A SCIENTIFIC OVERVIEW:

Compelling evidence for erythritol oral health benefits

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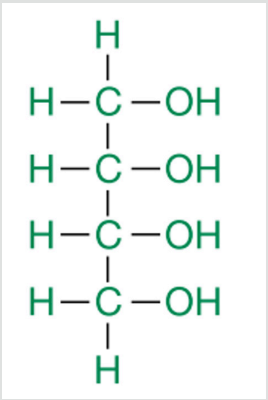
Naturally found in certain fruits and vegetables (and produced commercially via fermentation), erythritol is a four-carbon sugar alcohol (polyol) that is about 70% as sweet as sugar (sucrose) and is commonly used as a sugar replacer and bulking agent. Erythritol is recognized to have zero calories, does not impact blood glucose or insulin levels and is well-tolerated relative to other polyols such as xylitol and maltitol. As a result, erythritol is very useful in the food industry for reducing sugar and calories.

Erythritol can have other benefits beyond food uses, including oral health care applications. For example, the sweetener can be used to mask off-flavors in some oral care products, but research suggests that erythritol also offers other functional benefits. Erythritol has been shown to be non-cariogenic (does not contribute to tooth decay), whereas sugars can be metabolized and used as an energy source by oral bacteria, which produce acids and damage tooth enamel. Erythritol is not metabolized by oral cariogenic bacteria, and studies suggest that it may also slow the growth of oral cariogenic bacteria.

Many *in vitro* animal and human studies have evaluated the effects of erythritol to promote oral health. The following summary provides an overview of this work, including findings that suggest erythritol offers distinct oral care benefits as compared to xylitol and other polyols, which are also efficacious.

Proposed mechanisms for oral care benefits

Chemical composition of erythritol

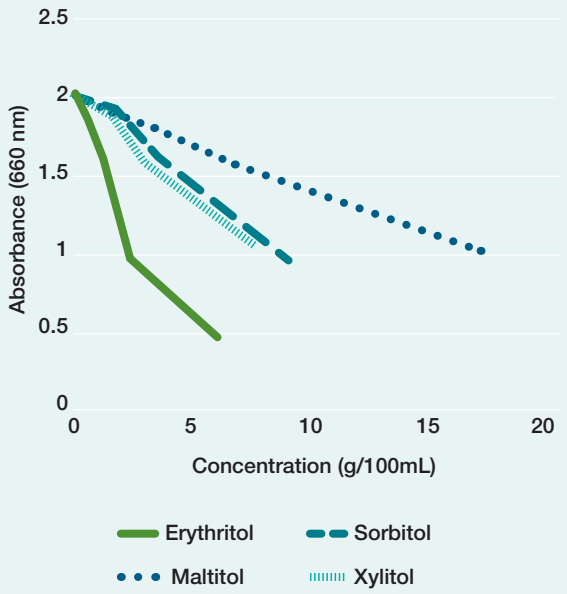


A central factor for poor oral health is the presence of cariogenic bacteria, such as *streptococcus mutans* and others. *Streptococcus mutans* produces dental plaque, which is a sticky biofilm that attaches to teeth. Left untreated, plaque can harden into tartar, which can act as a shield for bacteria. When large amounts of plaque are formed on teeth and fermentable sugars or starches are present, the *streptococcus mutans* convert the sugar into lactic acid, which causes demineralization and erosion, thus weakening tooth enamel. This ultimately leads to dental caries (cavities) in tooth enamel, which can spread to lower levels of the tooth (dentin) and cause permanent damage, tooth loss and gum disease. Dental caries is among the world's most prevalent health problems, largely affecting children, teenagers and older adults.

Unlike sugar, erythritol is non-cariogenic, so simply replacing sugars in foods and beverages with erythritol can, in itself, help benefit oral health. In addition, research suggests that erythritol offers some functional benefits to oral health.

Erythritol is not fermented by oral microflora, and has been shown through *in vitro* studies to inhibit cariogenic bacterial growth and lactic acid production. At concentrations ranging from 2%–16%, cariogenic bacterial growth (*Streptococci mutans, Streptococci sobrinus, Porphyromonas gingivalis, Streptococcus gordonii, Streptococci sobrinus* and *Streptococci wiggsiae*) has been inhibited by erythritol. Some studies have compared erythritol to other polyols and found erythritol to be more efficacious than sorbitol, maltitol and xylitol for oral health care (although these polyols show some efficacy). Erythritol has been shown to produce greater inhibition (by three- to seven-fold) of bacterial growth compared to xylitol, sorbitol and maltitol at the same osmolality (Makinen et al., 2002; 2005).

