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The Essential Role of Xylitol

Imparting preventive benefits for oral and systemic health and limiting the severity and possibly transmission of COVID-19

Mark L. Cannon, DDS, MS | John Peldyak, DMD

ABSTRACT

Severe outcomes of COVID-19 are associated with age and comorbidities such as metabolic dysfunction and oral disease; therefore, the importance of oral care in an overall wellness model needs to be recognized. Oral and overall systemic health can be enhanced by the simple adjunctive use of xylitol. Xylitol is a 5-carbon alditol that can be used as a low-calorie, low-glycemic sweetener to replace sugar and potentially improve the metabolic condition in the prediabetic and diabetic diet. With regular use, small amounts of xylitol can reduce the risk for dental caries and support periodontal health by stimulating saliva, reducing microbial adherence, promoting mineralization, and suppressing certain pathogens. Dietary xylitol can help establish and modulate a healthy microbiome. In a saline nasal spray, xylitol helps open the airway to encourage proper nasal breathing and prevent upper respiratory infections. A nasal spray containing xylitol has recently been shown to inactivate or block SARS-CoV-2. This article examines the benefits and clinical indications of xylitol; presents prevention strategies using xylitol products, including toothpastes, chewing gums, candies, mouth rinses, and nasal sprays; and discusses business considerations for implementing a xylitol-supplemented office-based prevention program to add value for patients and the practice.

LEARNING OBJECTIVES

- Describe the benefits of supplemental dietary xylitol in the maintenance of oral and systemic health.
- Explain how a prevention plan including xylitol can help reduce the severity of COVID-19 infection, limit related complications, and potentially block transmission of the virus.
- Identify some of the clinical indications for xylitol based on patient age, health condition, and other factors.
- Discuss the clinical applications of xylitol-based products, including toothpaste, chewing gum, candy, mouth rinse, and nasal spray.

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The global COVID-19 pandemic has renewed awareness of the crucial importance of oral hygiene in the prevention and mitigation of oral and systemic diseases.[1] The mouth is a gateway to the rest of the body,[2] and it has been recognized that dental disease can be a contributor to, as well as a consequence of, COVID-19.[3-6]

Although COVID-19 originates from the SARS-CoV-2 virus, severe cases with complications such as pneumonia and acute respiratory distress may be linked to bacterial superinfections.[3] Pathogenic oral microorganisms can be aspirated into the lower respiratory tract, where they have the potential to initiate or aggravate respiratory infections, and poor oral hygiene can contribute to this bacterial load.[3] Indeed, periodontal disease has been shown to be a risk factor for respiratory disease and severe COVID-19 complications.[4] Oral diseases contribute to chronic systemic inflammation by producing high circulating levels of IL-6, a pro-inflammatory cytokine.[5] Coronavirus infection dysregulates the host immune response, also elevating IL-6. Due to these factors, high IL-6 levels can be predictive of severe COVID-19 outcomes.

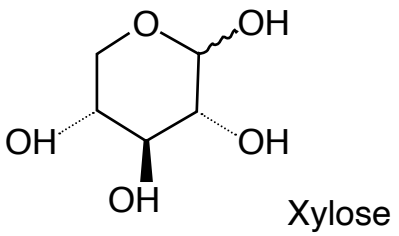
The importance of oral hygiene and periodontal health for individuals with respiratory conditions and COVID-19 infections should not be underestimated. Maintaining oral health can help reduce the severity of COVID-19 and limit related complications.[3,4] According to a literature review, COVID-19 patients who were older and experienced higher severity of the disease had more widespread and severe oral lesions, and lack of oral hygiene is considered one of the most important predisposing factors for the onset of oral lesions in COVID-19 patients.[6]

Coping with pandemic-related stress can

MARK L. CANNON, DDS, MS
Professor
Feinberg School of Medicine
Department of Otolaryngology
Division of Dentistry
Northwestern University
Chicago, Illinois

Private Practice
Long Grove, Illinois

JOHN PELDYAK, DMD
Co-owner
Advanced Developments, Inc.
Mt Pleasant, Michigan



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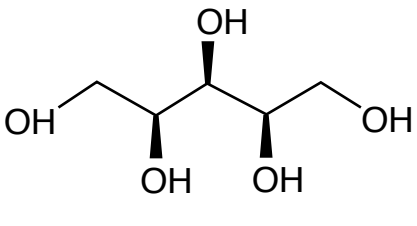
(5 carbon atoms with a free aldehyde group)



An alditol of the pentitol type
(5 carbon atoms with no free carbonyl group)

