The following is the double blind placebo study done at Loma Linda. This is a summary of the pocket depth reductions.

Baseline	# of Pockets	Change	% Change	Ave.Reading at 1 Month	% Improvement
4	243	0.93	23%	3.07	93%
5	93	1.71	34%	3.29	86%
6	26	2.81	47%	3.19	94%
7	17	3.13	45%	3.87	78%

Confidential report to:

PHARMADEN

Clinical Evaluation of a Nutraceutical for the Treatment of Periodontal Disease

LLU-99-014

By

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4/27/2000

SUMMARY:

The purpose of this study was to compare the effect of certain nutraceuticals (PerioTherapy) and a placebo tablet in the reduction of gingivitis, bleeding, probing depths and attachment levels, on a two month, two-cell, randomized, parallel, clinical trial for patients with Type II periodontal disease. Each cell consisted of 31-32 subjects for a total of 63 participants. Demographic information and medical history were randomly collected from each subject. Oral examinations of soft tissues and indices of gingivitis, bleeding, pocket depths and attachment levels were performed at baseline, one month and two months. In addition a subset of teeth that had probing depths of 4 mm or greater, was evaluated to determine if the treatments had greater effect on these teeth. GI, BI, AL and PD were analyzed using a one-way ANOVA, one-way repeated after factor ANOVA, paired t-test procedures. Overall the data shows a reduction in the GI, BI, PD for product 509 but no significant changes in the attachment levels. For product 299, there was little reduction in the GI, BI, and PD at any of the time periods. There were some significant changes for product 299 from one month to two months for the GI, BI and PD but no statistical changes from baseline to two months. Product 509 (PerioTherapy) was the most effective at reducing the GI, BI and PD, which were significantly different from product 299 (Placebo)($p<0.0001$). Neither of the two products was effective at reducing the AL for either males or females. For the teeth that had a pocket depth of 4 mm or greater, results indicate that subjects on PerioTherapy, had a significant improvement in the GI, BI and PD from baseline to one month ($p<0.0001$), baseline to two months ($p<0.0001$), but no difference between one month and two months ($p>0.2000$). The placebo treatment (299) resulted in a significant change in BI, GI and PD from baseline to one month, but not at the other two time periods. This improvement while statistically significant was very small compared to the PerioTherapy. The observed effect of the placebo on the GI, BI PD and AL was larger than expected and may be attributed to the Hawthorne effect. It is concluded that PerioTherapy is effective at reducing gingivitis, bleeding and periodontal pockets, but not attachment levels.

I.- PURPOSE

To evaluate the benefit of certain nutraceuticals in the treatment of periodontal disease.

II.- INTRODUCTION

Proanthocyanidin flavanols from Vitis vinifera (grape) seed extract has been found to bind to proline-rich proteins in bacterial membranes, preventing them from forming the aggregations that initiate the onset of periodontal disease. It also has been found to inhibit collagenase, elastase and serine protease secreted by bacteria and white blood cells, and along the way deactivating oxygen free radicals that lead to the destruction of the periodontium.

Echinacea stimulates cellular immunity and inhibits the release of bacterial hyaluronidase that allows bacteria to spread deeper into the gingival crevice. Ubiquinone (CoEnzyme Q10) enhances the production of ATP energy in the gingiva, which improves the healing response. Folic acid ensures the normal development of healthy squamous epithelium and binds to the plaque derived bacterial endotoxins preventing additional irritation.

Bioperine TM (Piper Nigrum) enhances the absorption and bioavailability of all the other ingredients. Taken orally, these ingredients of the neutraceutical PerioTherapy will enhance the ability to gain control of infections, gingivitis and periodontitis when added to conventional periodontal treatment regiments.

III.- STUDY DESIGN

A sixty-day, two-cell, randomized, parallel, clinical trial for patients with Type II periodontal disease was conducted. Each cell consisted of 31-32 subjects for a total of 63 participants. Qualified subjects in one cell received a vitamin tablet (PerioTherapy) with the active ingredients, while the other cell received a placebo tablet. Each subject took take the tablet twice a day for 60 days.

The treatment tablet (PerioTherapy) and the placebo tablet were provided by the sponsor with identical packaging which was labeled as A = 509 or B = 299, so that neither the subject nor the investigators knew the treatment. Clinical parameters that were evaluated included: 1) gingival index, 2) bleeding index, 3) periodontal probe depth and 4) attachment levels. All tests were carried out using modified indices. Clinical measures of efficacy were made at baseline, thirty and sixty days.

Subjects were asked to take the assigned tablet following instructions provided by the sponsor. To monitor compliance, subjects maintained daily logs of when they took the tablet.

IV.- PRE-STUDY VISITS, PROTOCOL AND PERSONNEL

In the summer of 1999, Mr. Douglas McGuinn approached the Center for Dental Research for the possibility of using the school of Dentistry for a periodontal study. The following personnel participated in the study:

1. **Carlos Muñoz, DDS, MSD** is Director of the Center for Dental Research and is the Principal Investigator. He had the overall responsibility for the administration of the study, including the coordination of all the study activities.

2. **Robert Kiger, DDS, MS;** is Chair of the Periodontics Department and was one of the two clinical examiners. Dr. Kiger has extensive experience in gingival indices and was calibrated prior to initiation of the study.

