative effect	Reference
4–4.5 g/d, 1 year	Decreased dental caries	None	Wang and Van Eys, 1981
5–15 g/d	Made in human body	None	Wang and Van Eys, 1981
8.4 g/d	Decreased otitis media	None	Uhari et al., 1996
10–85 g/d, 50d		Flatulence	Makinen, 2004
25 g/d	Improved glucose and lipid metabolism	None	Otto et al., 1993
30 g	Decrease in yeast	None	Salminen et al., 1985
45 g or higher		Diarrhea	Wang and Van Eys, 1981
1.6 kg/month	Decreased decayed, missing, or filled teeth	None	Wang and Van Eys, 1981
100 g/d		Transient diarrhea in half the subjects	Wang and Van Eys, 1981
400 g/d		1/2 had diarrhea	Wang and Van Eys, 1981

Two different enzymes are involved in the metabolism of xylitol. One is a nonspecific NAD-linked polyol dehydrogenase (EC 1.1.1.10) and other is a specific NADP-linked xylitol dehydrogenase (EC 1.1.9). Its metabolism yields 4.06 kcal/g and produces 35 mol ATP, as compared to 38 mol by glucose (Wang and Van Eys, 1981). Absorbed xylitol is used by the intestinal microflora in the distal part of the gut. The final products of bacterial fermentation of xylitol are mostly short-chain volatile fatty acids, besides, small quantities of the gases (H_2, CH_4, and CO_2) (Cummings et al., 1981; Grimble, 1989). These end products are absorbed by the intestine (Ruppin et al., 1980). Butyrate and acetate are efficiently absorbed by the liver and utilized by mitochondria to produce acetyl-CoA. Propionate is also metabolized by the liver and produced propionyl-CoA (Skutch et al., 1979; Cummings et al., 1987).

In vitro and in vivo experiments with xylitol and other polyols, it is concluded that about a quarter of ingested dose of xylitol is absorbed in the gastrointestinal tract, which is successfully metabolized by the glucuronate-pentose phosphate shunt and provides about 4 kcal/g. The absorbed three quarters of the ingested load is almost completely fermented by the intestinal flora. Based on thorough assessment, a metabolizable energy value of about 2.8–2.9 kcal/g xylitol can be calculated. Federation of American Society of Experimental Biology (FASEB) has assigned xylitol a net calorific value of 2.4 kcal/g (FASEB, 1994).

Xylitol Safety Issues

Xylitol has been shown to have a very low order of toxicity by all routes of administration. Conventional tests for embryotoxicity, tetrogenicity, and reproductive toxicity have consistently yielded negative results like in vitro and in vivo tests for mutagenesity and clastogenesity (WHO/FAO, 1977, 1978; Bar, 1985).

FDA approved xylitol as an additive for food (21CFR172.395) in 1986 and declared it safe for human use. The Joint FAO/WHO Experts Committee on food additives recommended an unlimited ADI for xylitol and suggested no additional toxicological studies are required. It is safe for utilization in foods, pharmaceuticals, and oral health care products, registered in more than 35 countries (Grizard and Barthomeuf, 1999).

Suitability for Diabetics and Glucose Level

Xylitol is not transported actively through the intestinal tract and does not require insulin for uptake by liver; therefore, it gives a low glycemic index. Slow and incomplete absorption by the upper gastrointestinal tract leads to very little effect on blood glucose. Xylitol is considered to be an ideal alternate sweetener for diabetic patients, as the control of blood glucose, lipid level, and weight control are the three most important objectives of diabetes management. Besides from minimum effect on blood glucose, it provides lower calories and a number of other health benefits. In a study conducted on diabetic patients, it was observed that the supplementation of xylitol in the diet up to the level of 30–60 g/day resulted in no harmful effects on diabetic patients, particularly in relation to fat and carbohydrate metabolism (Yamagata et al., 1969). It was initially considered that xylitol's lack of insulin responses would not be apparent when eaten with complex meal. To verify the hypothesis, a study was conducted using 30 g of xylitol or 30 g sucrose to substitute starch in a standardized meal as a part of diabetic diet. The results declared clearly that xylitol lowered blood glucose and insulin responses as compared to sucrose in the context of more complex meal (Hassinger et al., 1981).

It has been observed that xylitol fed diabetic rats restored their glycolytic function and increased glycogen synthesis. Schricker et al. (1995) concluded that xylitol use prevented high blood glucose concentrations and release of free fatty acids during the acute phase after trauma and sepsis. Natah et al. (1997) reported that the increase in carbohydrate oxidation with xylitol is one quarter of that caused by glucose (Hamber and Almdal, 1996). This study also concluded that xylitol metabolism resulted in a smaller increase in glucose, insulin, and thermogenic response as compared to glucose.