FIG. 1

(1.) Chemical structures of the sugar xylose and its sugar alcohol xylitol.

lead to an increase in disordered eating and snacking and the selection of sugary comfort foods.[7,8] These behaviors coincide with deteriorating metabolic and oral health. It is worrisome to note that obesity, hypertension, diabetes, and dental disease are all associated with more severe COVID-19 outcomes.[9] A comprehensive prevention plan would address dietary modification to promote oral health and, more broadly, translate to improved public health status.[10] One strategy for such a plan would be to utilize xylitol for sucrose replacement or as a targeted dietary addition.[10-13]

Benefits of Xylitol

Xylitol, a naturally occurring compound that is classified as an alditol—more specifically, a pentitol (5-carbon sugar alcohol)—can be used as a direct replacement for sucrose sugar. The human diet has always included xylitol from fruits, vegetables, and tubers. As much as 15 g of xylitol is generated daily as a metabolic intermediate linking critically essential pentose (5-carbon sugar) phosphate and glucuronic acid (detoxification) pathways.[14] Because xylitol is equal in sweetness with sucrose but lower in calories, low glycemic, and low insulinemic, it can displace equivalent amounts of sugar with notable metabolic benefits for individuals with diabetic and prediabetic conditions.[15,16] As such, it may be considered a dietary supplement.

Xylitol has been extensively researched and demonstrated to be safe and to have notable anticariogenic and anti-periodontal disease properties with appropriate use.[11-13] For about 50 years, xylitol has been used to replace sugar in sweet foods to help block the demineralization of tooth enamel, and it is also used in diabetic diets to reduce postprandial glucose and insulin excursions.[15] However, the benefits of added dietary xylitol go beyond the mere removal of sugar. Emerging evidence indicates that xylitol can play a number of functional roles to actively support the maintenance of oral and systemic health with anti-biofilm, antioxidant, anti-inflammatory, and antidiabetic effects.[14,15]

The health benefits of xylitol are not limited to oral hygiene. It efficiently stimulates and modulates the immune system. Although excess consumption can have a laxative effect, dental amounts of xylitol are well tolerated, especially after a brief period of adaptation. It then supports healthy digestion by increasing butyrate production. Xylitol has been shown to help in controlling blood sugar and obesity, facilitate wound healing, improve skin condition, reduce bone resorption, increase bone strength, and reduce ear and respiratory infections.[16-21]

Xylitol disrupts the growth and virulence of keystone oral disease initiators, such as *S. mutans* (caries), *C. albicans* (candidiasis), and *P. gingivalis* (periodontal disease), and as a prebiotic, it helps to establish, balance, and maintain a healthy microbiome, beginning with the oral gateway microbiome, which supports innate immunity and disease resistance.[21-26]

In a healthy mouth, saliva provides an environmental niche for protective probiotic microorganisms while preventing the overgrowth of pathogens, including fungal and viral pathogens. The oral cavity, via saliva and plaque, is strongly felt to be significant in the modes of transmission of COVID-19. Angiotensin-converting enzyme 2 (ACE2) is a critical receptor for coronavirus, and it is found in the epithelial cells of the mouth and salivary glands. Although xerostomia is a common complaint of the elderly, especially those taking medications, SARS-CoV-2 may induce acute and chronic sialadenitis, which aggravates dry mouth conditions, and hyposalivation is a potential risk factor for acute respiratory infection, notably in coronavirus exposure.[27-30] Xylitol is an excellent saliva stimulant that increases salivary pH and provides other protective factors.[31]

Recent research has identified xylitol as a potential "decoy target" to prevent the attachment of SARS-CoV-2 to cells.[32] Respiratory viruses may have evolved to attach to the D-xylose position of sulfated glycosaminoglycans (GAGs), particularly heparin sulfates, on the cell wall core protein, allowing contact of the virus to the appropriate cell receptor for endocytosis[32] to promote viral penetration and replication within the cell. In earlier research, xylitol demonstrated antiviral and anti-inflammatory effects in viral respiratory infections.[33,34] Therefore, the use of a xylitol-containing nasal spray has been recommended to further inhibit the spread of the SARS-CoV-2 virus,[35] especially for children returning to school. A citizen's petition to the US Food and Drug Administration and the US Centers for Disease Control and Prevention, which was signed by the authors of this article, has been filed to champion the movement for the use of readily available and safe supplements, such as xylitol. In addition, the use of xylitol nasal spray can enhance the comfort of healthcare providers who are required to wear substantial amounts of personal protective equipment, such as two masks and a face shield. A spray prior to donning the masks can significantly increase the

wearer's comfort and may provide protection from the SARS-CoV-2 virus.

