ORIGINAL ARTICLE

Evaluation of the Efficacy of Chlorhexidine Chewing Gum in Controlling Plaque Formation: A Clinical Trial

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ABSTRACT

Objective: The present study was conducted to evaluate the efficacy of chlorhexidine containing chewing gum in controlling plaque formation and compare its effects with chlorhexidine mouthwash.

Materials and Methods: Twenty dental students volunteered to participate in this double blind three times cross over study. Three, 7-day test periods were designed to utilize chlorhexidine mouthwash, chlorhexidine chewing gum and control chewing gum twice daily in different test periods respectively. Plaque scores were assessed at the end of each test period and the results were statistically analysed. Salivary samples were collected after using chlorhexidine mouthwash and chlorhexidine chewing gum to assess the substantivity of chlorhexidine upto 12 hours.

Results: Mean plaque scores for chlorhexidine mouthwash, chlorhexidine containing chewing gum and the placebo chewing gum were 1.51, 1.74 and 2.95 respectively. The substantivity of chlorhexidine in the oral cavity was found to be of similar for chlorhexidine mouthwash and chlorhexidine chewing gum.

Conclusion: This study demonstrated that chlorhexidine chewing gums were more efficient in controlling plaque formation as compared to control chewing gums. However, the chlorhexidine mouthwash was marginally better in controlling plaque formation as compared to the chlorhexidine chewing gum.

Keywords: Chewing gum, Chlorhexidine, Plaque

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INTRODUCTION

Although, numerous chemical agents directed against plaque are available, the use of chlorhexidine as an adjunct or even a short-term replacement to oral hygiene procedures has become well established.[1] Following the encouraging results for chlorhexidine mouthwashes to control plaque formation, a variety of vehicles have been utilized to deliver this antimicrobial including "chewing gums".[2,3] Addition of chemical agents to chewing gum has been tried since 1924 when the first medicated chewing gum; "Aspergum" (containing aspirin) hit the markets. Following this there has been a burst of activity around the globe involving incorporation of numerous agents into chewing gums (e.g. fluorides, nicotine etc.) although with varied success.

Early investigations revealed gum chewing to have no beneficial effect on gingival inflammation and calculus formation, although later work showed that sorbitol-containing gum reduced plaque and that xylitol gum reduced it even further.[4,5] Addy *et al*.[6] found that both sucrose gum and sugar free gum reduced plaque accumulation and removed established plaque, compared with no gum, albeit in the absence of oral hygiene measures. Similarly, numerous investigators have shown that chlorhexidine when delivered through chewing gum effectively prevents plaque growth.[3,4,7]

The present study was undertaken to evaluate chlorhexidine's efficacy in controlling plaque formation when delivered through the medium of a chewing gum. If proven beneficial it would pave the way for the routine use of this delivery system as an adjunct to mechanical plaque control.

MATERIALS AND METHODS

Present study was conducted in the Department of Periodontics, Manipal College of Dental Sciences, Manipal, Karnataka, India after obtaining the institutional ethical committee's clearance. A total of 20 dental students including 14 males and 6 females in the age group of 23-25 years volunteered to participate in this double blind placebo controlled cross over clinical trial. An informed consent before the start of the trial was obtained from all the participants. The subjects qualifying for the study had a minimum of 20 permanent teeth. Grossly carious, fully crowned or fully restored teeth and 3rd molars were not included in the tooth count.

The test chewing gum contained gum base 1.5 g, chlorhexidine gluconate 20 mg, artificial sweetener (Aspartame), mint and flavouring agents. The placebo chewing gum contained gum base 1.5g, artificial sweetener (Aspartame), mint and flavouring agents. The mouthwash used as a positive control contained 0.2% chlorhexidine gluconate, preservatives and flavouring agents. The chewing gums were manufactured at the College of Pharmaceuticals Sciences, Manipal and the mouthwash was prepared by the Pharmacy Manufacturing Wing, Kasturba Medical College and Hospital, Manipal.

Methodology: The study comprised of three, 7-days test periods (Phase I, Phase II and Phase III) during which the subjects used the test and placebo products twice daily. Same subjects crossed over to the next phase after a washout period of 20 days. Professional cleaning and polishing was instituted at the beginning of each test period to bring down the plaque scores to a minimum or baseline level. The subjects were recalled at the end of the study period to assess for the plaque scores through Turesky modification of the Quigley-Hein plaque index (Q-H Index) using a disclosing agent (erythrosine). In Phase I chlorhexidine mouthwash was given to the subjects, in Phase II chlorhexidine containing chewing gums and in Phase III the control chewing gums as revealed later by decoding the results. No mechanical oral hygiene measures like tooth brushing and flossing were allowed during the test periods. In all other aspects, the test subjects were advised to adhere to their normal dietary habits. However, during the washout periods the subjects were asked to return to their normal oral hygiene habits.

