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آموزش مهارت های کاربردی در تدوین و چاپ مقاله
Effect of xylitol on cariogenic and beneficial oral streptococci: a randomized, double-blind crossover trial

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ABSTRACT

Background/purpose: Although habitual consumption of xylitol reduces cariogenic streptococci levels, its effect on beneficial oral streptococci is less clear. The main aim of the study is to investigate the effect of short-term xylitol consumption on the oral beneficial streptococci level of saliva, Streptococcus sanguinis and S. mitis.

Material and Methods: Twenty four volunteers with a median age of 23.7 years (range: 20-28) harboring Streptococcus mutans, S. sobrinus, S. sanguinis and S. mitis participated in the randomized, double-blind, cross-over study. The experimental chewing gum (1.5 g/pellet) contained 70% xylitol w/w while the control gum contained 63% sorbitol w/w. Saliva samples were collected before and after two three-week test periods with a four-week washout interval. Colony-forming units (CFU)/ml were enumerated for the estimation of S. mutans levels on Mitis Salivarius-Mutans valinomycin (MS-MUTV), S. sobrinus on Mitis Salivarius-Sobrinus (MS-SOB), S. sanguinis on Modified Medium 10-Sucrose (MM10-S) and S. mitis on Mitis Salivarius Agar with Tellurite (MSAT) media.

Results: The S. mutans and S. sobrinus counts of the saliva samples decreased significantly (p = 0.01 and p = 0.011, respectively) in the xylitol gum group but not in the sorbitol gum group. The salivary S. sanguinis and S. mitis counts did not decrease in both xylitol and sorbitol gum groups.

Conclusions: Based on the findings of this study, xylitol consumption reduced S. mutans and S. sobrinus counts in saliva but appeared not to effect numbers of S. sanguinis and S. mitis in saliva. So, habitual consumption of xylitol reduces cariogenic streptococci levels without any effect on beneficial streptococci for the oral cavity.

Keywords: Cariogenic agents, Chewing gum, Sorbitol, Streptococcus, Xylitol

INTRODUCTION

Extensive epidemiological evidence has established a positive correlation between mutans streptococci (MS), most notably Streptococcus mutans and Streptococcus sobrinus and caries (1, 2). The coexistence of S. mutans and S. sobrinus in dental biofilm and saliva is associated with higher caries experience than if only S. mutans is detected (3, 4). Streptococcus sobrinus seems to be capable of producing more acid than S. mutans. Thus, S. sobrinus existence represents an important additional risk factor for caries due to its potential to exacerbate caries activity. As children grow up, the proportion of children positive for S. sobrinus may increase (5).

Streptococcus sanguinis, one of the major species of the indigenous oral biota colonizing dental plaque, is usually associated with tooth surfaces free of caries. The ratio of S. mutans to S. sanguinis might be indicative of risk for caries or caries outcome. Streptococcus sanguinis may play an antagonistic or
protective role against S. mutans colonization and it is associated with healthy periodontium. Thus, the colonization of certain oral streptococci such as S. sanguinis might be one factor offering protection against periodontitis (6, 7).

Streptococcus mitis plays an ecological role in the oral cavity. Streptococcus mitis releases rhammolipidlike biosurfactants, which interferes with adhesion of cariogenic MS strain. Biosurfactants effectively stimulate detachment of MS from exposed surfaces or in a salivary conditioning film by the dynamic trim forces that occur in the oral cavity (8).

Xylitol is a polyol sweetener, which is not fermented by oral bacteria. Xylitol practically neutralizes low pH-values in the oral cavity with beneficial effects on oral health. Regular xylitol consumption, at enough doses reduces MS level in both plaque and saliva (9-12). Streptococcus mutans takes xylitol into the cell via a fructose phosphotransferase system (PTS) and xylitol is metabolized to xylitol-5-phosphate, which cannot be utilized further and may even be toxic to bacteria (11). Since we found fructose-PTS genes using NCBI resources in S. sanguinis and S. mitis genomes as well as S. mutans, the hypothesis of the study would be, although xylitol consumption would result in prevention of caries by decreasing the numbers of cariogenic agent, S. sobrinus, decreasing the beneficial oral bacteria such as S. sanguinis and S. mitis in the period of using xylitol chewing gum would initiate the oral health endangerment such as periodontitis.