It should be noted that the terminology referring to xylitol as a sugar alcohol on food labels can be very misleading to consumers. Xylitol does not contain any ethanol. Specifically, sugar alcohols are reduction products of true sugars (ie, monosaccharide or disaccharide), which have a free carbonyl functional group (ie, aldehyde or ketone). All of the carbon atoms of the so-called sugar alcohols are bonded with the hydroxyl functional group (-OH) of alcohols, which is much more stable and less reactive than the corresponding carbonyl (C=O) (Figure 1). Alditols are a subset of polyhydroxy alcohols or "polyols."

Clinical Indications

The first potential indication for xylitol that should be considered is for the expecting or nursing mother. In pregnant women, xylitol has been reported to reduce periodontal disease, and this could help prevent miscarriages and preterm births.[36] In addition, for the nursing mother, xylitol has been well demonstrated to inhibit the transmission of *S. mutans* from mother to child, reducing the rate of caries development in the child by as much as 73%.[37,38] More directly, infants can benefit from xylitol wipes or syrup for further reduction of oral pathogens.[39] Research has shown that xylitol applied before the eruption of primary or permanent teeth creates a healthy environment for optimal mineralization and blocks pathogen colonization, resulting in long-lasting caries limitation.[40]

As soon as teeth have erupted, xylitol gel can be safely used as a dentifrice. Infants and toddlers may have their teeth brushed in the crib because the xylitol gel is 100% safe and digestible. The preservative, grapefruit seed extract, is not only very safe but also beneficial. Older children who are carefully instructed on the necessity of spitting may use a fluoride toothpaste with xylitol, which will outperform a toothpaste with fluoride only. Xylitol's ability to inhibit periodontal pathogens adds benefits that fluoride only toothpastes lack. One example would be for a young teen in full orthodontic appliances who has severe gingival issues. A xylitol mouth rinse would benefit this patient as it would any younger child capable of spitting after rinsing. Any patient who presents with plaque accumulation or a gingival pathosis should benefit from xylitol supplementation.[27,41]

TABLE 1. Addition of Xylitol to Saline Nasal Spray Increases Airflow 35%[72]

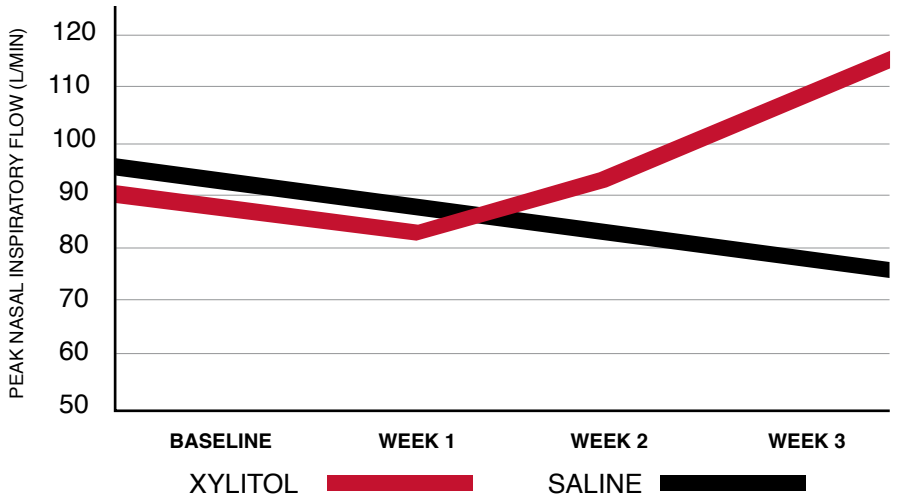
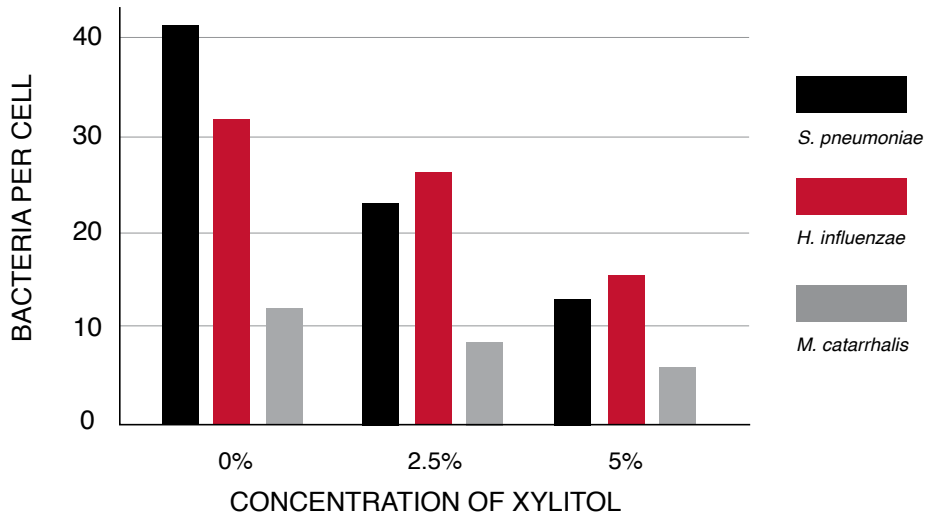


