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ORIGINAL ARTICLE

Effect of xylitol-containing chewing gums on interdental plaque-pH in habitual xylitol consumers

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Abstract

Objective. The aim was to investigate the effect of high and low amounts of xylitol on the interdental plaque-pH, directly and after sucrose challenge, in schoolchildren with habitual consumption. ***Material and methods.*** The study group consisted of 11 healthy children (10–15 years) with low caries risk and the experiment had a single-blind crossover (Latin square) design. After a 2-week run-in period with a daily 4.0 g xylitol intake, the children were subjected to single-dose exposures of chewing gums with (i) paraffin (CTR; no xylitol), (ii) low-dose xylitol (LX; 2.0 g xylitol), and (iii) high-dose xylitol (HX; 6.0 g xylitol) in a randomized order separated by a washout period of 1 week. Samples of chewing-stimulated whole saliva were collected prior to and after the experimental period for determination of bacterial counts. The outcome measures were *in situ* plaque-pH (micro-touch method) and area under the pH curve (AUC). ***Results.*** The AUC was significantly greater ($p < 0.05$) in the HX group compared to the LX and control groups during the first 5 min after chewing. After a 10% sucrose rinse, the interdental plaque-pH dropped in all groups but the HX regimen displayed significantly less reduction 0–5 min after chewing ($p < 0.05$). No significant alterations of the total viable counts or mutans streptococci levels in saliva were disclosed during the 4-week experimental period. ***Conclusions.*** The present results suggested that a high single dose of xylitol had a short and limited beneficial effect on interdental plaque-pH in habitual xylitol consumers, while a low single dose, resembling normal chewing gum use, did not differ from the control.

Key Words: *Chewing gums, mutans streptococci, plaque-pH, xylitol*

Introduction

Xylitol is a naturally occurring five-carbon sugar alcohol that has gained considerable attention as an anti-caries agent during recent decades [1–4]. Considered as non-cariogenic, xylitol is incorporated as a sweetener in chewing gums and tablets as well as in oral health care products such as dentifrices and mouth rinses. Although the mechanisms of action are not fully clear, the beneficial effects of xylitol are generally explained by reduced acid formation and inhibition of xylitol-sensitive mutans streptococci [5–7]. In the scientific community, it is a matter of controversy whether the main effect of xylitol in gums is attributed to the sugar-substitute *per se* or the saliva stimulation [2,8–12]. Likewise, the evidence for a dose–effect relationship is under debate, although recent reviews of clinical trials indicate that a habitual and long-term exposure to the teeth of xylitol corresponding to 4–5 g per day is needed to achieve a significant cariostatic effect [13,14].

We have previously demonstrated an inhibition of xylitol-sensitive mutans streptococci in patients with fixed orthodontic appliances exposed to a daily dose of 3.4 g xylitol, but this did not affect the plaque acidogenicity [15]. However, the measurements were carried out *ex vivo* in sucrose-challenged plaque suspensions, which may not adequately reflect the situation *in vivo*. Therefore, we adopted the micro-touch method that enables direct measurements of pH in dental plaque [16,17]. The effect of xylitol-containing chewing gums on sucrose-challenged plaque-pH has previously been investigated with this technique [18–23], but to our knowledge only Wennerholm et al. [24] have explored the effect of contrasting concentrations of xylitol. That study revealed no significant

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dose-related differences in pH in plaque after a sucrose rinse, but it should be noted that a mix of xylitol-sorbitol was used in the gums and that the subjects were not regular xylitol consumers. The possible effect of single dose exposures might differ between non-users and habitual users as well as with or without access to other sugars. Since xylitol-containing products are common and frequently used among schoolchildren in the Nordic countries [25], it was of interest to further investigate the effect of contrasting amounts of xylitol on plaque-pH in xylitol consumers of that age group. The aim of this study was therefore to investigate the effect of a high and a low single dose of xylitol administrated via chewing gums on the interdental plaque-pH in habitual xylitol consumers, directly and after a sucrose mouth rinse. The null hypothesis was that no differences between the different xylitol concentrations with respect to plaque-pH would be obtained.

Material and methods

Subjects

Eleven healthy children and adolescents (4 boys and 7 girls) with a mean age of 12.4 years (range 10–15 years) were invited to this study. The subjects were regular consumers of xylitol products (>2 times/week) and listed as recall patients at the Public Dental Clinics in Lycksele and Umeå, Sweden. The children volunteered to participate after verbal and written information was given and consent obtained from their care-takers. All exhibited a stimulated saliva secretion rate of >1 ml/min and were considered to have low caries risk. The mean DMFS was 1.3 (SD ± 1.2).