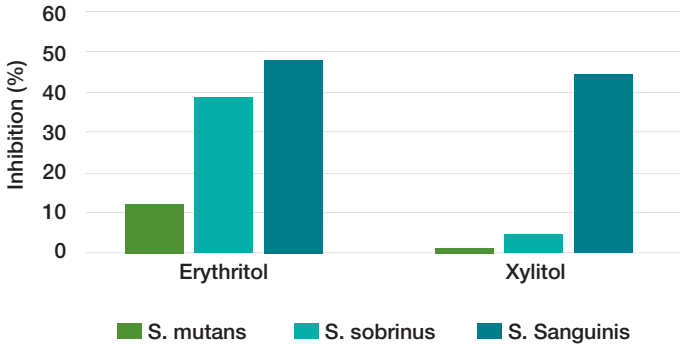
Fig 1. Effects of erythritol and polyols on growth inhibition of *S mutans in vitro* after 5 hours



Adapted from Makinen, et al; 2005 and Makinen, et al; 2001.

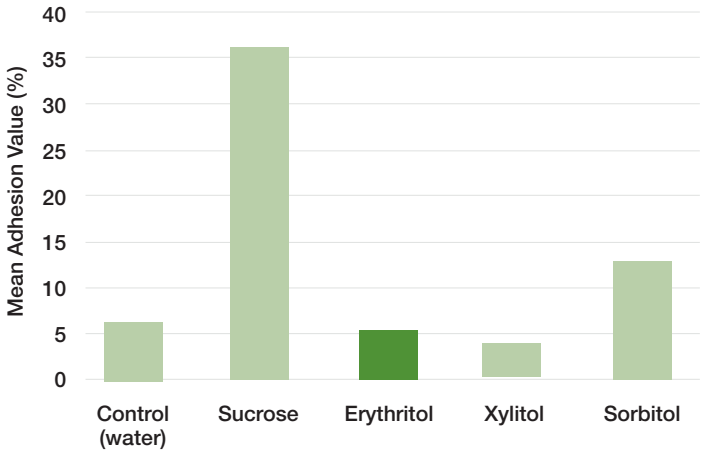
A proposed mechanism for cariogenic bacterial growth inhibition is that erythritol is believed to pass through the cell membrane and suppress genes and inhibit enzymes involved in glucose and sucrose uptake and metabolism pathways, particularly in the late stages (Hashino et al., 2013; Fujii et al., 2023) in *streptococci* and *staphylococcus* strains. Erythritol is also able to reduce lactic acid production, biofilm formation and adherence of *streptococci* and *staphylococcus* strains to smooth surfaces (Park et al., 2014; Fuhii et al., 2023; reviewed in de Cock et al., 2016). Glucosyltransferase (GTF) and fructosyltransferase (FTF) genes metabolize sucrose into glucose and fructose polymers (called glucans and fructans), which provide energy to cariogenic bacteria and promote adhesion of bacteria to dental surfaces.

Fig 2. Effects of erythritol and xylitol on biofilm formation (2% concentration)



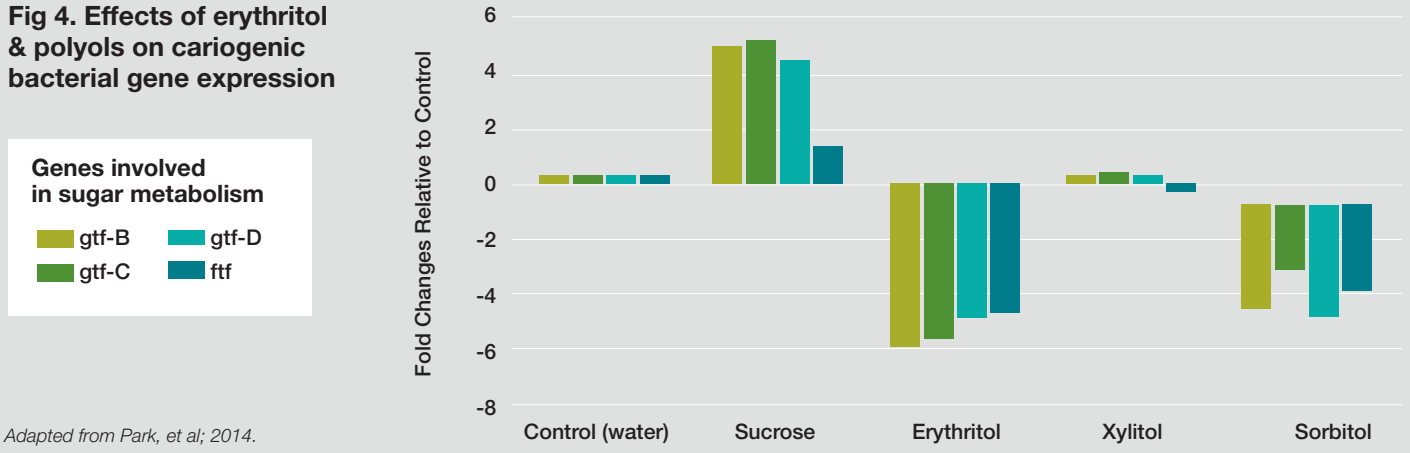
Adapted from Ghezelbash, et al; 2012.