3. **Joni Stephens, RDH, EdS;** is the former chair of the Dental Hygiene Department has also extensive experience in gingival studies and served as one of the coordinators for the study.

4. **Michele Johnson, RDH, BS;** served as one of the two clinical examiners. She also has participated in several gingival index studies and was also calibrated prior to the initiation of the study.

5. **Kerby Carambot,** Research Assistant, was primarily responsible for assisting in data collection and taking the clinical photographs.

6. **Alisa Wilson, RDA, OSA,** was the Clinical Coordinator. Her role was to schedule and coordinate appointments for the patients, distribute the product, and document progress notes and any other duties requested by Dr. Muñoz.

V.- INVESTIGATIONAL REVIEW BOARD

Loma Linda University requires the approval by the Institutional Review Board when initiating any research study involving human or animal subjects.

Prior to the initiation of the study, the protocol and the informed consent were submitted to the Investigational Review Board of Loma Linda University for approval.
On August 15, l999, the IRB application, along with the subject consent form were submitted and was approved on September 9, l999.

Before recruitment and enrollment into the study, each prospective candidate was given a full explanation of the study. When the investigator was assured the candidate understood the implications of participating in this study, the subject was asked to give consent to participate in the study by signing the informed consent form. The subjects were then given a copy of the signed informed consent.

As mandated by California Law and the Institutional Review Board, the study was conducted in accordance with ICH guidelines for Good Clinical Practices (GCP).

VI.- SUBJECTS ENROLLMENT AND RECRUITMENT

The Center for Dental Research had approximately 75 potential subjects. Sixty subjects were selected for the study. An additional three subjects were enrolled to compensate for early withdrawals or terminations.

Total # of subjects screened:	75
Total # of subjects that passed screening:	65
Total # of subjects on product:	63
Total # of subjects dropped:	0
Total # of subjects that completed the study:	63

Table 1 indicates the breakdown of the participant subjects by race, gender and age.

Inclusion/Exclusion Criteria

The screening process began on November, 1999 and the study was completed on February 18, 2000. All subjects were enrolled and on product by December 15, 1999. The last subject was evaluated February 18, 2000.

Inclusion criteria

Subjects were eligible to enter the study if they meet the following criteria:

1. Able to read, understand and sign the informed consent.
2. Be in good general health as evidenced by their medical history.
3. Be between the ages of 25 and 75.
4. Have a minimum of 20 natural teeth, including at least 5 maxillary and 5 mandibular anterior teeth, but excluding third molars.

5. Capable of understanding and following oral instructions as to the plan and scope
   of the study.
6.- Have a gingival index score of 2
7.- Had a moderate periodontitis in at least one quadrant of the mouth, each of which contain at least three pockets which measured 4 to 5 mm, and bleed to gentle probing. None of the qualifying sites should exceed a 7-mm periodontal pocket depth. Periodontal pockets in which the depth of the pocket corresponds to the apex to the tooth, as in a possible endodontic/periodontic condition, were not treated or evaluated.

Exclusion criteria:

Subjects with one or more of the following conditions were excluded from the study:

1. Be on chronic concomitant medications that would affect his/her soft tissue health
   (e.g. Dilantin, steroids, etc.).
2. The need for prophylactic antibiotic coverage for dental procedures.
3. Individuals with a chronic infectious disease with oral manifestations that would jeopardize his/her health or that of other health care providers.
4. Suspected or known allergy to acrylic resins or latex gloves.
5. Pregnant or nursing women.
6. Has a cardiac pacemaker.
7. Subjects not expected to demonstrate compliance, such as extensive travel commitments, lack of transportation, etc.
8. Smokers

VII. CLINICAL PROCEDURES

1.- Data collection and Subject Measurements

Clinical record forms (C.R.F.) were prepared for data collection for each subject. The investigators according to the following schedule will complete the forms:

a.- Baseline Examinations:

1.- Informed consent was signed
2.- Medical and health survey was taken
3.- Oral Soft Tissue examination
4.- Gingival Index
5.- Bleeding Index
6.- Probing depths
7.- Attachment levels
8.- Oral Soft Tissue examination
9.- Photographs of selected subjects
10.- Dispensing of new tablets and diary

b.- Thirty Day Examinations

1.- Medical and health update
2.- Oral soft tissue examination
3.- Gingival Index
4.- Bleeding Index
5.- Probing depths
6.- Attachment levels
7.- Photographs of selected subjects
8.- Collection of diary and unused tablets and dispensing of new tablets and diary

c.- Sixty Day Examinations (Final)

1.- Medical and health update
2.- Oral Soft Tissue examination
3.- Gingival Index
4.- Bleeding Index
5.- Probing depths
6.- Attachment levels
7.- Photographs of selected subjects
8.- Collection of diary and unused tablets

2.- Clinical Examinations:

The investigators according to the following evaluation criteria completed the subject record forms:

a.- Soft Tissue examination and Survey:

A complete soft and hard tissue examination was performed. The examination included observation of the face, lymph nodes, lips, buccal mucosa, floor of the mouth, tongue, hard palate, soft palate, gingiva and teeth. All findings were recorded as normal or abnormal.