TABLE 2. Exposure to Xylitol Reduces Adherence of Otopathogenic Bacteria[75]



Xylitol-based oral care products that are safe to swallow can support effective prevention programs for active people while they are away from home. These consumable items are especially valuable for patients who have special needs or are in care facilities.[42] Among adults, the periodontal protective effect of xylitol may help control chronic oral/systemic inflammation.[43-45] Elderly patients with exposed root structure are also candidates for xylitol supplementation because xylitol is a calcium carrier that can help reduce root caries and sensitivity. Patients who suffer from xerostomia are additional candidates. Xylitol mints can be used to stimulate salivary flow.[46,47] As one would surmise from the aforementioned indications, all patients could likely benefit in some manner from xylitol supplementation. Xylitol is a prebiotic and may be followed with a regimen of dental probiotics as part of a complete prevention program.

Clinical Applications

Xylitol may be used as an ingredient in toothpastes, chewing gums, candies, mouth rinses, and nasal sprays.[27] The usage guidelines for xylitol are suggestions that can be adjusted to accommodate individual circumstances. For caries limitation in adults, it may not be necessary to consume more than 10 g to 15 g (ie, less

than a tablespoon) of xylitol daily in three or more divided servings. Children older than 3 to 4 years only require about half of that amount, and younger children have been given smaller quantities under parental guidance.[48] For sustained long-term caries protection, the ideal time to initiate xylitol use is before tooth eruption. The use of xylitol should augment current prevention recommendations, not replace them.[48] Look for products that list xylitol as the sole or primary bulk sweetener. Several routine oral hygiene products and confectionaries now contain effective amounts of xylitol and can provide at least 5 g in three or more daily servings.[49,50]

Toothpaste

Implementing xylitol into dental practice can be very easily accomplished because of the numerous, readily available xylitol-based dental preventives on the market. First and foremost among the preventives would be the xylitol tooth gels and toothpastes. These are available with or without fluoride, depending on the age of the patient and his or her ability to expectorate. Because xylitol has been proven to efficiently prevent decay, young toddlers and individuals with special needs may be the most appropriate recipients for the fluoride-free formulations.[51] When compared with fluoride-only toothpastes, which reduce dental decay by an average of 24%, fluoride toothpastes with xylitol achieve an approximately 13 % greater reduction in dental decay.[52-59] However, the combination of fluoride in a low dose of only 200 PPM with xylitol, erythritol, and nanosized sodium trimetaphosphate averages the best remineralization.[60] This represents the first significant advancement in toothpaste technology in many years.

Chewing Gum

To achieve dental benefits, chewing gum is considered an ideal "delivery system" for xylitol and is the leading application for it worldwide. Xylitol is sweet enough to be used as the sole sweetener in gum. Chewing xylitol gum is recommended after meals and snacks to neutralize the potential harmful effects of fermentable carbohydrates.[61]

The great potential of xylitol in chewing gum was first demonstrated in the early 1970s when it's use was shown to achieve caries reduction nearly equivalent (ie, 80%) to the total substitution of dietary sucrose by xylitol.[62] Subsequently, several large trials have demonstrated impressive reductions in caries, even when the use of xylitol chewing gum was limited to school days.[63]

Candy

Xylitol-based candies can likewise be effective in caries limitation.[64] Dentally safe candy offers an opportunity to entice parents into substituting unhealthy sucrose and high fructose corn syrup snacks with xylitol. It is common for dental offices to dispense xylitol lollipops to children following restorative appointments. In addition, many parents purchase such snacks from local health-conscious grocery stores for occasions such as birthdays. The candies are also recommended for pregnant mothers or those who are breastfeeding. Research has demonstrated a decrease in miscarriages, premature births, and deliveries of low birth weight infants in mothers consuming xylitol.[65] Regarding breastfeeding, mothers who consume xylitol are far less likely to transmit *S. mutans* to their babies, and the children are less cavity prone for at least 5 years.[66]

