

The Effect of Xylitol Preparations on Salivary Gland Function and Oral Health

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الخلاصة

الأهداف: تهدف هذه الدراسة تقييم تأثير مستحضرات الزايليتول المختلفة (علكة المضغ والرقائق) على منسبات اللثة والصفحة الجرثومية وعلى بعض مكونات اللعاب مثل الكالسيوم والبروتين وحمض اليوريك. **المواد وطرائق العمل:** أجريت الدراسة على 29 طالباً من كلية طب الأسنان الذين تراوحت أعمارهم ما بين 20-24 عاماً. تم تقسيم المشاركين بصورة عشوائية إلى مجموعتين، أعطيت المجموعة الأولى علكة الزايليتول، بينما أعطيت المجموعة الثانية رقائق الزايليتول لمدة 21 يوماً. تم قياس منسب اللثة والصفحة الجرثومية قبل وبعد العلاج، كما تم جمع اللعاب في نفس الوقت لغرض قياس نسبة سريان اللعاب وتركيز الكالسيوم والبروتين وحمض اليوريك في اللعاب. **النتائج:** أظهرت النتائج التأثير الإيجابي في تغيير بيئة الفم بعد العلاج بالزايليتول في المجموعتين. كان هنالك تقليل في منسب اللثة والصفحة الجرثومية في المجموعتين ولكن التقليل كان دالاً إحصائياً في المجموعة المعالجة بالرقائق (ل > 0,0001 و ل > 0,01 على التوالي). أدى استخدام هذه المستحضرات إلى تقليل دالاً إحصائياً في تركيز البروتين في اللعاب في مجموعة الرقائق (ل > 0,05) ومجموعة العلكة (ل > 0,0001) عند مقارنتها مع القياسات الأولية (ما قبل العلاج). إن رقائق الزايليتول كان لها تأثير واضح على منسب اللثة (ل > 0,0001) عندما مقارنتها مع مجموعة علكة الزايليتول. **الاستنتاجات:** إن الاستخدام المنتظم لمختلف مستحضرات الزايليتول له تأثير وقائي في الحفاظ على صحة الفم. **الكلمات الدالة:** الزايليتول، قياس سريان اللعاب، منسب اللثة، منسب الصفحة الجرثومية، صحة الفم.

ABSTRACT

Aims: To evaluate the effect of different xylitol preparations (chewing gum and strips) on gingival, plaque indices and salivary fluid composition (calcium, total protein and uric acid). **Materials and Methods:** Twenty nine healthy dental students aged 20-24 years, were divided randomly into two groups, the first group used chewing gum sweetened with xylitol and the second took xylitol strips for 21 days. The plaque and gingival indices were examined at the baseline and at the end of treatment, together saliva samples were collected in the same periods for the measurement of salivary flow and salivary concentration of calcium, total protein and uric acid. **Results:** The results confirmed on going changeability of the oral cavity environment after treatment with xylitol preparations in both groups. There were reduction in plaque and gingival indices in both groups, but it was significantly reduced in strip treated group ($P < 0.0001$ and $P < 0.01$ respectively). Salivary concentration of total protein was significantly decreased in strip group ($P < 0.05$) and in gum group ($P < 0.0001$) against baseline Values. Xylitol strips have pronounced effect on the gingival index ($P < 0.0001$) when compared with xylitol gum. **Conclusions:** The regular use of different xylitol preparations has its protective effects on the oral health hygiene.

Key Words: xylitol, Salivary flow, Gingival index, Plaque index, Oral health.

