

NovaMin® Clinical Study Results

Study #1: Sensitivity Reduction vs. Placebo:

Objectives:

To evaluate the efficacy of a dentifrice containing 7.5 wt. % NovaMin® (DenShield™ or SootheRx®) compared to a negative control (placebo) dentifrice in relieving dentine hypersensitivity over a period of 4-weeks.

Material and Methods:

The study was a single site, double-blinded, two-arm parallel group study to assess the efficacy of a 7.5% w/w NovaMin® containing dentifrice in the reduction of tooth hypersensitivity. Subjects had a soft tissue oral examination, clinical assessment, and controlled stimuli to identify sensitive teeth. Subjects had to have at least two sensitive teeth to air stimulation with a measured VAS ≥ 30 but less than 85 on a scale of 0 to 100mm to be included in the study. Two measures of sensitivity were used in the study; a metered air blast (one-second duration) and cold water (3 ml) delivered from a syringe kept at 4°C. The time between measures on a given tooth was at least 3 minutes. Subjects were instructed to brush their teeth in their usual manner, for one minute, brushing no more than a total of two times per day for two weeks. At the two-week appointment, patients returned the unused toothpaste, and were given single doses and instructed to use the product only once a week for two additional weeks.

The study protocol was approved by the Ethics Committee at the Dental School of the University of Bologna, Italy. Patients were between the ages of 18 and 65 years old, signed informed consent, had a minimum of 10 natural evaluable teeth with at least two sensitive teeth and could read and follow instructions. Patients with chronic diseases with oral manifestations, orthodontic appliances, restorations or bridgework less than 5mm from a sensitive tooth were excluded from the study. In addition, patients with active infectious diseases such as hepatitis, HIV or tuberculosis, and females who might be pregnant or lactating were also excluded from the study.

A total of 20 patients were enrolled in the study, 10 in each group. There were no adverse events reported during the study. All patients completed the course of treatment.

Results:

A 2 (treatment) x 5 (time periods) repeated-measures ANOVA was conducted on the VAS score averaged across the cold water and air pressure methods. Table 1 and Figure 1 show that there were significant effects of treatment (NovaMin® was statistically better at reducing sensitivity than placebo, $p < .001$) and that the effects were statistically significant over the time periods as well ($p < .001$). Post hoc tests showed that there were no differences between the test and placebo group at baseline, but that the test group was statistically better at each time point than the placebo. The test group showed statistical decline in VAS score at each time point, and the placebo only showed a statistical decrease at the 3-week ($p < .021$) and 4-week ($p < .017$) time periods versus baseline. The data included in Table 1 and Figure 1 represents 10 patients in each group. At the baseline measurement the figure in parenthesis represents the number of teeth that were measured in each group.

Figure 1. *The Effects of Two Treatments on VAS scores Using Cold Water at Five Time Periods.* Error bars represent ± 1 standard error from each group's mean

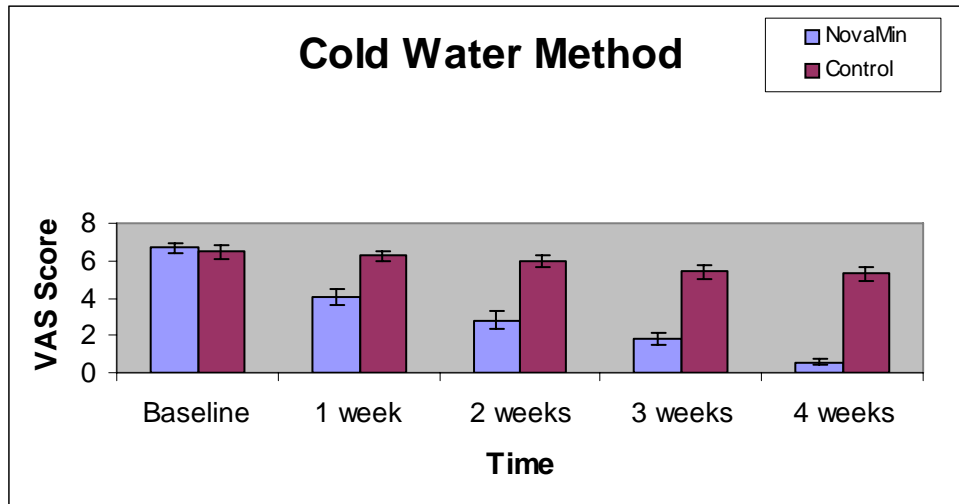
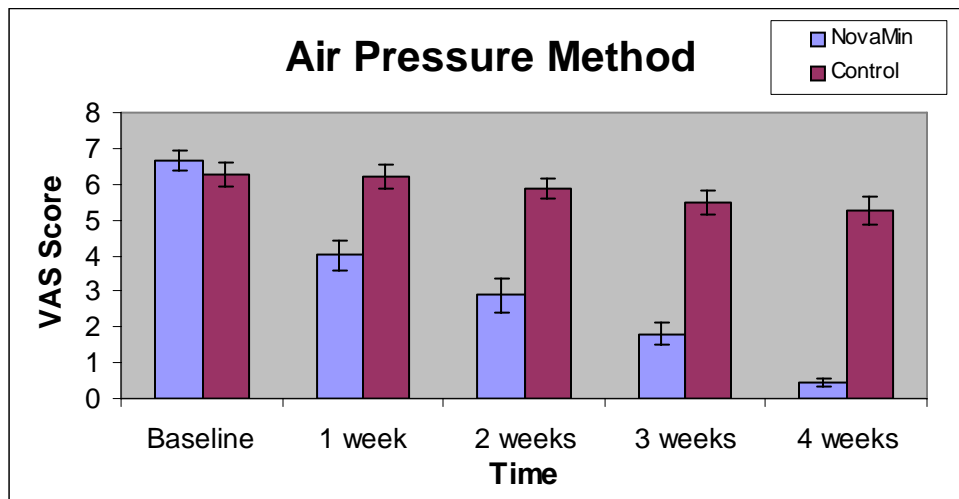


