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## RESEARCH ARTICLE

### EVALUATION OF A COMMERCIALY AVAILABLE GLYCCYRHIZAGLABRA FLAVORED CHEWING GUM FOR REDUCING DENTAL PLAQUE AND GINGIVITIS IN DIABETIC PATIENTS

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#### ABSTRACT

**Purpose:** Gingival inflammation in response to the accumulation of dental plaque is aggravated by systemic factors such as diabetes. In adults with type 2 diabetes, it may occur at higher rates than those in adults without diabetes. Many products have been researched to counter both inflammation and higher glucose levels, one such natural product is Glycyrrhizaglabra, also known as licorice and sweet wood which has many pharmaceutical properties such as anti-inflammatory, anti-hyperglycemic, anti-bacterial, anti-ulcer, anti-viral and anti-carcinogenic effects. Chewing gum has been used for centuries to clean the mouth and freshen the breath. Thus, in this study we are evaluating the use of flavored chewing gum as an adjunct to toothbrushing in diabetic patients.

**Materials and Method:** 20 subjects with diagnosed with diabetes (FBS-125-140mg/dl) and chronic generalized gingivitis were included in this randomized, clinical study. Initial clinical parameters plaque and gingival index were assessed and baseline unstimulated saliva collected. After completion of scaling patients were randomized into control and test group. Test group patients were asked to chew gum twice daily after brushing for 2 min. Control group were asked to chew placebo gum twice daily after brushing for 2min. Clinical measurements were repeated at 6 week interval.

**Results:** There was a significant decrease in plaque and gingival index within each group and were insignificant when both the groups were compared ( $p > 0.05$ ). There was no change in unstimulated saliva both within the group and on intergroup comparison.

**Conclusion:** Our results showed improvement in plaque score and gingival health when licorice was used along with tooth brushing. In future, higher concentrations or different concentrations of licorice in a long term study with larger sample size is required to ascertain the efficacy of glycyrrhiza or its extract in the treatment of gingival diseases.

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## INTRODUCTION

There is sufficient literature regarding the relationship between gingival disease and diabetes. It is generally admitted that diabetes alone will not give rise to the appearance of gingival disease. However, it does favor the modification of the gingival periodontal sphere and can make it easier for the clinical picture to deteriorate when the bacterial plaque presents as an initiating factor of the disease (Arrieto Blanco *et al.*, 2003). The gingival of untreated diabetics generally have an intense red color, is edematous and may be painful with suppuration. This situation makes it necessary for the patients to receive periodontal therapy as the first step towards a healthy mouth. Studies have demonstrated that long-term stability of the clinical benefits obtained via periodontal

therapy can be maintained only when cause-related treatment is followed by effective supportive periodontal care (SPC) (Becker *et al.*, 1984). Within this SPC program, self-performed plaque control is crucial in attaining the best long-term results after periodontal therapy (Lindhe *et al.*, 1984). As patient compliance with mechanical oral hygiene practices are not always as good as desired, chemical agents have been used to improve plaque control and to reduce gingivitis (Escribano *et al.*, 2010). Natural products such as propolis, mastic gum, green tea have been successfully used as an adjunct to mechanical plaque control and has thus, played a pivotal role in SPC. One such product Glycyrrhizaglabra, also known as licorice and sweet wood, is native to the Mediterranean and certain areas of Asia. The name Glycyrrhiza comes from the Greek words "glykos," meaning sweet and "rhiza," meaning root. It has many pharmaceutical properties such as anti-inflammatory, anti-bacterial, anti-ulcer, anti-viral and anti-carcinogenic effects (Jacobsen *et al.*, 2004). Various methods

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of delivery for these natural products have been used of which chewing gum has been found to be a convenient modified release drug delivery system (Monica Damle, 2014). Dry mouth (xerostomia) is a common known symptom among the diabetics which could be indirectly related to gingival disease as the salivary flow rate decreases favoring plaque accumulation (Arrieta-blancojj and bartolomé-villar, 2003). Flavored chewing gums have been found to be effective in increasing the salivary flow rate, thereby decreasing plaque accumulation. It was hypothesized that chewing gum incorporated with Glycyrrhizaglabra may act by its anti-inflammatory and anti-bacterial effect as well as improve the gingival condition of diabetics by increasing the salivary flow. Hence, this study was carried out to evaluate the use of Glycyrrhizaglabra flavored chewing gum as an adjunct to toothbrushing in diabetic patients.

