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Effect of mucoadhesive tablet containing herbal formulation on gingivitis

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Abstract

Gingivitis is the most common form of gum disease caused by oral bacteria. Previous research has shown the antibacterial activity of Sage, Echinacea, Lavender and Mastic gum against these bacteria. The aim of the study was to test their effect delivered using a mucoadhesive tablet on gingivitis as compared with a chemical mouthwash. Thirty healthy subjects presenting with signs of gingivitis were randomly assigned to one of the three test groups: herbal tablets, placebo and a 0.2% chlorhexidine mouthwash. Following baseline measurements subjects were instructed to use the products twice a day for one week. Baseline and follow up measurements included bleeding on probing and a gingivitis scores. Results showed that the herbal mucoadhesive tablet caused a significant reduction in bleeding and gingivitis. These results suggest that this mode of treatment is effective in the prevention of gingivitis and may be a viable alternative to chemical agents.

Keywords: Herbal, mucoadhesive, gingivitis

1. Introduction

Gingivitis is the most common form of gum disease affecting some 65% of the adult population [1]. It is characterized by the presence of inflammatory infiltrate and signs of soft tissue inflammation such as: redness, swelling, bleeding on probing and loss of tissue stippling, with no signs of loss of bony support [2]. Gingivitis is considered a reversible pathological condition however, if neglected this inflammatory process may progress to periodontitis which involves distraction of collagen fibers and an irreversible damage to the bony support of the dentition [3].

Gingivitis is bacterial in origin [4]. It results from the accumulation of microorganisms on the teeth and is associated with the increase of anaerobic Gram negative, motile rods in the biofilm [5]. These include bacterial species such as *Actinomyces*, *Fusobacterium*, *Villonela*, *Prevotella*, *Treponema*, and *Bacteroides*. However, the progression of this condition is largely dependent on the nature and extent of the inflammatory host-response [6].

Because of its bacterial etiology this condition reacts favorably to improved oral hygiene practice with an emphasis on interdental cleaning [7]. Furthermore, the use of antibacterial agents applied using toothpastes and mouthwashes have also demonstrated a beneficial effect on gingivitis [8].

Previous study demonstrated the antibacterial activity of four herbal medicinals: Echinacea, Mastic gum, Lavender and Sage against anaerobic oral bacteria [9]. Furthermore, an herbal formulation comprising of these four ingredients was effective in reducing oral malodor when delivered using a mucoadhesive sustained release delivery system [10, 11]. In the present study we tested the effect of this herbal formulation delivered using a palatal mucoadhesive tablets on gingivitis.

2. Materials and methods

2.1 Subjects

Thirty healthy subjects (mean age, 30.85±8.74 y, 20 females) positive for the presence of gingival inflammation (i.e. bleeding on probing ≥20%) were included in the study. Subjects who were smokers, took antibiotics within one month prior to the study, showed signs of periodontal disease (pocket depth >5mm) or presented with less than 20 natural teeth (not including wisdom teeth) were excluded. Informed consent was obtained and the experiment protocol was approved by the institutional ethics committee and registered at the NIH-FDA protocol registration system (NCT-000250289).

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2.2 Experimental Protocol

The study protocol is summarized in Table 1.

Table 1: Study design

Day 1	Week 1	Day 8	Week 2	Day 15
Baseline measurements	Mouthwash or tablet application twice a day in addition to regular tooth brushing	First follow-up measurements	Regular tooth brushing only	Second follow-up measurements