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INTRODUCTION

Xylitol is a naturally occurring form of the 5-carbon sugar alcohol. It is a true sugar replacement, have physiologic advantage of a pleasant and sweetness equal to

sugar with no after taste⁽¹⁾. Xylitol is currently available in many form, gum, mints, lozenges, tooth pastes and mouth washes⁽²⁾. Xylitol dissolve quickly and produces a cooling sensation in the mouth, stimu-

late saliva and sometimes used for relieving dry mouth⁽³⁾. Consumption of xylitol chewing gum is associated with a significant reduction in tooth decay because it inhibits the growth of bacteria which cause cavities^(4,5). In addition, regular xylitol consumption result in few cavities, improved periodontal health and reduce nasal sinus and throat infection^(6,7). Moreover, another study demonstrated that xylitol chewing gum decrease the amount and adhesiveness of plaque after regular xylitol consumption⁽⁸⁾. Experimental study concluded that dietary xylitol prevents weakening of bones in laboratory rats and actually improves bone density and appears to have potential as a treatment for osteoporosis⁽⁹⁾. Old study indicated that xylitol consumption caused a marked increase of amylase activity and total protein content in the parotid saliva⁽¹⁰⁾. However, recent study has showed that there was no linear association between salivary flow with total protein and no significant correlation with periodontal status⁽¹¹⁾.

Calcium is one of important inorganic content of salivary fluid⁽¹²⁾. Many studies have demonstrated the importance of salivary calcium with regard to both dental and gingival health. Sewon *et al.* (1998) Showed that a positive correlation between high salivary calcium content and periodontitis, and between high salivary calcium level and the number of intact teeth in selected groups of subjects⁽¹³⁾. Secretion of calcium in saliva depends upon salivary flow rate, so there is a negative correlation between calcium concentration and salivary flow rate⁽¹⁴⁾.

The concentration of uric acid in a mixed saliva has been reported as a range from 0.5 to 20.6 mg/100ml^(15,16). In recent years, it has been emphasized that the concentration of many of the constituents of saliva vary with flow rate and that composition of the saliva produced by individual gland differs from each others^(17,18).

The aim of this study is to evaluate the effect of xylitol preparation on the oral health and salivary flow and to measure the changes in some salivary fluid composition. In addition, this study was designed to show the effectiveness of xylitol strips and to compare its effectiveness with that of xylitol gum.

MATERIALS AND METHODS

1) Volunteer Selection

Healthy student volunteers in College of Dentistry / University of Mosul, (total number (n) =29, 9 males and 20 females) aged 20-24 year, were selected to participate in this study. All volunteers were non smokers and had no oral or systemic disease and were not taking any medication at the time of the study.

2) Method

The volunteers were randomly assigned into two groups. The first group (n=15), chewed the gum sweetened with xylitol (O2 + Xylitol 14%, Anadolu Eco-pack A-S, Turkey) for at least five minutes three times daily after meals for three weeks. Students in the second group (n=14) were asked to use Xylitol Strips (Fewei Fresh Breath Strips, Shanton Fewei Fruits and Nuts Manufacturing Co. Ltd. China). Three to five times a day immediately after eating and cleaning the mouth by swishing with water if possible. The duration of treatment for both groups were 21 days.

In order to determine the changeability of clinical and laboratory parameters, The evaluation was performed twice, at the beginning of the study on day 0, baseline assessment and after 21 day. The base line values was considered as the control negative group for this study and against which all the changes were evaluated. Oral cavity hygiene was evaluated using plaque index (PLI), and gingival index (GI) according to Silness and Løe index^(19,20). Saliva samples were collected on 0 and 21 days. All salivary samples were taken between 8.00 and 10.00 hours in the morning and the participants were instructed not to eat 1 hour prior to collection. Mixed resting saliva sample was collected after the subject had received their check up for oral hygiene⁽²¹⁾. The saliva was collected in special measuring bottle over a period of five minutes.

The concentration of calcium, total protein and uric acid were determined by colorimetric methods (O-Cresolphtalein complexone, Biuret and Uricase method respectively)⁽²²⁾ using a commercial kits (Biolabo reagents, Biolabo SA France).

3) Statistical analysis

Data were expressed as the mean \pm standard deviation (\pm SD), and percentage (%) throughout the paper. Means were compared using an independent or dependent sample Student's t-test as appropriate. To enable the reader to compare the changes in different parameters, the relative changes scores have been computed [relative change = ((post- pre) / pre) \times 100]⁽²³⁾. Computing this relative change index may result in different P values which were therefore also included. The relation

between the oral hygiene variables and biochemical parameters was explored by means of Pearson correlation coefficient(r). $P < 0.05$ was considered a statistically significant difference.

