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Remineralization of early caries by chewing sugar-free gum: A clinical study using quantitative light-induced fluorescence

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ABSTRACT: Purpose: To determine whether sugar-free gum can provide remineralization and caries control of active enamel caries lesions compared to baseline (before gum chewing) and to a no-gum group, following daily chewing for 12 weeks by school children; to determine whether chewing frequency can affect the extent of remineralization. **Method:** A pragmatic cluster-randomized controlled clinical trial with schools as the unit of randomization was employed. Three schools in Chengdu, PR China comprised the clusters. The study was approved by the Internal Review Board of Sichuan University. 177 school children, 8-13 years old, with at least one visible white-spot lesion were enrolled in the study. Each of the three clusters was randomly assigned to one of three groups: (1) no gum; (2) chew 2 pieces of sugar-free gum for 20 minutes, 3x per day; (3) chew 2 pieces of sugar-free gum for 12 minutes, 5x per day. White-spot lesions were examined by quantitative light-induced fluorescence (QLF) at baseline and after 4, 8, and 12 weeks of treatment. **Results:** 155 subjects completed the study. Of them, the mean values of fluorescence loss at baseline were 9.52, 9.83 and 9.17 for no-gum group, 3x per day group and 5x per day group, respectively. For the area, the mean values at baseline were 2.52, 2.61 and 2.57mm² for no-gum group, 3x per day group and 5x per day group, respectively. For ΔQ , the mean values at baseline were -27.91, -28.29 and -29.67 for no-gum group, 3x per day group and 5x per day group, respectively. To adjust for differences in groups at baseline, ANCOVA was used. After 12-weeks, for all QLF metrics, the absolute values of 5x per day group were the lowest and the no gum group was the highest; the differences among three groups were statistically significant ($P < 0.05$). For ΔQ , which was accepted as the most useful metrics of QLF system, the adjusted mean values at 12 weeks were -26.35, -19.81 and -17.58 for no-gum group, 3x per day group and 5x per day group, respectively. There were significant differences between groups. (*Am J Dent* 2014;27:291-295).

CLINICAL SIGNIFICANCE: The results suggested that sugar-free gum can provide remineralization and caries control of active enamel caries lesions following daily chewing; and increased daily frequency rather than the amount of time chewing promoted the greater effect.

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Introduction

Dental caries is a prevalent and ubiquitous oral health problem that affects children at a very early age as well as individuals throughout adolescence and adulthood.^{1,2} Dental caries is caused by fermentation of sugars to acids by the acid-producing bacteria present in dental plaque overlying the tooth. These acids dissolve calcium and phosphate, causing demineralization of the tooth enamel.^{3,4} However, not all incipient caries lesions progress to clinically visible cavities: an equilibrium between demineralization and remineralization normally occurs at the tooth surface. So as long the two rates are comparable, the enamel will remain healthy. However, when the rate of demineralization substantially exceeds that of remineralization, caries lesions can develop into severe cavities.⁵

The development of non-invasive methods for the detection and quantitative monitoring of dental caries at an early stage of formation can provide health and economic benefits ranging from timely preventive interventions to reduction of the time required for clinical trials of anti-caries agents.^{6,7} Therefore, there is a growing interest in the use of technologies to aid in detection, diagnosis and assessment of early stage caries lesions. In the past few years, a variety of devices have been developed to help dental practitioners diagnose caries early and treat cases conservatively.⁸⁻¹² The most widely used methods include: electronic caries monitoring,⁸ laser-induced fluorescence,⁹ and quantitative light-induced fluorescence (QLF).¹⁰⁻¹²

