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XYLITOL

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XYLITOL; HISTORY, PRODUCTION, HEALTH CLAIM, HEALTH BENEFITS AND SAFETY

Xylitol is a sugar alcohol that is used as a sweetener and has a much lesser effect on blood glucose than sucrose. Therefore, xylitol is considered suitable for diabetics and weight management.

Industrially xylitol is produced by chemical extraction, this has a high energy requirement though its multiple purification processes leading to a high-end cost. Xylitol can also be manufactured via microbial and enzymic extraction processes. Microbial extraction is time-consuming and not seen as a viable comparison on an industrial production scale, however enzymic production of xylitol produced from hemicellulose has gained great praise as a potential alternative to chemical production as it alleviates the environmental burden. Extensive interest and developments have been made.

History

Xylitol is a five-carbon sugar alcohol, a natural carbohydrate which occurs freely in fruits. Xylitol is also present in the metabolism of humans (Ur-Rehman et al 2015). Xylitol has been known to biochemists for at least 130 years with German and French researchers believed to be the first to make xylitol via chemical extraction with wood bark. Sodium amalgam creates a reduction of the wood sugars, known as D-xylose. The first xylitol preparation was a syrup-like mixture containing small amounts of other sugar alcohols along with the desires xylitol. The purification of xylitol was accomplished in the 1930's (Xu et al, 2019). However, the first successful crystallisation of xylitol using the method of purified D-xylose, took place during the Second World War but it’s form was not a stable (Bicas et al 2016).

Scientists did not discover the full properties of xylitol until researchers started to exploit its insulin independent nature, post-World War II (Kirk and Jacobson 2014). Frontrunners in xylitol developments were Japan, Germany and the Soviet Union. In Japan, xylitol was used in the resuscitation of patients from diabetic coma. Xylitol was used predominantly as a research chemical until the war-associated sugar shortage. This led chemists to search for alternative sweeteners. Scientists at the former Finnish Sugar Co. Ltd. succeeded to develop an industrial procedure for small-scale xylitol production from hardwood and paper production by-products (Bhattacharya et al 2014). The xylitol production process was refined and developed. In 1975 the Finnish company began the first large-scale production of xylitol. Swiss company, F. Hoffman La-Roche had also advanced their xylitol research with the aim of large-scale production (Mäkinen 2004). The two companies joined in 1976 under the name of Xyrofin. Xyrofin was then bought out by The Finnish Sugar Co.

Subsequently additional companies located in Eastern Europe, China, Japan, Germany, Italy had also started to produce xylitol for the domestic market where Xylitol was mainly used as a sweetener for diabetics or in parenteral nutrition (Bhattacharya et al 2014)

The usage of xylitol for dental benefits gained traction into the 1970s. in 1975 the first xylitol chewing gum was launched in Finland, with the USA following a year later (Bardach et al 2008).

Market

Modern consumers are seeking healthier options to replace refined white sugar. Xylitol offers excellent potential for future product development. Xylitol market was worth $700million in 2015 and projected to exceed $1.37billion by 2025. Growing at a rate of 6.6% CAGR. Xylitol is commercially one of the largest produced polyols with an approximate volume of 200 000 metric tones (Grand View Research, 2019).

Xylitol is reported to be one of top 12 high value-added intermediate chemicals that can be produced from biomass (Sibel et al 2017).

Processing

Xylitol is naturally found in many fruits, vegetables, yeasts, lichens, seaweeds and mushrooms but due to the high quantity of raw materials to extract a relatival small amount of xylitol it is not economical to do so. Therefore, research has focused on chemical and biotechnology production.

