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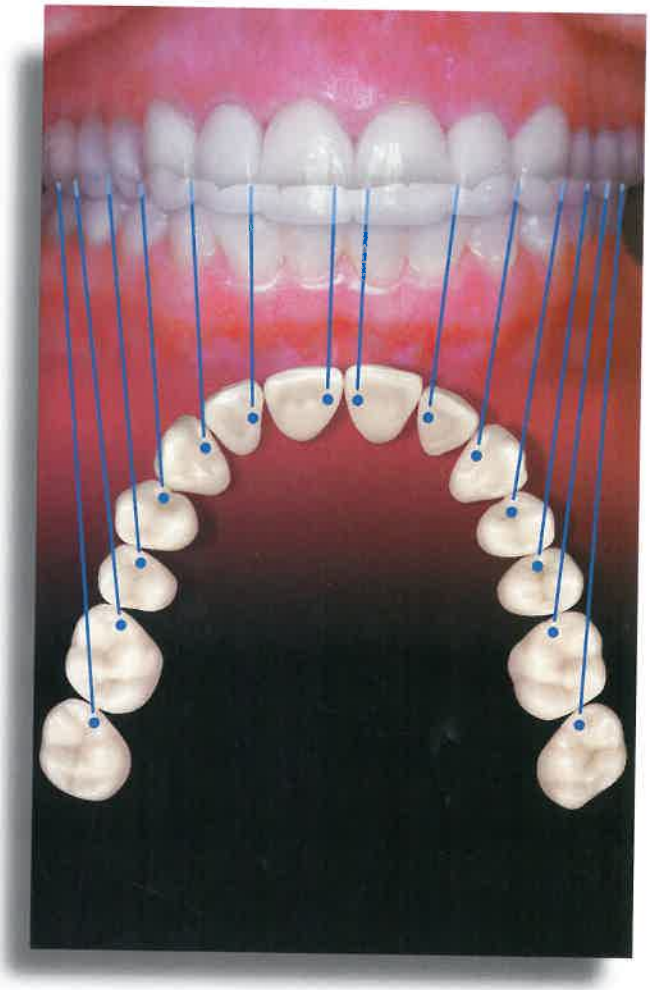

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Carlos A. Muñoz, DDS
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Effects of a Nutritional Supplement on Periodontal Status

CE 3

Carlos A. Muñoz, DDS, MSD
Director
Center for Dental Research

Robert D. Kiger, DDS, MS
Professor and Chair
Periodontics

Joni A. Stephens, RDH, EdS
Professor of Dental Hygiene

Jay Kim, PhD
Professor and Statistician

Alisa C. Wilson, RDA, OSA
Project Manager/Coordinator
Center for Dental Research

Loma Linda University
School of Dentistry
Loma Linda, California

Abstract: ***Among the recommendations for the maintenance of gingival and periodontal health, few have focused on the value of nutritional supplements. The purpose of this study was to compare the effect of certain nutritional and plant-derived nutraceuticals and a placebo tablet in the reduction of gingivitis, bleeding, probing depths, and attachment levels in a 60-day two-cell, randomized, parallel clinical trial for patients with Type II periodontal disease. The vitamin therapy was introduced as an adjunct to patient homecare to determine if there was a quantifiable improvement to soft-tissue health and periodontal damage. Sixty-three patients were randomly divided into two groups of 32 and 31 subjects and given either a vitamin tablet containing seven active ingredients (experimental treatment) or a placebo tablet. The clinical parameters assessed were the gingival index (GI), bleeding index (BI), periodontal pocket depth (PD), and attachment levels (AL), and were recorded at baseline and 60 days. Patients took the assigned tablet at breakfast and at dinner after brushing their teeth twice daily. After 60 days, the data showed a clinical reduction in the GI, BI, and PD for the experimental group (P < .0001). There were no significant changes for AL with either the experimental or the placebo group. When the data were further analyzed for pocket depths of ≥ 4 mm in patients receiving the experimental treatment, there were clinically significant improvements in the GI and PD from baseline to 60 days (P < .0001), but no significant differences in the BI and AL. There were no statistical differences in any of the indices when the data were compared between men and women. The results of the present study suggest that a multi-vitamin nutritional supplement might be a beneficial adjunct to the required established periodontal treatment.***

Learning Objectives:

After reading this article, the reader should be able to:

- describe the value of initial adjunctive therapy in the management of gingivitis and periodontal disease.
- discuss the role of vitamin supplements in inhibiting biological irritants on the gingival tissues.
- list the major components in a vitamin supplement and describe the role of each component.