At each visit, signs of sloughing, erythema, ulceration or edema was looked for. Sloughing is defined as necrotic superficial tissue separating from underlying epithelial tissue, but not extending into the lamina propria. Erythema is defined as a loss of surface necrotic tissue extending into the underlying lamina propria in response to inflammation. Edema is defined as abnormal amounts of fluid in the intercellular spaces resulting in visible swelling. Each parameter was scored as normal, slight, moderate or marked.

b.- Probing Depth Measurements

The probing depth measurements were done according to the method developed by Ramfjord using teeth # 3, 9, 12, 19, 25 and 28. A calibrated periodontal probe was inserted into the pocket with the long axis of the probe aligned parallel to the long axis of the tooth. A measurement was made from the tip of the probe to the level of the gingival margin. The distance was recorded in millimeters and rounded to the nearest whole number.

c.- Gingival Index

A modified Gingival Index of Silness and Loe was performed at each evaluation period from second right maxillary and mandibular premolars (#4 & # 20) to second left maxillary and mandibular premolars (# 13 and # 29) at 6 sites (mesiobuccal, buccal, distobuccal, mesiolingual, lingual and distolingual) per tooth, according to the following evaluation criteria:

0= Absence of inflammation
1= Mild inflammation - slight change in color and little change in texture
2= Moderate inflammation - redness, edema glazing and bleeding on probing
3= Severe inflammation - marked redness and hypertrophy.

d.- Bleeding on Probing

Bleeding on probing to the base of the pocket was performed at each evaluation period using the Eastman Bleeding Index according to the following criteria:

0 = No bleeding
1 = Presence of bleeding or a single bleeding point
2 = Interdental triangle is filled with blood
3 = Profuse bleeding is observed immediately after probing

e.- Clinical Attachment Level

To measure clinical attachment level, the cemento-enamel junction (CEJ) was used as a landmark. The end of the probe was manually placed against the enamel surface coronally to the margin of the gingiva on a 45-degree angle to the long axis of the tooth. The probe was then moved in an apical direction and the CEJ is then detected by either tactile sense or by a change in direction of the probe.

If the gingival margin is on enamel, the distance from the gingival margin to the CEJ was recorded first. Then, the probe was inserted further and the distance from the gingival margin to the bottom of the pocket was then recorded. The first measurement is then subtracted from the second measurement to obtain the clinical attachment level.

If the gingival margin is on cementum, the clinical attachment level was recorded as a direct measurement from the CEJ to be base of the pocket.

VIII.- ADVERSE EXPERIENCE REPORTING

All clinically significant changes occurring during or after the treatment, whether or not associated with the treatment were recorded on the case report form. At all evaluation visits, subjects were questioned regarding the occurrence of side effects. The subjects were also asked to contact us with any concerns or unexpected sequella caused by the tablet treatment.

Any adverse experiences which is considered as serious are those which: result in a life threatening event or death; require hospitalization as a result of the adverse experience;

result in a congenital anomaly or malignancy; are the result of an overdose; or result in a permanent disability.

No adverse experience was reported for any of the subjects.

IX.- STATISTICAL ANALYSIS

The sample size was estimated with the power analysis, which was performed at an α level of 0.05 and a β level of 0.2 using variance estimates from the literature of 0.3. To detect a change of 0.3 GI or PI units, 15 subjects per group would be required. To detect a change of 0.2 GI units, 30 subjects per group would be required. Again, based on the literature, a realistic expectation for a mean difference between groups is 0.2 units.

The primary analysis of the data was a repeated measures of variance using a 99% level of significance. This statistical model allows comparisons to be made between treatment groups, between time points and between treatment groups at each time point. Treatment groups were also be analyzed at post-treatment by analysis of covariance and at baseline using ANOVA.

X.- RESULTS AND DISCUSSION

The following clinical parameters were evaluated:

1. Gingival Index (GI)
2. Bleeding Index (BI)
3. Periodontal Probing Depths (PD)
4. Attachment Levels (AL)

- There were two (2) treatments: Treatment A = 509 (PerioTherapy) and Treatment B = 299 (Placebo).
- A total of 32 subjects was assigned randomly to A, and 31 subjects to B.
- The subjects were observed at three (3) time points: Baseline, 1 month, and 2-months.
- The data is presented in Tables 2-21 and Figures 1-16.
- Figures 17 – 32 shows the mean GI, BI, AL and PD for the 63 subjects at each of the three time periods.

All the subjects completed the two-month study.

Every effort was made to ensure the maximum subject compliance. It appeared that the instructions given by the Clinical Coordinator were effective, as subjects usually responded positively at each evaluation time.

Tables 2-4 summarize the results of the GI, BI, PD and AL, at baseline, one month and two months at a significant level of p-value < 0.0001. Overall, the data shows a reduction in the GI, BI, PD for product 509 but no significant changes in the attachment

levels. For product 299, there was little reduction in the GI, BI, and PD at any of the time periods. There were some significant changes for product 299 from one month to two months for the GI, BI and PD but no statistical changes from baseline to two months.

When the data were analyzed according to the time point, product 509 was the most effective at reducing the GI, BI and PD, which were significantly different from product 299 ($p<0.0001$)(Table 4).

When the data were further separated and analyzed by gender to determine the effect of the two treatments, product 509 was more effective than product 299 at reducing the GI, BI, and PD for both males and females. Neither of the two products was effective at reducing the AL for either males or females (Table 3).