QLF is a method that has been applied to imaging teeth to measure the area and degree of demineralization of early caries lesions.¹² QLF is based on observation of auto fluorescence from teeth.^{13,14} When enamel demineralization occurs, minerals are replaced by water from saliva, which reduces the light path in the tooth. This reduces light absorption by enamel, and thus, the intensity of fluorescence decreases in demineralized regions of enamel, which then appear as darker zones differing from sound tooth structures. By comparing the amount of fluorescence in the demineralized area to that of the surrounding sound enamel, the fluorescence loss (ΔF) can be calculated. By applying a threshold to the image based on the degree of fluorescence loss, the area of the lesion can be quantified. A further parameter known as ΔQ , calculated from the fluorescence loss and the area of the lesion, indicates the volume of the demineralized lesion.^{12,15} As a detection and assessment method of early caries, QLF enables studies to be conducted effectively in a relatively short time period with low cost, compared to traditional caries clinical trials. As a clinical diagnostic tool, QLF performs well against the gold standard of transverse microradiography (TMR) in studies of both natural and artificial caries lesions. QLF also shows a good accuracy and repeatability for detecting early caries lesions.¹⁶ Furthermore, QLF is non-destructive, and can be used to monitor progression/regression of natural caries lesions quantitatively.

Several studies have suggested that chewing sugar-free gum

can prevent the progression of early caries lesions to more serious cavities.¹⁷⁻²² Chewing sugar-free gum increases saliva flow, which increases oral clearance rates of fermentable carbohydrate, buffers the plaque pH, and promotes the remineralization of demineralized enamel.²³⁻²⁵ However, we are unaware of studies that address whether sugar-free gum can provide remineralization and caries control of natural early caries lesions. Moreover, the effect of chewing frequency of sugar-free gum on the extent of teeth remineralization has not been studied. This clinical study (1) determined the effect of a commercial sugar-free gum on tooth remineralization of active enamel caries lesions of school children and young adolescents; and (2) determined if the chewing frequency influences the extent of teeth remineralization using a QLF method.

Materials and Methods

This study was approved by the Ethics Committee of the State Key Laboratory of Oral Diseases. Prior to start of the study, all parents or legal guardians of subjects were required to read, sign and date an informed consent form which described the nature, purpose and duration of the clinical trial.

Subjects - Subjects from three schools were enrolled into the study based on meeting availability, age and health requirements. Three similarly-sized primary schools from Shuangliu Village, Chengdu City, were randomly selected; each grade had three classes and each class comprised about 45 students. Students from Grades 3 to 6 of each school were selected for screening. To be eligible, subjects were required to have at least four maxillary anterior teeth, and to have at least one early caries lesion on the labial smooth surfaces of those teeth. Subjects were also required to be able and willing to complete the 12-week clinical study. Subjects were excluded from the study if they had primary teeth, or permanent teeth that had not fully erupted; had fixed artificial teeth, or dental fluorosis visible to the naked eye; tetracycline-stained teeth, or teeth with enamel hypoplasia. Subjects were also excluded from the study if they had orthodontic bands and appliances, had severe congenital maxillofacial malformations, or were taking long-term medication due to chronic diseases, were allergic to substances in chewing gum, or had already reported regularly chewing gum. All subjects had the right to quit the study at any time for any reason.

As a result, 177 school children, 8-13 years old, from three schools met the inclusion and exclusion criteria and were recruited and enrolled. Students shared the same middle-class socioeconomic level. Fluoride concentration in the drinking water where the schools are located is approximately 0.3 ppm. One hundred fifty-five subjects completed this study.

Group allocation and compliance monitoring - A random allocation sequence based on the school cluster was devised by the principal investigator. There were three clusters and each of them was formed by all subjects who met the inclusion and exclusion criteria from one same school. Each of the three clusters was randomly assigned to one of three groups: (1) no gum; (2) chew two pieces of sugar-free gum for 20 minutes, 3x per day; (3) chew two pieces of sugar-free gum for 12 minutes, 5x per day. Chewing occasions for the 3x per day group were: post-breakfast, post-lunch and post-supper. Chewing occasions

for the 5x per day group were: post-breakfast, 2 hours prior to lunch, post-lunch, 3 hours prior to supper and post-supper. In order to assess the influence of chewing frequency on the extent of remineralization, the same total daily chewing time was maintained for both the 3x per day (Group 2) and 5x per day (Group 3), i.e., 60 minutes each day. Subjects in the control group did not chew any gum. All subjects were provided fluoride-free herbal toothpastes (Tianqi Toothpaste;^a non-fluoride herbal toothpaste) to use during the study. All groups were required to follow their respective protocols for 12 weeks.