Conventional nonsurgical treatment of periodontal dieseases has consisted of a combination of in-office therapy and a variety of at-home procedures performed by the patient. Proper brushing and flossing techniques are taught to enable patients to eliminate plaque accumulation and prevent the formation of calculus. In addition, dietary counseling is often provided to educate patients regarding the detrimental effects of the consumption of sugar and refined carbohydrates. However, scant attention has been given to the influence of nutritional supplements on gingival and periodontal tissues as part of a standard at-home oral hygiene protocol.

Research has shown that topical folate (folic acid) in a mouthrinse binds to plaque-derived endotoxins and reduces antigenic stimulation with a reduction in the level of gingival inflammation.[1] Although this mechanism of action is probably germane only to supragingival plaque accessible to a mouthrinse, daily systemic supplementation with 2 mg of folate has also been reported to reduce gingival inflammation.[2] The role of folate in improving gingival tissues by reducing inflammation remains ambiguous. In one study of pregnant patients, 5 mg of folic acid administered systemically proved ineffective,[3] while a 1% topical folate mouthrinse used for just 2 weeks reportedly produced a marked reduction in gingival inflammation.[4] Other reports have shown that folate intake is

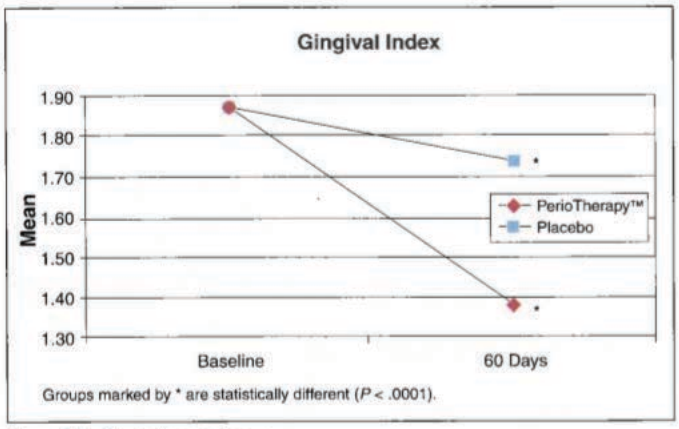


Figure 1A—Gingival score change.

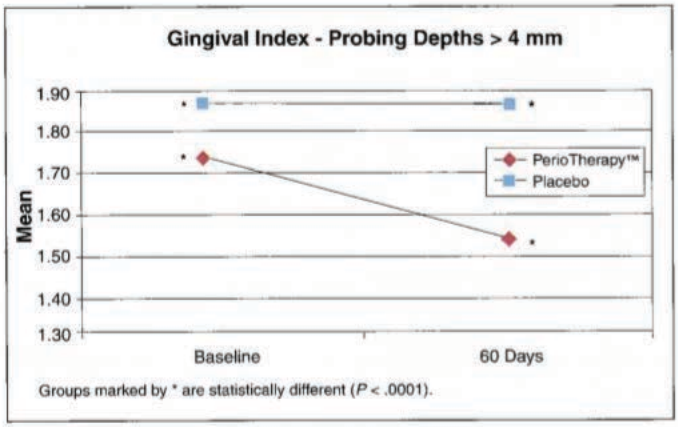


Figure 1B—Gingival score change for teeth that had a probing depth > 4 mm.

often inadequate[3] because of poor diet as well as the destruction of folic acid during food processing.[5] Therefore, the combination of poor eating habits and a heavy reliance on processed foods may limit a person's ability to obtain and maintain adequate levels of folic acid from food intake alone.

