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Effect of Xylitol Chewing Gum on Presence of *Streptococcus mutans* in Saliva

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Abstract

BACKGROUND: Oral disease ranks third among the most serious diseases in the world, after cancer and cardiovascular disease. Vietnamese population has suffered from various dental and oral diseases, of which the most common have been identified to be cavities and inflammation around the teeth.

AIM: The aim of the study was to evaluate the effectiveness of using xylitol gum on the status of *Strepptococus mutans* bacteria in saliva.

METHODS: The study design was an uncontrolled clinical study conducted at the Hanvinco Texture Factory (Hanoi). Two hundred and fifty-four subjects between the ages of 18 and 63 were included in the clinical trial. These subjects brushed their teeth for 2 weeks before providing a saliva sample for *S. mutans.* The 80 subjects with the highest number of salivary *S. mutans* were recruited for the further analysis (at least 10^4 CFU/ml). After each clinical intervention, participant chewed Lotte xylitol gum after each meal, two capsules each time and 1 time in the evening (total 4 times/day), continuously for 4 weeks. Saliva samples were quantified for *S. mutans* by real-time PCR method.

RESULTS: Quantitative analysis of *S. mutans* bacteria in saliva of 254 subjects showed that 19.7% had *S. mutans* detected within 105 CFU/ml of saliva. These result shows that nearly 20% of the subjects examined have a high risk of tooth decay. After continuous use of xylitol chewing gum 4 times a day for 4 weeks by 80 subjects, it showed a decrease in the number of *S. mutans* in the saliva of participants, and the difference was statistically significant.

CONCLUSIONS: The use of xylitol chewing gum taken 4 times/day is effective in reducing the number of *S. mutans* bacteria in saliva when combined with brushing your teeth.

Background

According to the World Health Organization (WHO), oral disease ranks third among the other serious diseases in the world, after cancer and cardiovascular disease [1]. Results of the National Oral Health Survey conducted in 2019 by Hanoi Central Dental Hospital showed that about 90% of the Vietnamese population suffered from dental and oral diseases, of which the most common were decay and gingival inflammation around the teeth [2]. Tooth decay not only affects the health of the patient but in the future may lead to costly treatment options. Many research programs as well as recommendations aimed at preventing tooth decay have been implemented by the World Health Organization over the years [3], [4], [5]. Although the rate of decay in the community has decreased significantly, it is still high and requires better preventive measures to meet the goals set by the World Health Organization.

Previously, conducted research has shown that the bacteria in the dental plaque break down sugars, causing formation of acid that causes destruction and forms cavities in the teeth. Among these bacteria, the role of *Streptococus mutans (Streptococus)* in tooth decay pathogenesis is emphasized. For instance, it was reported to have a direct relationship with tooth decay. According to previous studies, the higher the presence of Streptococus mutans in the oral cavity is, the more likely the tooth decay might be to occur [6], [7], [8], [9].

Creating good oral hygiene habits such as brushing the teeth with fluoride toothpaste, eating a healthy diet is another simple way to prevent dental diseases. Research has shown that xylitol is an effective sugar alternative [10], [11]. Xylitol is as sweet as sucrose but is only provides 1/3 of the calories and is found naturally within various fruits, vegetables, and from the bark of the Bulo tree [12].

Previously, conducted studies have shown that xylitol when used as a sweetener in chewing gum has a beneficial effect in reducing the amount of *S. mutans* bacteria in the mouth and helps reduce the incidence of the tooth decay [13], [14], [15]. However, in Vietnam, the total number of studies has been conducted on effect of xylitol on tooth decay. Therefore, the aim of

the study is to evaluate the effectiveness of using xylitol gum on the *S. mutans* present in the saliva.

Materials and Methods

Study design and select research subjects

The study design was a clinical study conducted at the Hanvinco Texture Factory (Hanoi). The study design is shown in Figure 1. The factory workers were interviewed and examined for eligibility for inclusion in the study.

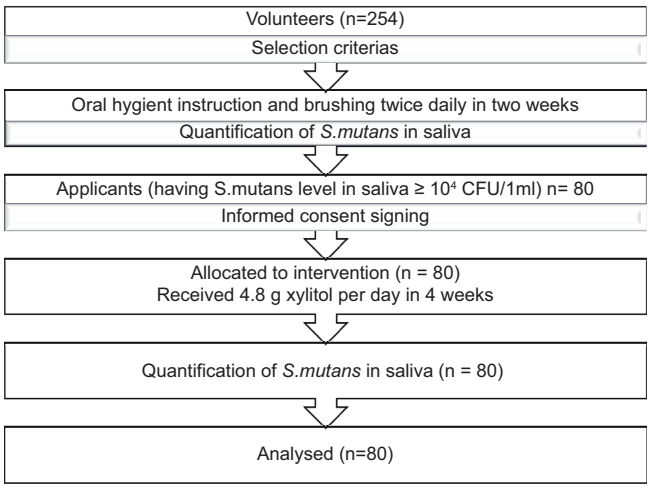

Figure 1: Flowchart of study design

Inclusion criteria were: The presence of at least 24 teeth, including at least 20 teeth without presence of caries on tooth, V-type cavity, more tartar or progressive periodontitis (that affected to effectiveness of Xylitol in oral bacterium). Participants were excluded if they were diagnosed with systemic diseases or were unable to follow the study protocol.