RESULTS

The data in table (1) represented the descriptive characteristics of both groups participated in the study.

Table (1): Descriptive characteristics of the volunteers

Characteristics	Xylitol chewing gum Group	Xylitol Strip Group	P- value
	Mean \pm SD N= 15	Mean \pm SD N= 14	
Male : Female	0 : 15*	9 : 4	.000
Age (years)	21.4 \pm 4.34	20.14 \pm 0.53	.292

N= Number of patients; * significant at $p < 0.001$

Differences between baseline values (control negative) of the analyzed parameters and those values obtained after 21 days of treatment could be observed in both groups. Table (2) shows the value obtained by chewing xylitol gum. The salivary flow rate was not significantly affected ($p = 0.208$), while GI and PLI were improved by 8.6% and 7.3% respectively, but this improvement were not statistically significant ($p = 0.323$ for GI and $p = 0.704$ for PLI). Salivary calcium and uric acid levels were elevated by 78% and 39.4%, but this was also not statistically significant ($p = 0.058$, and $p = 0.09$ respectively). Mean total protein level was decreased significantly ($p = 0.0001$) by 56.5%.

For the strip group, salivary flow rate was not significantly affect ($p = 0.322$), while both GI and PLI were significantly improved ($p = 0.0001$ and $p = 0.005$ respectively). The percentage of improvement

for GI was 56.5%, while it was 39.6% for PLI as shown in table (3). Also, the total protein level was significantly lowered ($p = 0.013$) by 44.8%. Salivary calcium and uric acid levels were elevated (84.5% and 31.5% respectively), but this changes were not statistically significant ($p = 0.247$ and $p = 0.892$).

There were no significant differences between both groups at beginning on day 0 (control) for all of the parameters measured except for the PLI which was significantly lower ($p < 0.05$) in the first (chewing gum) group (0.796 ± 0.45) when compared with the second group (1.11 ± 0.28) (table 4).When comparing the effect of the two xylitol preparations with each other, GI was significantly improved ($p < 0.05$) in the xylitol strip when compared with those obtained from xylitol gum group, as shown in table (4).

Table (2): Changes in Mean Oral Cavity Hygiene Indices and Salivary Composition From the Baseline Sample to the 21 Days After Treatment in Xylitol Chewing Gum Group.

	control Mean ± SD	21 days after treatment Mean ± SD	% of hanges	P- value
Salivary flow rate (ml /5 min)	2.6 ± 1.08	2.3 ± 0.97	-11.5%	.208
GI	1.02± 0.37	0.93 ± 0.44	-8.6%	.323
PLI	0.8± 0.45	0.74 ± 0.35	-7.3%	.704
Ca (mMol/L)	1.55± 0.10	2.76±0.29	78%	.058
Total protein (g/100ml)	0.55±0.23	0.24 ± 0.099*	-56.5%	.000
Uric acid (mMol/L)	1.38±0.71	1.92 ± 1.51	39.4%	.09

significant at $p < 0.05$

Table (3): Changes in Mean Oral Cavity Hygiene Indices and Salivary Composition From the Baseline Levels (control) to the 21 Days After Treatment in Xylitol Strip Group.

	Control Mean ± SD	21 days after treatment Mean ± SD	% of changes	P -value
Salivary flow rate (ml /5min)	3.65 ± 1.68	3.4±1.44	-6.9%	.322
GI	1.14±0.41	0.5±0.46***	-56.5%	.000
PLI	1.11± 0.28*	0.67±0.43**	-39.6%	.005
Ca (mMol/L)	1.1± 0.05	2.03±0.26	84.55%	.247
Total protein (g/100ml)	0.43±0.22	0.24±0.27*	-44.8%	.013
Uric acid (mMol/L)	1.86±1.14	1.92±1.29	31.5%	.892

*** significant at $p < 0.0001$, ** $p < 0.01$, * $p < 0.05$

Table (4): Comparison between Mean(\pm SD) of Changes in Oral Cavity Hygiene Indices and Salivary Composition for Xylitol chewing Gum and Strip Treated Groups.