There does not appear to be a clear relationship between vitamin B deficiency and either gingivitis or acute necrotizing ulcerative gingivitis.[6] One study found that a large percentage of the patients evaluated were deficient in vitamins A, C, B complex, and iron,[7] all of which are vital for the maintenance of healthy gingival tissues. Such nutritional deficiencies render patients less able to defend against the cycle of bacterial growth, acid production, and plaque formation.[7]

Patients with vitamin C deficiency (scurvy) generally present with periodontal disease, gingival bleeding, tooth mobility, and loss of gingival attachments.[8] Studies have found a relationship between vitamin C and periodontal health.[9-10] Gingival bleeding, which generally increases during periods of vitamin C deficiency, has been shown to revert to baseline when vitamin C levels are returned to normal.[9]

According to Salvi and colleagues, research on the relationship between nutrition and vitamin deficiencies (as they relate to periodontal health) remains unclear largely because of the lack of longitudinal studies on human subjects.[11] Furthermore, much of what has been learned about the relationship between periodontal disease and nutrition is derived largely from laboratory studies rather than clinical investigations with human subjects. More importantly, there has been a decided lack of control for possible confounding variables with this type of research. There is a need for well-controlled longitudinal studies involving human test subjects in the effort to identify the effect of these nutritional supplements in periodontal disease.

This study was undertaken to determine if the administration of a nutritional supplement (PerioTherapy™[a]) could be beneficial in improving gingival and periodontal health in human subjects. PerioTherapy™ tablets are composed of specially formulated ingredients that the manufacturer claims are made of a proprietary blend. These ingredients, referred to as nutraceuticals by the manufacturer, reportedly are manufactured using pharmaceutical-grade ingredients and the purest and highest quality extracts and nutrients.

Folic Acid (Folate)—Folic acid (folate) helps promote the normal development of healthy squamous epithelium and binds to the endotoxins from bacterial plaque thereby preventing additional irritation.[1-2,12]

Cyanocobalamin (Vitamin B_{12})—Cyanocobalamin (vitamin B_{12}) helps patients with anemia and has been shown to prevent elevated levels of monocysteine, which is known to be a factor in the onset of arteriosclerosis.[13]

Ascorbic Acid (Vitamin C)—Ascorbic acid (vitamin C) is an intracellular and intercellular aqueous antioxidant that works synergistically with bioflavonoids and vitamin E to prevent the oxidation of the cells of the body.[14,15]

Echinacea Angustifolia (Purple Cone Flower)—Echinacea angustifolia may stimu-

[a]Pharmaden, Inc, Scottsdale, AZ 85260; (800) 910-5523

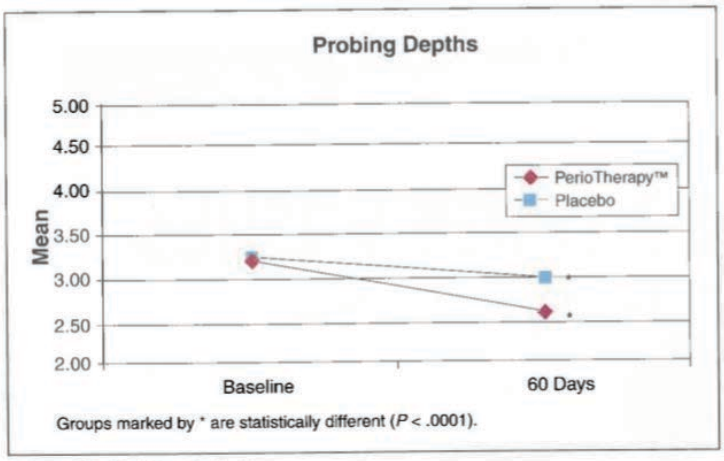


Figure 2A—Probing depth change.