To evaluate the effect of the treatment products on the GI, BI, PD and AL, of the teeth that had a pocket depth of 4 mm or greater, a separate analysis was conducted. This was done to evaluate if the treatment products had a significantly higher effect on teeth with greater pocket depths than the rest of the teeth (Tables 2-4).

Results indicate that subjects on product 509, had a significant improvement in the GI, BI and PD from baseline to one month ($p<0.0001$), baseline to two months ($p<0.0001$), but no difference between one month and two months ($p>0.2000$). The placebo treatment (299) resulted in a significant change in BI, GI and PD from baseline to one month, but not at the other two time periods. This improvement while statistically significant was very small compared to the PerioTherapy (599). These results indicate that PerioTherapy was more effective at reducing the GI, BI, and PD for subjects with a 4-mm or greater probing depth in the first 30 days, and maintained the effect thereafter. For subjects taking the placebo, results indicate that this product was not effective in reducing the GI, BI or PD over a two-month period, even though there was a slight improvement from baseline to one month.

Table 5 indicates the mean delta change at the three time periods. At BL-1M there was a substantial reduction on the GI, BI and PD and AL. At 1M-2M there was further improvement in BI, and GI but no improvement in the PD and Attachment levels. At BL–2M there was further change in the GI, BI and PD and an increase in the attachment levels.

The observed effect of the placebo on the GI, BI PD and AL was larger than expected at the one-month period. This observed effect might be attributed to the Hawthorne effect, which is associated with the subject's knowledge of participating in the study (Darby and Bowen, 1983). It is possible that since the subjects knew that they were participating in a clinical study, their oral hygiene might have improved (because they knew they were being examined) during the course of the study. However, even with the Hawthorne effect, the two-month data showed that PerioTerapy was more effective in preventing or reducing gingivitis.

A six to twelve month study needs to be conducted to evaluate the long term effectiveness of PerioTherapy

XI.- CONCLUSIONS

Under the conditions of the present study, the following conclusions are made.

1.- PerioTherapy showed significant efficacy in reducing the GI, BI and PD. The observed effects of the placebo tablet may be associated with the Hawthorne effect.
2.- PerioTherapy is effective in reducing gingivitis. The effect appears to be stabilized after the first month.
3.- Gender has little impact on the effects of the PerioTherapy or placebo tablets.
4.- Neither the PerioTherapy nor the placebo tablet had any effect at increasing the attachment levels in the present study.
5.- There were no additional attachment loss with either the PerioTherapy or the Placebo during the course of the study.
6.- On teeth with probing depths of 4 mm or more, PerioTherapy was more effective at reducing the probing depths than the placebo.

XII.- REFERENCES

Caton JG, Polson AM (1985). The interdental bleeding index: a simplified procedure for monitoring gingival health. *Compend Cont Ed Dent* 6:88, 90-92

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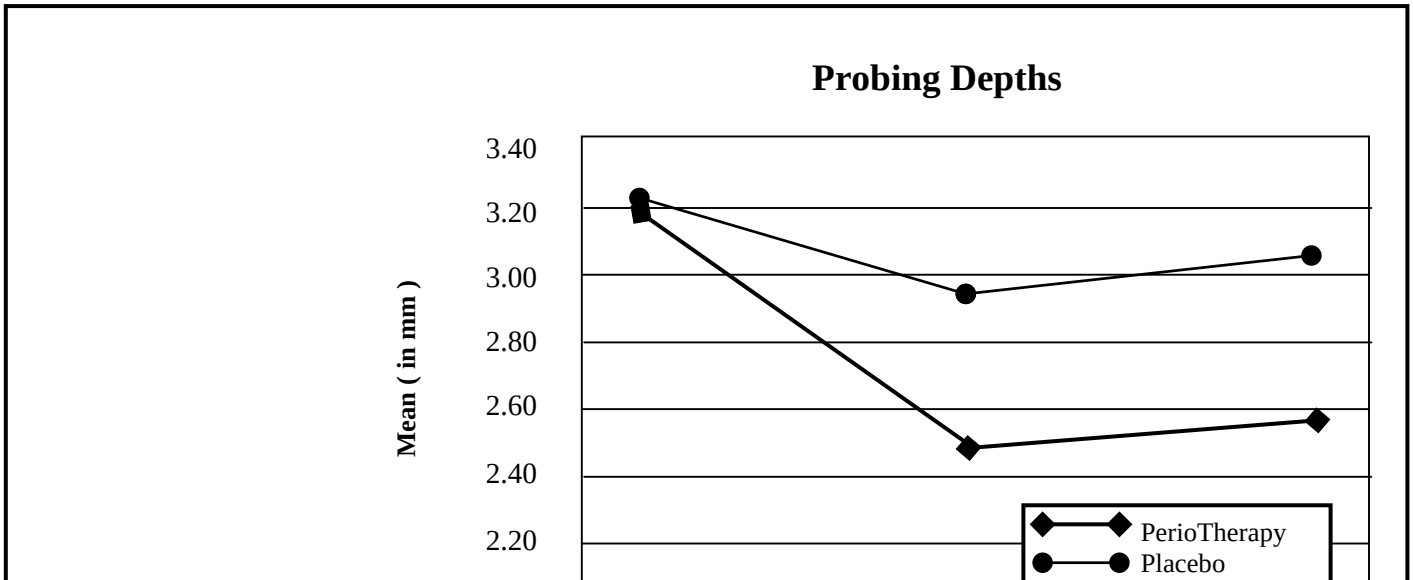