At each participating school, the headmaster appointed teachers to supervise students' gum chewing activity. Teachers were aware of the group allocations. They monitored whether students were chewing their gum by following the study protocol, and documented any deviations. Parents were also required to monitor the compliance of the study protocol, and to document any deviations. Study investigators met regularly with school monitors and parents over the course of the entire clinical trial to collect the compliance data.

The chewing gum employed in this study was a sugar-free, commercially available pellet gum (Wrigley's Extra Melon^b). The piece weight was 1.4g, and the serving size was 2.8g (two pieces per serving).

Dental assessment - All subjects underwent an initial baseline examination, when investigators recorded the age, gender, and class of each participant, as well as clinical history, medication history, and drug sensitivities. Each subject received a soft oral tissue examination according to the recommendations of the Third National Oral Health Survey of China.²⁶ They were also examined for caries using the decayed, missing and filled teeth (DMFT) index. Finally, the labial surfaces of the anterior maxilla were examined by QLF to quantify demineralization. After initial oral examination, subjects underwent a 4-week lead-in period, during which they were not allowed to chew gum or use any other oral hygiene means except the toothpaste and toothbrush provided for the study. Subjects were advised to brush their teeth twice daily for the entire duration of the study. Subsequently, subjects entered into the 12-week intervention period, during which they either chewed the test gum three times per day, or five times per day, or did not chew any gum. At the end of 4, 8, and 12 weeks, subjects received oral examinations which involved the same assessments as of those at baseline. The clinicians who performed the baseline and subsequent examinations were blinded to the group allocation of subjects.

QLF examination - The labial surfaces of the anterior maxilla were examined using a QLF system.^c During fluorescence measurements, ambient light was minimized by using blackout curtains and by switching off all lights. Before fluorescence measurements, all tooth surfaces were thoroughly cleaned by brushing with non-fluoride toothpaste or by manual cleaning. The labial surfaces of the anterior maxillary teeth were visually examined under natural light to identify definite or possible early caries lesions. The teeth were then dried by gently blowing compressed air for 5 seconds per tooth. Subsequently, QLF images were acquired. Six images were taken for each subject to ensure that all maxillary anterior teeth were included. QLF patient software^c (version 3.0.3.30) was em-

Table 1. Baseline characteristics of subjects who completed the whole study in each group.

Group	No gum (n=50) Mean or %	3x per day (n=53) Mean or %	5x per day (n=52) Mean or %
Age (years)	10.5 ± 1.2	10.6 ± 0.7	10.9 ± 0.5
Gender (%)	F: 48.0 M: 52.0	F: 45.3 M: 54.7	F: 40.4 M: 59.6
ΔQ	-27.91 ± 1.21	-28.29 ± 1.34	-29.67 ± 1.86
Area	2.52 ± 0.09	2.61 ± 0.10	2.57 ± 0.11
ΔF	-9.52 ± 0.35	-9.83 ± 0.16	-9.17 ± 0.16

F: female; M: male.

ployed to analyze QLF images and extract ΔF (loss of fluorescence of demineralized enamel compared to neighboring healthy enamel), Area (area of lesions), and ΔQ (total loss of fluorescence).

Statistical analysis - The data were analyzed by a statistician. The fluorescence loss (ΔF), area of white spot and ΔQ (ΔF×Area) were collected after QLF image analysis. The three study groups and all three outcomes (ΔF, Area and ΔQ) were compared using covariance analysis to correct for differences in baseline score. Within each testing group, the differences of ΔF, Area and ΔQ changes at 4, 8, and 12-week time points were compared to the baseline by pair-wise t-test. Statistical analysis was performed using the SAS^d 8.0 software program.

Sample size calculation - The sample size was determined based on a sample size estimation formula for a case-control study that assumed a two-tailed test $\alpha=0.05$, a general statistical power of $\beta=0.1$, a difference of the primary outcome (ΔQ) between the test and control group means of $\delta=10$, and a within-group standard deviation of $\sigma=15$. These variables were obtained from a pilot QLF study in which ΔQ was also the primary outcome.¹³ The result of the estimation formula showed that a minimum number of 48 subjects was needed, and 55 subjects were recruited for each group.