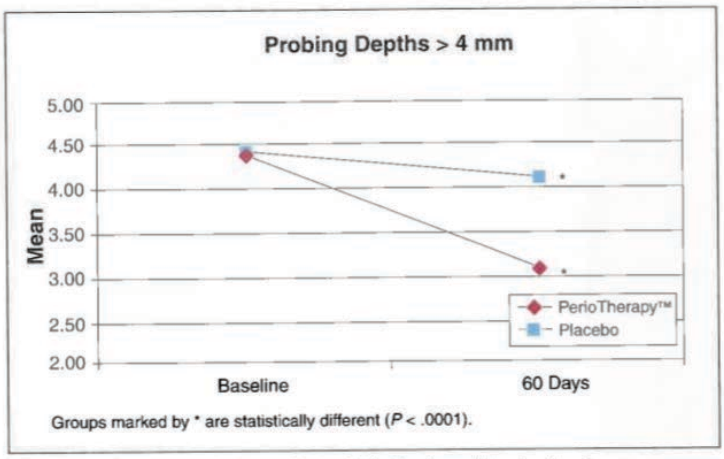


Figure 2B—Probing depth change for teeth that had a probing depth > 4 mm.

late cellular immunity and inhibit the release of bacterial hyaluronidase that permits bacteria to spread deeper into the gingival crevice.

Vitis Vinifera (Grape) Seed—Vitis vinifera (grape) seed proanthocyanidins have been shown to bind to proline-rich proteins in bacterial membranes preventing them from forming the aggregations that play a role in the onset of periodontal disease. They also inhibit collagenase and serine protease secreted by bacteria and white blood cells and deactivate oxygen-free radicals that lead to the destruction of the periodontium.[16]

Ubiquinone (Coenzyme Q10)—Ubiquinone (coenzyme Q10) is added to enhance the production of adenosine triphosphate (ATP) energy in the gingiva itself to promote health.[17]

Piper Nigrum (Black Pepper) Extract—Piper nigrum (black pepper) extract is included because it enhances the absorption and bioavailability of all the other ingredients.[18]

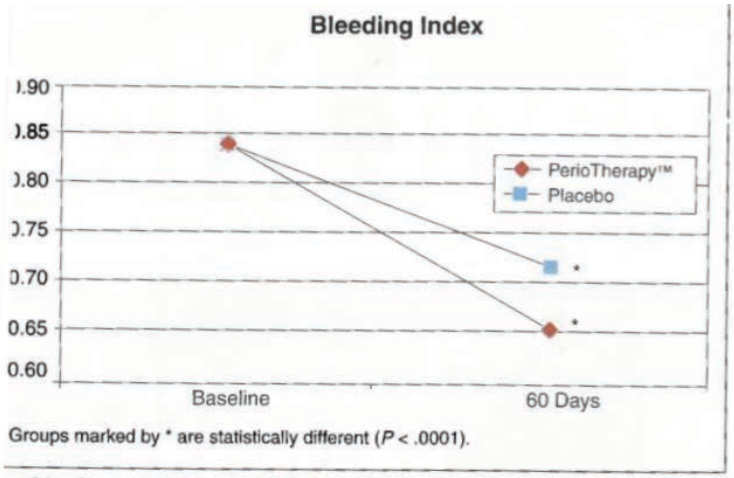
Materials and Methods

Population

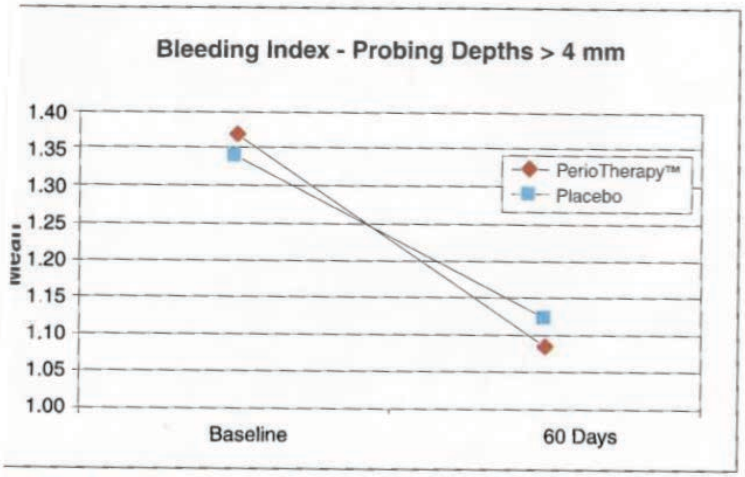
Sixty-three patients ranging in age from 20 to 70 years and diagnosed with gingivitis and Type II periodontal disease were selected for a 60-day double-blind clinical trial. The inclusion criteria included the ablility to read, understand, and sign the informed consent form as well as the patient being in a state of general good health and having a minimum of 20 natural teeth. Study participants were either referred to the Loma Linda University School of Dentistry by their private dentist or chosen from patients who were diagnosed with periodontal disease by the school's Department of Periodontology. The mean Gingival Index score at the beginning of the study was > 1.7. In addition, the patients had to have moderate periodontitis in at least one quadrant of the mouth and have at least three periodontal pockets that measured 4 mm to 5 mm in depth (not to exceed 7 mm) that bled on gentle probing. Patients with periodontal pockets in which the depth of the pocket corresponded to the apex of the tooth, as in a possible endodontic/periodontic combined lesion, were not selected. Likewise, patients who chronically used concomitant medications that could potentially affect soft-tissue health or individuals diagnosed with a chronic infectious disease who presented with oral manifestations were also excluded from the study. Subjects with allergies to acrylic resins or latex gloves, pregnant or nursing women, and smokers were excluded as well.