Parameters	Control		P- value	21 days after treatment		
	Xylitol chewing gum Group Mean \pm SD N= 15	Xylitol Strip Group Mean \pm SD N= 14		Xylitol chewing gum Group Mean \pm SD N= 15	Xylitol Strip Group Mean \pm SD N= 14	P- value
Salivary flow rate (ml / 5 min)	2.6 \pm 1.08	3.65 \pm 1.68	.231	2.3 \pm 0.97	3.4 \pm 1.44	.152
GI	1.02 \pm 0.37	1.14 \pm 0.41	.414	0.93 \pm 0.44	0.5 \pm 0.46*	.015
PLI	0.8 \pm 0.45	1.11 \pm 0.28*	.031	0.74 \pm 0.35	0.67 \pm 0.43	.662
Ca (mMol/L)	1.55 \pm 0.10	1.1 \pm 0.05	.144	2.76 \pm 0.29	2.03 \pm 0.26	.478
Total protein (g /100ml)	0.55 \pm 0.23	0.43 \pm 0.22	.154	0.24 \pm 0.099	0.24 \pm 0.27	.956
Uric acid (mMol/L)	1.38 \pm 0.71	1.86 \pm 1.14	.184	1.92 \pm 1.51	1.92 \pm 1.29	.990

* significant at $p < 0.05$

There were no significant different in other parameters measured. This difference was confirmed by analyzing the relative changes between the groups as shown in table (5), in which the significant improvement of GI in xylitol strips group

($p < 0.0001$) was confirmed when compared with the chewing gum group (figure 1), but there were no significant differences between other parameters measured in both groups.

Table (5): Mean Relative Changes Scores (%) in Oral Cavity Hygiene Indices and Salivary Composition for Xylitol chewing Gum and Strip Treated Groups.

	Xylitol chewing gum Group Mean \pm SD N= 15	Xylitol Strip Group Mean \pm SD N= 14	P -value
Salivary flow rate(%)	3.488	3.49	.384
GI (%)	6.38	62.01***	.000
PLI (%)	9.16	36.29	.145
Ca (%)	-72.94	-211.37	.276
Total protein (%)	49.36	40.86	.630
Uric acid (%)	-45.84	-70.91	.717

*** significant at $p < 0.0001$

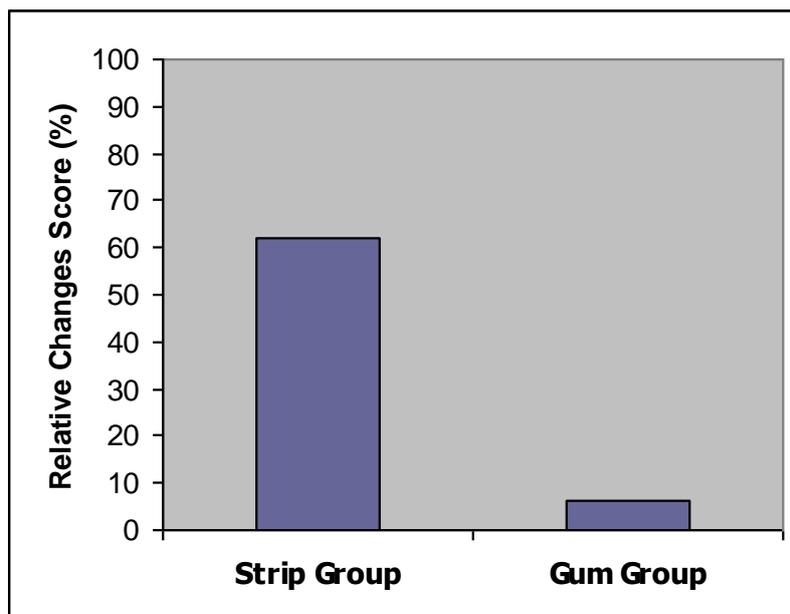


Figure (1): Comparison Between Mean Relative Changes Scores (%) in Gingival index for Xylitol Chewing Gum and Strip Treated Groups.