Results

A total of 177 students from three schools were recruited and screened for this clinical trial. 155 subjects were enrolled and finished the study. The age of these subjects ranged from 8-13 years (mean 10.68 ± 0.42). 55.5% of subjects were male (Table 1). No adverse events were reported in any of the testing groups during the course of the study. The mean baseline values for ΔF, Area and ΔQ for the three study groups are also shown in Table 1. The mean values of fluorescence loss at baseline were 9.52, 9.83 and 9.17 for the no-gum group, 3x per day group and 5x per day group, respectively. For the area, the mean values at baseline were 2.52, 2.61 and 2.57 mm² for no-gum group, 3x per day group and 5x per day group, respectively. For ΔQ, the mean values at baseline were 27.91, 28.29 and 29.67 for no-gum group, 3x per day group and 5x per day group, respectively. There was no statistically significant difference between the three study groups for any of the baseline measurements.

Least square means for each group after analysis of covari-

Table 2. Least square mean for each group after analysis of covariance with baseline adjusted.

Metrics		Adjusted mean values			
		Baseline	4 weeks	8 weeks	12 weeks
ΔQ	No gum	-28.64	-26.91 ± 0.20*	-26.42 ± 0.25*	-26.35 ± 0.20*
	3x group		-25.19 ± 0.19*	-22.07 ± 0.24*	-19.81 ± 0.19*
	5x group		-24.56 ± 0.20*	-21.36 ± 0.25*	-17.58 ± 0.21*
Area	No gum	2.57	2.46 ± 0.014*	2.43 ± 0.02*	2.41 ± 0.02*
	3x group		2.49 ± 0.013*	2.32 ± 0.02*	2.15 ± 0.02*
	5x group		2.41 ± 0.013*	2.25 ± 0.02*	2.09 ± 0.01*
ΔF	No gum	-9.50	-9.39 ± 0.03	-9.41 ± 0.03	-9.40 ± 0.03
	3x group		-8.82 ± 0.03*	-8.17 ± 0.04*	-7.48 ± 0.04*
	5x group		-8.54 ± 0.03*	-8.03 ± 0.04*	-7.14 ± 0.04*

* Significant difference compared with baseline within groups (P<0.05).

ance with baseline adjusted are shown in Table 2. At the 4-week examination, the values of ΔQ were 26.91, 25.19 and 24.56 for no-gum group, 3x per day group and 5x per day group, respectively. For area, the mean values were 2.46, 2.49 and 2.41 mm² for no-gum, 3x per day and 5x per day groups, respectively. For ΔF, the mean values at the 4-week examination were 9.39, 8.82 and 8.54 for no-gum, 3x per day and 5x per day groups, respectively.

For ΔF and ΔQ, the differences among three groups were statistically significant at the 4-week period (P<0.05). The difference between the 3x per day and 5x per day groups of the area was not statistically significant for the same period (P>0.05).

At the 8-week period, the ΔQ value was 26.42, 22.07 and 21.36 for no-gum, 3x per day and 5x per day groups, respectively. The lesion areas were 2.43, 2.32 and 2.25 mm² for no-gum, 3x per day and 5x per day groups, respectively. ΔF values were 9.41, 8.17 and 8.03 for no-gum, 3x per day and 5x per day groups, respectively. For all QLF metrics (ΔF, Area and ΔQ), the differences among three groups were statistically significant at the 8-week period (P<0.05).

At the 12-week time point, the ΔQ values were 26.35, 19.81 and 17.58 for no-gum, 3x per day and 5x per day groups, respectively. The lesion areas were 2.41, 2.15 and 2.09 mm² for no-gum, 3x per day and 5x per day groups, respectively. ΔF values were 9.40, 7.48 and 7.14. This represents an improvement from baseline of 5.6%, 30.0% and 40.7% (measured by ΔQ) for no-gum, 3x per day and 5x per day groups, respectively. Again, for all QLF metrics, the differences among three groups were statistically significant at the 12-week period (P<0.05).