Study Design

Patients were randomly assigned to either the experimental group (32) or to the control group (31). The experimental treatment consisted of one tablet of PerioTherapy™ to be taken at breakfast time after brushing their teeth and a second one in the evening after dinner and brushing. Patients in the control group received a similar looking placebo tablet. Patients in both groups were given an adequate supply of tablets, a new toothbrush, and a tube of toothpaste with written instructions on the protocol for administration, but were not told if they were receiving the experimental or control treatment. To monitor compliance, all patients were asked to maintain a diary and daily log of their activity and record any unusual events.



ıre 3A—Gingival bleeding score change.



ıure 3B—Gingival bleeding score change for teeth that had a probing depth > 4 mm.

Clinical Parameters

Measurements of the gingival inflammation, bleeding, pocket depth, and attachment levels were recorded at baseline and 60 days. The following criteria were used for the clinical evaluation:

Soft-Tissue Examination and Survey—A complete soft- and hard-tissue 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 either normal or abnormal. Any abnormal findings were noted on the appropriate evaluation form. Each parameter was scored as normal, slight, moderate, or marked. Soft-tissue examinations were performed by one examiner at each visit.

Gingival Index—The Gingival Index (GI) of Silness and Löe[19] was performed at each evaluation period from the second right maxillary and mandibular premolars (teeth Nos. 4 and 29) to the second left maxillary and mandibular premolars (teeth Nos. 13 and 20) at 6 sites (mesiobuccal, buccal, distobuccal, mesiolingual, lingual, and distolingual) per maxillary and mandibular tooth. The following criteria were used:

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 as well as a tendency to spontaneous bleeding [elicited by air syringe] and/or ulceration).

Probing Depth Measurements—The probing depth (PD) measurements were obtained according to the method developed by Ramfjord using teeth Nos. 3, 9, 12, 19, 25, and 28.[20] 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. In the absence of one of these teeth, the adjacent counterpart was used.

Bleeding on Probing—Bleeding on probing (BI) to the base of the pocket was performed at each evaluation period using the Eastman Bleeding Index[21] 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.

Clinical Attachment Level—To measure the clinical attachment level (AL), the cementoenamel junction (CEJ) was used as a landmark. The end of the probe was placed against the enamel surface coronal to the margin of the gingiva on a 45° angle to the long axis of the tooth. The probe was then moved in an apical direction, and the CEJ was then detected by either tactile sense or by a change in direction of the probe.