Fig 3. Effects of erythritol & polyols on bacterial surface adherence



Adapted from Park, et al; 2014.

Fig 4. Effects of erythritol & polyols on cariogenic bacterial gene expression



Adapted from Park, et al; 2014.

The proposed mechanisms for improving oral health via erythritol include:

1. **Inhibiting growth and decreasing acid production of the principal bacterial species** associated with caries development.
2. **Decreasing adherence of 14 common streptococcal oral bacteria to tooth surfaces**, due in part to a decrease in expression of bacterial genes involved in metabolism of sugar(s) (glucosyltransferase [GTF] and fructosyltransferase [FTF]) genes, resulting in a reduced production of glucans and fructans.
3. **Decreasing *in vitro* biofilm formation** and *in vivo* dental plaque weight.

Summary of *in vitro* studies of erythritol and oral health

Numerous *in vitro* studies show erythritol benefits to oral care, including inhibition of cariogenic bacteria, as well as reduction in plaque formation, smooth-surface adhesion and lactic acid production. These studies include:

Incubation studies on growth inhibition and surface adherence

- ***5-hour incubation.*** A 0.1M to 0.6M solution of erythritol was incubated for five hours with *Streptococci mutans* strains, inhibiting their growth at a 3x–7x higher rate compared to sorbitol, xylitol and maltitol, which also reduced growth (Makinen et al., 2005).
- ***Overnight incubation.*** Solutions of erythritol at 2% and 4%, incubated overnight, inhibited the adherence of 14 strains of polysaccharide-forming oral *streptococci*, including *Streptococcus mutans*, to a glass surface or microtiter plates; this result was independent of growth inhibition (Soderling et al., 2010; Ghezelbash et al., 2012).
- ***48-hour incubation.*** Erythritol solutions at concentrations of 0.5% or 8–16% incubated in growth medium for 48 hours demonstrated inhibited growth of *Streptococcus mutans* and *Streptococcus sobrinus* (Yao et al., 2009; White et al., 2015).

Dose response studies on growth inhibition and biofilm formation

- ***4% solution.*** A 4% erythritol solution slowed growth of *Streptococcus mutans* and biofilm production by 56% and 36% respectively (Saran et al., 2015).
- ***10% solution.*** A 10% erythritol solution had an inhibitory effect on the microstructure of a biofilm composed of *Porphyromonas gingivalis* and *Streptococcus gordonii* compared to erythritol and xylitol (Hashino et al., 2013).
- ***5% & 10% solutions.*** Erythritol solutions at 5% and 10% in a human-stimulated saliva dose dependently inhibited biofilm formation after nine days (i.e., it induced a compositional shift from periodontitis- and gingivitis-related taxa) and contributed to a healthy oral ecosystem *in vitro* (Janus et al., 2017).

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- ***15% solution.*** A 15% erythritol solution inhibited biofilm formation of *Streptococcus mutans* (up to 85%) and *Streptococcus sobrinus* (up to 69%), as well as a newly recognized bacterium highly associated with caries in early childhood, *Streptococcus wiggsiae* (Koljagl et al., 2020; Tanner et al., 2011).
- ***2.5%, 5% & 10% cultures.*** Throat cultures were incubated with 2.5%, 5% and 10% solutions of xylitol and erythritol to evaluate the inhibitive effects on growth of *Streptococcus pyogenes*, which causes peritonsillar abscesses (collection of pus related to tonsilitis) in adolescents and young adults. Both xylitol and erythritol were efficacious in inhibiting the growth of *Streptococcus pyogenes* (by 48% to 98%), with xylitol being more efficacious (Koljagl et al., 2020).
- ***Impedance spectroscopy study.*** A study using impedance spectroscopy and a Real Time Cell Analyzer (RTCA) to evaluate the effects of erythritol and xylitol on real-time monitoring of biofilm formation by *Streptococcus mutans* strains found that both polyols inhibited real-time biofilm formation at the early stages, inhibited different *Streptococcus* strain growth and inhibited surface attachment (Loimaranta et al., 2020).