Actually little is known about the clinical trial effects of xylitol and sorbitol on the caries-protective bacteria. Since several studies (9-12) have shown the effects of xylitol on S. mutans levels in saliva, we use S. mutans as internal control in this study. Considering no cross-over randomized study on the effect of xylitol and sorbitol on S. sobrinus, S. sanguinis and S. mitis, the aim of the present study is to evaluate the effect of xylitol on S. sobrinus, S. sanguinis and S. mitis.

MATERIALS AND METHODS

Subjects. Between Dec 2009 and Jun 2010 twenty-four healthy dental students from The Islamic Azad University-Dental Branch (Tehran, Iran) were participated in the study. The inclusion and exclusion criteria were as reported in Table 1. The included subjects were chosen on the basis of a pre-screening for the presence of S. mutans, S. sobrinus, S. sanguinis and S. mitis.

Experimental and Control Chewing Gums. The experimental chewing gum (1.5 g/pellet) contained 70% xylitol w/w (Orion Food Vina Co., Ltd. Binh Duong, Vietnam). The control gum was as the same as xylitol gum in pellet but the main sweetener was sorbitol, with a concentration of 63%. Gum containing sorbitol (Shantou Slg Foods Co., Ltd. Shantou, Mainland), was included in this study because it is also commonly used as a sweetener in many chewing gums; in fact, being less expensive, sorbitol is more frequently used than xylitol (13). They were packed in identical plastic containers which were colour-coded, yellow and red. The codes of the test gums were revealed after the results had been fed into SPSS files.

Study Design. The investigation had a cross-over randomized double-blind prospective design with two arms (14) (Fig. 1) that was approved by The Islamic Azad University Teaching and Research Ethics Committee (IAUTREC), Tehran, Iran. The study and intervention involved were completely explained to all participants, and written consent was obtained from all subjects. Following screening, subjects were randomly allocated into one of two groups. Subjects entered a four-week wash-out period followed by a three-week treatment period (Group AB/ part 1). At the end of this period there was a four week wash-out period. Subjects then entered a second three-week treatment period when they received the alternative treatment (Group BA/ part 2). Group AB consisted of two xylitol chewing gum pieces at a time, three times a day, after meals for three-weeks followed by four weeks wash out then matched control gum as the same as xylitol gum. Group BA consisted of control gum for three-weeks, four week washout, and then xylitol gum for three-weeks. The recommended chewing time was 10 min. The gum consumption resulted in a daily xylitol dose of approximately 6.6 g. The gum is not used during the washout periods.

The pre-experimental and post-experimental saliva were collected into sterile Flat-top cap for BD Falcon™ 50 ml conical centrifuge tubes (Becton, Dickinson; Tokyo, Japan). During this time the subjects were educated not to use mouthwashes, antibiotics or xylitol products, but to continue their usual tooth brushing and consume their normal diet. The subjects were instructed not to use tooth
brushing and other oral hygiene procedures for 24 hours before sample collection and not to eat or drink for 1 hour before the sampling. At the appointments the subjects were also interviewed about confounding factors like acute infectious diseases and use of antibiotics. The subjects and researchers in this study were blinded throughout the study. Also the microbiological analyses in Tehran University of Medical Sciences (TUMS) were carried out blinded.

**Microbiological Analysis.** The saliva samples were homogenized by ultra-sonication under ice-cold water for 10 s; 20 µl aliquots of 10-fold diluted samples were plated on the following selective media: Mitis Salivarius-Mutans valinomycin (MS-MUTV), Mitis Salivarius-sobrinus (MS-SOB), Modified Medium 10-Sucrose (MM10-S) and Mitis Salivarius Agar with Tellurite (MSAT) (QUELAB, UK). MS-MUTV medium is useful for the isolation of *S. mutans* alone from clinical samples (15). The usage of MS-SOB medium resulted in growth inhibition of *S. mutans* and oral streptococci other than *S. sobrinus* (16). *Streptococcus sanguinis* were selected from MM10-sucrose agar (17) based on their firm, adherent, star-shaped colony morphology. Growth of *S. mitis* on the MSAT agar appears as small or minute blue colonies (18). After 72 h of incubation at 37°C in an anaerobic atmosphere, colony-forming units (CFU) were enumerated for the estimation of *S. mutans* levels on MS-MUTV, *S. sobrinus* on MS-SOB medium, *S. sanguinis* on MM10-S, *S. mitis* on MSAT media. For confirmation of the selectivity of media, colonies were identified biochemically using a rapid ID 32 STREP system (bioMérieux, France).