Study design

The experiment had a randomized single-blind crossover (Latin square) design, as outlined in Figure 1, and the study protocol was approved by the local ethics committee at Umeå University. At the initial visit, the subjects were supplied with xylitol chewing gums and instructed to chew 6 pieces per day (2 pieces in the morning, 2 pieces after lunch, and 2 pieces in the evening) throughout the entire 4-week study period. They were recalled for three test occasions (A, B, and C) after 2, 3, and 4 weeks, respectively. The participants were told to avoid oral hygiene for 2 days before each test occasion and not to eat or drink in the 2 h prior to the test. The subjects were randomly assigned to three groups testing single intakes of (i) paraffin (CTR; no xylitol), (ii) low-dose xylitol (LX; 2.0 g xylitol), or (iii) high-dose xylitol (HX; 6.0 g xylitol) in randomized order with a washout period of 1 week. The tests were performed in exactly the same way on each occasion. After a thorough mouthrinse with tap water, the subjects were asked to chew on the assigned chewing gums for

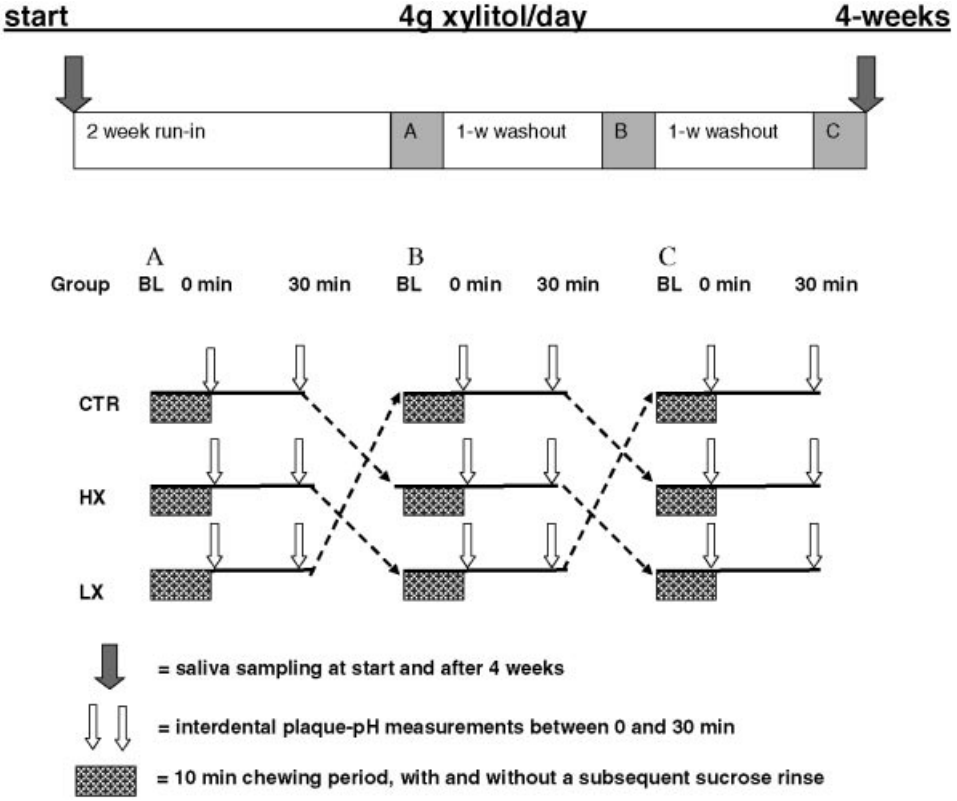

Figure 1. A schematic overview of the randomized single-blind crossover design. A, B, and C denote the chewing episodes. BL = baseline, CTR = paraffin gum, LX = low xylitol gum and HX = high xylitol gum.

10 min. The interdental plaque pH was measured before chewing (baseline), directly after chewing (0 min), and then at 2, 5, 10, 15, 20, 25, and 30 min after chewing. Thereafter, the children rinsed the mouth with water and a new baseline pH was established. A new 10-min chewing period was followed by a 1-min rinse with 10% sucrose solution, after which the pH measurements were carried out as above. The investigator carrying out the recordings was unaware of the chewing gum regimen.

