

RE: Pharmanex Study at the University of the Pacific

This is a summary of the final report for the Pharmanex study entitled:

“The Effects of a Nutritional Supplement on Periodontal Condition, Antioxidant Levels, and C-Reactive Proteins” at the University of the Pacific.

An abstract on the study has been submitted to the IADR/AADR (<http://www.dentalresearch.org/>) meeting for next March 2007.

RESULTS Summary:

Eighty-five subjects completed the study with forty assigned the active supplement and forty-five assigned the placebo. Both groups showed improvement in attachment level (gain), bleeding score (decrease), probing depths (decrease), and gingival index score (decrease). There was a slight decrease in C-Reactive Protein for the placebo and a larger increase in C-Reactive Protein for the active supplement. The placebo showed a small decrease in scan score while the active supplement showed an increase. The data were analyzed for significant differences using a t-test on difference scores and a repeated measures analysis of variance. (Results were identical on all such tests, as expected). There were no significant differences between the two groups in any of the parameters evaluated except the active supplement showed a statistically significant increase in scan score ($p < 0.01$).

When only sites with a probing depth of 4 mm or greater were analyzed for changes in bleeding score, gingival index score, probing depth and attachment

level, both experimental and control groups showed a decrease in all four parameters. However, the experimental group showed a statistically significant decrease in gingival index score ($p < 0.02$) when compared to the control. The experimental group also demonstrated a marginally significant decrease in bleeding score ($p < 0.07$) when compared to the control. There was no statistically significant difference between the experimental and control group for probing depth or attachment level. Pages 19-26 show the graphic results and the statistical analysis. Pages 19-22 show results when all sites were analyzed. Pages 23-26 show results when only sites with probing depths greater than or equal to 4 mm were analyzed.

Two-factor ANOVA tests (active / placebo and initial pocket depth < 4 mm / $4+$ mm); analyses of covariance with patient age, gender, C-reactive protein level, and scan score as covariables; and step-wise multiple regression tests were also performed. The 2×2 ANOVA generally confirmed the results of the t-tests on difference scores for sites with initial pocket depths of 4 mm or greater. Gingival inflammation was reduced significantly in the experimental group ($p = .028$), but differences were not found for bleeding, pocket depths, or attachment. The results of the analysis of covariance were more complex and, perhaps, more suggestive of the mechanism of operation involved in treatment. With gingival inflammation as the criterion measure, scan score was highly significant as a covariate ($p = .005$) and treatment group dropped out of significance as a predictor. High scan scores are associated with greater reduction in gingival inflammation. This suggests that decreased gingival inflammation is entirely a function of the elements in the treatment that are

associated with scan score. When bleeding is the criterion, scan score is again a significant covariate ($p = .007$) but the direction of effect is reversed, with high scan scores being associated with decreased reduction in bleeding. However, holding this and other factors statistically constant (the purpose of the analysis of covariance), the treatment group emerged as an important factor in reducing bleeding ($p = .005$). This complex effect was confirmed through multiple regression analysis controlling the order of entry of the predictor variables. Considering both scan score and treatment together, each unit increase in scan score retards improvement in bleeding by .016 units and being a member of the treatment group improves bleeding score by .177 units. The proportion of variance explained by both factors together is $R^2 = 5\%$, $p = .01$. There were no remarkable findings with regard to pocket depth or attachment using this approach to analyzing the data. The statistical reports supporting these analyses appear on pages 29-40.

A note from the Principle Investigator:

I feel very excited about our findings. The scanner readings were statistically significant when the supplement was compared to the placebo. In our second analysis we focused on only the 4mm+ pockets. After doing this further analysis, the gingival index was statistically significant when the supplement was compared to the placebo, and the bleeding index was marginally statistically significant for the supplement compared to the placebo. There were no significant statistical differences when pocket depth and attachment levels were compared. I am not surprised about this as I would expect to see changes in gingival inflammation and bleeding rather measurable differences in the pockets and attachment levels over a short eight week study period. This is likely what we might find in clinical practice. I had hoped, however, that we

might find a significant correlation with the C-Reaction Protein test, but there are some plausible explanations for this. The CRP test (cardio-specific) picks up markers of inflammation, which are not specific for the gingiva (gums). Some subjects in the study reported various illnesses while participating (colds, flu, etc.) and some others reported an upset stomach from taking the supplement. These could contribute to our CRP findings.