## MATERIALS AND METHODS

Commercially available Glycyrrhizaglabra flavored chewing gum was used.

### Study population

A total of 20 subjects from Department of Periodontology, JSS Dental College a constituent of JSS university, Mysuru were taken for the study. Screening and selection of volunteers were carried out by a single investigator who explained the study and obtained signed consent from the participants. The subjects recently diagnosed with diabetes (Fasting blood sugar 120-170 mg/dl) with no other systemic disease, both males and females in the age range of 35-50 years with at least 20 natural teeth, who experienced bleeding of gums and erythematous gingiva were selected. The exclusion criteria included systemic problem other than diabetes, recession, other signs of periodontitis, temporomandibular joint disorders, mal occlusions and chronic onychophagia. The female subjects enrolled were not pregnant or nursing. In particular, no subject had received mouth rinses, gels, or chewing gums containing antimicrobial agents in the preceding 3 months.

### Study Design

The study was designed as a randomized, parallel arm controlled study. All procedures performed in study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The effect on plaque growth and gingivitis of a chewing gum containing glycyrrhizaglabra was assessed in a randomised clinical trial with 20 adult volunteers. At baseline, Plaque index: By Sillness and Loe (PI) and Loe-Sillness gingival index (GI) was recorded and unstimulated saliva was collected by asking the patient to sit in a relaxed and upright position and to allow all saliva to drain into a beaker by drooling or gentle spitting. They were instructed not to masticate, swallow, or speak. Saliva was collected for a period of 5 min. All the subjects received phase I therapy (full mouth scaling and root planning). Then the subjects were randomly allocated using coin toss method into the control group (toothbrushing only) comprising of 10 volunteers while the remaining 10 were categorized under test group (toothbrushing and licorice flavored gum). Patients in control group were asked to brush their teeth twice daily using a standard toothbrush and toothpaste following the Roll technique for 2 min and to chew

a placebo gum. Patients in test group were asked to chew the flavored gum (1 pellet, 1.3g) twice daily in addition to brushing using standard toothbrush and Roll method of brushing for 2 min. At 6<sup>th</sup> week patients returned and refrained from all oral hygiene on the day of examination. This provided a standardised period since the last tooth cleaning and use of product of approximately 10-12hr. Patients were recalled after 6 weeks for recording of the clinical parameters and unstimulated saliva was also collected at a 5 min interval.

### Statistical Analysis

The values obtained from the clinical data were subjected to following statistical analysis

- Descriptive statistics (mean and standard deviation)
- Student 't' test for independent samples

The statistical package for social science (SPSS version 22) for windows software was used. The level of significance was set at  $p < 0.05$ .

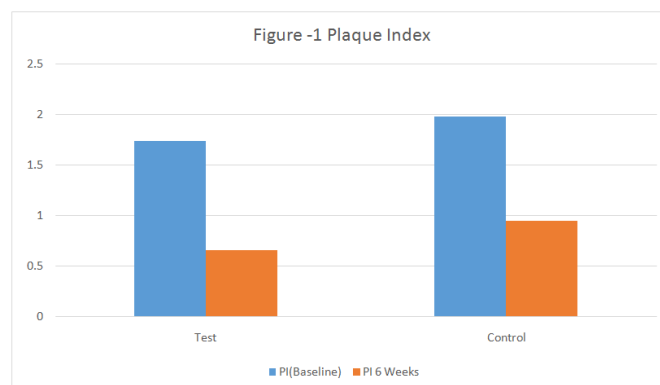
## RESULTS

### Plaque index (Table I) (Figure 1)

The means and standard errors for the plaque indices of the two groups at baseline and 6 weeks are shown in the table I. There were no significant baseline differences plaque indices for the 2 groups ( $p > 0.05$ ). Plaque scores were significantly lower within the test group and control group at 6<sup>th</sup> week evaluation. However, there were no significant differences in 6<sup>th</sup> week plaque scores when compared between control (toothbrushing only) and test (toothbrushing and chewing gum) group.

