Xylitol in Chewing Gums

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Abstract: Xylitol is a naturally occurring sweetener that cannot be metabolized by oral microorganisms. When used as sugar substitute, it can lead to a reduction in dental caries incidence. The use of xylitol and other sugar alternatives is not common practice in restorative dentistry. One reason for this could be the lack of understanding of the proper rationale for utilizing such a preventive modality. This effort aims to summarize the literature concerned with xylitol in chewing gums and provides a concise guideline for the use of this preventive approach in clinical practice.
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Introduction

Dental caries is a bacterial disease with a multifactorial etiology. Caries occurs due to an imbalance between the protective and pathological factors within the oral environment (Figure 1). This same concept can also be expanded to include recurrent caries (also known as secondary caries) which is basically primary caries related to the margins of existing dental restorations. Dental caries is still widely spread in many regions of the world and is considered the most common chronic disease affecting the human population(Petersen, Bourgeois et al. 2005; Jin, Lamster et al. 2016).

Management of dental caries involves several approaches. Until recently, the surgical excavation of the infected tooth structure was the only method for dealing with the disease. In some parts of the world, this is the primary method that dentists use to manage the disease. In fact, from personal interaction with patients, they are expecting the use of rotary instruments when visiting the dental office. The focus on preventive and minimally invasive methods is starting to get traction. Among these, dietary restriction of fermentable carbohydrates is a viable option. As patients are accustomed to the sweet taste, the use of sugar substitutes can be a very effective strategy to restrict the consumption of caries-inducing sugars.

There is a direct benefit to limiting dietary intake of sucrose and other fermentable carbohydrates. Given the major effect that sugar ingestion plays in the development of caries, strategies restricting the exposure to sugars can be used to counteract certain parts of the etiology by replacing sugars with other ingredients(Burt 2006). The use of these sugar alternatives, or substitutes, is increasingly getting more attention owing to the multifactorial nature of the caries process. Sugar substitutes are low- or non-cariogenic sugars that cannot be metabolized effectively by cariogenic bacteria. Multiple reports have documented the benefits of sugar-free chewing gums in reducing dental caries (Burt 2006; Deshpande and Jadad 2008; Mickenautsch and Yengopal 2012).

The purpose of this report is to provide clinicians interested in utilizing the preventive actions of xylitol, especially xylitol-containing chew gums, to manage their patients and to incorporate the chewing gums into caries prevention regimens. A concise overview of xylitol characteristics, mechanism of action, and evidence of caries prevention as well as the reported dosage will be presented. By providing answers for five simple questions: "what, how, how much, who, and what if…" dentists and dental students as well as policy makers can have a general understanding of the benefits and implications for incorporating such a modality in the established clinical system.

Xylitol… [*the what…?*]

Carbohydrates in general can be divided into simple and complex based on the composition. Simple sugars (also known as monosaccharides) tend to be utilized readily by the body owing to their simple structure that is made of a single carbon atom. Consequently, it can be fermented by cariogenic bacteria leading to rapid production of lactic acid in the dental biofilm and saliva. Examples of simple sugars include glucose, fructose, and galactose. Disaccharides are another category of simple sugars that contains two carbons and are usually made of at least of two units of simple sugars. Among these, sucrose is the most cariogenic since it can be broken down into two molecules of glucose leading to large energy production and byproducts by oral bacteria(Peldyak and Makinen 2002). Complex sugars (also known as polysaccharides) require local digestion by oral enzymes in order to be broken down to a form that can be utilized by cariogenic bacteria. It

tends to be less cariogenic unless it is consumed in conjunction with simple sugars. These sugars cumulatively along with sugar alcohols (polyols) are referred as bulk sweeteners and used in baking and confectionery products such as chewing gum, candies, chocolates, and mints. Also, they can be used in dentifrices and mouth rinses and cough syrups and throat lozenges (Zero 2008).

To counteract the effect of sugar fermentation of the sugars mentioned above, sweeteners were introduced. These sugar substitutes can be divided into intense (high intensity) and bulk sweeteners (Table 1). Among these sugar substitutes, Xylitol is very important owing to its non-cariogenic properties. Furthermore, sometimes xylitol can be considered as anti-cariogenic because it affects the metabolism of oral bacteria(Peldyak and Makinen 2002; Zero 2008). Xylitol is found naturally in birch trees and xylan-producing trees as well as in small amounts in fruits and vegetables. Xylitol has the same sweetness as sucrose(Natah, Hussien et al. 1997)and was found previously to be metabolized slowly or not effectively by *Streptococcus mutans*leading to reduction in the incidence of dental caries (Shaw 1976; Pihlanto-Leppala, Soderling et al. 1990).