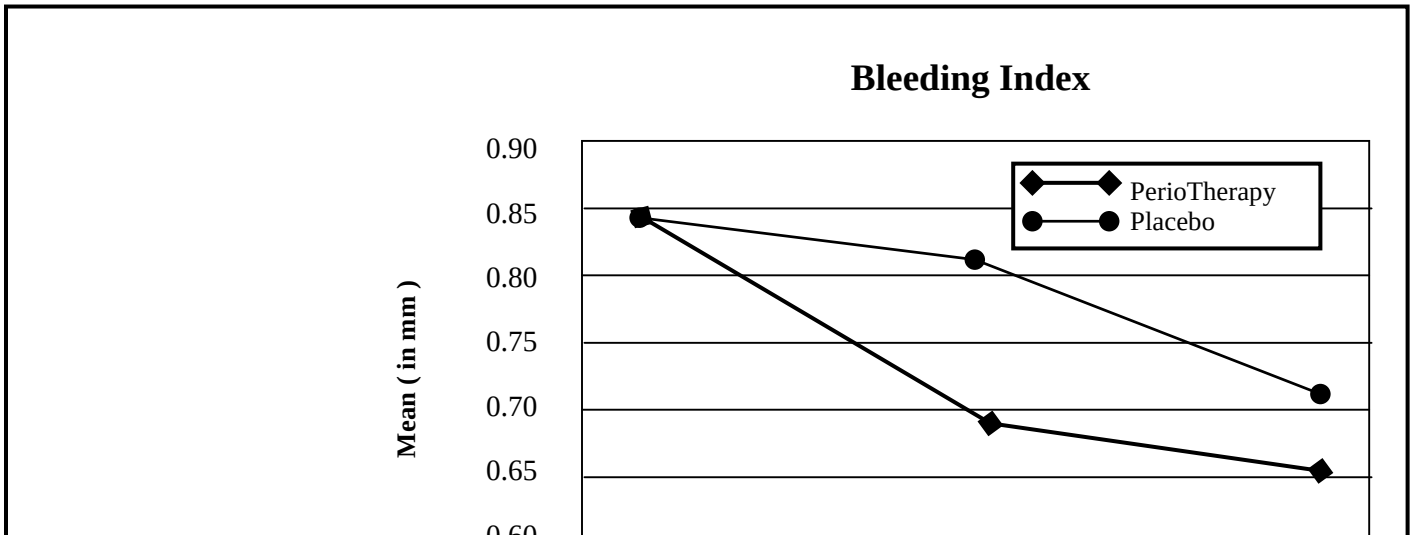
Bleeding Index
Mean (in mm)
0.90
0.85
0.80
0.75
0.70
0.65
0.60
PerioTherapy
Placebo

Table 1.- **Subjects Arranged by Age, race and Gender**

	Male	Female	Totals

Subjects	27	36	63
Age			
Oldest	54	70	
Youngest	27	20	
Race			
Caucasian	20	22	42
Hispanic	2	9	11
African American	0	4	4
Asian	3	1	4
Native American	0	0	0
Other	2	0	2
Totals	**27**	**36**	**63**

Table 2.- Comparison Within Time Periods and Gender

Comparisons	BL – 1M P Value	Significance	BL - 2M P Value	Significance	1M – 2M P Value	Significance
Gingival Index						

A = 509						
All	0.0001	Yes[a]	0.0001	Yes[a]	0.5575	No[c]
> 4 mm All	0.0002	Yes[a]	0.0001	Yes[a]	0.2150	No[c]
B = 299						
All	0.0001	Yes[a]	0.5720	No[c]	0.0010	Yes[b]
> 4 mm All	0.0104	Yes[a]	0.0910	No[c]	0.8966	No[c]
Bleeding Index						
A = 509						
All	0.0001	Yes[a]	0.0001	Yes[a]	0.1336	No[c]
> 4 mm All	0.0001	Yes[a]	0.0001	Yes[a]	0.0059	Yes[b]
B = 299						
All	0.6184	No[c]	0.3999	No[c]	0.0004	Yes[a]
> 4 mm All	0.0030	Yes[a]	0.1851	No[c]	0.0001	Yes[a]
Attachment Levels						
A = 509						
All	0.0774	No[c]	0.7678	No[c]	0.3395	No[c]
> 4 mm All	0.2581	No[c]	0.5499	No[c]	0.0840	No[c]
B = 299						
All	0.0026	Yes[a]	0.7473	No[c]	0.0009	Yes[a]
> 4 mm All	0.0491	Yes[a]	0.6781	No[c]	0.0573	No[c]
Probing depths						
A = 509						
All	0.0001	Yes[a]	0.0001	Yes[a]	0.0076	Yes[a]
> 4 mm All	0.0001	Yes[a]	0.0001	Yes[a]	0.6503	No[c]
B = 299						
All	0.0001	Yes[a]	0.2591	No[c]	0.1084	No[c]
> 4 mm All	0.0104	No[a]	0.2961	No[c]	0.0004	Yes[b]

a = Decrease over time period
b = Increase over time period
c = No change over time period