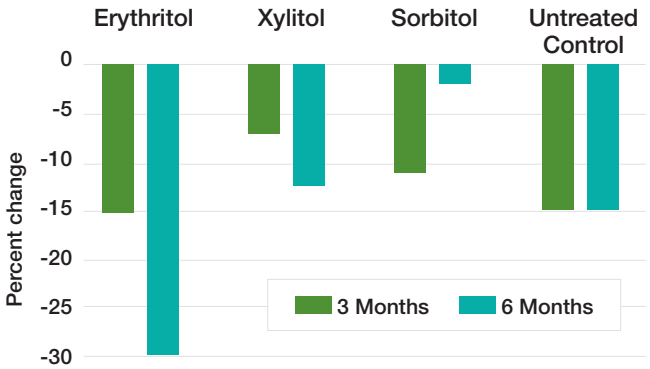
Summary of human clinical studies on oral health with erythritol

Human clinical studies further confirm the oral health benefits of erythritol. This research spans more than three decades and evaluates the effects of erythritol on oral health in diverse sets of individuals, including healthy adults, teenagers and children.

In a study by Makinen et al. (2002), 98 individuals were administered a chewable containing either 5.4g/day sorbitol (Group S) or xylitol (Group X), or 2.7g/day of a 1:1 mixture of xylitol:erythritol (Group XE) or sorbitol:erythritol (Group SE) for 64 days. There was a significant reduction in plaque and saliva *Streptococcus mutans* in Groups X and XE.

In another study by Makinen et al. (2005), researchers used a much-larger sample size, erythritol dose and study duration. In this study, 136 teenagers received either 7g/day of erythritol, sorbitol or xylitol combined with 2x/daily use of toothpaste with the same polyols for 6 months. Both erythritol and xylitol significantly reduced dental plaque, as well as saliva and plaque levels of *Streptococcus mutans*, but sorbitol did not. In addition, levels of erythritol and sorbitol could be found in dental plaque, and to a lesser extent, xylitol.

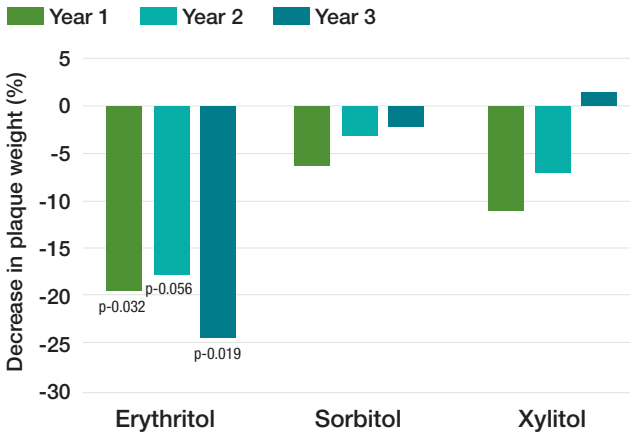
Fig 5. Change in fresh dental plaque weight



Adapted from Makinen, et al; 2005.

The first study performed in children (Honkala et al., 2014) evaluated long-term effects of erythritol, sorbitol and xylitol on the incidence and propagation of dental caries in a randomized double-blind, controlled prospective trial. 374 children aged 8-9 years at the beginning of the trial were given chewable tablets containing either 7g of erythritol, sorbitol or xylitol. The children were given a toothbrush and oral care advice and were seen by a trained dental examiner at 12, 24 and 36 months. At baseline and at 12 months, there were no significant differences in dental caries. At the 24-month follow-up, there were significantly fewer caries; and at the 36-month follow-up, there was significantly lower mixed dentition in the erythritol group than in the xylitol group.

Fig 6. Effects of erythritol on fresh plaque weight



Adapted from Runnel et al., 2013.

Compared to xylitol and sorbitol over the 3-year period, the erythritol group had significantly fewer tooth surfaces developing into enamel or dentin caries, and significantly less enamel caries on tooth surfaces developing into dentin caries.