Neither the subjects nor the dental examiner were aware of the group to which they belonged for the use of test product (chewing gum). The test product was assigned to the subjects by a third person at the start of each period. The chewing time for the test product as determined by the pilot study was 20 minutes and the mouthwash was used as per the standard mouth rinsing time i.e. 60 seconds.[1]

Parameters recorded: Plaque scores (Q-H Index) were recorded at baseline, and end of each phase. To assess the oral retention (persistence) of the drug (chlorhexidine) in the oral cavity, salivary samples from 10 subjects divided into 2 groups (5 each in a group) were obtained immediately after using the test products (chlorhexidine mouth rinse for 60 seconds and chlorhexidine containing chewing gum for 20 minutes) at 0, 1, 2, 4, 6, 8, 10 and 12 hours. The salivary samples were subjected to spectrophotometric analysis to determine the amount of drug present in saliva at a particular time interval.

Statistical Analysis: The data collected was analysed using the statistical package, SPSS/pc+. Students-'t' test and Kruskal Wallis test were employed in order to compare the associations among the different phases. P-value of less than 0.05 and 0.001 were considered to be statistically significant and statistically very highly significant respectively.

RESULTS

At the beginning of each phase the plaque scores were brought down to zero by professional cleaning and polishing. The increase in mean plaque scores with standard deviation at the end of 7-day test period for phase I (chlorhexidine mouthwash) was 1.51 (0.28), for phase II (chlorhexidine containing chewing gum) was 1.74 (0.35) and for phase III (placebo chewing gum) was 2.95 (0.38) (Table I) (Fig. 1 to 4).

Table I: Plaque (Turesky Modification of Q-H plaque Index) scores with mean and standard deviation (SD) at the end of each phase.

Phase	Minimum	Maximum	Mean	SD
I (Chlorhexidine mouthwash)	0.98	1.86	1.51	0.28
II (Chlorhexidine chewing gum)	1.27	2.38	1.74	0.35
III (Control chewing gum)	2.16	3.52	2.95	0.38

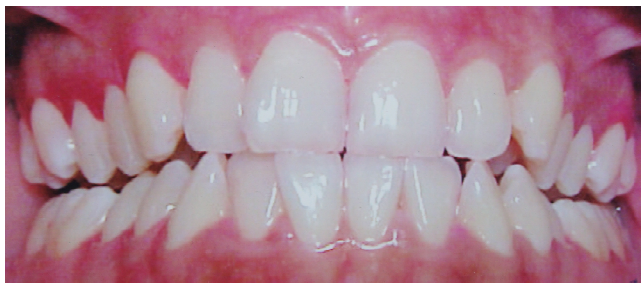

Figure 1: Immediate after scaling and polishing.

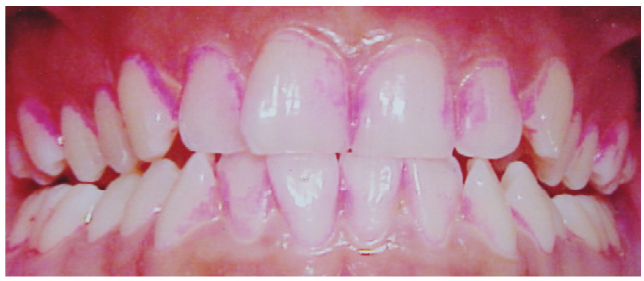

Figure 2: After using chlorhexidine mouthwash.

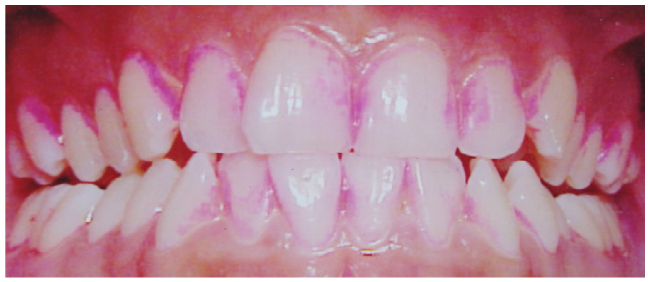

Figure 3: After using chlorhexidine chewing gum.