Figure 2. *The Effects of Two Treatments on VAS scores Using Air Pressure at Five Time Periods.* Error bars represent ± 1 standard error from each group's mean



Conclusion:

The results of the current study support the previous conducted studies, demonstrating the rapid and continuous relief from tooth hypersensitivity using a 7.5% w/w concentration NovaMin[®] in a non-fluoride toothpaste. There were no adverse events reported in this study.

Study #2: Sensitivity Reduction vs. Strontium Chloride:

Objectives:

To evaluate the efficacy of a dentifrice containing 5 wt.% NovaMin® (Oravive®) compared to a positive control (SrCl₂) and negative control (placebo) dentifrice in relieving dentine hypersensitivity over a period of 6-weeks.

Material and Methods:

The study design was a randomized, double-blinded, parallel-group, experiment with a positive and negative control group. Test dentifrices containing NovaMin®, a positive control previously clinically proven as an anti-sensitivity toothpaste, and a negative control dentifrice without NovaMin®. Seventy- five (75) qualified volunteers took part in the study according to the inclusion and exclusion criteria. Tooth sensitivity was recorded by marking the degree of discomfort on a 10-cm long visual-analogue scale (VAS) when elicited by an evaporative stimulus and cold-water stimuli at an interval of 5 minutes. A soft tissue examination of the whole mouth was carried out to assess any adverse effects of the study dentifrice on oral soft tissues. The protocol was reviewed and approved by the Medical Ethical Committee of the University before the study was conducted. Changes were assessed for statistical significance using ANOVA.

Results:

Change in Sensitivity (VAS) vs. Baseline

Test Article	2-weeks		6-weeks	
	Air pres.	Cold H2O	Air pres.	Cold H2O
NovaMin®	-20%	-5%	-36%	-40%
SrCl ₂	-15%	+2%	-23%	-24%
Negative control	-14%	+3%	-9%	-17%

Seventy-one subjects finished the study, the age ranges from 20 to 56 years old. The results showed that the mean values of the VAS scores resulting from the air stimulus, cold water and overall assessment of sensitivity were reduced significantly (p<0.01) in both test and positive control group after six weeks of tooth brushing. No product related adverse events on oral soft tissue were found in this six weeks study.

Conclusion:

The results of this study showed that the test dentifrice containing NovaMin® and the positive control toothpaste reduced dentine sensitivity significantly over the 6-weeks period study.

Study #3: Sensitivity Reduction vs. Potassium Nitrate and Stannous Fluoride:

Objective:

The purpose of this clinical study was to evaluate the effectiveness of three dentifrices containing 5% potassium nitrate, 0.4% stannous fluoride and 7.5% sodium calcium phosphosilicate (NovaMin®) containing dentifrice respectively in the treatment of dentinal hypersensitivity.