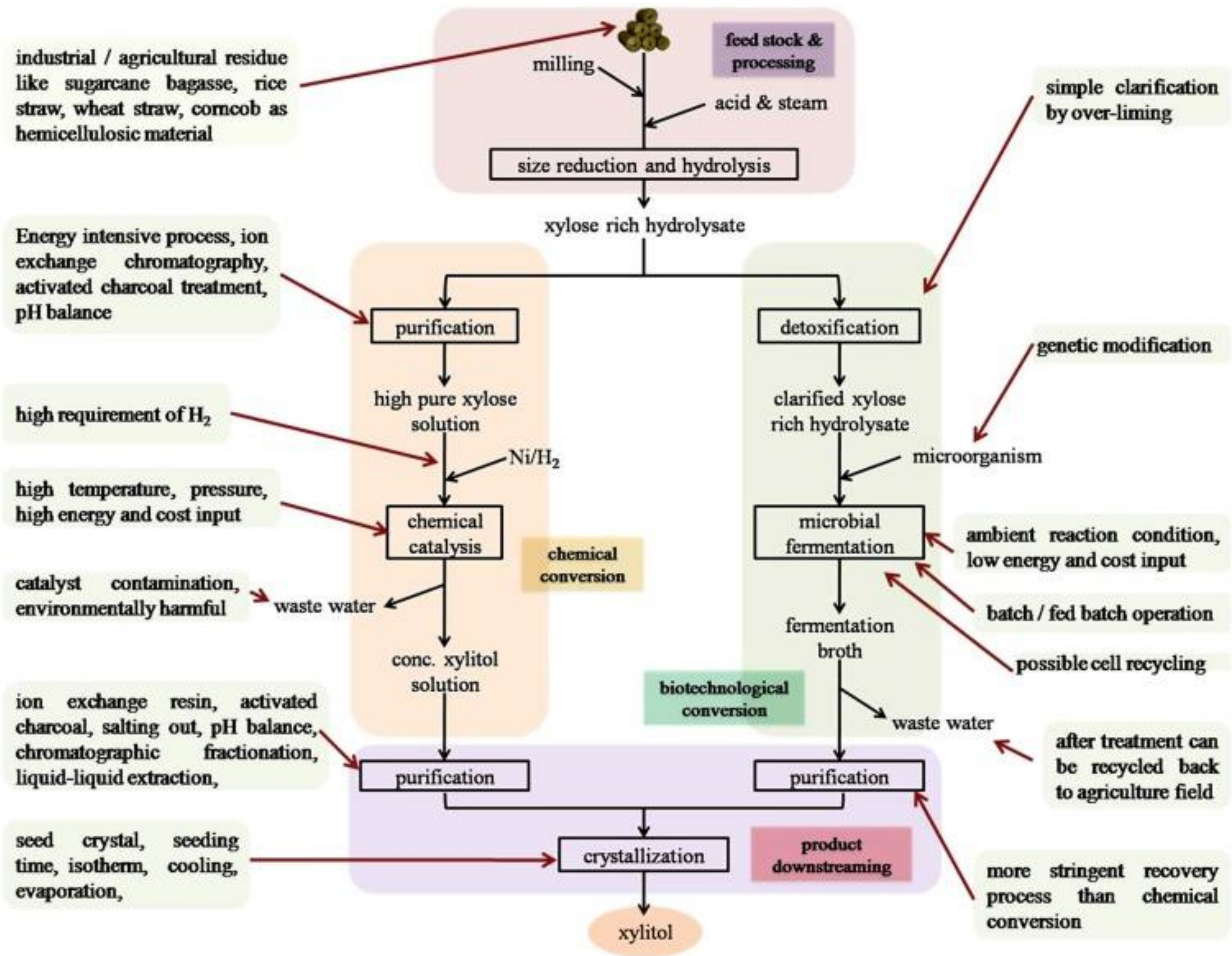

Figure 1; Xylitol processing overview using chemical and biotechnological recovery (**Hector Hernandez-Escoto et al, 2014** ***).***

Xylitol is industrially manufactured by reducing pure xylose from hardwood; hemicellulosic hydrolysate, via Raney nickel catalyst (XR). There are four processes involved in the chemical extraction of xylitol. These include 1) hydrolysis of the lignocellulosic biomass material by mineral acid, 2) purification and separation to obtain the pure xylose (crystals or solution), 3) reduction of the xylose into xylitol and 4) separation of the xylose and xylitol crystals (Arcaño et al 2018). The chemical process yields 8-15% xylitol of the raw material. The low yield makes chemical processing expensive and energy intensive. However, the advantages are that it provides a pure product that is suitable for commercial usage.