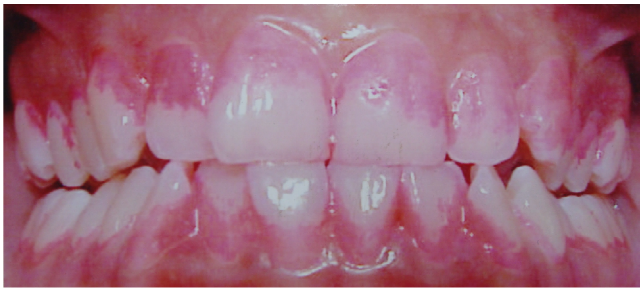

Figure 4: After using placebo chewing gum.

When a comparison of mean plaque scores among the 3 phases was done, it was not statistically significant ($p>0.05$) between phase I and phase II, but very highly significant ($p<0.001$) between phase I and phase III and phase II and phase III (Table II).

Table II: Comparison of mean plaque scores among the three phases (Kruskal Wallis Test).

Comparison	z	P*	Remarks
Phase I vs Phase II	1.820	0.069	Not significant
Phase I vs Phase III	5.126	0.000	Very highly significant
Phase II vs Phase III	5.049	0.000	Very highly significant

(*$p<0.001$ is considered as very highly significant)

When salivary samples were collected after a single rinse with 10 ml 0.2% chlorhexidine mouthwash for 1 minute, at 0, 1, 2, 4, 6, 8, 10 and 12 hours and analyzed spectrophotometrically for the drug persistence the result showed a substantial amount of drug retention in the oral cavity upto 12 hours. It was also seen that there was not much difference between the concentration of chlorhexidine found in saliva during the initial part and at the end of the experiment (Table III) (Fig. 5).

Table III: Mean values for chlorhexidine in salivary samples

Time (hours)	Chlorhexidine from Chlorhexidine Mouthwash (g/mg of saliva)	Chlorhexidine from Chlorhexidine containing Chewing gum (g/mg of saliva)
0	2.33	1.73
1	2.60	1.98
2	2.57	2.59
4	2.09	2.18
6	2.30	2.20
8	2.51	2.40
10	2.44	1.26
12	1.63	1.15

Similarly, a single piece of chlorhexidine containing chewing gum when chewed for 20 minutes and the salivary samples

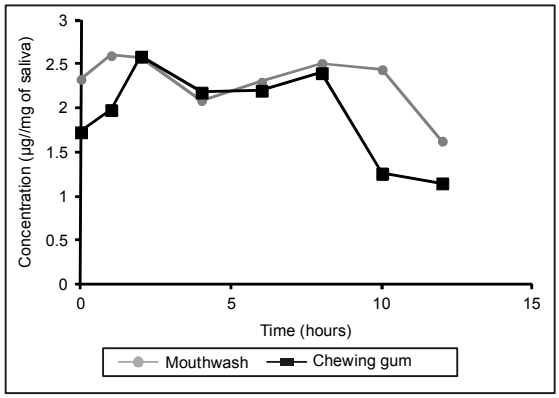

Figure 5: *In vivo* concentrations of chlorhexidine in saliva after using the chlorhexidine mouthwash and chlorhexidine chewing gum.

analyzed at 0, 1, 2, 4, 6, 8, 10 and 12 hours showed a substantial amount of drug retention upto 12 hours. It was noted that the concentration of chlorhexidine in the saliva during the initial part of the experiment with chewing gum was considerably less when compared with the mouthwash. However, the concentration became equivalent to that of the mouthwash by 2 hours from the start of the experiment.

DISCUSSION

Commercially viable chlorhexidine chewing gum by the name of Chew-X was introduced in Switzerland as documented by Imfeld.[8] However, it is yet to be popularized in the other parts of the world. In India, none of the companies manufacturing chewing gums have ventured into this field. Hence, present study utilised custom made chewing gums. Another rationale of using custom made mouthwash and chewing gum was to standardize the products and to keep the variables at minimum for example use of same flavouring agents and sweeteners. Plaque formation was substantially inhibited by the chlorhexidine containing chewing gum when compared with the placebo chewing gum with the results being statistically very highly significant. However, when the results of chlorhexidine containing chewing gum were compared with the chlorhexidine mouth rinse it was seen that the mouth rinse had a marginally better plaque inhibiting properties. These results are consistent with the earlier findings of Ainamo *et al.*,[2] Smith *et al.*,[9] Tellefsen *et al.*[10] and Simons *et al.*[11] who have also demonstrated substantial plaque inhibition via chlorhexidine containing chewing gums. This suggests that chlorhexidine containing chewing gums can be used as an adjunct to routine oral hygiene procedures. Also, Simons *et al.*[12] suggested that its use may be considered for hospitalized and dependent geriatric patients as there is an ease of dispensing and not requiring the use of water. Patients with xerostomia and those at high caries risk may benefit this product as there is an increase in salivation using a chewing gum; however, further studies are required before an actual implementation is made.