**Statistical Analysis.** The data concerning *S. mutans*, *S. sobrinus*, *S. sanguinis* and *S. mitis* salivary levels at the four sampling phases were analyzed for a normal distribution. Differences between groups were assessed using the ANOVA test. The level of statistical significance was set at $p < 0.05$. The statistical software package used was SPSS 14.0 (SPSS Inc., Chicago, Ill., USA). For statistical analyses, where no bacterium detected, the levels of detection limit were 50 CFU/ml for each bacterial species (7).

![Fig. 1. Algorithm of the study design.](image-url)
Fig. 1. Algorithm of the study design. Yr, year; W, week.

Fig. 2. Flowchart of the subjects in the study.

Excluded-N = 11
Absent of S. mutans, S. sobrinus, S. sanguinis or S. mitis

*2 Cancelled their participation due to personal reasons
*3 excluded on antimicrobial therapy
*1 excluded on dietetic criteria

Table 2. The effect of xylitol vs. sorbitol chewing gum on the cariogenic and beneficial oral streptococci.

| Microorganisms | Xylitol chewing gum | Sorbitol chewing gum |
|----------------|---------------------|----------------------|
|                | Mean                | SD                   | Minimum | Maximum | Variance |
|                | Mean                | SD                   | Minimum | Maximum | Variance |
|                | Mean                | SD                   | Minimum | Maximum | Variance |
|                | Mean                | SD                   | Minimum | Maximum | Variance |
|                | Mean                | SD                   | Minimum | Maximum | Variance |
| S. mutans      | 3.38                | 0.55                 | 2.39     | 4.46    | 0.30     |
|                | 2.47                | 1.69                 | 3.86     | 4.17    | 0.49     |
|                | 27                  | 2.30                 | 4.17     | 0.23    | 0.16     |
| S. sobrinus    | 2.88                | 0.53                 | 2.00     | 4.11    | 0.38     |
|                | 2.15                | 0.65                 | 1.69     | 0.46    | 0.17     |
|                | 75                  | 2.00                 | 3.88     | 0.17    | 0.24     |
| S. sanguinis   | 5.02                | 0.30                 | 4.36     | 5.64    | 0.09     |
|                | 4.97                | 0.40                 | 4.14     | 5.97    | 0.16     |
|                | 2                   | 4.41                 | 5.49     | 0.07    | 0.06     |
| S. mitis       | 4.35                | 0.88                 | 2.54     | 5.81    | 0.79     |
|                | 4.23                | 1.07                 | 1.69     | 6.63    | 1.16     |
|                | 3                   | 2.84                 | 5.65     | 0.66    | 0.74     |

The counts (log_{10} CFU/ml) of each microorganism per saliva sample are expressed as logarithmic Values of mean ± SD, Minimum, Maximum and Variance. † and ‡ denotes a statistically significant difference (p = 0.01 and p = 0.011, respectively).
RESULTS

Twenty-four (18 female and 6 male) of 30 Pre-
cluded subjects, with a median age of 23.7 years
(range: 20-28) completed the study. Two subjects
cancelled their participation due to personal reasons,
3 persons excluded on antimicrobial therapy and 1
excluded on dietetic criteria (Fig. 2).

Since bacterial colony forming unit (CFU/ml) did not
exhibit a normal distribution, the data were transform-
ed to logarithms to confer homogeneity among the
groups and then submitted to variance analysis with
repeated measures. The original logarithmic values of
CFU/ml data in Table 2 showed that there were very high
variables of counts, particular in S. mitis, although all
the xylitol groups indicated higher inhibitory tendency. All
of studied subjects showed a reduction in S. mutans and
S. sobrinus salivary levels in relation to baseline data. As
shown in Table 2, the average S. mutans and S. sobrinus
salivary levels were 3.38 and 2.88 (log10 CFU/ml) at
baseline, respectively. After the experimental period the
average levels of S. mutans and S. sobrinus in saliva
decreased to 2.47 and 2.15 (log10 CFU/ml), respectively.
In S. mutans salivary levels, the mean percentage of
logarithmic value in the xylitol group dropped to
73% after 3 weeks, and this difference was statistically
significant (P = 0.01) in comparison to those in the control/
sorbitol gum group. The mean percentage difference of
logarithmic value for S. mutans between the xylitol
gum group and the sorbitol gum group was slightly
larger than the percentages for S. sobrinus (75%). The
mean percent reduction of logarithmic values amongst
S. mutans and S. sobrinus by xylitol were 27% and 21%,
versus baseline, respectively. Variance analysis using
ANOVA test revealed that the decrease in S. mutans
and S. sobrinus levels observed in subjects after the
xylitol chewing gum–phase and baseline was statistically
significant (p = 0.01 and p = 0.011, respectively).