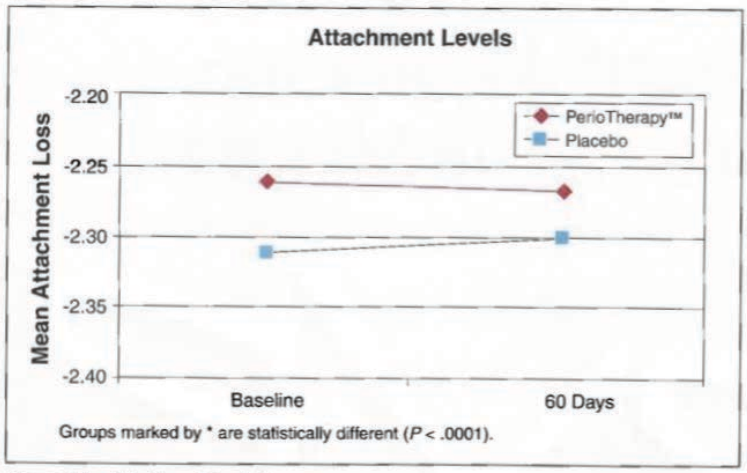


Figure 4A—Attachment level change.

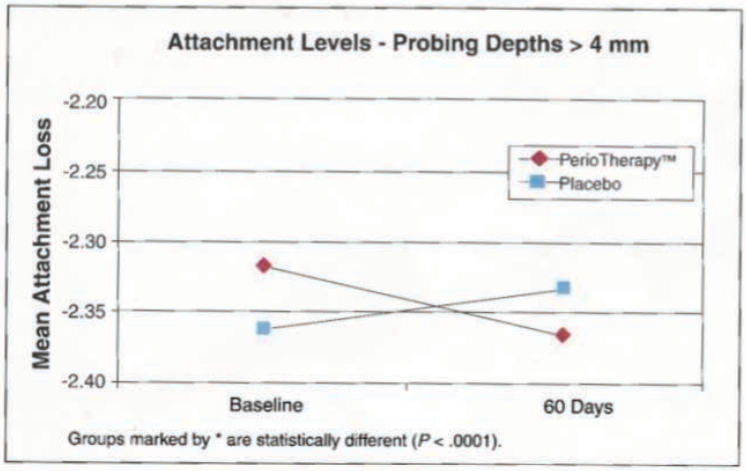


Figure 4B—Attachment level change for teeth that had a probing depth > 4 mm.

If the gingival margin was on enamel, the distance from the gingival margin to the CEJ was first recorded. The probe was then inserted further and the distance from the gingival margin to the bottom of the pocket was recorded. The first measurement was subtracted from the second measurement to obtain the AL. If the gingival margin was on cementum, the AL was recorded as a direct measurement from the CEJ to the base of the pocket. Teeth Nos. 3, 9, 12, 19, 25, and 28 were each measured at six sites. All the measurements were made by one experienced, calibrated examiner with previous experience in soft tissue dental indices studies.

Data Analysis—Comparisons of the mean values for the GI, BI, PD, and AL were analyzed using a one-way analysis of variance (ANOVA) when the variables were normally distributed and the U-Mann-Whitney test was used for non-normally distributed variables. A post-hoc test was used to identify differences when found. A paired *t* test was used to compare gender and time treatments. The level of statistical significance was established at $P < .05$.

Results

There was no statistical clinical difference in periodontal response between the subjects who were men and women. Based on these findings, the data were pooled for all of the subjects (men and women). The data are presented in Figures 1A through 4B and Tables 1 and 2. At baseline, the data showed that overall the four evaluated parameters were similar for both the experimental and the placebo groups (Table 1). When the data at baseline were separated for pocket depths > 4 mm, again all of the parameters were statistically similar with the exception of GI, which was different between the experimental and the placebo groups (Table 1). To determine if there were any differences within the experimental group, a *t* test indicated that there was a statistical significant difference for the GI, PD, and BI ($P < .0001$) from baseline to 60 days; however, no difference was found among these parameters for the placebo group (Table 1). The same trend was found within the experimental and the placebo groups with pocket depths > 4 mm (Table 1).

At the 60-day evaluation point, all subjects receiving the experimental treatment (PerioTherapy™) had significant reductions in the GI (0.49 average) and PD (0.61 average). The subjects taking the placebo experienced only a 0.14 and 0.22 average reduction, respectively (Table 2). When the effect was compared among treatments there were statistical differences and clinically significant reductions in the GI and PD (Table 1 and Figures 1A through 2A). When the data were separated for pocket depths > 4 mm, the results indicated a moderate yet statistically significant reduction in the GI (0.19 average) and clinically significant reduction in the PD (1.37 average) for the experimental group as compared to the placebo group, which had an average GI change of 0.01 and an average PD change of 0.27 ($P < .0001$) (Table 2 and Figures 1B and 2B).