Analyzing the relations between different parameters after treatment a linear correlation was demonstrated between GI and PLI ($r = +0.452, p = 0.014$) (figure 2), and between calcium and GI ($r = +0.416, p = 0.012$) as shown in figure (3). While salivary calcium has a positive correlation with the uric acid ($r = + 0.483, p$

$=0.008$) (figure 4). A positive linear correlation was obtained also between GI and total protein($r=+0.327, P=0.016$) as shown in figure (5).

During the whole study period, no negative side effects such as stomach troubles were reported.

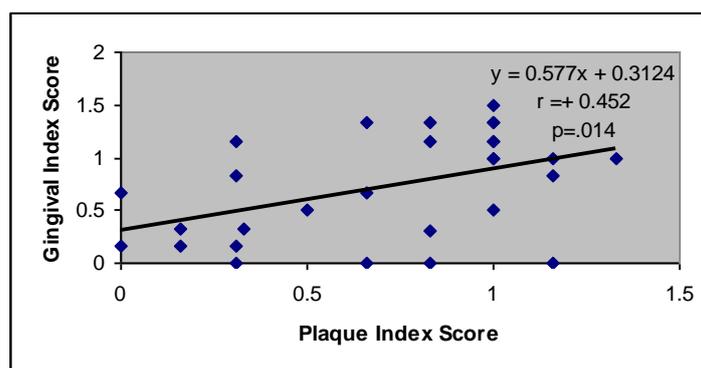


Figure (2): Linear correlation between GI and PLI.

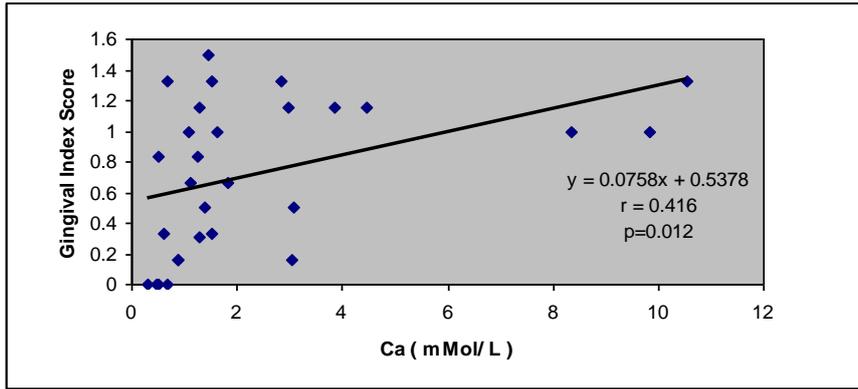


Figure (3): Linear correlation between GI and Salivary Calcium.

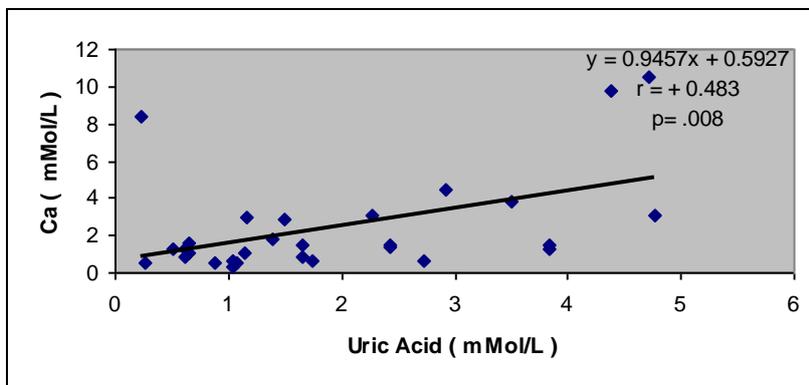


Figure (4): Linear correlation between Salivary Calcium and Uric Acid.