Fig 7. Effects of erythritol, xylitol and sorbitol on developing dental caries *over* 3 years (%)

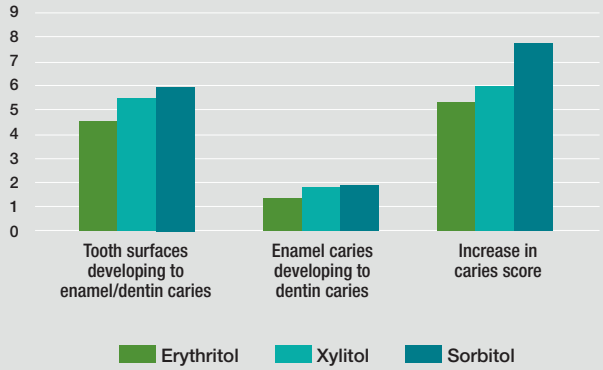
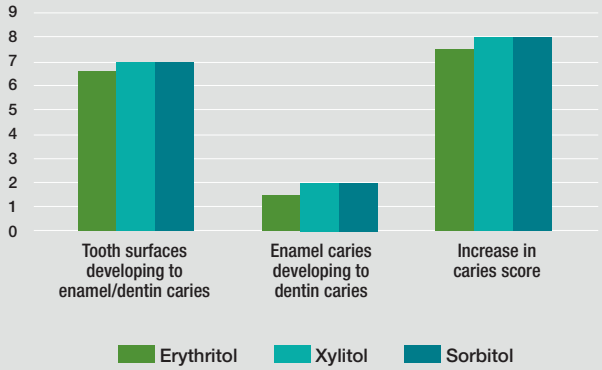


Fig 8. Effects of erythritol, xylitol and sorbitol on developing dental caries *after* 3 years (%)



Adapted from Honkala, et al; 2014.

In addition, the time required for enamel or dentin caries lesions to develop, and dentin caries to progress, was significantly longer in the erythritol group compared to the sorbitol and xylitol groups. The authors report that the erythritol group had 143 fewer dental treatments (tooth restorations by a dentist) as compared to the control. Saliva and plaque were collected at the time of dental examination for determination of salivary and plaque counts of *S. mutans* and salivary counts of *Lactobacillus*.

At years 1 and 3, a significant reduction in the weight of freshly collected dental plaque was observed in the erythritol group vs. the sorbitol and xylitol groups. (Runnel et al., 2013). Analysis of the plaque found no effect on plaque levels of protein, glucose, glycerol or calcium, but the erythritol-receiving children displayed significantly lower levels of *Streptococcus mutans*, acetic acid and propionic acid, and a trend toward less lactic acid than that of subjects who had received xylitol or sorbitol. Three years following cessation of the polyol interventions, a subsection of the children was reevaluated using the same procedures (ICDAS examination) for decayed, missing and filled teeth/surfaces. No significant differences between the intervention groups were noted; however, in the erythritol group, percentages of surfaces developing enamel/dentin caries, or dentin caries subject to dentist intervention, were reduced compared to the other polyol groups.

Conclusion

Erythritol has been evaluated for its effects on oral health over a wide dosage range in diverse populations over various time periods. Taken together, these studies show that erythritol is efficacious in improving oral care across a range of doses, timeframes and when compared to other polyols, including xylitol.

The scientific literature supports oral-care benefits of erythritol, mainly through the bacteriostatic effects on cariogenic bacterial species, reductions in plaque weight, reductions in bacterial adhesion and reduction in acid production. Based on these findings, erythritol offers distinct oral care benefits over other polyols and should be explored and promoted as an oral care ingredient for humans.

Explore erythritol's possibilities for oral-care benefits.

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SOURCES:

De Cock, P; Makinen, KK; Honkala, E; Saag, M; Kennepohl, E; Eapen, A. “Erythritol is More Effective than Xylitol and Sorbitol in Managing Oral Health Endpoints.” *International Journal of Dentistry.* 2016;2016:9868421.

Fujii, T; Tochio, T; Nishifuji, K. “Erythritol Alters Gene Transcriptome Signatures, Cell Growth, and Biofilm Formation in Staphylococcus Pseudintermedius.” *BMC Veterinary Research*, 2023 Sep 7;19(1):146.

Ghezelbash, GR; Nahvi, I; Rabbani, M. “Comparative Inhibitory Effect of Xylitol and Erythritol on the Growth and Biofilm Formation of Oral Streptococci,” *African Journal of Microbiology Research*, vol. 6, no. 20, pp. 4404–4408, 2012.