Chewing gums

The xylitol chewing gum used was Xylimax (Fennobon Oy, Finland) with a xylitol content of 66 weight percent. The habitual xylitol intake during the experimental period was therefore approximately 4.0 g per day. At the pH experiments, the high xylitol gum group chewed 3×3 pieces corresponding to ≈ 6.0 g xylitol. The low xylitol group chewed 3 pieces (≈ 2.0 g xylitol in a single intake), while the paraffin group was given 3 pieces (3.0 g) of non-flavored paraffin.

In situ pH measurements and samplings

The pH in supragingival interdental plaque was measured *in situ* at pre-selected proximal sites with visible plaque accumulation according to the microtouch method described by Scheie et al. [16]. Predominantly, sites between the premolars in the upper quadrants were selected in order to facilitate insertion of the electrode. Several sites within each subject was analysed but only one within each designated time series. The following equipment was used: a Beetrode pH electrode (NMPH5) and a reference electrode (DRIREF 5SH) from World Precision Instruments, Inc., Sarasota, USA; the pH meter (Model 340) was from Mettler Toledo AG Schwerzenbach, Switzerland.

Bacterial cultivation and enumeration

At baseline and at the 4-week follow-up, samples of paraffin-stimulated whole saliva were collected for microbiological enumeration. After a thorough mouthrinse with tap water, the subjects were asked to collect 1 ml of saliva in a test tube during paraffin chewing. The samples were serially diluted in 10-fold steps with a 25 mM potassium phosphate buffer with 0.5% NaCl (pH 7.0). Aliquots of 50 µl were placed in duplicate on trypticase/proteose-peptone-glucose agar (BBL, Boston, Mass., USA) supplemented with 4% horse blood, vitamin K, and trace elements for detection of total viable counts and on mitis salivarius bacitracin (MSB) agar for enumeration of mutans streptococci [26]. The agar plates were incubated at 37°C under aerobic conditions for 3 days. The mutans streptococci strains were identified by morphological characteristics and the number of colonies was counted with the aid of a stereomicroscope (10–30 × magnification) and expressed as colony forming units (CFU) per ml.

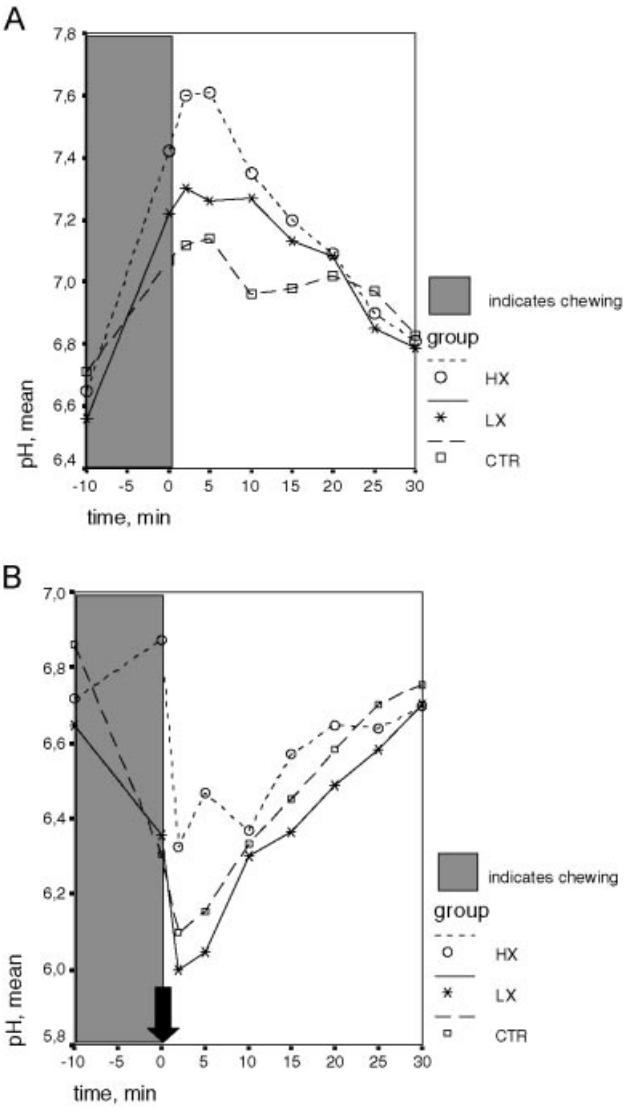

Figure 2. Mean pH in dental plaque at baseline and after 0, 2, 5, 10, 15, 20, 25, and 30 min after (a) chewing 10 min with paraffin (CTR), 2.0 g xylitol (LX), and 6.0 g xylitol (HX) and (b) chewing as above followed by rinsing with 10% sucrose solution for 1 min (black arrow).