To eliminate the influence of the baseline differences among three groups, we subtracted the values of ΔF, Area, and ΔQ from those of the baseline and obtained the change of ΔF, Area, and ΔQ. The Figure shows the change of ΔF, Area, and ΔQ values from baseline for three testing groups. The Figure also indicates statistical significance within the group as well as between group comparisons.

Comparison within the group revealed that the area of the lesions, as well as the ΔQ values, showed statistically significant improvements after 4, 8 and 12 weeks of treatment versus baseline for all testing groups (including the no-gum group). The change in control group suggests an auto remineralization effect of the white spot lesion. However, this auto remineralization was limited.

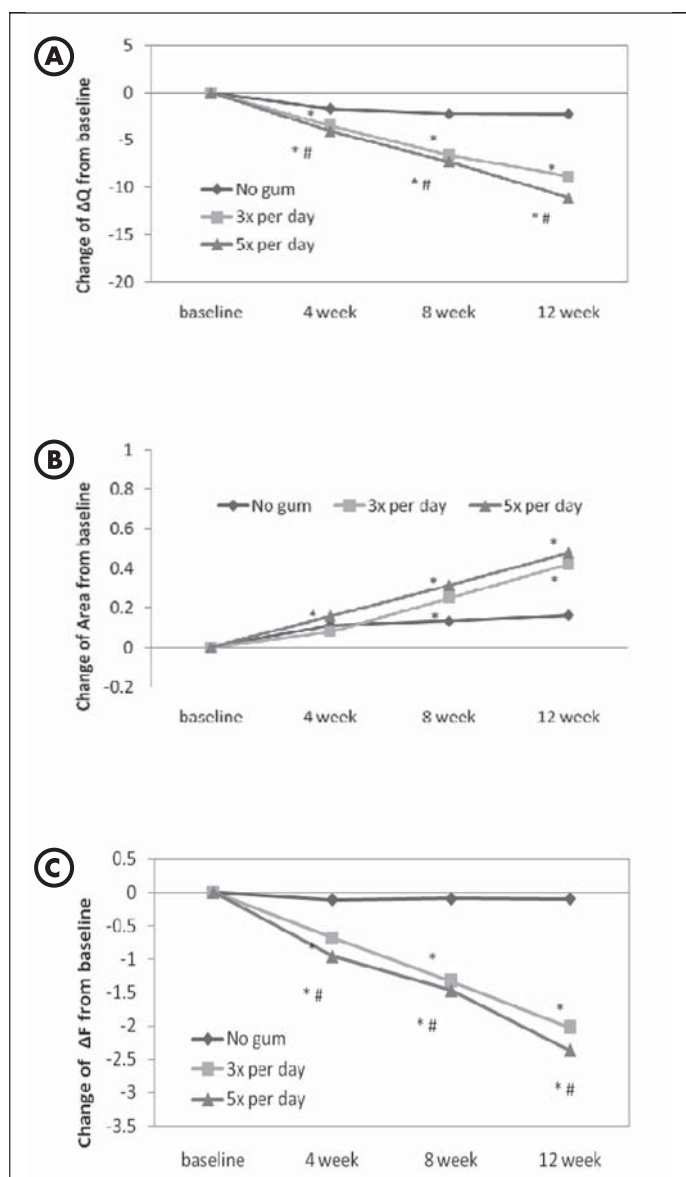


Figure. Changes of adjusted mean value of A. ΔQ , B. area, C. ΔF from baseline for three groups at 4, 8 and 12 weeks.

* Significant difference when compared with no-gum group ($P < 0.05$).

Significant differences when compared with 3x per day group ($P < 0.05$).

Discussion

Several studies have shown that chewing sugar-free gum can help prevent cavities. The present study further supported this evidence. In the current study, chewing of sugar-free gum resulted in improvements in ΔQ from baseline scores of 5.6%, 30.0% and 40.7% after 12 weeks for no-gum, the 3x per day, and 5x per day groups, respectively. At 4, 8 and 12-week time points, the difference between the negative control (no-gum) group and both experimental groups were statistically significant for all QLF metrics measured (ΔF , Area and ΔQ) ($P < 0.05$). Furthermore, for the primary outcome variable, ΔQ , the difference between the 5x per day and 3x per day groups was statistically significant after 12 weeks of treatment ($P < 0.05$).