Hashino, E; Kuboniwa, M; Alghamdi, SA; et al., “Erythritol Alters Microstructure and Metabolomic Profiles of Biofilm Composed of Streptococcus Gordonii and Porphyromonas Gingivalis,” *Molecular Oral Microbiology*, vol. 28, no. 6, pp. 435–451, 2013.

Honkala, S; Runnel, R; Saag, M; et al, “Effect of Erythritol and Xylitol on Dental Caries Prevention in Children,” *Caries Research*, vol. 48, no. 5, pp. 482–490, 2014.

Kõljalg, S; Smidt, I; Chakrabarti, A; Bosscher, D; Mändar, R. “Exploration of Singular and Synergistic Effect of Xylitol and Erythritol on Causative Agents of Dental Caries. *Scientific Reports*. 2020 Apr 14;10(1):6297. doi: 10.1038/s41598-020-63153-x. PMID: 32286378; PMCID: PMC7156733.

Loimaranta, V; Mazurel, D; Deng, D; Söderling, E. “Xylitol and Erythritol Inhibit Real-Time Biofilm Formation of Streptococcus Mutans.” *BMC Microbiology*. 2020 Jun 29;20(1):184. doi: 10.1186/s12866-020-01867-8. PMID: 32600259; PMCID: PMC7325245.

Makinen, KK; Isotupa, KP; Kivilompolo, T; Makinen, PL; Toivanen, J. and Soderling, E. “Comparison of Erythritol and Xylitol Saliva Stimulants in the Control of Dental Plaque and Streptococcus Mutans,” *Caries Research*, vol. 35, no. 2, pp. 129–135, 2001.

Makinen, KK; Isotupa, KP; Kivilompolo, T; et al. “The Effect of Polyol-Combinant Saliva Stimulants on S. Mutans Levels in Plaque and Saliva of Patients with Mental Retardation,” *Special Care in Dentistry,* vol. 22, no. 5, pp. 187–193, 2002.

Makinen, KK; Saag, M; Isotupa, KP; et al. “Similarity of the Effects of Erythritol and Xylitol on Some Risk Factors of Dental Caries,” *Caries Research*, vol. 39, no. 3, pp. 207–215, 2005.

Park, Y-N; Jeong, SS; Zeng, J. et al., “Anti-Cariogenic Effects of Erythritol on Growth and Adhesion of Streptococcus Mutans,” *Food Science and Biotechnology*, vol. 23, no. 5, pp. 1587–1591, 2014

Runnel, R; Makinen, KK; Honkala, S; et al. “Effect of Three-Year Consumption of Erythritol, Xylitol and Sorbitol Candies on Various Plaque and Salivary Caries-Related Variables,” *Journal of Dentistry,* vol. 41, no. 12, pp. 1236–1244, 2013.

Saran, S; Mukherjee, S; Dalal, J; Saxena, RK. “High Production of Erythritol from Candida Sorbosivorans SSE-24 and its Inhibitory Effect on Biofilm Formation of Streptococcus Mutans,” *Bioresource Technology*, vol. 198, pp. 31–38, 2015.

Soderling, E.M. and Hietala-Lenkkeri, AM. “Xylitol and Erythritol Decrease Adherence of Polysaccharide-Producing Oral Streptococci,” *Current Microbiology,* vol. 60, no. 1, pp. 25–29, 2010.

Štšepetova, J; Truu, J; Runnel, R; Nõmmela, R; Saag, M; Olak, J; Nõlvak, H; Preem, JK; Oopkaup, K; Krjutškov, K; Honkala, E; Honkala, S; Mäkinen, K; Mäkinen, PL; Vahlberg, T; Vermeiren, J; Bosscher, D; de Cock, P; Mändar, R. “Impact of Polyols on Oral Microbiome of Estonian Schoolchildren.” BMC Oral Health. 2019 Apr 18;19(1):60. doi: 10.1186/s12903-019-0747-z. PMID: 30999906; PMCID: PMC6471963.

White, K; Le, C; Cannon, M; et al. “Inhibition of Streptococcus Mutans and Sobrinus by Xylitol and Erythritol (poster),” in *Proceedings of the 93rd General Session of the International Association for Dental Research*, Boston, Mass, USA, 2015.

Yao, J; Zhang, JL; Wu, YQ; Lu, ZJ. “Contrasting Study of Erythritol and Xylitol on Streptococcus Mutans,” *West China Journal of Stomatology*, vol. 27(6), 603–605, 2009.

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