After selective examination, 254 subjects between the ages of 18 and 63 were included in the clinical trial. Study subjects included 50 men (accounting for 19.7%) and 204 women (accounting for 80.3%) all following normal oral hygient regime. The saliva samples were taken to quantify the levels of *S. mutans* in saliva. The demographic characteristics of the participants are shown in Table 1.

Table 1: Demographic characteristics of participants

Parameters	Values
Age	
Mean age	37, 87
Range age	18–63
Sex:	
Male	50 (19.7%)
Female	204 (80-3%)

All 254 participants received oral hygiene instructions, and received standard toothpaste and toothbrush. These participants brushed their teeth for 2 weeks before providing a saliva sample for *S. mutans*. The 80 subjects, 70 (87.5%) males and ten females (12.5%), with the highest number of salivary *S. mutans* were recruited for the further analysis.

Clinical intervention methods

The study used Lotte xylitol chewing gum with a content of 0.6 g xylitol sweetener circulated in Vietnam under License No. 307/2015/YTBD-XNCB. Each clinical intervention participant strictly followed the intervention protocol as follows: Chewed Lotte xylitol gum after each meal, two tablets each time (at work under the supervision of research collaborators) and 1 time in the evening (total 4 times/day), continuously for 4 weeks. It was chewed for no more than 5 min and the participants were instructed not to brush their teeth for at least 1 h after chewing. This xylitol intake has been recommended in the previous studies by Abdelwahab *et al*. [16] and Ribelles Llop *et al*. [17]. Participants were advised to not have any other chewing gum at the same time and to follow oral hygiene protocol using toothbrush and toothpaste. After 4 weeks, saliva samples of these subjects were collected spontaneously (non-stimulated saliva) into eppendorf tubes containing sterile physiological saline and transferred to laboratory within 1 hour for storage and preparation of quantitative tests.

Sampling saliva and quantification of S. mutans

Participants were instructed not to swallow their saliva for 1 min and then split out non-stimulating saliva into a sterile graduated test tube. Participants were asked to give 1 ml of saliva. All saliva samples were stored in a cold storage box at 4°C and then transferred to the lab for microbiological testing.

Saliva samples were quantified containing *S. mutans* by real-time PCR method at Central Laboratory, Central Hospital for Tropical Diseases of Vietnam, following the three-step process: DNA extraction (Using QIAamp DNA Mini Kit from Qiagen Company), Real-time PCR implementation (using the genesig gene Standard Kit *Streptococcus mutans* from Primerdesign) and the results were evaluated.

As the standard curve of this real-time PCR method was linear for samples containing from 10^4 cells to 10^8 cells per ml, only samples containing at least 10^4 cells/ml were used for analysis before and followed after intervention.

Statistical analysis

For statistical analysis, software SPSS version 11.5 (IBM, Chicago) was used for data

analysis. The normality of the data was analyzed using Anderson–Darling normality test. The changes in *S. mutans* counts were compared using a paired t test and Wilcoxon–Signed Ranks test. Mc Nemar test and Chi-square test were used to compare the differences between *S. mutans* counts before and followed intervention. Statistical significance was established at $p < 0.05$.

Ethics approval

The study was conducted in accordance with the ethical principles for clinical research described in the Declaration of Helsinki. The study protocol was approved by the Scientific and Ethical committee of the National Hospital of Odonto-Stomatology, Hanoi, Vietnam (no. 314/QD-TCCB signed May 30, 2018). The study took place at the National Hospital of Odonto-Stomatology from June 2018 to October 2018 in accordance with CONSORT guidelines for clinical trials. All participants of the study signed an informed consent form.

Results and Discussion

Quantitative results of *S. mutans* bacteria in saliva of 254 subjects showed that over 50% of subjects had no or too little *S. mutans*; 1.2% of subjects with *S. mutans* quantity below 10^4 CFU/ml of saliva; 26% of subjects had *S. mutans* quantity of 10^4–10^5 CFU/ml of saliva, the rest had *S. mutans* quantity of over 10^5 CFU/ml of saliva (19.7%). This result shows that nearly 20% of the subjects examined had a high risk of tooth decay. For subjects in saliva, in addition to normal oral hygiene measures, additional oral care measures are required to prevent tooth decay (Table 2).