Mode of action… [*thehow…?*]

Xylitol and other polyols were first approved by the FDA in 1998 as preventive agents for dental caries. The reported mechanisms for the inhibitory action of xylitol in chewing gum are shown in Figure 2. These effects are mostly due to the inhibitory effect of xylitol to the metabolic pathways of caries-producing oral microorganism (Makinen 2000). In addition of not being metabolized by *S.mutans* (Ghezzi 2014), xylitol interferes with the adherence of cariogenic bacteria to dental hard tissues by affecting the extracellular polysaccharides production. These microorganisms cannot adhere properly to the tooth structure leading to a reduced overall caries experience (Loesche, Grossman et al. 1984) and vertical transmission (Trahan, Soderling et al. 1992). Further, a significant decrease in *S. mutans* quantities in saliva and plaque was reported with the frequent use of xylitol (Trahan 1995).

Recent systematic reviews show evidence that the frequent use of xylitol-containing chewing gums can reduce the occurrence of dental caries(Deshpande and Jadad 2008; Mickenautsch and Yengopal 2012). Even though this evidence was recorded with the use of other polyols such as sorbitol, the non-cariogenic potential of xylitol renders it more attractive for preventive and management protocols.

Chewing gum is increasingly utilized for the delivery of multiple active ingredients (Dodds 2012). Typically, chewing gum for the delivery of polyol, including xylitol, tends to be cheaper than other alternatives. This would allow it to be easily incorporated into preventive protocols for individual as well as on small community scales. The delivery of xylitol via chewing gum has been previously reported as convenient and as effective in producing adequate salivary stimulation (Tanzer 1995; Edgar 1998). Up to 12 folds increase in salivary flow rate can take place while chewing gum (Dawes 2010). This effect can last for up to seven minutes and tapers down to a sustained two fold increase after the gum sweetness fades (Dawes and Kubieniec 2004). Increased salivary flow will enhance the cleansing action of saliva as well as facilitate remineralization of incipient lesions due to the abundance of minerals found in the saliva.

Several investigators compared xylitol chewing gum to placebo and found a significant difference between the caries experience in the two groups (Kandelman and Gagnon 1990; Makinen, Bennett et al. 1995; Hildebrandt and Sparks 2000; Campus, Cagetti et al. 2009). These authors attributed the caries reduction compared to non-chewing gum controls to the salivary stimulation effect while chewing. Still, several investigations showed a direct effect for chewing gum containing xylitol on caries increments compared to negative controls as well as to chewing gums containing other sugar alcohols (Van Loveren 2004; Soderling 2009).

Many clinical trials suggest greater reduction in caries from chewing gums sweetened with xylitol than from sorbitol-sweetened gums (Makinen, Bennett et al. 1995; Machiulskiene, Nyvad et al. 2001; Van Loveren 2004). In a study that was a part of the Turku sugar research, the control group received chewing gum sweetened with sucrose and the study group received xylitol-sweetened gum (50% xylitol and 6% sorbitol). The control group developed 3 new DMFS, while DMFS in the xylitol group decreased by 1 (Scheinin, Makinen et al. 1975). Evidence also shows that habitual use of gum sweetened with xylitol can reduce dental biofilm accumulation (Makinen, Chen et al. 1996) as well as provide a marked decrease in patient's caries risk compare to sorbitol-containing chew gums (Burt 2006).

Effective dose… [*the how much…?*]

The recommended dose of xylitol to achieve caries preventive effect can be set around the consumption of 6 grams per day divided into multiple sessions(Twetman 2010). Still, a range between 4 and 12 g per day can be found in the literature as well (Peldyak and Makinen 2002). Clinical guidelines state that the maximum recommended dose of xylitol for individuals over 6 years of age not to exceed 10 g per day (Jenson, Budenz et al. 2007). The consumption of the chewing gum should be extended for approximately 10 minutes to achieve the maximum

benefit for the exposure to xylitol (Hurlbutt and Young 2014).