Table 3.- Comparison Within Time Periods and Gender

Comparisons	BL – 1M P Value	Significance	BL - 2M P Value	Significance	1M – 2M P Value	Significance
Gingival Index						
A = 509						
Females	0.8105	No[c]	0.8105	No[c]	0.8105	No[c]

Males	0.8105	No[c]	0.8105	No[c]	0.8105	No[c]
> 4 mm Females	0.0002	Yes[a]	0.0001	Yes[a]	0.9068	No[c]
> 4 mm Males	0.0374	Yes[a]	0.0010	Yes[a]	0.0338	Yes[a]
B = 299						
Females	0.8105	No[c]	0.8105	No[c]	0.8105	No[c]
Males	0.8105	No[c]	0.8105	No[c]	0.8105	No[c]
> 4 mm Females	0.9869	No[c]	0.0010	Yes[b]	0.0012	Yes[b]
> 4 mm Males	0.0002	Yes[a]	0.0124	Yes[b]	0.1941	No[b]
Bleeding Index						
A = 509						
Females	0.0001	Yes[a]	0.0016	Yes[a]	0.0088	Yes[a]
Males	0.0001	Yes[a]	0.0001	Yes[a]	0.2285	No[c]
> 4 mm Females	0.5867	No[c]	0.5867	No[c]	0.5867	No[c]
> 4 mm Males	0.5867	No[c]	0.5867	No[c]	0.5867	No[c]
B = 299						
Females	0.0066	Yes[a]	0.0010	Yes[a]	0.6522	Yes[a]
Males	0.1426	No[c]	0.0059	Yes[a]	0.1934	No[c]
> 4 mm Females	0.5867	No[c]	0.5867	No[c]	0.5867	No[c]
> 4 mm Males	0.5867	No[c]	0.5867	No[c]	0.5867	No[c]
Attachment Levels						
A = 509						
Females	0.9144	No[c]	0.9144	No[c]	0.9144	No[c]
Males	0.9144	No[c]	0.9144	No[c]	0.9144	No[c]
> 4 mm Females	0.1630	No[c]	0.1630	No[c]	0.1630	No[c]
> 4 mm Males	0.1630	No[c]	0.1630	No[c]	0.1630	No[c]
B = 299						
Females	0.9144	No[c]	0.9144	No[c]	0.9144	No[c]
Males	0.9144	No[c]	0.9144	No[c]	0.9144	No[c]
> 4 mm Females	0.1630	No[c]	0.1630	No[c]	0.1630	No[c]
> 4 mm Males	0.1630	No[c]	0.1630	No[c]	0.1630	No[c]
Probing depths						
A = 509						
Females	0.0001	Yes[a]	0.0001	Yes[a]	0.9151	No[c]
Males	0.0001	Yes[a]	0.0001	Yes[a]	0.3077	No[c]
> 4 mm Females	0.0921	No[c]	0.0921	No[c]	0.0921	No[c]
> 4 mm Males	0.0921	No[c]	0.0921	No[c]	0.0921	No[c]
B = 299						
Females	0.0001	Yes[a]	0.0883	No[c]	0.0026	Yes[b]
Males	0.0001	Yes[a]	0.0032	Yes[a]	0.1459	No[c]
> 4 mm Females	0.0771	No[c]	0.0771	No[c]	0.0771	No[c]
> 4 mm Males	0.0771	No[c]	0.0771	No[c]	0.0771	No[c]

a = Decrease over time period
b = Increase over time period
c = No change over time period

Table 4.- Comparisons Between Treatments and Time

Comparisons	Baseline P Value	Significance	One Month P Value	Significance	Two Months P Value	Significance
Gingival Index						
A vs B	0.9920	No[d]	0.0001	Yes[e]	0.0001	Yes[e]
A vs B > 4 mm	0.0001	Yes[e]	0.0001	Yes[e]	0.0001	Yes[e]

Bleeding Index						
A vs B	0.9760	No[d]	0.0001	Yes[e]	0.0058	Yes[d]
A vs B > 4 mm	0.4594	No[d]	0.0001	Yes[e]	0.7110	No[d]
Attachment Levels						
A vs B	0.9760	No[d]	0.2758	No[d]	0.4238	No[d]
A vs B > 4 mm	0.4663	No[d]	0.2346	No[d]	0.3889	No[d]
Probing Depths						
A vs B	0.5092	No[d]	0.0001	Yes[e]	0.0001	Yes[e]
A vs B > 4 mm	0.7566	No[d]	0.0001	Yes[e]	0.0001	Yes[e]

d = No difference between A and B
e = A lower than B
f = B higher than A

Table 5.- Descriptive Statistics of the Difference in Means for the GI, BI, PD and AL

	BL-1M	BL-2M	1M-2M
Gingival Index			
A	-0.490	-0.478	0.011
B	-0.258	-0.135	0.123
>4 mm A	-0.143	-0.189	-0.046
>4 mm B	-0.095	0.004	0.099
Bleeding Index			
A	-0.139	-0.186	-0.046
B	-0.016	-0.123	-0.107
>4 mm A	-0.585	-0.274	-0.858
>4 mm B	-0.148	-0.214	-0.066
Probing Depths			
A	-0.707	-0.667	0.040
B	-0.303	-0.222	0.081
>4 mm A	-1.396	-1.368	0.029
>4 mm B	0.515	-0.266	0.249
Attachment Levels			
A	-0.204	0.031	0.235
B	-0.354	0.044	0.398
>4 mm A	-0.268	0.109	0.310
>4 mm B	-0.354	0.077	0.471