**Table I. Plaque index scores recorded at baseline and 6 weeks**

	Baseline(mean)	6 weeks(mean)	p value
Test	1.73	0.65	0.00
Control	1.9	0.9	0.00
Comparison done using Student T test			
Inter group p value - 0.78			
P<0.05-significant			



### Gingival index (Table II) (Figure 2)

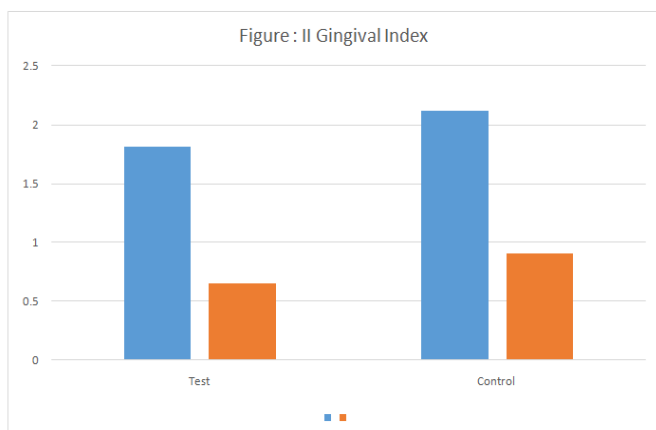
The means and standard errors for the gingival indices of the two groups at baseline and 6 weeks are shown in the table II. There were no significant baseline differences gingival indices for the 2 groups ( $p > 0.05$ ). Gingival scores were significantly

lower within the test group and control group at 6<sup>th</sup> week evaluation. However, there were no significant differences in 6<sup>th</sup> week gingival scores when compared between control (toothbrushing only) and test (toothbrushing and chewing gum) group.

**Table II. Gingival index scores recorded at baseline and 6 weeks**

Gingival index	Baseline(mean)	6 weeks(mean)	p value
Test	1.8	0.65	0.0
Control	2.1	0.9	0.0

Comparison done using Student T test  
Inter group p value- 0.8  
P<0.05-significant



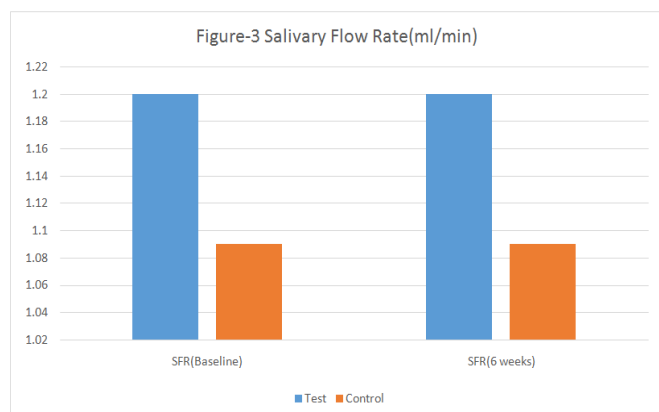
### Unstimulated saliva (Table III) (Figure 3)

The means and standard errors for the unstimulated saliva of the two groups at baseline and 6 weeks are shown in the table III. There were no significant baseline differences in unstimulated saliva for the 2 groups ( $p>0.05$ ).

**Table III. Unstimulated saliva (ml/min) recorded at baseline and 6 weeks**

Salivary Flow Rate(SFR)	Baseline	6 Weeks	p value
Test	1.2	1.25	0.06
Control	1.09	1.2	0.00

Comparison done using Student T test  
Inter group p value - 0.25  
P<0.05-significant



Unstimulated saliva showed no differences within the test group and control group at 6<sup>th</sup> week evaluation. Also, there were no significant differences in 6<sup>th</sup> week unstimulated saliva when compared between control (toothbrushing only) and test (toothbrushing and chewing gum) group.

