Clinical Evidence for Polyol Efficacy

P. Milgrom[1]*, E.M. Söderling[2], S. Nelson[3], D.L. Chi[1], and Y. Nakai[4]

[1]University of Washington, Box 357475, B-509 Health Sciences, University of Washington, Seattle, WA 98195-7475, USA; [2]University of Turku, Lemminkaisenkatu 2, Turku, Finland; [3]Case Western Reserve University, Cleveland, OH, USA; and [4]Okayama University, Okayama, Japan; *corresponding author, dfrc@u.washington.edu

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APPENDIX

This Appendix includes a brief review of pilot studies or definitive studies that are too small to include in the main body of the paper. They are included here for completeness.

The protocol for a Cochrane systematic review of xylitol studies was published (Hildebrandt and Lee, 2009), but no results have been issued. Nadimi and co-workers (2011) presented a broad review of sugar-free products but without meta-analyses. They also concluded that xylitol, as well as sorbitol, decreased caries risk. However, the main purpose of their paper was to caution that the polyols may have side-effects. However, most of the evidence presented was from *in vitro* or *in situ* studies; none was based on clinical trials. Mickenautsch and Yengopal (2012) sought to conduct a systematic review of studies that compared the effectiveness of xylitol with that of topical fluoride. Studies with chewing gum were excluded. They concluded that this was not possible because of extensive clinical heterogeneity, publication bias risk, and confounding.

A small survey study of Chilean orthodontists revealed lack of knowledge about the indications for sugar-free chewing gum, and the fact that they never recommended it to their patients (Petrasic and Cifuentes, 2009). The extent to which this finding would be similar in a larger sample and in other countries is unknown.

Lee and colleagues (2008) reported an *in situ* remineralization study including maltitol and xylitol chewing gums in comparison with gum base and "sugar gum". The study followed a cross-over design in which 24 adult participants chewed the test gums 7 times daily for 5 min for 1 wk while wearing an acrylic mandibular removable appliance in which enamel chips were mounted. There was a wash-out period of 1 wk between treatments. In a blinded analysis, the investigators concluded that microhardness was greater and surface roughness lower in samples from participants who chewed the maltitol and xylitol gums *vs.* those who chewed "sugar" gum or gum base.

Fontana and colleagues (2009) conducted a pilot study to examine the acquisition of cariogenic bacteria by infants of mothers who chewed xylitol (4.2 g/day) or sorbitol gum during the child's first year of life beginning 0-5 mos after birth. No effect was shown, which the authors attributed to the young age at which the children were sampled, a large loss to follow-up, and a low dose of xylitol.

An Italian study has investigated the effects of a 6-month exposure to xylitol (11.6 g/d total divided into 5 doses) or sorbitol gums *vs*. a no-gum control in schoolchildren 8-9 yrs old who were evaluated 18 mos after exposure (Lingström *et al.,* 2010). The authors' abstract concluded that the xylitol gum reduced the caries increment more than both the sorbitol gum or the no-gum control, but that the sorbitol gum was also effective. The formal publication from this trial has not appeared, so the work cannot be fully evaluated.

A Japanese study examined the effect of xylitol gum in 3- to 4-year-old children (Seki *et al*., 2011). The children were enrolled in 3 comparable preschools: 1 school was randomly selected as a no-treatment control group (N = 106). Within the other 2 schools, children (N = 142) chewed a 1.3-g xylitol pellet 4 times *per* day for 3 mos. The primary outcome assessed was plaque MS level at 6 and 9 mos, expressed as the mean score from plaque taken from 8 prespecified interdental spaces and analyzed separately. The Dentocult scores ranged from 0 to 3, where higher scores represent greater amounts of SM within the plaque. Secondary measures were caries scores (dfs), and plaque levels (visually assessed as yes/no) were also collected. The investigators reported an analysis of only 76 of the original 142 children in the treatment group, excluding the majority because of failure to use at least 100 pellets of gum. Actual mean gum usage was reported to be 3.33 g/day, but it is unclear if this is for the entire study population or just those included in the analysis. The mean Dentocult scores for the children included in the analysis were 0.5 (SE = 0.1) for xylitol and 0.7 (SE = 0.1) for the controls, suggesting that the children had low levels of SM. The investigators reported that 19% of the xylitol group and 36% of the control group had a salivary MS score greater than 0 at baseline but did not provide the mean level. In the first 6 mos after baseline, 3 mos after the cessation of the gum, the xylitol group showed no change in mean Dentocult score, while the control group decreased 0.2 units. Compared with the 9-month score, the xylitol group dropped a mean of 0.1 units, while the control group increased by 0.2 units 6 mos post-gum-chewing. The same curious reversal is reported in the dfs scores.

Kawamorita and colleagues (2010) reported a non-randomized trial in which 40 young adult participants used a 5% xylitol mouthrinse (10 mL/dose, 1 min *per* treatment, 3 times/day). Salivary *S. mutans* was assessed. The authors reported that

counts were reduced 65% after 4 wks in the xylitol group and 10% in the sorbitol group. No comparison was made as to the comparability of the groups at baseline.

An ongoing Japanese study compares a 10% xylitol oral spray (0.01 g/spray, intended total dose 1 g/day) with a spray containing 10% maltitol in a group of 120 individuals aged 10 to 40 yrs (Y. Nakai, personal communication). MS are to be measured at baseline and at 1 and 3 mos.

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