To reach the daily recommended dose of xylitol in chewing gum, dentists should know the concentration of xylitol in the recommended products. Not all products can deliver the recommended dose efficiently. In a report by Bouges and colleagues, the authors reviewed 49 products carrying the "sugar free" label. Only two out of ten brands of chewing gum can deliver the 6 g/day xylitol with the use of a reasonable number of gum pellets (Bouges, Awn et al. 2017). This dose should by divided over the course of the day. Exposure to xylitol for three times daily is the minimum frequency to achieve effective caries reduction (Makinen, Bennett et al. 1995).

Pathologic factors (negative forces)		Medium		Protective factors (positive forces)
Low flow rate (<0.7 mL/min.)/ Inadequate buffering/ Dehydration	→	**Salivary**	←	Adequate flow rate (≥0.7 mL/min.)/ Adequate buffering/ Adequate body hydration
High Streptococcus mutans and Lactobacellus counts (≥100,000 CFUs)	→	**Bacterial count**	←	Low Streptococcus mutans and Lactobacellus counts (<100,000 CFUs)
High in fermentable carbohydrates	→	**Dietary content**	←	Low in fermentable carbohydrates
Multiple exposures to fermentable carbohydrates and cariogenic snacks between meals	→	**Dietary habits**	←	Less frequency of exposure to fermentable carbohydrates and healthy snacks with meals
Inconsistent brushing habits	→	**Brushing**	←	At least brushing twice daily with a fluoridated toothpaste
Inadequate fluoride exposure	→	**Fluoride exposure**	←	Multiple sources of fluoride
Presence of health issues that can affect salivary flow/ Physical disability	→	**Systemic conditions**	←	No major health issues affecting salivary/ No radiotherapy/ No medications affecting saliva/ No physical disability

Figure 1. Force field analysis of the balance between pathological and protective factors in the oral cavity that contribute to dental caries

Target population [*the who…?*]

The use of sugar-free products is potentially beneficial to certain groups of people who have issues with increased consumption of sugars. Still, in order to decrease the caries risk for the patients, multiple factors including: saliva, fluoride, and improving oral hygiene play a role along with the reduction of sugars (Featherstone 2004). Xerostomic patients, elderly patients with susceptibility to root caries, pregnant and nursing women can benefit from incorporating xylitol-containing chewing gums in their caries preventive protocols(Makinen, Pemberton et al. 1996).

There is established evidence that the early use of xylitol by parents and care givers can lead to a

reduction in caries incidence in the offspring. This is mainly attributed to the decrease in the vertical transmission of *S. mutans* from mother to child (Isokangas, Soderling et al. 2000; Soderling, Isokangas et al. 2000). As the child-mother interaction is the primary source of acquiring the cariogenic species (Li and Caufield 1995), mothers and care givers can be instructed to use xylitol products to decrease such transmission. Its utilization during the "window of infectivity" period, which spans between ages of 19 and 35 months (Caufield, Cutter et al. 1993; Kohler and Andreen 1994), can reduce or delay *S. mutans* transmission leading to fewer DMFS scores later in life (Straetemans, van Loveren et al. 1998).

Safety and side effects [*the what if…?*]

So does xylitol have side effects and what are the safety considerations if the recommended dose is exceeded? Xylitol, as well as other sugar alcohols, can be consumed without side effects up to concentrations in the range of 8 to 10 g/day (Forster, Quadbeck et al. 1982); however, at such quantities a laxative effect was reported. In fact, a study reported that laxative effect can take place only when doses as high as 15 g/day are used (Jang, Ju et al. 2012). To reach such a high concentration, the patient needs to consume more than ten gum sticks per day (Dodds 2012). Even though the use of chewing gum is considered safe in general, dentists should refrain from recommending gum chewing for small children below the school age to avoid potential choking hazards. Also, the use of chewing gum is not advisable for patients with temporomandibular dysfunction or for patients suffering from jaw pain or stiffness (Christensen, Tran et al. 1996).

Recommendations [the *What…? So what…? and Now what…?*]

Secondary preventive measures such as the use of chewing gums are seldom used by dental professionals(Longbottom, Ekstrand et al. 2009). Since the effectiveness of such modalities has been recognized, it is essential to increase the awareness of dentists in utilizing such effective modality than can be a valid alternative to surgical measures for caries management(Longbottom, Ekstrand et al. 2009; Tellez, Gomez et al. 2013).

