Effects of maltitol and xylitol chewing-gums on parameters involved in dental caries development

ABSTRACT

Aim The effects on plaque parameters of sugar free chewing-gums (CG) sweetened with either maltitol or xylitol were assessed to better understand the role polyols can play in dental caries prevention.

Materials and methods A double-blind, parallel, randomised, controlled study was conducted in China. Subjects (N = 258, age = 13 to 15 years-old) were divided into 4 groups: 2 receiving polyols CG, containing respectively maltitol or xylitol, a group receiving gum base (placebo) and a negative control group not receiving any gum. CG were chewed for 30 days. This corresponds to a 10 g consumption of polyol per day. Plaque parameters (growth, pH, bacteria and insoluble glucans) were evaluated throughout the experimental period.

Results All parameters studied were significantly modified with gum base compared to no-gum: plaque pH increased; plaque growth, bacteria (S. mutans, S. sobrinus, A. viscosus and Lactobacillus) and insoluble glucans decreased. Maltitol and xylitol CG led similarly to a higher plaque pH (AUC, \( p \leq 0.05 \)) on short (at baseline after the first CG consumption) and long term (after 4 weeks of daily CG consumption), with or without saliva stimulation compared to both control and placebo groups. They led to a decrease in plaque growth (\( p=0.02 \)) over the experimental period compared to controls. Moreover, they significantly reduced the concentration of 4 cariogenic bacteria species (\( p \leq 0.05 \)) in dental plaque compared to gum base.

Conclusion Sugar free CG sweetened with either maltitol or xylitol can similarly reduce plaque acidogenicity compared to gum base through a decrease in oral bacteria presence. The use of a gum base placebo allowed to isolate effects on parameters involved in dental caries development specific to maltitol and xylitol, and to show these effects were similar.

Keywords Dental caries; Maltitol; Polyol; Xylitol.

Introduction

According to the World Health Organization [WHO, 2001], dental caries is a multifactorial disease linked to the presence of microorganisms (e.g. Streptococcus mutans and Streptococcus sobrinus) and to the frequency of fermentable carbohydrates (e.g. sugars) ingested. The prevalence of this disease is a matter of concern in both children and adults and in both developed and developing countries [Petersen, 2009]. Consequently, a global health programme was initiated by the WHO in 2004 to increase oral health awareness worldwide [Petersen, 2009]. Large epidemiological studies were performed in some countries to identify high risk population categories according to their income or location. In China, this study ended with a national information campaign aiming at the systematic implementation of preventive oral care as well as community-oriented health programmes [Wang et al., 2002]. The present study was conducted in an urban area where drinking water contains 0.6 ppm of fluoride [Wang et al., 2002].

According to a 2009 ILSI (International Life Science Institute) report, dental caries is a disease affecting the hard tissues of the teeth and resulting in progressive decay. The main prerequisites involved in tooth decay development are tooth, dental plaque and substrate. Diet recommendations to prevent sugar consumption could contribute to reduce the amount of substrate given to the oral bacteria. Dental plaque is a biofilm reinforced by bacterial product, salivary proteins and food substances from the diet. Many techniques to reduce dental plaque such as tooth brushing and dental floss are largely promoted both in developed countries as in developing ones. Lactobacillus, Streptococcus mutans and Streptococcus sobrinus are known to be major components of the oral microflora able to produce acid through the fermentation of sugars from our diet. This fermentation phenomenon can induce a decrease of plaque pH leading to a partial dissolution
of tooth mineral. Mineral dissolution can be followed by formation of a dental cavity, which in turn can be infected by oral bacteria. The continuous salivary flow allows for a perpetual clearance of the mouth and a buffering of the oral environment. Polyol CG are known to increase salivary flow [Dawes and Kubieniec, 2004; van Loveren, 2004]. The second prerequisite for dental caries development is substrate presence for acidogenic bacteria. The WHO recommended a reduction in simple sugar intake between meals to decrease caries occurrence. Sugar substitutes could be a way to eliminate this second prerequisite, as polyols are not fermented by oral bacteria [Wursch & Koellreutter, 1982].