Statistical methods

All data were processed with the SPSS software (v. 11.5, Chicago, Ill., USA). The area under the pH-curve was calculated and compared between groups with the aid of analysis of variance (ANOVA). Data on bacterial counts were subjected to ANOVA in order to test differences between baseline and the 4-week follow-up. The level of statistical significance was set at 5%.

Results

The mean interdental plaque-pH at baseline and at the designated follow-ups is shown in Figure 2a, b,

Table I. Area under the pH-curve (AUC, mean ± SD) during 30 min after chewing of paraffin or xylitol-containing chewing gums for 10 min followed by no rinse or a sucrose rinse in 11 children. CTR = paraffin gum; LX = low-xylitol gum (2.0 g); HX = high-xylitol gum (6.0 g)

	Time				
Group	0–2 min	0–5 min	0–10 min	0–15 min	0–30 min
No rinse					
CTR	14.2 ± 0.8[a]	35.5 ± 1.8[b]	70.2 ± 4.5	105.4 ± 5.0	208.6 ± 8.0
LX	14.5 ± 0.8	36.2 ± 2.0	72.5 ± 4.1	107.7 ± 5.5	210.1 ± 7.6
HX	15.0 ± 0.9[a]	37.6 ± 2.1[b]	73.8 ± 4.5	109.6 ± 7.0	213.4 ± 12.1
Sucrose rinse					
CTR	12.4 ± 1.4	31.1 ± 3.2	63.2 ± 6.5	95.7 ± 8.2	195.9 ± 15.5
LX	12.4 ± 1.0	31.0 ± 2.2[c]	63.3 ± 4.8	95.4 ± 6.6	195.9 ± 11.5
HX	13.2 ± 1.0	33.4 ± 2.7[c]	66.2 ± 4.5	100.8 ± 7.3	203.6 ± 12.2

[a, b, c] Statistically significant difference, $p < 0.05$.

and the area under the curve (AUC) is presented in Table I. Without subsequent sucrose rinse, the 10-min chewing period increased the interdental plaque-pH in all groups but the elevation was higher in the high xylitol (HX) group compared with the low xylitol (LX) and the control (CTR) groups. The difference between the HX and the CTR groups was statistically significant ($p < 0.05$) during the first 5 min after chewing with respect to the AUC. Conversely, when the chewing was followed by a sucrose rinse, the plaque-pH dropped in all groups, although this was less pronounced in the HX group. A statistically significant difference between the HX and LX groups during the initial 5 min after the sucrose challenge was disclosed. The number of subjects with plaque recordings below pH 6.0 is shown in Table II and, as can be seen, the pH drop was clearly counteracted in the HX group. All subjects harbored detectable levels of salivary mutans streptococci, although the mean pre-experimental levels of total viable counts and mutans streptococci in saliva were generally low, $4.2 \times 10^6 \pm 2.3 \times 10^6$ and $1.6 \times 10^3 \pm 0.7 \times 10^3$ CFU/ml, respectively. No significant alterations were displayed at the end of the experimental period.

Discussion

This study was undertaken to obtain information on a possible dose-related effect of xylitol when administered as a single sweetener in chewing gums with and without a subsequent sucrose rinse. All children consumed xylitol gums more or less frequently before the experiments, but the 2-week run-in period with standardized consumption of xylitol was planned to ascertain comparable habitual levels within the study group. The background level of approximately 4.0 g per day was chosen as this was the amount that was used by a number of the subjects at the time of inclusion. The low xylitol single dose was intended to resemble "normal" chewing gum behaviour, while the high xylitol single dose represented a contrasting excessive use. The crossover study design was highly suitable for this purpose, although it was not possible to keep it double blind. We used commercial chewing gums and the subjects had to chew more gums to achieve the high xylitol single dose. In order to keep the bolus similar in size and comparable between the groups, three pieces of gums were given at the start of the 10-min chewing period in the high xylitol group, and they were then renewed after 3 and 6 min. The secretion rate during the 10-min chewing periods was checked in a pilot set-up before the study and no significant difference was obtained between the chewing gum regimes. Nevertheless, the paraffin control pieces were non-sweetened and this factor may have resulted in less active chewing. The investigator carrying out the pH measurements was unaware of the chewing gum regimen. The cooperation and compliance with the study protocol was regularly checked and judged as excellent and no side effects of the xylitol regimen were reported during the 4-week test period. It should be noted, however, that the test persons were not regarded as caries risk individuals, a fact that was underlined by their relatively low counts of mutans streptococci in saliva. Thus, the findings may be valid for the average Swedish schoolchild and should not be generalised or extrapolated to caries active children or to children with high caries risk.