These results indicate that regular chewing of sugar-free gum can help to arrest and reverse early caries lesions after 4, 8 and 12 weeks. The study further demonstrated that the frequency of daily chewing, rather than chewing time, has the

greater impact on the extent of tooth remineralization. Increase of chewing frequency can lead to a significant remineralization even when chewed for a shorter duration.

A traditional anti-caries study often involves over 1,000 subjects, and lasts for 2 years or longer.⁸ In the current study, aided by QLF methodology, we were able to observe the difference between three treatment groups by the QLF metrics after 12 weeks of intervention, which is a relatively short duration. In QLF metrics, ΔQ measures the volume of the caries lesion, which represents a combination of fluorescence loss (ΔF) and the area of lesion. ΔQ plays the most important role in remineralization analysis. It is more sensitive compared with the traditional decayed, missing, filled surface (DMFS) index.¹³ The QLF method has been reviewed extensively at the “2005 Clinical Models Workshop: Remin-Demin, Precavitation, Caries” sponsored by the National Institute of Dental and Craniofacial Research, and the Task Force of Design and Analysis in Dental and Oral Research. QLF has also been shown to correlate well with the “gold standard” for content validity, i.e., transverse microradiography. The correlation coefficients between the two technologies range from 0.64 to 0.86.²⁷⁻²⁹ In addition, QLF shows a good accuracy and repeatability for detecting early caries lesions, with sensitivity ranging from 0.94 to 0.97 and specificity from 0.67 to 0.75.³⁰

Many studies have shown that chewing sugar-free gum can promote tooth remineralization. Most studies evaluated the extent of tooth demineralization either by microradiography,³¹ or polarized light microscopy.³² In these studies, participants typically chew sugar-free gum once a day and continue for 2-3 weeks, and the extent of demineralization and remineralization is measured in artificial caries-like lesions in enamel sections from extracted teeth carried in intra-oral appliances. None of the studies addressed the effects of gum-chewing frequency on the extent of tooth remineralization. The present study quantitatively assessed pre-cavitated natural caries occurring within the subjects' own dentitions. In the current study, we demonstrated that frequently chewing sugar-free gum can reduce both the area of the demineralized lesion as well as the volume of the lesion. Chewing sugar-free gum increases saliva flow, which increases oral clearance rates of fermentable carbohydrate, buffers the pH inside the mouth, and promotes the remineralization of demineralized enamel. The current study indicated that chewing frequency, rather than chewing time, has the greater impact on the extent of tooth remineralization. This outcome supports the hypothesis that high salivary flow, initiated by the first few minutes of chewing, will enhance the buffer capacity to neutralize the acids produced by fermentable carbohydrates. Dawes & Kubieniec³³ showed that with the chewing gums, the salivary flow rate and salivary pH could remain significantly higher than the unstimulated flow rate for 2 hours. Increased salivary pH also raises the pH of dental plaque by buffering plaque acids from bacterial carbohydrate metabolism.³⁴ In addition, stimulated saliva is expected to promote the remineralization of the tooth surface.³⁵ Machiulskiene et al³⁶ showed that the caries preventive effect of chewing gum is related to the chewing process itself rather than being an effect of gum sweeteners or additives, such as polyols. The sugar-free gum employed in this study was a commercial pellet gum (Wrigley's Extra Melon), with a piece weight of 1.4 g and a serving size of 2.8 g. It contained 36% xylitol and 32% sorbitol.

The total daily intake of xylitol was 3.0 and 5.0 g for the 3x per day and 5x per day groups, respectively. We do not expect a significant contribution of anti-caries effect from xylitol or other sugar alcohols in this study. The total amount of xylitol employed was well below the threshold of laxative effect for school children, which was reported as 40 g of daily intake.³⁷ Sorbitol and other sugar alcohols have a much higher laxative threshold. In the current study, no adverse effects were observed, including a laxative effect. Daily intake of sugar-free gum even at five times per day should not therefore impose any side effects on school children.