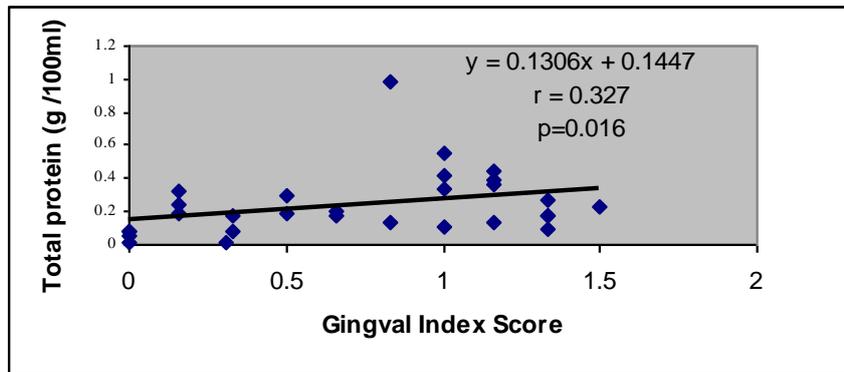


Figure (5): Linear correlation between GI Score and Salivary Total protein.

DISCUSSION

This study is a part of an investigation in the effect of different xylitol preparations on salivary composition. Xylitol is a sweet – sugar substitute that has been approved for use in more than 35 countries and has along safety history. It is relatively well accepted in the body, although ex-

cessive intake may cause intestinal side effect ^(1,2,5). In our study no any side effects were reported.

The results in this study showed that xylitol uses for 21 days has no effect on salivary flow rate for both preparations and this results are consistent with that of Soderling *et al*(1989) were no effects of

xylitol chewing gum on salivary flow were observed, in contrast to other studies where a significant increment in salivary flow rate were reported^(25,26). Gum chewing, could attribute to the context of salivary stimulation since it has been shown to elicit a continued flow of saliva during prolonged mastication. Jenkins and Edgar (1989) found that two weeks of daily chewing of sugar less gums increase salivary flow, PH and buffer capacity of unstimulated saliva⁽²⁶⁾.

In this study the large differences in salivary flow rates among subjects were observed for the unstimulated state, and this could explain while no significant statistical effect on salivary flow rate were reported.

The improvement in the GI and PLI were similar to those observed in other studies^(2,25,26). Autio-Gold *et al* (2005) studied the effect of xylitol gum by measuring the levels of salivary *mutans streptococci* before and after a three week chewing period in (3 – 4) years old children, chewing the xylitol gum reduced the levels of salivary *mutans streptococci* there by possibly reducing the risk for dental caries in those children. Xylitol actually inhibits the growth of the bacteria that cause cavities because these bacteria cannot utilize xylitol to grow⁽²⁾. Over time with xylitol use the quality of the bacteria in the mouth changes and fewer decay causing bacteria survive on tooth surfaces, less plaque forms and the PLI will be lowered. In conjunction, these studies^(2,4,5,27) provide evidence that by the chewing of sugar free gum, the plaque PH fall following consumption of fermentable carbohydrates can rapidly returned towards resting levels, where it persists for the duration of the experiment. Researches now believe that gum sweetened with xylitol can prevent chronic sinusitis and some of the more serious throat and lung infections. This is tremendously significant since recurrent otitis media is the number one reason for children's visits to doctors⁽²⁸⁾. It is also possible that the virulent bacterial flora present in the aero-digestive tract can be favorably affected by systemic xylitol use⁽²⁹⁾.

Xylitol reduces the incidence of periodontal disease by preventing bacterial

adhesion to the epithelia cells⁽²⁹⁾. Researchers demonstrated that the mucosal attachment of *Streptococcus Pneumonia* and *Haemophilus Influnzae* will be reduce by 68% and 50% respectively⁽⁷⁾, this could explain the improvement in the GI seen in this study. The differences in the effect of both preparations on the GI could be explained by the fact that xylitol strips contain thymol and peppermint oil in their composition, and both of them have strong anti inflammatory and wide antibacterial activities⁽³⁰⁾.