Many clinical trials were conducted to study the effects of sugar-free CG on oral health and dental caries occurrence [Deshpande and Jadad, 2008; Gopinath et al., 1997; Twetman, 2009]. In the present study, we aimed at comparing the effects of 2 different sugar-free CG recipes on several parameters involved in dental caries development.

Materials and methods

All research procedures in this trial were performed in strict accordance with a predefined protocol that was approved by all researchers and a local Ethic Committee (named IRB food health committee from Shanghai Food Nutrition Society) including a signed informed consent before participation.

Subjects

Subjects were recruited from the XuShe Middle School in YiXing, in the JiangSu Province of the People's Republic of China.

The recruitment of subjects occurred one month before the beginning of the study. Enrollment was based on a two-step design. First, individuals were subjected to inclusion criteria; then, those who passed the inclusion step were checked for exclusion criteria.

In order to be included in the study, children had to fit the following criteria: be between 13 and 15 years-old, healthy and non-smokers; have their permanent dentition; neither eat CG or sugar-free candies on a regular basis; neither have active cavities, nor periodontal diseases, nor gingivitis; show a salivary Streptococcus count lower than $10^5$ Colony Forming Units (CFU)/ml and a Decayed, Missing and Filled Teeth, DMFT, index of 1.2. The participants also had to have a normal salivary flow (>0.25ml/min).

Finally 288 parental consenting male and female children were included for this study. Eligible subjects were then randomised and started on the allocated study group as soon as they were enrolled. They were randomly allocated to four groups (n = 72 per group) according to a gender and baseline plaque index stratification after the 2 weeks of recruitment and 16 days prior to the beginning of the study. Before the beginning of the CG supplementation, there was a 2-week period with no consumption of sugar-free or sugar-based gum/candy, followed by a 2-day washout period during which volunteers in the CG groups (maltitol, xylitol and gum-base groups) chewed gum-base CG identically to what will be performed during the study. The no gum group did not have a wash-out period because the subject did not consume any CG.

Study design

This study had two treatment groups, one placebo group and one control group.

The group receiving maltitol CG chewed 2 pellets 5 times a day for 10 minutes. Pellets were chewed after each meal (breakfast, lunch, snack and dinner) and before going to bed in lieu of brushing. The same supplementation schedule was also followed by the xylitol group. For technical reasons, the gum base pellets of the gum base control group were produced to obtain the same quantity of gum base to chew in one control pellet as in two maltitol or xylitol pellets. Consequently, the gum base group chewed one pellet on the same schedule as the two other groups. Finally, the no-gum control group received no CG. In order to control CG intake and chewing duration, 3 daily intakes out of 5 took place during class hours. During the study, the children were asked not to consume sugar-free products; to refrain from using mouth wash or dental floss throughout the study and to respect one tooth brushing per day (in the morning) consistent with the Chinese norm [Zhu et al., 2003] using herbal tooth paste and tooth brushes that were provided.

The treatment period lasted 30 days. The different measurements were performed at baseline, after the first CG consumption in order to assess the short-term effects, and after 4 weeks of CG consumption on a daily basis in order to observe the long-term effects.

Product recipe

Each xylitol CG was made up of 0.35g gum base (Cafosa S.A., Barcelona, Spain), 0.5 g xylitol (XYLISORB®, Roquette Frères, Lestrem, France), 0.01 g maltitol syrup (LYCASIN HBC 80/55, Roquette Frères, Lestrem, France), 0.004g glycerine (The Dow Chemicals Company, Midland, U.S.A.) and 0.009g spearmint flavour (Mane S.A., Le Bar-sur-Loup, France). Each maltitol CG was made up of 0.35g gum base, 0.49 g maltitol (SweetPearl®, Roquette Frères, Lestrem, France), 0.02 g maltitol syrup, 0.004 g glycerine and 0.009g spearmint flavour. The gum base control CG was made up of 0.7 g gum base, 0.24 g talc (Talc de Luzenac, Rio Tinto Minerals-Luizenac Operations, Luzenac, France) and 0.03 g spearmint flavour.