No significant changes were seen in the beneficial
bacteria counts of the xylitol gum group in comparison
to those in the control/sorbitol gum group.

Statistical analysis of the saliva samples from
subjects after the control chewing gum–phase and
baseline did not demonstrate significant differences
amongst the different groups of bacteria (p > 0.05).

DISCUSSION

This study is part of a series to explore the selective
xylitol activity that can be used as anti-cariogenic
agent. Although xylitol chewing gum has been report-
ed to significantly reduce the mutans streptococci
(MS) levels in plaque and saliva (9-12); its effect
against S. sobrinus in a clinical trial has not been
explored. Another pilot study in this series assessed
the effect of xylitol on the composition of the oral flora.
The results revealed xylitol consumption reduced
MS counts in plaque but appeared not to affect the
total microbial composition of plaque or saliva (7).
In the present study, we tested the effectiveness of
xylitol and sorbitol chewing gums in reducing load
of S. mutans and S. sobrinus, as cariogenic agents
and S. sanguinis and S. mitis, as oral health agents.
The results showed that 3 weeks of xylitol chewing
gum consumption reduced the levels of S. mutans
and S. sobrinus in saliva compared to baseline levels
and did not affect the S. sanguinis and S. mitis level.
This supports the findings of previous studies proving
xylitol reduces MS (10, 11).

In vitro studies have demonstrated that MS are
target organisms of xylitol (19, 20). The inhibition
effect of xylitol varies among MS strains (21, 22).
It is reported that the ability of xylitol to act as an
anti-cariogenic agent is most likely due to its ability
to be transported into caries-causing oral bacteria,
inducible fructose phosphotransferase system (PTS)
and inhibiting fermentation either by depleting the
cell of high-energy phosphate or by poisoning the
glycolytic system (23, 24). Since fructose-PTS
genes are detected in S. mitis and S. sanguinis as
well as S. mutans and S. sobrinus using GenBank
database, and their resistance to anticariogenic
property of xylitol, it is suggested that there may
be other unknown mechanisms of the xylitol effect
against S. mutans and S. sobrinus. Söderling et al.
(9) demonstrated that xylitol consumption did not
reduce counts of either total salivary streptococci
or streptococcal species determined with the DNA-
DNA hybridization technique, S. oralis, S. gordonii,
S. salivarius or S. sanguinis. Several oral lactobacilli
also possess the fructose PTS pathway and thus could
be inhibited by xylitol (25-27). The idea that xylitol
consumption reduces counts of oral lactobacilli is
controversial. Loesche et al. (28) found no effects
induced by xylitol consumption on oral lactobacilli
counts, but Mäkinen et al. (29) in the clinical trial
demonstrated a xylitol-associated decrease in salivary
lactobacilli. This result may, however, reflect a
xylitol-induced elevation of the oral pH and therefore
an indirect effect on salivary lactobacilli.
It was shown \textit{in vitro} that xylitol could reduce adherence of \textit{S. mutans} contributing to plaque and biofilm formation and induced changes in the virulence with an approach not dependent on growth inhibition (22, 30). In contradiction to the \textit{in vitro} study of Sahni et al. (24), the present study showed that xylitol did not inhibit \textit{in vivo} \textit{S. sanguinis} in saliva. \textit{In vitro} tests demonstrated the xylitol concentration of 12.5\% was required for inhibiting the growth of \textit{S. sanguinis}; however, \textit{S. mutans} was inhibited significantly at a xylitol concentration of 1.56\% (24). Kontiokari et al. (31) showed \textit{in vitro} effectiveness of xylitol in reducing \textit{S. mitis}. This is incompatible to the finding of the present study, which suggested that xylitol chewing gum consumption did not effect on \textit{in vivo} growth of \textit{S. mitis}. It is possible that xylitol selectively affects and reduces \textit{S. mutans} and \textit{S. sobrinus} levels without altering load of \textit{S. mitis} and \textit{S. sanguinis}, the bacteria implicated in development of oral health.