Biotechnological processes are based on the use of microorganisms or isolated enzymes as alternatives to the chemical process. The most promising bio-tech processes are the microbial process and the enzymic approach utilising isolated XR. The microbiological process uses bacteria, fungi, yeast and recombinant strains to produce xylitol from pure xylose or hemicellulosic hydrolysate.

Bacterial production research has identified some bacterial strains that can produce small quantities of xylitol. Multiple bacteria strains have been studied with a range of differing results. The highest reported production was a yield of 29.2g/l xylitol after a 27hour incubation period, using intact cells as the enzyme source (Rice 2019). However, the research into xylose fermenting bacteria is not extensive due to the low yield of xylitol produced in the process.

Fungi production of xylitol has been studied to a lesser extent than bacterial and chemical production. Production via fungi Aspergillus, Byssochlamys, Gliocladium. Myrothecium, Penicillium, Rhizopus and Neurospora sp. have shown to produce modest quantities of xylitol in xylose containing solutions (Shah 2019).

Yeast production of xylitol has been deemed as effective. Several types of yeast have been used for the fermentation process to produce xylitol. Multiple studies have been documented with 44 strains of yeast to documented to establish the most effective converter of xylose to xylitol. Candida tropicalis presented the most effective, producing the highest quantities of xylitol (Mountraki et al 2017). Appendix 1 tabulates the yeast productions tested to produce xylitol.

Enzymic production of xylitol using enzyme technology is an emerging and promising method with the chemical reaction process dependant on NAD(P)H. Results are initiated with 1 mole of coenzyme to produce 1 mole of xylitol; resulting in an efficient equimolar process. Furthermore, the coenzyme is retained during the process and can recovered using membrane reaction (Mountraki et al 2017). In order to maximise catalysed reactions for xylitol synthesis the optimal pH, temperature, concentration of substrate and enzyme concentration is essential. Studies indict that conversion of xylose to xylitol is obtained at 35*C and pH 7.5 after a 24hour period.

Once the conversion has been achieved, the product needs to be recovered and purified; this process is the time consuming and finically costly.

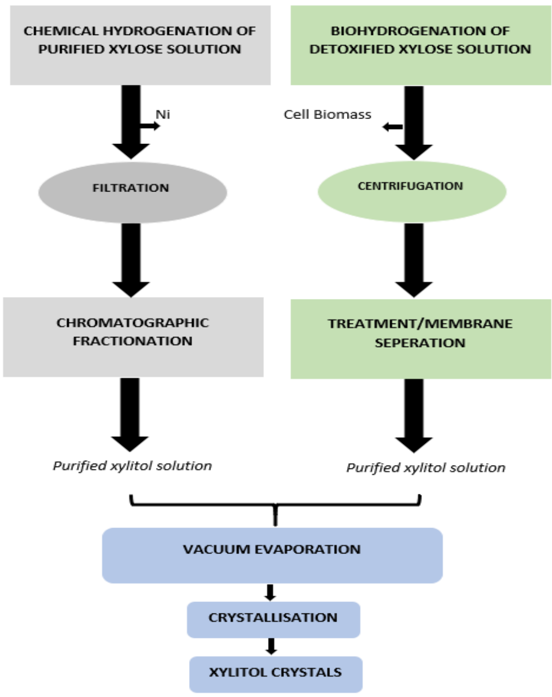

Figure 2; Process flowchart for chemical and bio-hydration for the recovery of xylitol (modified flow diagram form Mountraki et al 2017)

Alternative biomass wastes include agricultural, industrial and forest residues which can provide alternative energy sources and serve as potential low-cost raw materials used to produce xylitol. Currently wood bark, wheat straw, corn waste and cobs, apple waste, banana stalks and waste, peanut husks, pomegranate waste, sugar waste, barley stalks and chaff can be used in the production of xylitol. The areas of expansion to utilise food and agriculture industry waste are extensive with great opportunities to be researched.