Methods

Measurements were performed at baseline on 2 days before the first day of supplementation (day 0),
and during the last 2 days of supplementation. Several days of clinical measurements were necessary to allow the various measurements and sample collections (Fig. 1). During the two last and two first clinical days, the children were asked to refrain entirely from brushing their teeth in order to observe the effects of CG on dental plaque formation. Plaque growth was evaluated through dental examination using the Quigley and Hein Index at baseline and on day 30. A suitable disclosing solution such as Bismarck Brown was painted on all exposed tooth surfaces. Accumulations were scored according to the following plaque index system: 0 corresponds to “No plaque”, 1 to “Separate flecks of plaque at the cervical (top) margin of the tooth”, 2 to “A thin continuous band of plaque (up to 1 mm) at the cervical margin of the tooth”, 3 to “A band of plaque wider than one mm but covering less than one-third of the crown of the tooth”, 4 to “Plaque covering at least one-third but less than two-thirds of the crown of the tooth” and 5 to “Plaque covering two-thirds or more of the crown of the tooth”. After all teeth were examined and scored, the index was calculated by dividing the total score (summation of both surfaces for all teeth, upper and lower) by the number of surfaces examined (a maximum of $2 \times 2 \times 16 = 64$ surfaces).

Plaque pH was evaluated through direct measure at baseline and on day 30, under saliva stimulation for 10 minutes with the CG used in the subject’s group (at 0, 5, 10, 20, 30 and 45 min) using a miniature pH electrode (Dental Beetrode NMPH 1, WPI, UK) and a pH meter (Model SA-210, Orion Research, Tampa, Florida, USA). Areas under the curve (AUC) were calculated as described by Ludwig and Goldberg [1956], which consisted in centrifuging an aliquot of plaque in saline solution at 2000 g for 10 minutes, discarding the supernatant and retaining pellet, washing the pellet and re-suspending it by agitation in 1 ml of distilled water. To determine glucose content 50 µl of suspension were used. Results were expressed in µmol/min.

**Statistical analysis**

The primary outcome of this study was plaque index measurement. The secondary outcomes were the measurement of plaque pH and the quantification of plaque bacteria. Simulation-based methods which postulate various scenarios for effect size – based on dichotomizing the Quigley and Hein score and using odds ratios – indicated a benefit for the treated groups.
compared with the no-gum control group and gum base placebo group. These simulation methods showed that it was necessary to enroll 288 participants to allow dichotomizing the Quigley and Hein score and obtain a 17% attrition rate with a statistical power of at least 90%.

Means and standard deviations were used to describe continuous outcomes. Comparisons between the four groups were conducted with univariate analyses such as ANOVA or Kruskal Wallis as appropriate. To measure continuous outcome, constancy of the error variance structure was tested, and a least-squares-based modelling approach was employed to correctly identify the potential effects in both treated groups against the control group and the placebo group. Multiple comparisons for plaque pH kinetics, longitudinal comparison and area under the curve were controlled using Duncan’s and Dunnette’s approaches. Overall significance level for the statistical tests of differences among the groups was set to 0.05.

Results

Eleven percent of the eligible subjects dropped out from the study, but our statistical hypothesis was validated. The main reason for dropout was lack of compliance in both control and placebo groups. As gum base was not tasty, the gum base group registered 15 dropouts. In the control group, as they did not receive any treatment, the children could forget about the study, in the no-gum group 9 subjects dropped out from the study. Clinical examination indicated lack of presence of any significant differences among the groups with respect to these characteristics and very healthy indicators among these children. At the end of the study, the placebo group had 57 children and exhibited an average plaque index score of $2.26 \pm 1.43$. The control group had 63 children and exhibited an average plaque index score of $2.44 \pm 1.23$. The xylitol group had 66 children and exhibited an average plaque index score of $2.41 \pm 1.32$. The maltitol group had 68 children and exhibited an average plaque index score of $2.32 \pm 1.25$. This shows that the dropouts did not affect group homogeneity.

As the children were asked to chew 10 CG per day in both polyol groups, this corresponds to a 10g consumption of maltitol or xylitol per day.