When the experimental and placebo groups were compared for the BI at baseline

Table 1—A Comparison of Treatments and Time Periods

Comparisons	Baseline *P* Value	Significance	2-Month *P* Value	Significance
Gingival Index				
PerioTherapy™ vs Placebo	.9920	No	.0001	Yes
PerioTherapy™ vs Placebo > 4 mm	.0001	Yes	.0001	Yes
Probing Depths				
PerioTherapy™ vs Placebo	.5092	No	.0001	Yes
PerioTherapy™ vs Placebo > 4 mm	.7566	No	.0001	Yes
Bleeding Index				
PerioTherapy™ vs Placebo	.9760	No	.0058	Yes
PerioTherapy™ vs Placebo > 4 mm	.4594	No	.7110	No
Attachment Levels				
PerioTherapy™ vs Placebo	.8134	No	.9261	No
PerioTherapy™ vs Placebo > 4 mm	.8632	No	.8674	No

(0.18 average change) there was no statistical difference, but at 60 days (0.12 average change), there was a clinical and statistical difference ($P < .0001$) between the two groups (Tables 1 and 2). There were no statistical changes in the BI for subjects with > 4 mm for either the experimental or the placebo groups ($P = .7110$) (Table 1 and Figures 3A through 3B).

None of the patients in either group demonstrated any change in AL (Figure 4A through 4B). The pooled data indicated that all subjects had a combined average attachment loss of –2.28 mm at baseline. At 60 days, the experimental group had a net loss of –0.02 mm and the placebo group had a net change of –0.04 mm. No adverse experiences were reported by any of the subjects participating in this study.

Discussion

Although the changes for the placebo group indicated a reduction in the GI, BI, and PD, the changes were small compared to patients who received PerioTherapy™ in the experimental group. In fact, the observed effects of placebo treatment on GI, BI, PD, and AL were greater than anticipated and may be attributed to the Hawthorne Effect with these subjects.[22] It is possible that since the subjects knew they were participating in a clinical trial and would have dental examinations, they improved their oral hygiene. However, even with the Hawthorne Effect taken into consideration, the 60-day data showed that the experimental treatment was more effective in reducing gingivitis and pocket depths (Figures 1A and 3B and Table 1).

The results of this investigation showed that subjects in the experimental group had a reduction in their GI and BI at the end of the 60 days. Teeth with probing depths of ≥ 4 mm receiving the experimental treatment had pocket depths reduced by an average of 1.37 mm in 60 days compared to subjects in the placebo group (0.27 mm) despite the possible influence of the Hawthorne Effect.

Health-conscious Americans have shown a growing interest and participation in medical treatments generally referred to as alternative therapies. From 1990 to 1997, there has been a 25% increase in the proportion of the US population undergoing some form of nontraditional alternative treatment.[23] Individuals 25 to 49 years of age who have higher incomes and more education, spent an estimated $36 billion dollars on alternative medicines and services.[23] In addition, approximately $14.8 billion of those dollars were used to purchase nutraceuticals with the balance spent on alternative services.[23] This growing awareness and increasing concern have also manifested themselves by individuals taking a greater share of the responsi-