Table 2: Quantitative results of *S. mutans* bacteria in saliva of 254 subjects

None		<10^4 CFU/ml		10^4–10^5 CFU/ml		≥10^5 CFU/ml	
N	%	N	%	N	%	N	%
135	53.1	3	1.2	66	26.0	50	19.7

Of the 80 participants included in the further studies, 57.5% initially had a *S. mutans* quantity of 10^4–10^5 CFU/ml of saliva; the rest of the *S. mutans* quantity exceeded 10^5 CFU/ml of saliva (Table 3).

Table 3: Saliva levels of *S. mutans* in participants using xylitol gum at baseline

	10^4–10^5 CFU/ml		≥10^5 CFU/ml		Total	
	N	%	n	%	N	%
Male	7	70.0	3	30.0	10	100.0
Female	39	55.7	31	44.3	70	100.0
Total	46	57.5	34	42.5	80	100.0

After 4 weeks of using xylitol chewing gum, the number of participants having the number of *S. mutans* more than 10^5 CFU/ml of saliva showed a reduction in levels from 42.5% to 30%, and 25% participants had no or too little *S. mutans* (Table 4). Thus, in our study, after using xylitol gum continuously 4 times/day for 4 weeks, the study results showed a decrease in the amount of *S. mutans* in the saliva of participants and the difference is statistically significant with $p < 0.001$. Our result is similar to the results of previously conducted studies such as the study of Ribelles Llop *et al.* [17].

Table 4: Saliva *S.mutans* level in participants using xylitol gum at 4 weeks

	None		<10^4 CFU/ml		10^4–10^5 CFU/ml		≥10^5 CFU/ml		Total	
	N	%	n	%	N	%	N	%	N	%
Male	4	40.0	0	0.0	4	40.0	2	20.0	10	100.0
Female	16	22.9	1	1.3	35	43.3	24	31.4	70	100.0
Total	20	25.0	1	1.3	35	43.8	24	30.0	80	100.0

Bacteria that can ferment sugars into lactic acid that exist in the oral cavity are considered to cause tooth decay. They mainly belong to three groups of microorganisms: *Streptococcus (Streptococcus mutans, Streptococcus sorbrinus, Streptococcus salivarius, Streptococcus milleri etc.), Lactobacillus (Lactobacillus acidophilus, Lactobacillus casei etc.), and Actinomyces*. Among these bacteria, *S. mutans* is always found in human saliva, plaque, and in very high numbers in tooth decay areas [18], [19].

S. mutans is considered the main cause of tooth decay as this bacterium has strong acidogenicity (ability to produce acid), good acid resistance, and the ability to create extracellular and intracellular polysaccharide, the main component of dental plaque. *S. mutans* has been isolated in saliva, plaque, and in cavities. The presence of *S. mutans* has also been associated with the progression of tooth decay, which gets reduced or lost in the absence of *S. mutans* [20], [21], [22]. On the other hand, being infected of *S. mutans* in experimental animals caused tooth decay in these animals. Therefore, measures to reduce *S.mutans* bacteria in the oral environment are necessary to reduce the risk of tooth decay [23].

Studies conducted under different conditions have shown that the use of xylitol effectively reduced tooth decay significantly in the high-risk group (with a high incidence of cavities, nutrition, and hygiene. poor mouth) as well as the low-risk group (with a low incidence of cavities, using all of the present preventive measures) [24], [25], [26]. Until now, sugar-free chewing gum using the main sweetener, xylitol, has been certified by many dental associations around the world.

Research evidence shows that *S. mutans* was xylitol target tissue in *in vivo* studies; *S. mutans* was reduced or low in studies with prolonged use of xXylitol as well as when use was discontinued; use of xylitol has the effect of reducing plaque accumulation; pregnant and lactating mothers using xylitol has the potential to reduce the risk of transmitting *Streptococus mutans* from mother to child; xylitol reduces the incidence of tooth decay in children [27], [28], [29].

Subjects with *S.mutans* in saliva above 10^5 CFU/ml were considered to be at high-risk of tooth decay. In this study, up to 42.5% of the intervention research subjects belong to this group. The study results showed that, after using Lotte xylitol gum continuously 4 times/day for 4 weeks, the number of subjects with high amount of *S.mutans* in saliva was statistically significantly (<0.05) decreased (Table 5).

Table 5: Changes in percentage of volunteers having high level of saliva S.mutans (≥ 105 VK/ml) at baseline and 4 weeks

	$<10^5$ CFU/ml	$\geq 10^5$ CFU/ml	Total
Baseline	46 (57.5%)	34 (42.5%)	80
At 4 weeks	56 (70%)	24 (30%)	80
P		<0.05*	

*Mc Nemar Test, Chi-Square test.

Conclusions

Clinical study on 80 adults showed that using Lotte xylitol gum containing 4.8g of xylitol, used 4 times/day, was effective in reducing the number of *S.mutans* bacteria in saliva when used daily in combination with tooth brushing.

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