Measurements (described in detail below) included bleeding on probing scores, and gingivitis scores using clinical photos evaluated by three examiners. Following baseline measurements subjects were randomly assigned into one of the three treatment groups: (i) herbal mucoadhesive tablets (HMT; n=11), (ii) placebo muoadhesive tablets (Placebo; n=9), and (iii) 0.2% chlorhexidine mouthwash (Corsodyl; n=10). Mucoadhesive tablets were prepared with or without the herbal active ingredient as previously described [10]. Briefly, the adhesive polymers hydroxypropyl cellulose (Hercules Co.,Wilmington, DE), and carbopole (Goodrich Co., Cleveland, OH) were mixed in a ratio of 4:1. 250 mg of the mixture with or without an active ingredient (as control) were pressed for 30 seconds at a pressure of 3 ton/cm² into a mold using a laboratory Carver press (Carver Machine Works, Inc, In, USA). This process produced tablets of 12 mm in diameter and 2.5 mm in thickness with one side flat and the other side curved to fit the shape of the palate. The active ingredient was an herbal formulation composed of equal shares of four herbal medicinals: Echinacea (*Echinacea augustifolia*), Mastic gum (*Pestacia lentiscus*), Lavender (*lavandula augustifolia*) and Sage (*salvia officinals*), supplied as dried powders (SupHerb. Nazeret Ilit IL).

Subjects were instructed to apply the mucoadhesive tablets to their palate twice a day (after dinner and after breakfast) for a week. The mouthwash group was instructed to rinse for 30 seconds twice a day (before bedtime and on the morning) for a week. The use of other products besides their regular tooth brushing was not allowed during the two weeks of the experiment. First follow up measurements were conducted after a week of treatment use (day 8) and second follow-up measurements were done after another week without treatment besides regular tooth brushing (day 15).

2.3 Measurements

2.3.1 Bleeding on probing: Probing was done by a single clinician blinded to the treatment on each natural tooth at six points (mesial, middle and distal for the buccal and lingual aspects of each tooth). Scores were recorded as percentage of bleeding sites from the total.

2.3.2 Gingivitis scores: Clinical photos were obtained at baseline and at the first and second follow-up. Photos were arranged randomly and scored by three clinicians on a 0-2 scale [12] with description as follows: 0-no signs of inflammation (healthy appearance, pink color, stippling), 1-mild signs of inflammation (reddish color, light swelling), 2-severe signs of inflammation (red to purple shade, swollen without stippling).

2.4 Statistical analysis

The effect of the various treatments was compared for each measured parameter using ANOVA. The level of correlations among the different examiners was determined using spearman correlation coefficient. All the tests applied were two-tailed and $p \leq 0.05$ was considered statistically significant.

3. Results & Discussion

The mean results (\pm S.D.) of the bleeding on probing scores and gingivitis scores for the three treatment groups at baseline (before treatment) and at first and second follow up (following treatment and a week after treatment was ended) are presented in Figures 1 and 2.

Figure 1.

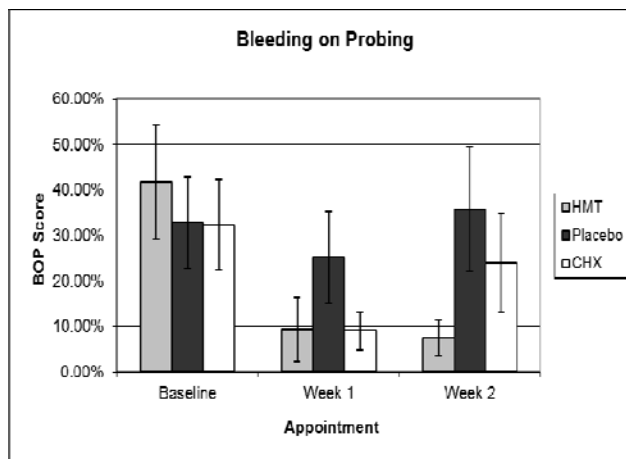


Fig 1: Shows the mean results (\pm SD) of the bleeding on probing scores for the three treatment groups. The herbal mucoadhesive tablet group (HMT) showed significant reduction ($p < 0.001$) in both first and second follow-up measurements.

Figure 2.