## DISCUSSION

Current study was designed to investigate the clinical therapeutic effect of *Glycyrrhizaglabra* (licorice) as an adjunct to tooth brushing in the treatment of chronic gingivitis in diabetic patients. It has been observed that still large part of the world's population use herbs and other traditional medicines for their primary health care needs and *Glycyrrhizaglabra*, is one of the widely used herb in traditional medicine. There are many useful compounds in licorice root such as, glycyrrhizin (saponin- like glycoside -50 time sweeter than sugar) and its aglycone, glycyrrhetic acid which are clinically used for hyperlipidemia (Tamir *et al.*, 2001). Licorice flavonoid constituents mainly include flavones, flavonals, isoflavones, chalcones, bihydroflavones and bihydrochalcones. Pharmacological investigations indicate that they have antioxidant, antibacterial and anti-inflammatory activities (Vaya *et al.*, 1997). Gingivitis index has been found to be high in diabetic population and it has been established that diabetes is a risk factor for periodontitis. Among the factors which link diabetes and periodontitis increase in matrix metalloproteinases in salivary matrix is seen. A study by Shirin *et al* concluded that licorice extract can prevent the production of MMPs by host cells and can be as useful as antibiotics like doxycycline to cure periodontal and other inflammatory diseases. Hence, in this study glycyrrhizaglabra was used. Gingivitis index was measured using Loe and Silness index which correlates with the plaque accumulation in the marginal gingiva. Both groups showed a significant decrease from baseline till 6 months. In the test group where toothbrushing and chewing gum was given there was improved gingival health which is in accordance with a study where a mouthrinse containing 0.05% CPC, 0.02% triclosan and 0.02% DPZ (dipotassium glycyrrhizinate) reduced supragingival plaque and gingivitis. This could be attributed to the anti-inflammatory effect of licorice which was reported by Charles Bodet *et al* who observed that the licorice extract exhibited potent anti-inflammatory properties, inhibiting the periodontopathogen LPS-induced IL-1 $\beta$ , -6, and -8 and TNF- $\alpha$  responses of macrophages (Charles Bodet *et al.*, 2008). The licorice extract inhibited the phosphorylation of important macrophage intracellular signaling proteins, including nuclear factor-kappa B p65 nuclear transcription factor and Jun proto-oncogene-encoded activator protein (AP) 1 transcription factor, which are involved in inflammatory signaling pathways. Both groups showed significant improvement in plaque score from baseline till 6 weeks. A commercially available chewing gum was used for the study, the concentration of glycyrrhiza incorporated was not specified, the additional benefit of glycyrrhiza could not be assessed. FDA acceptable daily intake is 0.015–0.229mg glycyrrhizin/kg body weight/day. In the present study there was no significant difference on inter group comparison which may be due to the Hawthorne effect as well as the mechanical efficacy of placebo gum to provide effective plaque control. No side effects were reported.

Unstimulated saliva lubricates the oral cavity for the majority of the day and is therefore a critical factor for the prevention of dry mouth symptoms. A study by Jenkins *et al* found that regular chewing of gum for 8 weeks, 4 sticks a day had elevated unstimulated salivary flow rate particularly in subjects with low baseline flow rates. In the present study there was no change in the salivary flow rate due to the fact that decreased salivary flow rate is mostly seen corresponding to uncontrolled

diabetes (HbA1C values more than 9) also the patients were only on lifestyle modification and not on any hypoglycemics. In the best of the author's knowledge this is the first study where a commercially available glycyrrhizaglabra flavored chewing gum has been investigated for its efficacy in plaque removal and anti-gingivitis activity in diabetics. As the required dosage of glycyrrhizic acid for anti-plaque and anti-gingivitis is not known in future studies utilizing gums containing different concentrations of the product need to be evaluated in a large population, to establish its effect.

## Conclusion

This was a pilot study using commercially available chewing gum containing licorice and our results showed improvement in plaque score and gingival health when licorice was used along with tooth brushing which was in agreement with the previous studies. Though licorice showed anti-plaque and anti-gingivitis effect it was not superior to the control group. In this study the concentration of licorice could have been too low to show the desired improvement as an adjunct. Future studies with different concentrations of glycyrrhiza need to be studied along with the drug release pattern of the herb in a larger population to ascertain the efficacy of glycyrrhiza or its extract in the treatment of gingival diseases. Its exact role in diabetics also need to be researched.

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