E 3

Table 2—Mean Scores Within Treatments and Time Periods

	All Combined			> 4 mm		
	Mean	SD	*P* Value	Mean	SD	*P* Value
Gingival Index						
PerioTherapy™ (BL)	1.86	0.34		1.74	0.44	
PerioTherapy™ (60 day)	1.38	0.49		1.55	0.50	
Difference	(0.48)		.0001	(0.19)		.0001
Placebo (BL)	1.86	0.45		1.85	0.42	
Placebo (60 day)	1.72	0.51		1.86	0.45	
Difference	(0.14)		.5720	(0.01)		.0910
Probing Depths						
PerioTherapy™ (BL)	3.20	1.12		4.47	0.83	
PerioTherapy™ (60 day)	2.59	0.81		3.10	0.94	
Difference	(0.61)		.0001	(1.37)		.0001
Placebo (BL)	3.23	1.27		4.45	1.18	
Placebo (60 day)	3.01	1.32		4.18	1.20	
Difference	(0.22)		.2591	(0.27)		.2961
Bleeding Index						
PerioTherapy™ (BL)	0.83	0.04		1.38	0.72	
PerioTherapy™ (60 day)	0.65	0.07		1.11	0.78	
Difference	(0.18)		.0001	(0.27)		.0001
Placebo (BL)	0.83	0.08		1.34	0.76	
Placebo (60 day)	0.71	0.08		1.13	0.83	
Difference	(0.12)		.3999	(0.21)		.1851
Attachment Levels						
PerioTherapy™ (BL)	-2.26	0.89		-2.27	0.94	
PerioTherapy™ (60 day)	-2.27	0.92		-2.29	0.91	
Difference	(0.01)		.9661	(0.02)		.8355
Placebo (BL)	-2.31	0.73		-2.37	0.84	
Placebo (60 day)	-2.37	0.72		-2.33	0.93	
Difference	(0.06)		.9153	(0.04)		.8964

bility to improve their health by seeking out new therapies or preventive measures.

Gingivitis and periodontal disease are inflammatory processes that involve microorganisms also linked to medical conditions. These bacteria can appear in plaques that build up in arteries and restrict blood flow or play a role in the formation of bacterial endocarditis. Health-conscious people aware of these risks often search for ways to prevent and treat such conditions outside traditional medical and dental avenues.

The introduction of a dietary supplement is intended to offer periodontal patients an adjunctive therapy to improve their oral condition.

The introduction of a dietary supplement is intended to offer periodontal patients an adjunctive therapy to improve their oral condition while also inhibiting biological irritants such as bacteria and endotoxins associated with gingivitis and periodontitis. The alternative therapy evaluated in this investigation with PerioTherapy™ relies on biological plant extracts, selected co-enzymes, and specific vitamins to strengthen host resistance and nourish the tissues of the oral cavity. Health-conscious periodontal patients might find this new therapy appealing.

The authors acknowledge the sensitive balance required when portraying the relative merits of nutritional supplements within the new federal guidelines that went into effect in February 2000.[24] The Food and Drug Administration (FDA), which oversees the multi-billion market of dietary supplements, has stressed the need to differentiate between acceptable and unacceptable claims to avoid

an FDA product review. Basically, any supplement claiming a cure of a disease is subject to FDA review. In contrast, products that promote health or help maintain healthy function rather than cure a specific disease or condition are less likely to require FDA approval.

Multi-vitamin therapy may be beneficial by promoting optimal tissue health. The resulting healthy tissues may be better able to resist attack by disease-causing microorganisms.

While the results of this study suggest that PerioTherapy™ improved the GI, BI, and PD in subjects, further studies are needed to evaluate the effect of plaque control and root planing and scaling in conjunction with the use of PerioTherapy™. Because this was a 60-day study, the long-term effect on the gingival tissues is unknown.

This study was conducted on healthy nonsmoking men and women and nonpregnant women. It is well documented that two of the biggest factors for changes in the GI and BI are smoking and hormonal changes during pregnancy. This study did not evaluate the beneficial effect of the experimental tablet on these two populations and further evaluation is needed in this area.

Although additional research is encouraged, the results of this investigation suggest that one tablet of PerioTherapy™ taken twice daily can lead to improvements in bleeding index, gingival index, and pocket depth when coupled with a regimen of home oral care. The manufacturer recommends a daily supplement for 30 to 90 days.

Conclusion

This new intervention involving the use of nutritional and plant-derived nutraceuticals for oral administration is not intended to replace routine oral hygiene, scaling and root planing, and surgical intervention in the treatment of gingivitis and periodontitis. On the contrary, PerioTherapy™ appears to offer patients a noninvasive, systemic, adjunctive protocol to add to their at-home, oral hygiene regimen in an effort to nourish gingival tissues and promote a healthy periodontal complex in preparation for conventional periodontal treatment by their dental professional.

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