Aside from xylitol, studies involving sugar alcohols, most commonly sorbitol, suggests that they have little effect on actively reducing MS levels (32). This is consistant with our study, which showed no \textit{in vivo} growth inhibition of sorbitol control gum for tested bacteria. So, it has suggested that the observed caries reduction through the sorbitol chewing process can be ascribed to stimulation saliva flow, increase in plaque pH, lack of sucrose and the inability of bacteria to metabolise polyols into acids instead of effect on reduction cariogenic bacterial level (33). Limitations of this study are as follows: diet uptake by each individual, small sample sizes and bias due to the nature of community intervention studies.

In conclusion, the results of the present study support the idea that \textit{S. mutans} and \textit{S. sobrinus} represent main target organisms of xylitol. It shows that consumption of xylitol in chewing gum reduces \textit{S. mutans} and \textit{S. sobrinus} in saliva but has no effect counts of \textit{S. sanguinis} and \textit{S. mitis}. Thus, we advocate that xylitol chewing gum consumption to maintain healthy ecology of the oral cavity.

**CONFLICT OF INTEREST**

None to declare

**REFERENCES**

1. Loesche WJ. Role of \textit{Streptococcus mutans} in human dental decay. \textit{Microbiol Rev} 1986; 50: 353-380.

2. Brighten D. The complex oral microflora of high-risk individuals and groups and its role in the caries process. \textit{Community Dent Oral Epidemiol} 2005; 33: 248-255.

3. Fontana M, Zero DT. Assessing patients’ caries risk. \textit{J Am Dent Assoc} 2006; 137: 1231-1239.

4. Seki M, Yamashita Y, Shibata Y, Torigoe H, Tsuda H, Maeno M. Effect of mixed mutants streptococci colonization on caries development. \textit{Oral Microbiol Immunol} 2006; 21: 47-52.

5. Rupf S, Merte K, Eschrich K, Kneist S. \textit{Streptococcus sobrinus} in children and its influence on caries activity. \textit{Eur Arch Paediatr Dent} 2006; 7: 17-22.

6. Saravia ME, Nelson-Filho P, Ito IY, da Silva LA, da Silva RA, Emilion CG. Morphological differentiation between \textit{S. mutans} and \textit{S. sobrinus} on modified SB-20 culture medium. \textit{Microbiol Res} 2011; 166: 63-67.

7. Ge Y, Caufield PW, Fisch GS, Li Y. \textit{Streptococcus mutans} and \textit{Streptococcus sanguinis} colonization correlated with caries experience in children. \textit{Caries Res} 2008; 42: 441-448.

8. van Hoogmoed CG, van der Kuijl-Booij M, van der Mei HC, Busscher HJ. Inhibition of \textit{Streptococcus mutans} NS adhesion to glass with and without a salivary conditioning film by biosurfactant- releasing \textit{Streptococcus mitis} strains. \textit{Appl Environ Microbiol} 2000; 66: 659-663.

9. Söderling E, Hirvonen A, Karjalainen S, Fontana M, Catt D, Seppä L. The effect of xylitol on the composition of the oral flora: a pilot study. \textit{Eur J Dent} 2011; 5: 24-31.

10. Milgrom P, Ly KA, Roberts MC, Rothen M, Mueller G, Yamaguchi DK. Mutans streptococci dose response to xylitol chewing gum. \textit{J Dent Res} 2006; 85: 177-181.

11. Tanzer JM, Thompson A, Wen ZT, Burne RA. \textit{Streptococcus mutans}: fructose transport, xylitol resistance and virulence. \textit{J Dent Res} 2006; 85: 369-373.

12. Mickenautsch S, Leal SC, Yongopal V, Bezerra AC, Cruvinel V. Sugar-free chewing gum and dental caries: a systematic review. \textit{J Appl Oral Sci} 2007; 15: 83-88.

13. Tapiainen T, Kontiokari T, Sammalkivi L, Ikäheimo I, Koskela M, Uhari M. Effect of xylitol on growth of \textit{Streptococcus pneumoniae} in the presence of fructose and sorbitol. \textit{Antimicrob Agents Chemother} 2001; 45: 166-169.

14. Hutchings HA, Wareham K, Baxter JN, Atherton P, Kingham JG, Duane P, Thomas L, et al. A Randomised, Cross-Over, Placebo-Controlled Study of Aloe vera in Patients with Irritable Bowel Syndrome: Effects on Patient Quality of Life. ISRN Gastroenterol. 2011; 206103. Epub 2010; 11: PubMed PMID: 21991499.

15. Takada K, Hirasawa M. A novel selective medium for isolation of \textit{Streptococcus mutans}. \textit{J Microbiol Methods} 2005; 60: 189-193.