In the present study the amount of chlorhexidine incorporated in the test chewing gum was 20 mg/piece i.e. total daily dosage of 40 mg chlorhexidine. This was done in order to match the daily dosage of 0.2% chlorhexidine mouth rinse that was utilized 10 ml twice daily. Although Ainamo *et al*.[2] had utilized 50 mg total daily dosage of chlorhexidine in their study, they optimized it to 20 mg in a subsequent short-term trial conducted in 1990. According to them even at this dosage plaque inhibitory activity of chlorhexidine was maintained when delivered through chewing gum and was comparable to 0.2% chlorhexidine mouth rinse. They also reported that dosages less than 20 mg of chlorhexidine did not provide sufficient plaque inhibition effect. Smith *et al*.[9] confirmed this finding in a long-term study conducted over a year in 151 subjects where chlorhexidine chewing gums were used as an adjunct to mechanical oral hygiene procedures.

Since chlorhexidine is poorly absorbed from the GIT and exhibits a remarkably low level of toxicity, a 40 mg total daily dosage in the present study appears to be harmless even if swallowed in its entirety. None of the participants in the present study reported any adverse reaction with the use of chlorhexidine when delivered through the chewing gum as also reported by Tellefsen *et al*.[10] This low toxicity of chlorhexidine and its poor penetrability through the mucosa has earlier been demonstrated by Haugen and Johansen,[13] who have attributed this property of chlorhexidine to its cationic nature.

Another observation made during the conduct of this study was that the test chewing gum had a more pronounced effect on the posteriors when compared to the anterior teeth, with regard to plaque inhibition. Even in the anterior teeth there was a difference with facial surfaces showing more plaque formation than the oral surfaces. This variation could be attributed to the mechanical cleaning action of the chewing gums itself and more importantly the muscular action of the cheek and tongue on the surfaces of the posterior teeth during chewing. Similar findings have also been reported by Glavind *et al*.[14]

The results obtained from the salivary samples show a substantial amount of chlorhexidine even 12 hours after rinsing with the chlorhexidine mouth rinse for 60 seconds and chewing of the test chewing gum for 20 minutes. However, the concentration of the chlorhexidine found in the saliva of the subjects who rinsed with the mouth rinse was considerably higher during the first 2 hours than in those who used the test chewing gum. This suggests that there was a higher amount of chlorhexidine that was available immediately after using the mouth rinse. This study confirms the previously established property of substantivity exhibited by chlorhexidine in the oral cavity. Rolla[15] and Roberts[16] had shown substantivity of chlorhexidine upto 5 hours whereas Loe and Schiott,[1] and Bonesvoll *et al*.[17] reported a substantivity of 12 hours with traces being found even after 24 hours of usage of chlorhexidine. Observation periods need to be extended if this product is considered for longer-term use. In addition, future studies should include observations of staining, change in the gingival status, site specificity for the action of chewing gums and the optimal dosage of the medicament being delivered through the chewing gums.

Microbiological assessment for the efficacy of chlorhexidine containing chewing gum may be considered in future studies. Although, Marwaha and Bhat[18] in their clinical trial reported that 20 mg daily dosage of chlorhexidine effectively reduced the levels of salivary *Streptococcus mutans*, the effect of chlorhexidine chewing gum on the varied plaque bacteria is still an open arena for future research.

Thus, the use of this medicament containing chewing gum can be recommended as an adjunct to routine oral hygiene procedures. Also, the thought of substituting mechanical hygiene measures with an effective chewing gum product has significant appeal from a convenience and compliance perspective. Based on these observations of the present study, it can be concluded that chlorhexidine containing chewing gum may prove beneficial for plaque control.

- Chlorhexidine chewing gum has been shown to inhibit plaque formation effectively when compared to the control chewing gum (placebo).
- The 0.2% chlorhexidine mouth rinse had a marginally better plaque control effect than the chlorhexidine chewing gum.
- The chewing gum and the mouth rinse used in this study showed comparable oral persistence of the drug at 12 hours.

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