The changes in the oral health indices were associated with some changes in the salivary fluid composition and this was seen by the increase in calcium and uric acid levels associated with significant decrement in total protein levels and this is in agreement with many studies^(9,10,25).

The regular use of chewing gum had been shown to be one of the means that promote remineralization due to the accompanying enhancement of salivary flow and buffering capacity^(2,7,31). The concentration of calcium in the fluid phase surrounding teeth is one of the primary factors that determines whether a tooth remineralizes or demineralizes⁽¹³⁾. Xylitol binds with calcium and other polyvalent cations, contributing to remineralization of the enamels^(31,32,33). The calcium – xylitol complexes facilitate calcium absorption through the gut wall, this suggests that xylitol may play a role in preventing osteoporosis⁽⁹⁾. The increase in calcium levels also was associated with the improvement in the GI and this is in agreement with other studies^(13,14). These studies have demonstrated the importance of salivary calcium with regard to both dental and gingival health, they Showed that there were a positive correlation between high salivary calcium content and periodontitis, and between high salivary calcium level and the number of intact teeth in selected groups of subjects. Those studies^(13,14) and others^(8,4,11) have revealed that various biological and physiochemical functions mediated by both inorganic and organic component of the saliva are co-responsible for the dynamics of the processes contribute for good oral cavity environment, particularly saliva and dental plaque, as well as bacteria, which provide

conditions that facilitated teeth demineralization. It is therefore still an open question whether the use of oral hygiene products like xylitol preparations and appropriate sanitation procedures (fluoride, chlorhexidine) may change the existing tooth - dental plaque - saliva equilibrium.

Statistically significant difference could be observed between the level of total protein at baseline and after three weeks of treatment. This is consistent with the finding of others^(25,26), where total protein were found to be lowered and associated with caries activity in these studies. Total protein is selected as one of the reference for total antioxidant parameters in the mouth because of its complex nature and presence of albumin as one of its major constituent⁽¹⁸⁾; in addition saliva osmolarity are dependent partly on protein concentration and this will affect the process of diffusion that occur between the solid and liquid phases in the oral cavity⁽¹⁷⁾, and this may explain the linear association between the total protein content with improvement in the GI as confirmed in this study. Early study had found that whole saliva amylase activity increased during xylitol consumption⁽¹⁰⁾, but this was opposed by others^(18, 26). It may, therefore, be said that xylitol administration had lead to a new state of equilibrium between the parameters that characterize oral cavity environment.

Uric acid is the most abundant aqueous antioxidant in humans^(34,35). It constitute one of the three main salivary antioxidants(uric acid, ascorbic acid, and albumin)^(15, 16). The presence of antioxidant bathing the gingival cervices may be of major importance in damping down inflammatory processes initiated by bacterial infection⁽¹⁸⁾. No study was found to report the effect of xylitol on uric acid levels in saliva, but one study had found that xylitol increases serum antioxidant activity in a dose related manner when administered intravenously to healthy human volunteers⁽³⁵⁻³⁷⁾, and this may explain the increment of uric acid level in this study. The linear association between calcium and uric acid levels after treatment could explain the protective effect of xylitol on general oral health, and its effective role in preventive programs.

CONCLUSIONS

This study clearly show's the benefit of xylitol preparations on oral health, and that breath strips were more effective than chewing gum as a Xylitol delivery vehicle to be used especially habit of chewing is unacceptable in our society and breath stripes are more accepted and easy to be used and more safe because chance of choking is minimal if not their as the strip will immediately dissolve in the saliva once it touches the tongue.

Using xylitol preparations should be promoted in our society as it may offers an additional efficacious, cost effective oral health preventive strategy for small children and adult when other preventives methods are difficult to implement.

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