Mouth Rinse

Xylitol mouth rinses are very well tolerated by children and do not negatively affect the oral microbiome.[67] Important oral gluten metabolizers are significantly inhibited by other common mouth rinses; however, they are relatively un-affected by xylitol mouth rinses.[68] Several antimicrobial mouth rinses have been shown to raise the blood pressure of patients and increase the rate of type 2 diabetes.[69,70] Unlike xylitol-based ones, these antimicrobial mouth rinses significantly inhibit the nitrate reducing bacteria necessary for nitric oxide homeostasis. Nitric oxide regulates blood pressure by vascular dilation, mediates capillary growth, maintains nitric oxide homeostasis, and initiates cardiac muscle repair.[71]

Nasal Spray

When xylitol is added to normal saline, it creates a hypertonic nasal spray that can draw excess fluid from edematous tissue, thereby opening the airway and facilitating nasal breathing (see Table 1).[72] Xylitol/saline nasal spray also helps to moisturize, thin secretions, relieve congestion, and rinse away allergens and irritants.[73] In addition, xylitol has anti-biofilm and anti-adhesive effects on upper airway pathogens (see Table 2).[74,75] It is recommended to use a xylitol/saline nasal spray at least twice each day. This use can easily be linked with routine toothbrushing.

Use of a xylitol-containing nasal spray prior to donning an N95 respirator can benefit dental and healthcare personnel because it aids in breathing and reduces nasal airway discomfort. Its use can also benefit patients with mild sleep apnea, either alone or when used prior to wearing a continuous positive airway pressure (CPAP) machine.

Concerning COVID-19

An article published in the June 2020 issue of the *British Dental Journal* concluded that poor oral hygiene may be connected to serious COVID-19 complications due to high levels of harmful oral bacteria.[76] The need for supportive, self-administered oral hygiene strategies is obvious, especially for vulnerable underserved populations, such as elderly patients in care facilities. Xylitol can play an essential role because its use is simple, pleasant, convenient, and effective.[39,42,49,61,62,77-79] Xylitol should be recognized for its ability to improve the health of all Americans, but its use is particularly important during the health crisis of the COVID-19 pandemic.

A patient may be advised to use a xylitol-supplemented toothpaste and mouthwash in the morning and at night as well as xylitol chewing gum or candies after meals and snacks. Similarly, dental healthcare providers should strive to achieve 5 g to 15 g of daily exposure as a dietary supplement and a dental preventive in the same manner as they would recommend for their patients. This can help them better relate to patients how xylitol benefits oral and systemic health.

Business Considerations

The addition of xylitol supplementation to an office-based prevention program requires an inventory of dental preventives, such as toothpastes, gels, sprays, rinses, and probiotics. The dental team should be trained on the benefits of providing the best in preventive care and the necessity of maintaining the sufficiency of this inventory for patient use.

Some patients do not follow up on the recommendations of their healthcare professionals; however, if xylitol-containing products are made readily available at the dental office, many will purchase them and follow through with the recommended prevention program. At later appointments, it is quite

common for patients to purchase additional products to continue the prevention program.

For a busy dental practice with a dentist and two hygienists that averages 4,000 visits per year, a purchase rate of 800, each at $20 to $100, would predict approximately $16,000 to $80,000 in additional gross revenue for the office with a net of approximately $6,400 to $20,000. But the most important financial consideration is the effect on patient referrals and patient retention. It should be recognized that adopting a "patient-centric" approach has been shown to help drive new patient acquisition and retention.[80]

The success of an office's program can be readily evaluated by the lack of recurrent caries or advanced periodontal pathoses among its participants, and the dental team may become very enthused as they see the benefits of providing patients with state-of-the-art preventive care. Being patient centric means providing patients with the care that they truly need and desire, which includes education about the causes of dental disease and systemic illnesses and the means to positively affect their own health. When patients receive all that they need for their complete health, they become empowered to assume overall responsibility for their care.

Conclusion

The addition of xylitol preventives to the dental office is easily accomplished and encourages the entire dental team to participate in a new paradigm shift in preventive dental care. The shift to patient-centric care demonstrates to patients that the practice cares about not only their oral health but also their total health. Many patients are now aware of the oral-systemic link and how important the maintenance of good oral health is to overall body health. Offering xylitol oral and nasal products enhances the total body care that should be provided by all oral healthcare professionals.

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