Effect on Blood Lipid (Cholesterol and Triglycerides)

Substitution of xylitol in food may have an effect on decreasing triglycerides and cholesterol levels. Mechanism for lowering effect is the viscous nature of the fiber that binds the dietary or biliary cholesterol in the intestinal lumen and increase in fecal excretion of the bile acids. A net stimulation of hepatic cholesterogenesis results, through an increased activity of

3-hydroxy-3-methylglutaryl CoA reductase (HMG-CoA). Cholesterol lowering effect may also stimulate the uptake of liver-lipoprotein cholesterol by up-regulation of low-density lipoprotein (LDL) receptor activity. A study was conducted on rats with diets of 10–15% oligosaccharide which resulted in a decline in body fat, phospholipidaemia, and triglyceridaemia (Mazur et al., 1990).

EFFICACY STUDIES

A study was conducted on male Fisher rats, fed on diets containing glucose without or with either 10% or 20% sorbitol or xylitol for a period of eight weeks following a four weeks adaptation period. Sugar alcohols addition decreased both food intake and body weight gain. Liver glucose-6-phosphate dehydrogenase and malic enzyme were also decreased by the use of sugar alcohols in the diet. These sugar alcohols had very little influence on plasma insulin and blood glucose levels. Triglycerides and cholesterol levels were decreased with sugar alcohols. However, xylitol and sorbitol increased plasma alkaline phosphatase. Relative liver and ceacum weights significantly increased with the addition of sugar alcohols in the diet (Ellwood et al., 1999; Mushtaq, 2011).

In a sub-acute toxicity study, it was administered to 20 female and 20 male rats per group by daily gastric intubations for a period of 14 days. Level of doses given was 1.25, 2.5, 5.0, and 10.0 g/kg. The animals receiving 1.25 g xylitol/kg during the first nine days received 10.0 g xylitol/kg during the last seven days. In the control groups, animals received 0, 2.5, and 5 g sucrose/kg of animal/day. The animals were killed after 2, 5, and 14 days. Heart, spleen, liver, kidneys, and stomach were weighed. These organs and jejunum, colon, pancreas, and brain were histological examined in 2 and 5 days treatment groups, while in 14 days treatment group, this study was only carried out on liver. Except for a decrease of the FFA content in the blood at all xylitol dose levels, no effects were observed in this study. Also, no evidence of hepatotoxicity was recorded (Truhaut et al., 1977).

In another study, in a 13 weeks experiment period four groups of eight female and eight male Charles River CD rats weighing 120–150 g were fed 0, 5, 10, and 20 g dietary xylitol/kg/day. Blood glucose, urine analyses and hematology of five male and five female rats of each group were carried out at 4, 8, and 12 weeks. Alkaline Phosphatase, GOT, bilirubin, and uric acid in serum were determined up to 13 weeks. Food consumption and body weights were reduced particularly in male rats that were dose dependent. No significant changes were observed except for transient diarrhea in a number of treated animals. No histopathological lesions related to xylitol administered were noticed (Swarm and Banziger, 1970).

Short-chain Fatty Acids Production

During metabolism of xylitol, it passes through the upper gastrointestinal tract and reaches the ceacum as an impending source for fermentation by the inhabitant saccharolytic microorganisms. The nondigestible carbohydrates which enter the distal part of a gut are fermented by these microorganisms and produce beneficial intermediates end products. These by-products are short-chain fatty acids (acetate, propionate, and butyrate), gases (hydrogen, carbon dioxide, and methane), organic acids, and ethanol. Short chain fatty acids (SCFAs) produced by fermentation are absorbed and metabolized; propionate, lactate, and acetate by the liver and muscle; butyrate by the colonic epithelium.

Indeed, these organic acids can provide about 10% of daily energy needs (Topping, 1996). The SCFAs are acidic in nature which lower the pH in the colon and further reduces the bioavailability of alkaline cytotoxic compounds. It can also inhibit the growth of pH-sensitive microorganisms and can easily dissolve minerals like calcium and magnesium. However, all SCFAs enhance the relaxation of resistance vessels, which maintains the supply of blood to the colon and liver. Moreover, absorption of cations is increased by acetates, while the muscular contraction of colon is increased by propionates. These propionates enhance the propagation of the colonic epithelium and colonic electrolyte transport. According to Topping (1996), butyrates are chief energy sources for metabolism of the colonocytes which enhance the colonic electrolyte transport. Gibson and Rastall (2004) reported that SCFAs help out in cognitive ability and stress but the mechanism is unknown. Moreover, they are important in many areas such as immune function modulation, gut integrity, calcium absorption, and cholesterol maintenance (Douglas, 2004). Different "starved bowel" disorders collectively known as irritable bowel syndrome (IBS), are generally associated with insufficient SCFAs production and poor balance of gut microflora (Topping, 1996).

These SCFAs are essential in many areas; immune function modulation, gut integrity, and calcium absorption cholesterol maintenance (Douglas, 2004). Various "starved bowel" disorders, such as those known collectively as IBS, are generally linked to inadequate SCFAs production and a poor balance of gut microorganism (Topping, 1996).