16. Hirasawa M, Takada K. Susceptibility of \textit{Streptococcus mutans} and \textit{Streptococcus sobrinus} to cell wall inhibitors and development of a novel selective medium for \textit{S. sobrinus}. \textit{Caries Res} 2002; 36: 155-160.

17. Caufield PW, Dasanayake AP, Li Y, Pan Y, Hsu J, Hardin JM. Natural history of \textit{Streptococcus sanguinis} in the oral cavity of infants: evidence for a discrete
window of infectivity. *Infect Immun* 2000; 68: 4018-4023.
18. Maeda Y, Elborn JS, Parkins MD, Reihill J, Goldsmith CE, Coulter WA, *et al.* Population structure and characterization of viridans group streptococci (VGS) including Streptococcus pneumoniae isolated from adult patients with cystic fibrosis (CF). *J Cyst Fibros* 2011; 10: 133-139.
19. Bradshaw DJ, Marsh PD. Effect of sugar alcohols on the composition and metabolism of a mixed culture of oral bacteria grown in a chemostat. *Caries Res* 1994; 28: 251-256.
20. Vadeboncoeur C, Trahan L, Mouton C, Mayrand D. Effect of xylitol on the growth and glycolysis of acidogenic oral bacteria. *J Dent Res* 1983; 62: 882-884.
21. Miyasawa-Hori H, Aizawa S, Takahashi N. Difference in the xylitol sensitivity of acid production among *Streptococcus mutans* strains and the biochemical mechanism. *Oral Microbiol Immunol* 2006; 21: 201-205.
22. Söderling EM, Hietala-Lenkkeri AM. Xylitol and erythritol decrease adherence of polysaccharide-producing oral streptococci. *Curr Microbiol* 2010; 60: 25-29.
23. Trahan L, Bareil M, Gauthier L, Vadeboncoeur C. Transport and phosphorylation of xylitol by a fructose phosphotransferase system in *Streptococcus mutans*. *Caries Res* 1985; 19: 53-63.
24. Sahni PS, Gillespie MJ, Botto RW, Otsuka AS. In vitro testing of xylitol as an anticariogenic agent. *Gen Dent* 2002; 50: 340-343.
25. Saier MH Jr, Ye JJ, Klinke S, Nino E. Identification of an anaerobically induced phosphoenolpyruvate-dependent fructose-specific phosphotransferase system and evidence for the Embden-Meyerhof glycolytic pathway in the heterofermentative bacterium Lactobacillus brevis. *J Bacteriol* 1996; 178: 314-316.
26. Kaplan H, Hutkins RW. Fermentation of fructooligosaccharides by lactic acid bacteria and bifidobacteria. *Appl Environ Microbiol* 2000; 66: 2682-2684.
27. Helanto M, Aarnikunnas J, Palva A, Leisola M, Nyyssölä A. Characterization of genes involved in fructose utilization by Lactobacillus fermentum. *Arch Microbiol* 2006; 186: 51-59.
28. Loesche WJ, Grossman NS, Earnest R, Corporon R. The effect of chewing xylitol gum on the plaque and saliva levels of Streptococcus mutans. *J Am Dent Assoc* 1984; 108: 587-592.
29. Mäkinen KK, Alahari P, Isokangas P, Isotupa K, Söderling E, Mäkinen P, *et al.* Thirty-nine-month xylitol chewing-gum programme in initially 8-year-old school children: a feasibility study focusing on mutants streptococci and lactobacilli. *Int Dent J* 2008; 58: 41-50.
30. Söderling EM, Xylitol, mutants streptococci, and dental plaque. *Adv Dent Res* 2009; 21: 74-78.
31. Konttinen T, Uhari M, Koskela M. Effect on xylitol on growth of nasopharyngeal bacteria in vitro. *Antimicrob Agents Chemother* 1995; 39: 1820-1823.
32. Wennerholm K, Arends J, Birkhed D, Ruben J, Emilson CG, Dijkman AG. Effect of xylitol and sorbitol in chewing-gums on mutants streptococci, plaque pH and mineral loss of enamel. *Caries Res* 1994; 28: 48-54.
33. Edgar WM. Sugar substitutes chewing gum and dental caries: a review. *Br Dent J* 1998; 184: 29-32.
گزارش‌های آموزشی مرکز اطلاعات علمی

مقاله نویسی علوم انسانی

اصول تنظیم قراردادها

آموزش مهارت های کاربردی در تدوین و چاپ مقاله