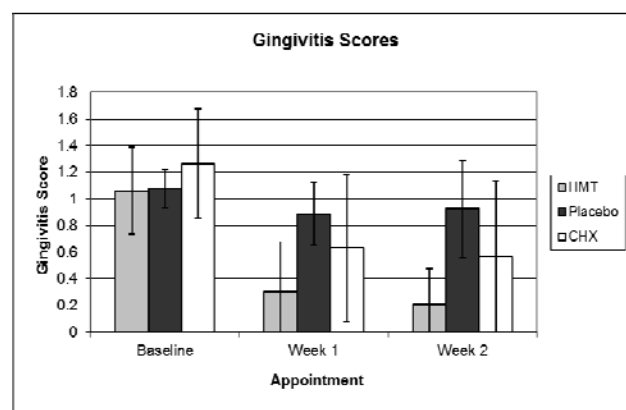


Fig 2: Shows the mean results (\pm SD) of the gingivitis scores for the three treatment groups. The herbal mucoadhesive tablet group (HMT) showed significant reduction ($p < 0.001$) in both first and second follow-up measurements.

No significant differences were observed between the three groups at baseline measurements for both parameters. In the first follow up measurements both the herbal mucoadhesive tablet (HMT) and the 0.2% chlorhexidine mouthwash (CHX) groups had shown a statistically significant reduction in bleeding scores (Figure 1; $p < 0.001$ and $p = 0.002$, respectively) resulting in bleeding scores of under 10%. However, in the gingivitis scores only the herbal mucoadhesive tablet (HMT)

showed a significant reduction as compared to the placebo (Figure 2; $p=0.004$). In the second follow-up (day 15) only the active mucoadhesive tablet group showed a significant reduction for both bleeding and gingivitis as compared to the placebo ($p<0.001$).

The level of correlation between the three gingivitis examiners is presented in Table 2.

Table 2: Pearson correlation coefficients between examiners.

	Examiner 2	Examiner 3
Examiner 1	$r=0.57$ $p<0.001$	$r=0.63$ $p<0.001$
Examiner 2		$r=0.50$ $p<0.001$

The spearman correlation analysis yielded correlation coefficients ranging from 0.50 to 0.63 with a significance level of $p<0.001$.

We previously showed the antimicrobial properties of four herbal medicinals against anaerobic oral bacteria [9]. We have also demonstrated the effect of these active ingredients on oral malodor reduction using a mucoadhesive delivery system [10, 11]. In the present study we tested the effect of these herbal ingredients on gingivitis using mucoadhesive tablets applied twice a day for one week as compared with placebo mucoadhesive tablets and 0.2% chlorhexidine mouthwash.

Results showed that the application of the herbal mucoadhesive tablets caused a significant reduction in gingival bleeding as well as in visible signs of gingivitis following one week of treatment. Bleeding scores were also reduced in the 0.2% chlorhexidine group however; they rose back in the second follow-up one week after treatment was stopped. These results suggest that apart from the antibacterial activity the herbal active ingredients may possess an anti-inflammatory effect. Indeed some of these herbal ingredients (e.g. Echinacea) have been reported to demonstrate immunomodulating activities [13].

Previous study by Greenstein and co-workers [14] showed that both bleeding on probing and visible signs of inflammation (swelling, color) were closely associated with the inflammatory response within the gingival tissues. In the present study we employed a visual scale evaluated using clinical photos. This type of evaluation offered several advantages such as recordings of the results at the various stages of the study and the ability to score gingivitis by a panel of examiners under the same conditions in a blinded manner without subjecting the patients to repeated examinations. All the evaluators in this study were trained experienced dentists and the levels of correlations between them ranged from 0.50 to 0.63 yielding high level of significance ($p<0.001$).

Similar to our results other studies have also reported the ability of 0.2% chlorhexidine mouthrinse to effectively reduce gingivitis [15]. However, the prolonged use of this material (e.g. more than 10 days) has been reported to be associated with various side effects such as discolorations, altered taste, burning sensations and sloughing [16]. The use of a sustained release mucoadhesive delivery system that allows for a prolonged exposure time of the herbal formulation might explain better results gained by this mode of treatment.

4. Conclusions

Results of the present study clearly show that the herbal formulation delivered by the mucoadhesive tablets is effective in reducing gingivitis. As suggested, we hypothesized that apart from its antibacterial properties it may also have an anti-inflammatory activity, however this warrants further study.

5. References

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