The most recent investment for xylitol production comes from Finnish grain specialist, Fazer, who have funded $40m to produce xylitol from Finnish oat by-products. Fazer aim to be the only xylitol manufacturer producing xylitol from a plant-based raw material with Finnish origin. This is important for Fazer's confectionery business as Fazer is the only company producing chewing gum in Finland and bring xylitol back to its historical origin (Bioenergy International 2019).

Accredited health claims

Xylitol holds 3 accredited EFSA health claims that apply for children and adults. The health, claim, category, conditions of use and EFSA reference is listed in the table 1.

Table 1; Xylitol EFSA claims and regulations for use

Claim type	Nutrient, substance, food or food category	Health claim	Conditions of use of the claim (including restrictions)	Health relationship	EFSA opinion reference
Art.13(1)	Sugar replacers, i.e. intense sweeteners; xylitol, sorbitol, mannitol, maltitol, lactitol, isomalt, erythritol, sucralose and polydextrose; D-tagatose and isomaltose	Consumption of foods/drinks containing instead of sugar* contributes to the maintenance of tooth mineralisation * In the case of D-tagatose and isomaltulose this should read "other sugars"	In order to bear the claim, sugars should be replaced in foods or drinks (which reduce plaque pH below 5.7) by sugar replacers, i.e. intense sweeteners, xylitol, sorbitol, mannitol, maltitol, lactitol, isomalt, erythritol, D-tagatose, isomaltose, sucralose or polydextrose, or a combination of them, in amounts such that consumption of such foods or drinks does not lower plaque pH below 5.7 during and up to 30 minutes after consumption	maintenance of tooth mineralisation by decreasing tooth demineralisation	2011;9(4):2076, 2011;9(6):2229
Art.13(1)	Sugar replacers, i.e. intense sweeteners; xylitol, sorbitol, mannitol, maltitol, lactitol, isomalt, erythritol, sucralose and polydextrose; D-tagatose and isomaltulose	Consumption of foods/drinks containing instead of sugar* induces a lower blood glucose rise after their consumption compared to sugar-containing foods/drinks * In the case of D-tagatose and isomaltose this should read "other sugars"	In order to bear the claim, sugars should be replaced in foods or drinks by sugar replacers, i.e. intense sweeteners, xylitol, sorbitol, mannitol, maltitol, lactitol, isomalt, erythritol, sucralose or polydextrose, or a combination of them,	reduction of post-prandial glycaemic responses	2011;9(4):2076, 2011;9(6):2229

			so that foods or drinks contain reduced amounts of sugars by at least the amount referred to in the claim REDUCED [NAME OF NUTRIENT] as listed in the Annex to Regulation (EC) No 1924/2006. In the case of D-tagatose and isomaltose, they should replace equivalent amounts of other sugars in the same proportion as that referred to in the claim REDUCED [NAME OF NUTRIENT] as listed in the Annex to Regulation (EC) No 1924/2006.		
Art.14(1)(a)	Chewing gum sweetened with 100% xylitol	Chewing gum sweetened with 100% xylitol has been shown to reduce dental plaque. High content/level of dental plaque is a risk factor in the development of caries in children	Information to the consumer that the beneficial effect is obtained with a consumption of 2-3g of chewing gum sweetened with 100% xylitol at least 3 times per day after the meals	not specified	Q-2008-321