Negative values represent amount of decrease

Table 6.- Gingival Index: Descriptive Statistics for Males and Females Combined

		n	Mean	SD
Tx	A	3,454	1.5394	0.5284
	B	3,301	1.7316	0.5795

Time	Baseline	2,251	1.8627	0.4058
	1-month	2,255	1.4860	0.6476
	2-month	2,249	1.5514	0.5320
Tx(Time)	A(BL)	1,150	1.8626	0.3494
	B(BL)	1,101	1.8629	0.4576
	A(1-mon)	1,152	1.3724	0.5618
	B(1-mon)	1,103	1.6047	0.7075
	A(2-mon)	1,152	1.3837	0.4936
	B(2-mon)	1,097	1.7274	0.5140

Table 7.- Gingival Index: Descriptive Statistics for Males vs Females

		n	Mean	SD
Tx(Time)				
Females:	A(BL)	646	1.8111	0.3995
	B(BL)	639	1.8545	0.4840
	A(1-mon)	648	1.3673	0.5705
	B(1-mon)	641	1.6474	0.6735
	A(2-mon)	648	1.3410	0.4873
	B(2-mon)	635	1.7827	0.4127
Males:	A(BL)	504	1.9286	0.2578
	B(BL)	462	1.8745	0.4184
	A(1-mon)	504	1.3790	0.5508
	B(1-mon)	462	1.5455	0.7489
	A(2-mon)	504	1.4385	0.4967
	B(2-mon)	462	1.6515	0.6194

Table 8. - Gingival Index for Males & Females Combined with Probing depths > 4 mm

		n	Mean	SD
Tx(Time)				
	A(BL)	352	1.7486	0.4464
	B(BL)	407	1.8575	0.4262

	A(1-mon)	347	1.6052	0.4954
	B(1-mon)	387	1.7623	0.6025
	A(2-mon)	365	1.5589	0.5027
	B(2-mon)	398	1.8618	0.4528

Table 9.- Gingival Index for for Males and Females with Probing Depths > 4 mm

Time	Tx	Sex	n	Mean	SD
Baseline	A	F	205	1.7463	0.4473
		M	147	1.7279	0.4466
	B	F	213	1.8498	0.4617
		M	194	1.8660	0.3844
1-month	A	F	205	1.5659	0.5066
		M	142	1.6620	0.4747
	B	F	208	1.8269	0.4903
		M	179	1.6872	0.7050
2-month	A	F	204	1.5784	0.5049
		M	161	1.5342	0.5004
	B	F	214	1.9766	0.3553
		M	184	1.7283	0.5143

Table 10.- Bleeding Index: Descriptive Statistics for Males and Females Combined

		n	Mean	SD
Tx	A	3,451	0.7279	0.7834
	B	3,301	0.7895	0.8140
Time	Baseline	2,250	0.8360	0.8504
	1-month	2,255	0.7570	0.7275
	2-month	2,247	0.6809	0.8074
Tx(Time)	A(BL)	1,149	0.8364	0.8478

	B(BL)	1,101	0.8356	0.8535
	A(1-mon)	1,152	0.6970	0.6958
	B(1-mon)	1,103	0.8196	0.7544
	A(2-mon)	1,150	0.6504	0.7880
	B(2-mon)	1,097	0.7129	0.8264

Table 11.- Bleeding Index: Descriptive Statistics for Males vs Females

		n	Mean	SD
Tx(Time)				
Females:	A(BL)	645	0.8264	0.8364
	B(BL)	639	0.8435	0.8383
	A(1-mon)	648	0.7052	0.7128
	B(1-mon)	641	0.7878	0.7344
	A(2-mon)	647	0.6708	0.7858
	B(2-mon)	635	0.7244	0.8262
Males:	A(BL)	504	0.8492	0.8629
	B(BL)	462	0.8247	0.8748
	A(1-mon)	504	0.6865	0.6740
	B(1-mon)	462	0.8636	0.7799
	A(2-mon)	504	0.6243	0.7909
	B(2-mon)	462	0.6970	0.8274

Table 12.- Bleeding Index for Males & Females Combined with Probing depths > 4 mm

		n	Mean	SD
Tx(Time)	A(BL)	390	1.3846	0.7212
	B(BL)	428	1.3458	0.7695
	A(1-mon)	390	1.9692	0.7376
	B(1-mon)	429	1.1981	0.7333
	A(2-mon)	389	1.1105	0.7836
	B(2-mon)	425	1.1318	0.8336

Table 13.- Gingival Index for for Males and Females with Probing Depths > 4 mm

Time	Tx	Sex	n	Mean	SD
Baseline	A	F	225	1.3467	0.7226
		M	165	1.4364	0.7182
	B	F	228	1.3553	0.7574
		M	200	1.3350	0.7848
1-month	A	F	225	0.9644	0.7551
		M	165	0.9758	0.7153
	B	F	229	1.1747	0.7405
		M	200	1.2250	0.7260
2-month	A	F	225	1.1378	0.7698
		M	164	1.0732	0.8031
	B	F	228	1.1360	0.8258
		M	197	1.1269	0.8446