Effect of Xylitol on Bifidobacteria and Lactobacilli Growth and Benefits

Xylitol is a prebiotic sweetener which can modify the colonic microorganisms and enhance the growth of health promoting bacteria particularly *bifidobacteria* and *lactobacilli* (Kaur and Gupta, 2002; Huebner et al., 2007). The primary benefit of the enhancing colonic *lactobacilli* and *bifidobacteria* is a protection against infectious intestinal diseases and cancer by reducing the putrefactive bacteria (such as *Clostridium perfringens*) and pathogenic bacteria (such as *Salmonella, Listeria, Escherichia coli, Shigella,* and *Clostridium difficile*). This may be due to the secretion of *bifidobacteria* baceriocin-like material against *E. coli, Campylobacter, Salmonella,* and *Shigella* and decline in pH (Gibson and Wang, 1994; De Sousa et al., 2011). The

decreased pH may also encourage the production of mucus enhancing endothelial wall thickness of the colon and enhances the blood flow (Roberfroid and Delzenne, 1998; Mushtaq, 2011). It improves the glucose, cholesterol and lipid metabolism. Glucose and insulin are considered to be the factors in the regulation of triglyceride and fatty acid synthesis, thus regulating glucose and insulin levels can lead to decrease in fatty acids, triglycerides, and even VLDL secretions by the liver (Kok et al., 1996). The exact mechanism of SCFAs in decreasing cholesterol is still unknown. This would be important, such as acetate, a metabolic precursor of cholesterol, may be a possible reason of hypercholesterolemia; while propionate may be considered responsible for lowering serum cholesterol level can be linked with inhibition of hydroxymethylglutaryl-CoA reductase (Roberfroid and Delzenne, 1998).

Xylitol consumption decreases the renal nitrogen excretion due to the effect in fiber-like properties. It has been reported that decreasing formation of ammonia and various end products protein catabolism may reduce the risk for colon carcinogenesis. It also increases the bioavailability of essential minerals, production of folic acid, and vitamins B1, B6, B12 (Gibson and Wang, 1993). Study carried on rats show that a 5% oligosaccharide diet can enhance calcium absorption 15–30% and magnesium absorption 20–40% (Morita et al., 1998). This is considered to be due to the lowering of pH and SCFA production, which enhances the mineral's solubility (Grizard and Barthomeuf, 1999). Another benefit of normal stool consistency is the prevention of diarrhea and constipation (Ouwehand et al., 2005; Macfarlane et al., 2006). Gibson et al. (1995) reported that 1.3 and 2.0 g of prebiotic feeding increased the stool wet weight/g. Krishnan et al. (1980a) reported that an increase in the total amount of fecal content was observed on feeding xylitol diet. This increase in biomass is considered to have several benefits in the same context such as fall in nitrogen excretion, ulcerative colitis, cancer, and glucose tolerance (Jenkins et al., 1999).

Besides this, xylitol is considered to be a probable fermentable carbohydrate for several important strains of bacteria. Krishnan et al. (1980b) reported that an increase in Gram-positive bacteria and *Lactobacillus casei* and *Klebsiella pneumoniae* in ceacal microorganisms of rats with xylitol was recorded. Moreover, the growth of *lactobacilli* and *bifidobacteria* decreases the growth of opportunistic pathogens through competition for growth medium and adhesive area. Two opportunistic pathogens *Candida albicans* and *Escherichia coli* are normally present in the colonic microflora with no harmful effects at low concentrations, but when given the chance to proliferate, such as in the use of antibiotics, they can grow and cause major problems. Therefore, controlling their growth is of major benefit. Increased population of *C. albicans* has been linked with diarrhea, vaginitis, and stomatitis. Xylitol has been reported as a possible inhibitor of *C. albicans,* since they grow on glucose (Vargas et al., 1993). Salminen et al. (1985) observed a decrease in number of yeast in human stool after only one dose of xylitol (Salminen et al., 1985). Pizzoferrato (2003) also reported a decrease in adhesion of *C. albicans* in the oral cavity, inhibiting the occurrence of infections such as thrush (Pizzoferrato, 2003). In addition, Krishnan et al. (1980a) observed that *E. coli* was not able to consume xylitol as a metabolic substrate, while Salminen et al. (1985) reported a decrease in fecal aerobic *streptococci* of xylitol fed rats.

CONCLUSION

Potential of agricultural wastes for the production of xylitol; its utilization in various foods and pharmaceutical and health effects and safety issues have been reviewed. Xylitol is a low calorific sweetener which is attracting global attention due to its various potential applications in food and pharmaceutical sectors. Xylose is the raw substrate used for xylitol production either by chemical hydrogenation or bioconversion with certain microbial species. Chemical production is cost intensive and energy consuming. 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, 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 best for xylitol production. Microbial production of xylitol is influenced by various process parameters like pH and temperature. Xylitol can successfully be utilized in food product for instance confectionery, dairy and bakery products. Also it has a potential to be incorporated in various medicines such as in cough syrups and tonics for diabetics and health cognizant people. About two-third of ingested xylitol is metabolized by intestinal bacteria which exerts prebiotic effect by producing SCFAs, lowering blood glucose, cholesterol, and triglyceride level.

Focus should be fixed on understanding the nature of hydrolysate materials, hydrolysis procedure, detoxification methods, bioconversion environment for xylitol production, and xylitol incorporation in various foods. Furthermore, metabolic effects of xylitol on health need to be well thought-out.

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