Clinical studies involving school children pose challenges to researchers, given the fact that the participants are very young. Sometimes it is difficult to have all subjects comply with the study protocol. Consequently, frequent monitoring is often required. Nevertheless, in the present study it was worthwhile to invest the extra effort to minimize the risk of bias from compliance deviations by increasing monitoring frequency, and collecting data from both school staff and parents/guardians, who agreed to assist the investigators in ensuring that participants adhered to their protocols.

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References

1. Beltran-Aguilar ED, Beltran-Neira RJ. Oral disease and conditions throughout the lifespan. 1. Diseases and conditions directly associated with tooth loss. *Gen Dent* 2004; 52:21-27.
2. Thomson WM. Dental caries experience in older people over time: What can the large cohort studies tell us? *Br Dent J* 2003;196:89-92.
3. Anderson M. Risk assessment and epidemiology of dental caries – Review of literature. *Pediatr Dent* 2002;24:377-385.
4. Bowen WH. Do we need to be concerned about dental caries in the coming millennium? *Crit Rev Oral Biol Med* 2002;13:126-131.
5. Featherstone JD. The science and practice of caries prevention. *J Am Dent Assoc* 2000;131:887-899.
6. Pereira AC, Eggertsson H, Martinez-Mier EA, Mialhe FL, Eckert GJ, Zero DT. Validity of caries detection on occlusal surfaces and treatment decisions based on results from multiple caries-detection methods. *Eur J Oral Sci* 2009; 117:51-57.
7. Featherstone JD. The continuum of dental caries - Evidence for a dynamic disease process. *J Dent Res* 2004; 83(Sp No C):39-42.
8. Pretty IA. Caries detection and diagnosis: Novel technologies. *J Dent* 2006;34:727-739.
9. Lussi A, Imwinkelried S, Pitts N, Longbottom C, Reich E. Performance and reproducibility of a laser fluorescence system for detection of occlusal caries in vitro. *Caries Res* 1999;33:261-266.
10. de Josselin de Jong E, Sundstrom F, Westerling H, Tranaeus S, ten Bosch JJ, Angmar-Mansson B. A new method for in vivo quantification of changes in initial enamel caries with laser fluorescence. *Caries Res* 1995;29:2-7.
11. Higham SM. The quantitative light fluorescence (QLF) model. In: Stookey GK. Proceedings of the 7th Indiana Conference Clinical Models Workshop: Remin-Demin, Precavitation, Caries. 2005; 273-276.
12. Yin W, Hu DY, Fan X, Feng Y, Zhang YP, Cummins D, Mateo LR, Pretty IA, Ellwood RP. A clinical investigation using quantitative light-induced fluorescence (QLF) of the anticaries efficacy of a dentifrice containing 1.5% arginine and 1450 ppm fluoride as sodium monofluorophosphate. *J Clin Dent* 2013;24 (Sp Is A):A15-A22.
13. Feng Y, Yin W, Hu D, Zhang YP, Ellwood RP, Pretty IA. Assessment of autofluorescence to detect the remineralization capabilities of sodium fluoride, monofluorophosphate and non-fluoride dentifrices. *Caries Res* 2007;41:358-364.
14. Tranaeus S, Shi XQ, Lindgren LE, Trollsås K, Angmar-Mansson B. In vivo repeatability and reproducibility of the quantitative light-induced fluorescence method. *Caries Res* 2002;36:3-9.
15. de Josselin de Jong E, Sundstrom F, Westerling H, Tranaeus S, ten Bosch JJ, Angmar-Mansson B. A new method for in vivo quantification of changes in initial enamel caries with laser fluorescence. *Caries Res* 1995;29:2-7.
16. Ando M, Hall AF, Eckert GJ, Schemehorn BR, Analoui M, Stookey GK. Relative ability of laser fluorescence techniques to quantitate mineral loss in vitro. *Caries Res* 1997;31:125-131.