Health attributes and associated health benefits

Dental; Xylitol is used mostly in toothpaste and chewing gum due to being non-cariogenic and because it does not contribute to tooth decay by preventing or reducing the incidence of dental decay forming. Xylitol reduces the amount of plaque and the number of harmful bacteria within plaque and mouth. No other polyol has been shown to function in this way. Xylitol can also re-mineralise teeth when exposed to xylitol on a regular basis over a 8 week period or more (Takeuchi et al 2018)

Skin; Skin applications of xylitol acts as an anti-microbial agent has shown to reduce skin moisture losses when combined with essential oils, bees wax of petroleum jelly. Current research suggests that xylitol is effective for those with dry skin conditions such as eczema. Another study also found that xylitol reduced the glycation of skin collagen, associated with skin aging (Sali et al 2019).

Digestive tract; Xylitol is not digested by human enzymes and approximately 50% of the consumed xylitol is absorbed through passive diffusion in the small intestines. The remining 50% of the dietary xylitol enters the colon where it can serve as an energy and carbon source for the intestinal microbiota and leads to the formation of short-chain fatty acids which provide energy to the host and support immunity. These properties from xylitol are very similar to what is expected from a prebiotic where xylitol can be utilised by the hosts microflora presenting multiple health benefits (Lugani et al 2017)

Gas chromatography analysis has shown that the mechanism of xylitol on the microflora of the gut stimulated the increased formation or butyric acid compared to studies compared with non- supplemented controls (Sali et al 2019). The production of butyric acids in the colon is considered beneficial for colonic health.

Cholesterol; 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 fibre that binds the dietary or biliary cholesterol in the intestinal lumen and increase in faecal excretion of the bile acids (Zhang et al 2018)

Impact on blood glucose; The glycaemic index of xylitol is low because it is not actively transported through intestinal tract. The high tolerance of xylitol by diabetics is due to its metabolism in humans by two different pathways, such as direct absorption (mainly in liver) and indirect metabolism by intestinal bacteria (Arcaño et al 2018). Both mechanisms of xylitol metabolism are independent to insulin and hence it acts as promising ideal alternate sweetener for diabetics.

Table 2; Glycaemic index of natural sugars

Natural sweetener	Glycaemic index of natural sweetener
Stevia	0
Xylitol	8
Agave nectar	15
Fructose	17
Coconut sugar	35
Apple juice	40
Honey	50 (raw sugar 30)
Maple syrup	54
Molasses	55
Refined white sugar	99

Diabetes; Xylitol controls blood glucose, lipid level and weight control, which are the three important objectives for diabetes management. It is poorly absorbed by the human digestive system and thus acts as a dietary soluble fibre to maintain healthy gut flora (Wölnerhanssen et al 2019).

Xylitol is as sweet as sugar and contains fewer calories. Therefore, xylitol is an ideal sugar substitute.

Table 3; Comparison of natural and artificial sweetened and sugars (Mooradian 2017)

Sugar substitute	Times sweeter than table sugar	Artificial or natural sweetener	Notable effects
Refined sugar		4cal per gram	
Saccharin	200-300	Artificial – no calories	
Aspartame K	200	Artificial – no calories	Cannot be processed in the body by individuals with phelketonutria
Sucrose	600	Artificial – no calories	Suitable for cooking
Neotame	8000	Artificial – no calories	
Stevia/Erythritol	300	Natural – no calories	
Sorbitol	0.5-0.7	Natural – low calories	Laxative if dose is exceeded
Mannitol	0.7	Natural – low calories	Laxative if dose is exceeded
Xylitol	1	Natural – low calories (2.4cal per gram) Can also be man made	Natural anti-tooth decay properties. Laxative if dose is exceeded

Xylitol applications

Food industry applications for xylitol are to improve product shelf life, colour and taste. Xylitol does not reduce the nutritional value of proteins as xylitol dose not undergo Millard browning reaction (Sahin et al 2019).