As reported above, there is strong evidence that the regular use of xylitol-containing chewing gum can prevent dental caries if used in conjunction with other oral measures. This concept can also be expanded to community-level initiatives as a public-health preventive approach. As suggested by management protocols of Caries Management by Risk Assessment (CAMBRA) model, the incorporation of sessions of chewing xylitol-sweetened guminto the regimen is effective. Of course this should be considered in addition to the use of other measures such as fluoride and oral hygiene practices. The additive effect of these measures can promote a healthier oral environment.

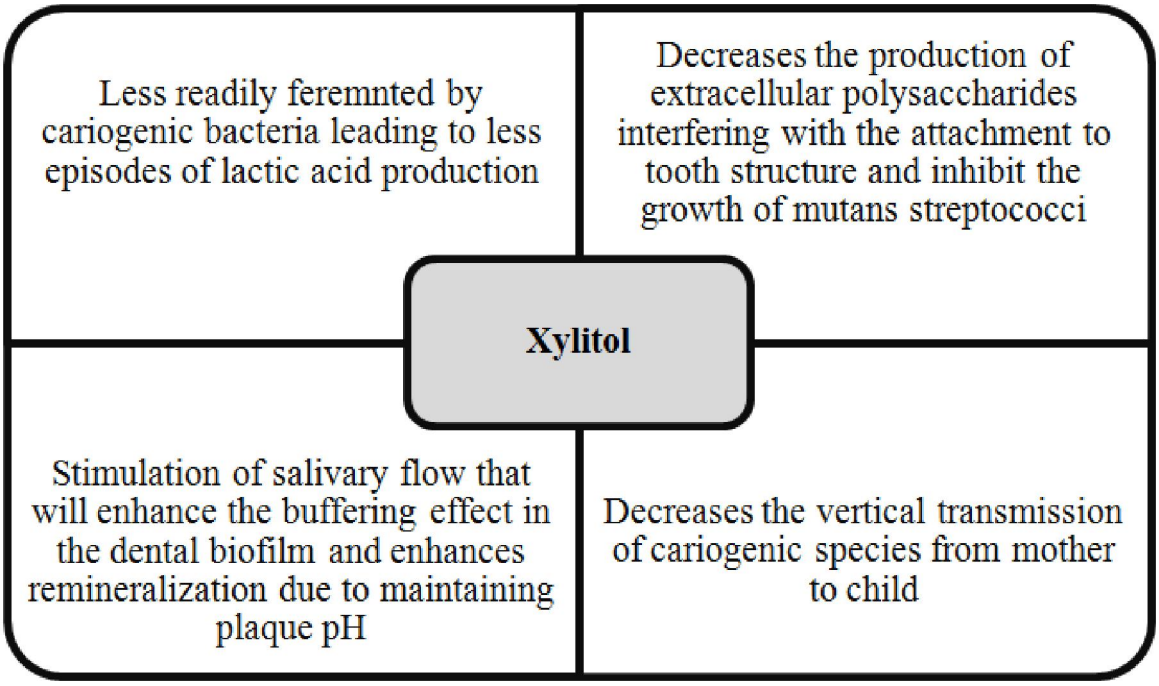

Figure 2. Possible caries preventive mechanisms of xylitol

Table 1. Types and properties of sweeteners (Van Loveren 2004; Ly, Milgrom et al. 2008) – *adapted.*

Sweetener		Uses	Examples	Calories (Kcal/g)	Relative sweetness compared to sucrose	Caloric	Acido-genic	Cario-genic
Bulk	Sugars	Dietary sweeteners	Sucrose	4.0	1.0	Yes	Yes	Yes
			Fructose	4.0	1.5			
			Lactose	4.0	0.2			
			Glucose	4.0	0.7			
	Sugar alcohols (polyols)	Chewing gums, mints and oral care products	Sorbitol	2.6	0.6	Yes	Low	Low/ none
			Maltitol	2.1	0.9			
			Mannitol	1.6	0.5			
			Lactitol	0.02	0.4			
			Isomalt	2.0	0.5			
			Xylitol	2.4	1.0	Yes	No	None/ anti-
			Erythritol	0.02	0.8			
Intense sugars		Table sugar replacement, in diet beverages and in reduced calorie foods	Acesulfame-K	0.0	200	No	No	No
			Aspartame	0.0	180			
			Saccharin	0.0	300			
			Sucralose	0.0	600			

Declaration of interests

The author declares no conflict of interest.

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