Table II. Number of subjects in the experimental groups with interdental plaque recordings below pH 6.0 at baseline, immediately after a 10% sucrose rinse (0 min) and at designated times thereafter. CTR = paraffin gum; LX = low-xylitol gum (2.0 g); HX = high-xylitol gum (6.0 g)

Group	Base line	0 min	2 min	5 min	10 min	15 min	20 min
CTR ($n = 11$)	0	6	7	5	4	2	1
LX ($n = 11$)	0	6	5	5	2	2	0
HX ($n = 11$)	0	0	4	3	2	1	0

Previous studies have investigated the effect of xylitol in mouth rinses, chewing gums, and lozenges on the pH in sucrose-challenged dental plaque with conflicting findings [18–22,24,27–30]. The majority of the studies suggested a certain advantage for polyol, while others found minor or no effects in the pH response to sucrose [27–29]. The present results indicate that a dose–response relationship may be evident and that a high amount of xylitol was needed to affect the interdental plaque-pH in habitual xylitol consumers. Thus, the null hypothesis was rejected, but it should be emphasized that such a high amount of xylitol is far above what is commonly advocated by clinicians and what is considered as convenient and realistic for patients from economic and practical points of view. The finding of a short-term increase in plaque pH following gum chewing, mimicking an "after-meal" situation, was in harmony with previous reports [18–23]. After the sucrose rinse, the pH drop was

counteracted in the high xylitol group during a 5-min period, while no significant differences between the low xylitol and control regimens were displayed. This was in agreement with Wennerholm et al. [24] and Lingström et al. [27], who also found that much of the "xylitol effect" disappeared immediately after sucrose mouthrinses. In general, however, the pH drop after the sucrose rinse was not very dramatic in our setting, probably reflecting the protective properties of chewing and possibly also that the children were regular xylitol consumers. In fact, values below the critical pH 5.5 were recorded in only 3 subjects in the control and low xylitol groups, and in no case after the high xylitol dose. Although the effect of the high xylitol dose on the plaque-pH seemed limited, it may still be of clinical importance in light of the current ecological plaque hypothesis [31]. According to this, a low oral pH is most crucial for selection of aciduric micro-organisms in dental plaque and the main factor that drives the carious process. However, we found no significant alteration of the salivary bacterial counts, which was expected in the light of our own report and those of others [4,6,14,15] and the relatively short experimental period. It should be noted that the salivary mutans streptococci estimation was not intended as a primary outcome measure but rather a control on the fact that microbial conditions were stable during the crossover episodes.

As mentioned earlier, the beneficial effects of xylitol involve different mechanisms of action [1–7]; (i) hampering of bacterial growth and metabolism, (ii) selection of less adhesive strains of oral mutans streptococci, and (iii) stimulation of saliva secretion. In light of our limited present findings regarding the first alternative, it may be speculated whether or not the anticipated xylitol-induced shift in the microbial plaque community is a key event apart from chewing itself. It is thought that less adhesive xylitol-resistant strains of mutans streptococci are favored during long-term exposure to xylitol, but these cells do not seem to be less cariogenic than the xylitol-sensitive strains [32]. In the clinical situation, the oral microflora is complex and the bacteria are exposed to a variety of natural and artificial sugars at the same time, and an increased bacterial tolerance to xylitol cannot be ruled out [33]. Furthermore, it is not clear whether the above-mentioned xylitol-induced mechanisms play an equal role in caries reduction or whether one or two factors may be dominant under given conditions. The relative importance of the different events may vary with factors such as total xylitol amount, administration vehicle, single or fragmented doses, and the peak concentration of xylitol in saliva or in the liquid phase of the plaque. For example, a clinical plaque reduction may require another amount of xylitol than an interference with the mother–child transmission of mutans streptococci [34,35]. These issues need to be further elucidated in clinical studies.

In conclusion, the present study suggests that high amounts of xylitol in chewing gums may have a short and limited beneficial effect on interdental plaque-pH in habitual consumers with increased pH-values after chewing and a counteracted pH-drop after sucrose challenge. In contrast, a low single dose of xylitol, resembling a normal chewing gum situation, did not differ from non-xylitol controls. Obviously, clinicians have to advocate a very frequent daily use of xylitol-containing chewing gums if additional effects besides saliva stimulation by chewing are to be expected.

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