Identifying and counting bacteria in dental plaque samples

After 28 days of CG supplementation, a significant decrease in Streptococcus mutans presence was observed in the maltitol and xylitol groups compared to both control and placebo groups (-5%, $p<0.05$ compared to gum base and -8%, $p<0.05$ compared to no-gum). Moreover, the gum base group showed a significantly lower Streptococcus mutans count than the no-gum group (-3%, $p<0.05$) (Fig. 2). At baseline, the count for Streptococcus sobrinus was the same in every group. At the end of the experimental period, a significant decrease in the Streptococcus sobrinus count was observed in the maltitol and xylitol groups compared to both gum base (-3.5%, $p<0.05$) and no-gum (-5%, $p<0.05$) groups (data not shown). The results obtained for Actinomyces viscosus (AV) were similar to those obtained for Streptococcus mutans, except that maltitol had a significantly stronger effect than xylitol (data not shown). After 30 days of CG supplementation, a significant decrease in Lactobacillus occurrence was observed in the maltitol group against both the gum base (-1%, $p<0.05$) and the no-gum (-2.2%, $p<0.05$) groups as well as the xylitol group (data not shown).

Considering longitudinal comparisons, maltitol and xylitol CG supplementation triggered a significant decrease in the presence of all tested bacteria over the experimental period compared to placebo and negative control (Fig. 2).

Measuring plaque pH

For the sake of consistency, the no-gum group did not undergo saliva stimulation. Consequently, the plaque pH of the no-gum group did not vary over 45 minutes. Conversely, plaque pH increased significantly in the gum base group against the no-gum group ($p<0.05$). This increase began with saliva stimulation (data not shown). The maltitol and xylitol groups showed similar plaque pH measurements. Indeed, this parameter increased
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Table 1: Area under the curve (AUC) for plaque pH measurement at baseline (D0) and after 30 days of supplementation (D30). Numbers that do not share the same upper letter (a, b, c, d) are statistically different (P≤0.05).

<table>
<thead>
<tr>
<th>GROUP COMPARISON</th>
<th>AT BASELINE (D0)</th>
<th>AFTER 30 DAYS OF SUPPLEMENTATION (D30)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>No-gum</td>
<td>-0.75A</td>
<td>2.17</td>
</tr>
<tr>
<td>Gum base CG</td>
<td>3.35B</td>
<td>2.10</td>
</tr>
<tr>
<td>Maltitol CG</td>
<td>4.41C</td>
<td>2.33</td>
</tr>
<tr>
<td>Xylitol CG</td>
<td>5.41D</td>
<td>2.39</td>
</tr>
</tbody>
</table>

Measuring plaque index through Quigley and Hein score and quantifying insoluble glucans

The CG supplementation led to a significant decrease in the concentration of insoluble glucans compared to the no-gum group (-24.4% for the gum base group, P<0.05, data not shown). This decrease was significantly larger for both maltitol and xylitol groups (respectively -48 and -39% compared to control, P<0.05, data not shown).

At baseline, no difference in plaque index was observed over the two days of formation without oral hygiene. Indeed, the plaque index scores were measured after 2 days of formation, consequently we were able to visualise the effect of our treatment on dental plaque formation. After 30 days of CG supplementation, a significant decrease in plaque index formation over the two last days was observed in the maltitol and xylitol groups compared to the no-gum (-43%, P<0.05, data not shown).