17. Szöke J, Bánóczy J, Proskin HM. Effect of after-meal sucrose-free gum-chewing on clinical caries. *J Dent Res* 2001;80:1725-1729.
18. Glass RL. A two-year clinical trial of sorbitol chewing gum. *Caries Res* 1983;17:365-368.
19. Beiswanger BB, Boneta AE, Mau MS, Katz BP, Proskin HM, Stookey GK. The effect of chewing sugar-free gum after meals on clinical caries incidence. *J Am Dent Assoc* 1998;129:1623-1626.
20. Kovari H, Pienihakkinen K, Alanen P. Use of xylitol chewing gum in daycare centers: A follow-up study in Savonlinna, Finland. *Acta Odontol Scand* 2003;61:367-370.
21. Machiulskiene V, Nyvad B, Baelum V. Caries preventive effect of sugar-substituted chewing gum. *Community Dent Oral Epidemiol* 2001;29:278-288.
22. Alanen P, Isokangas P, Gutmann K. Xylitol candies in caries prevention: Results of a field study in Estonian children. *Community Dental Epidemiol* 2000;28:218-224.
23. Manning RH, Edgar WM, Agalamanyi EA. Effects of chewing gums sweetened with sorbitol or a sorbitol/xylitol mixture on the remineralisation of human enamel lesions in situ. *Caries Res* 1992;26:104-109.
24. Pollard KE, Higgins F, Orchardson R. Salivary flow rate and pH during prolonged gum chewing in humans. *J Oral Rehabil* 2003;30:861-865.
25. Milgrom P, Ly KA, Roberts MC, Rothen M, Mueller G, Yamaguchi DK. Mutans streptococci dose response to xylitol chewing gum. *J Dent Res* 2006;85:177-181.
26. Qi XQ. Report of the third national oral health survey. Beijing: People's Medical Publishing House, 2008;60-64.
27. Emami Z, al-Khateeb S, de Josselin de Jong E, Sundström F, Trollsås K, Angmar-Mansson B. Mineral loss in incipient caries lesions quantified with laser fluorescence and longitudinal microradiography. *Acta Odontol Scand* 1996;54:8-13.
28. Shi XQ, Tranaeus S, Angmar-Mansson B. Comparison of QLF and DIAGNodent for quantification of smooth surface caries. *Caries Res* 2001;35:21-26.
29. Lagerweij M, van der Veen M, Ando M, Lukantsova L, Stookey G. The validity and repeatability of three light-induced fluorescence systems: An in vitro study. *Caries Res* 1999;33:220-226.
30. Ando M, Hall AF, Eckert GJ, Schemehorn BR, Analoui M, Stookey GK. Relative ability of laser fluorescence techniques to quantitate mineral loss in vitro. *Caries Res* 1997;31:125-131.
31. Creanor SL, Strang R, Gilmour WH, Brown J, Geddes DA, Hall AF. The effect of chewing gum use on in situ enamel lesion remineralization. *J Dent Res* 1992;71:1895-1900.
32. Manning RH, Edgar WM, Agalamanyi EA. Effects of chewing gums sweetened with sorbitol or a sorbitol/xylitol mixture on the remineralization of human enamel lesions in situ. *Caries Res* 1992;26:104-109.
33. Dawes C, Kubieniec K. The effects of prolonged gum chewing on salivary flow rate and composition. *Arch Oral Biol* 2004;49:665-669.
34. Gopinath V K, Tandon S, Shirwaikar A. The effect of chewing gums acidogenicity of plaque after a sucrose challenge. *J Clin Pediatr Dent* 1997;22:77-81.
35. Manning RH, Edgar W M. Salivary stimulation by chewing gum and its role in the remineralization of caries-like lesion in human enamel in situ. *J Clin Dent* 1992;3:71-74.
36. Machiulskiene V, Nyvad B, Baelum V. Caries preventive effect of sugar-substituted chewing gum. *Community Dent Oral Epidemiol* 2001;29:278-288.
37. Storey D, Lee A, Bomet F, Brouns F. Gastrointestinal tolerance of erythritol and xylitol ingested in a liquid. *Eur J Clin Nutr* 2007;61:349-354.