Table 14.- Attachment Levels: Descriptive Statistics for Males and Females Combined

		n	Mean	SD
Tx	A	3,446	-0.1666	3.1860
	B	3,302	-0.2153	3.1077
Time	Baseline	2,251	-0.1102	3.0426
	1-month	2,255	-0.3876	3.3578
	2-month	2,242	-0.0727	3.0228
Tx(Time)	A(BL)	1,149	-0.1088	3.0711

B(BL)	1,102	-0.1116	3.0139
A(1-mon)	1,152	-0.3125	3.3823
B(1-mon)	1,103	-0.4660	3.3317
A(2-mon)	1,145	-0.0777	3.0918
B(2-mon)	1,097	-0.0675	2.9505

Table 15.- Attachment Levels: Descriptive Statistics for Males vs Females

		n	Mean	SD
Tx(Time)				
Females:	A(BL)	645	0.1488	2.8377
	B(BL)	640	-0.2781	3.1180
	A(1-mon)	648	-0.2191	3.3231
	B(1-mon)	641	-0.6677	3.1977
	A(2-mon)	648	0.1128	2.8286
	B(2-mon)	635	-0.2661	3.0891
Males:	A(BL)	504	-0.4385	3.3199
	B(BL)	462	0.1190	2.8508
	A(1-mon)	504	-0.4325	3.4565
	B(1-mon)	462	-0.1861	3.4934
	A(2-mon)	498	-0.3253	3.3905
	B(2-mon)	462	0.2056	2.7283

Table 16.- Attachment Levels for Males & Females Combined with Probing depths > 4 mm

		n	Mean	SD
Tx(Time)	A(BL)	388	-0.1418	2.9136
	B(BL)	424	-0.2925	2.9702
	A(1-mon)	347	-0.3436	3.6151
	B(1-mon)	387	-0.6462	3.6108
	A(2-mon)	365	-0.0336	2.9304
	B(2-mon)	398	-0.2151	2.9752

Table 17.- Attachment Levels for for Males and Females with Probing Depths > 4 mm

Time	Tx	Sex	n	Mean	SD
Baseline	A	F	224	0.2232	2.6371
		M	164	-0.6402	3.1949
	B	F	228	-0.5439	3.1135
		M	196	0.0000	2.7735
1-month	A	F	226	-0.1150	3.6179
		M	164	-0.6585	3.5986
	B	F	228	-0.9956	3.3113
		M	196	-0.2398	3.8999
2-month	A	F	226	0.2788	2.6394
		M	161	-0.4720	3.2540
	B	F	227	-0.5330	3.1724

Table 18.- Probing Depths: Descriptive Statistics for Males and Females Combined

		n	Mean	SD
Tx	A	3,451	2.7627	0.9674
	B	3,301	3.0591	1.2727
Time	Baseline	2,250	3.2173	1.1974
	1-month	2,254	2.7081	1.0265
	2-month	2,248	2.7976	1.1145

Tx(Time)	A(BL)	1,149	3.2010	1.1210
	B(BL)	1,101	3.2343	1.2726
	A(1-mon)	1,151	2.4944	0.7688
	B(1-mon)	1,103	2.9311	1.2000
	A(2-mon)	1,151	2.5934	0.8181
	B(2-mon)	1,097	3.0119	1.3245

Table 19.- Probing Depths: Descriptive Statistics for Males vs Females

		n	**Mean**	**SD**
Tx(Time)				
Females:	A(BL)	645	3.2341	1.1405
	B(BL)	639	3.1189	1.1617
	A(1-mon)	647	2.5054	0.8381
	B(1-mon)	641	2.8752	1.1096
	A(2-mon)	647	2.5533	0.9040
	B(2-mon)	635	3.0520	1.1601
Males:	A(BL)	504	3.1587	1.0952
	B(BL)	462	3.3939	1.3975
	A(1-mon)	504	2.4802	0.6700
	B(1-mon)	462	3.0087	1.3124
	A(2-mon)	504	2.6448	0.6899
	B(2-mon)	462	2.9567	1.5215

Table 20.- Probing Depths for Males & Females Combined with Probing depths > 4 mm

		n	**Mean**	**SD**
Tx(Time)	A(BL)	389	4.4730	0.8388
	B(BL)	420	4.4500	1.1866
	A(1-mon)	390	3.0769	0.8449
	B(1-mon)	421	3.9359	1.2829
	A(2-mon)	390	3.1051	0.9441
	B(2-mon)	413	4.1840	1.2028

Table 21.- Probing Depths for for Males and Females with Probing Depths > 4 mm

Time	Tx	Sex	n	Mean	SD
Baseline	A	F	225	4.4889	0.8970
		M	164	4.4512	0.7538
	B	F	227	4.2996	1.0594
		M	193	4.6269	1.3013
1-month	A	F	226	3.0885	0.9386
		M	164	3.0610	0.6979
	B	F	228	3.8553	1.1728
		M	193	4.0311	1.3991
2-month	A	F	226	3.0796	1.0720
		M	164	3.1402	0.7338
	B	F	227	4.1410	1.1200
		M	186	4.2366	1.2978