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Discussion

The no-gum group reflected no treatment at all, whereas the gum base group allowed the isolation of the effects of polyol and its comparison to that of chewing. The need for two comparison groups was identified a long time ago [Edgar and Geddes, 1990]. In addition, parallel groups were studied, and no cross-over design was used in order to avoid long-term effects visualisation and wrong conclusions [Makinen, 2009]. These two characteristics of the present study account for the attribution of the conclusions to xylitol itself or to maltitol itself. Assessed parameters were significantly influenced by gum base chewing, due to the mechanical action on dental surfaces. Nevertheless, the modulation of the four tested bacteria and of the plaque pH (baseline T0) was significantly larger in both polyol groups against the gum base group, underlying the fact that maltitol and xylitol have specific effects on the parameters involved in dental caries development. Maltitol and xylitol CG consumption led to a significant decrease in the presence of *Streptococcus mutans*, *Streptococcus sobrinus*, *Actinomyces viscosus* and *Lactobacillus* compared to both no-gum and gum base groups (Fig. 2). According to an 88-variable statistical model using the Projection on Latent Structures (PLS) method, pathogenic bacteria occurrence in dental plaque was the main factor for predicting caries development [Nordlund et al., 2009]. In addition, the role *Streptococcus mutans* plays in dental plaque acidification and dental caries development was demonstrated a long time ago (Edwardsson, 1970). Nowadays, this parameter is used to test the cariostatic properties of some plant extracts (Percival et al., 2006; Smullen et al., 2007).

The decrease in SM presence in the dental plaque was

![FIG. 4](image-url)
correlated to a higher plaque pH thanks to two different putative mechanisms. Polyol CG chewing would not bring fermentable sugars to oral bacteria as demonstrated by Würsch et al. [Würsch and Koellreuter, 1982]. Moreover, after at least one month of supplementation, polyol CG decreased the level of pathogenic bacteria in dental plaque. Consequently fewer oral microorganisms would be challenged with sucrose or fermentable nutrients during an ordinary meal. As the pH increase has been demonstrated to be inversely correlated to bacteria concentration [Ryan and Kleinberg, 1995], the observed increase in interdental plaque pH (Fig. 3) could be explained by these 2 mechanisms. At baseline, the non-availability of both maltitol and xylitol for oral bacteria was observed during 45 minutes after the beginning of saliva stimulation (Fig. 3). After 30 days of supplementation, this non-availability was still observed during 45 minutes after saliva stimulation had begun. Additionally, a significantly higher pH was measured at T0 in the groups supplemented with CG compared to the no-gum group, showing clearly that the decrease in bacteria occurrence led to a higher basal plaque pH (Fig. 3). These results put the light on the fact that sugar free CG sweetened with polyols could help to neutralise plaque pH after the first mastication and after 30 days of everyday consumption. Nevertheless, special attention has to be paid on the short duration of this trial. We cannot extrapolate our results to a very long range study on several years.

As dental plaque results from bacteria deposition and secretion (insoluble glucans) on dental surfaces, the lower bacteria occurrence triggered lower plaque index scores. This phenomenon has been previously described for sugar free CG containing either xylitol, maltitol, erythritol or sorbitol [Holgerston et al., 2007; Mäkinen et al., 2005; Twetman, 2009]. The most commonly studied polyol is xylitol. In the present study, it has been showed that maltitol exhibited similar effects on pathogenic bacteria, plaque pH and index as xylitol. All three supplementations with CG led to a significantly smaller quantity of insoluble glucans and a significantly lower plaque formation using the Quigley and Hein scale (Fig. 4). A decreasing trend was observed for both polyol groups compared to the gum base group. The non-significance of this result could be linked to an insufficient supplementation period, or to the subjectivity of the Quigley and Hein scoring method. Moreover, longitudinal comparisons showed significant decreases for all groups throughout the experimental period, including for the no-gum group. This can be attributed to the fact that the subjects, because of their participation to the study, became more aware of the importance of oral hygiene. Consequently, their oral health habits improved thanks to the study, leading to a lower plaque index in every group.

In conclusion compared to both placebo and control groups, the 30-day supplementation with maltitol or xylitol CG led to a significant decrease in the presence of 4 pathogenic bacteria: *Streptococcus mutans*, *Streptococcus sobrinus*, *Actinomyces viscosus* and *Lactobacillus*. This first result was directly linked to an increase in plaque pH after 30 experimental days. As polyols are not fermented by oral bacteria, plaque pH was also increased at baseline under saliva stimulation. A significant decrease in plaque index was observed compared to the no-gum control group. All together, these results demonstrate that both maltitol and xylitol CG can increase plaque pH against gum base CG through a decrease in oral bacteria presence, showing that sugar free CG sweetened with maltitol or xylitol can improve general oral health in a similar way.

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References

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