Xylitol is added to confectionery for both infants and adults' products and used on its own or in combination with other sugar substitutes to produce sugar-free chocolate, chewing gum, boiled sweet, cough pastilles, and reduced sugar products for diabetics. Sugarless pectin jelly sweets can be produced with a combination of xylitol and hydrogenated starch. Crystalline xylitol can be used as an effective alternative to sugar coating confectionery (Nutra Foods (2019)

Baking; The xylitol addition in bakery products provides the characteristic flavour and colour to baked goods. In cakes, xylitol proved to be a good substitute. The xylitol cake resembled closely to that of sucrose cake in respect of colour and texture. Cookies prepared with xylitol have contained brown spots, due to poor solubility of xylitol in the dough. 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 flavour of cookies. Cookies containing 50% of xylitol maintained the maximum sensory scores including taste, colour, flavour, and texture (Mushtaq et al., 2010). Rusks were prepared with different quantities of sucrose with xylitol and concluded that it could be replaced up to 50% in the product as higher levels decreased the colour development and the texture of the rusks became hard (Ahmad, 2010).

Chewing gum; 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 and it provides rapid sweetness, flavour and cooling effects. Due to its rapid drying and crystallization properties, it is often used to coat pellet forms of sugar-free chewing gum (Bouhet et al 2016).

Pharmaceutical applications; Xylitol can be used as a sweetener in many pharmaceutical preparations. As in foods, the advantages are xylitol's suitability for diabetic, noncariogenic properties, and no fermentability. It also prevents the growth of mould (Sachdev 2018). Cough syrups, tonics, and vitamin preparations can contain xylitol.

Safety

Xylitol is deemed safe as a food additive, for pharmaceutical use and in cosmetics. Xylitol has 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 (EFSA 2019). Xylitol is also known as E976 and under goes regular assessment via the EFSA food additive panel. The accredited health claims issued by the EC demonstrate that xylitol is a safe product to consume. However, side effects from high intakes of xylitol can cause laxative effects, gastrointestinal tract discomfort and flatulence.

Summary

Xylitol is a low calorific sweetener which is attracting great global attention due to its potential applications in food and pharmaceutical sectors. Xylitol can successfully be utilised in food products such as confectionery and bakery products and can be incorporated in various medicines for diabetics and general public.

Xylitol is metabolised by intestinal bacteria which presents a prebiotic effect, lowering blood glucose and cholesterol. Xylitol holds 3 accredited health claims for its positive effects on dental health and glycaemic index.

Xylose is the raw substrate used for xylitol production by chemical or bioconversion using microbial species. Chemical production is cost intensive and energy consuming. Xylose consuming microbial research shows that Candida species are best suited for xylitol production.

Microbial production of xylitol is influenced by various process factors such as pH, time and temperature.

Further research is required to maximise the production of xylitol from biomass to create a product that moves from a liner system to a circular one. Xylitol's applications can elevate the environmental impact of sugar production whilst positively impacting the consumers health.

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Appendix 1; Yeast strains researched

Microbial strain	Raw material	Fermentation time (hour)	Max. xylitol production (g/L)
Candida tropicalis HPX2	D-Xylose	24	40
C. Tropicalis BSXDH-3	D-Xylose and Glycerol	Unknown	Unknown
C. guillermondi FT1-20037	D-Xylose	78	77.2
C. tropicalis IFO 0618	D-Xylose	Unknown	Unknown
C. tropicalis DSM 7524	D-Xylose	800	220
C. Boidinii NRRL T-17213	D-Xylose	336	53.1
C. Mogii ATCC 18364	D-Xylose	Unknown	Unknown
Debaryomyces hansenii NRRL Y-7426	Sugarcane bagasse	48	10.54
Candida sp. 550-9	D-Xylose	120	173
Hansenula polymorpha	D-Xylose and Glycerol	96	58
C. tropcalis	D-Xylose and Glucose	284	110
Pichia sp.	D-Xylose	50	25
D. hansenii UFV-170	D-Xylose	24	5.84
C. tropicalis JH030	Rice straw	71	31.1
C. tropicalis SS2	Xylose and Glucose	67	220