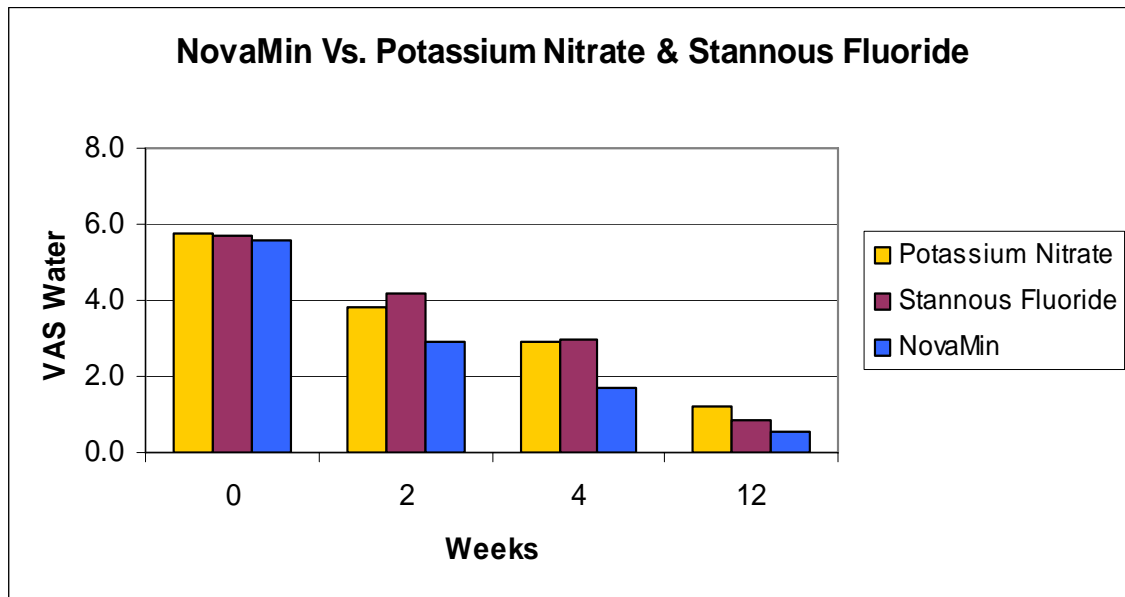
Materials & Methods:

The study was a randomized, double-blinded, clinical trial. The study included 120 volunteers, which were balanced for gender and selected based on an evaluation of sensitivity. Sensitivity was measured using a measured cold water and cold air blast onto identified teeth (canines, incisors or pre-molars). Those scoring between 4 and 10 on a visual analogue scale of 0-10 were

included (0=no pain, 10= extreme pain). Participants were randomly divided into three groups. Each was given a test dentifrice and instructed to brush twice daily for about 2 minutes. Patients were recalled at 2, 4 and 12 weeks for measurement via the cold air and cold water methods.

Results:

For air at weeks 2 and 4, there were significant main effects for group with NovaMin® more effective than the other two groups, which did not differ between themselves. For air at week 12, the effect of group was not significant. For water at weeks 2 and 4, there were significant main effects for group with NovaMin® more effective than the other two groups, which did not differ between themselves. For water at week 12, there was a significant main effect for group with the only significant pair-wise effect being NovaMin more effective than the potassium nitrate group.



Conclusion:

All three products reduced sensitivity, with the NovaMin containing product showing much greater reductions at the 2- and 4-week time periods.

Study #4: Gingivitis Reduction:

Objective:

To evaluate the anti-gingivitis and anti-plaque efficacy of a dentifrice containing 5 wt.% NovaMin® (Oravive®) and a negative control dentifrice (without NovaMin®) in a 6-weeks clinical trial study.

Material and Methods:

The study design was a randomized, double-blinded, controlled clinical trial. One hundred (100) volunteers took part in the study according to the inclusion and exclusion criteria. The subjects received a supragingival prophylaxis to remove all plaque, calculus and extrinsic stain. Following the baseline examination subjects were instructed to brush with their

assigned dentifrice and toothbrush twice per day. The levels of Silness & Loe Plaque Index (PLI) and Gingival Bleeding Index (PBI) were determined for the baseline and 6-week assessments.

The protocol was reviewed and approved by the Medical Ethical Committee of the University before the study was conducted. Student t-test was used to compare the effect between the test and control group; P value was set at 5% level.

Results:

Ninety-five subjects finished the study, the age ranges from 20 to 48 years old. The results showed that the PBI and PLI were significantly reduced respectively over 6-weeks period in the test group (n=47) and there was no difference in the PBI and PLI over 6-weeks period in the negative control group (n=48):

Change in Index vs. Baseline

Test Article	Bleeding Index	Plaque index
NovaMin®	-59%	-16%
Placebo	-14%	-2%

Conclusion:

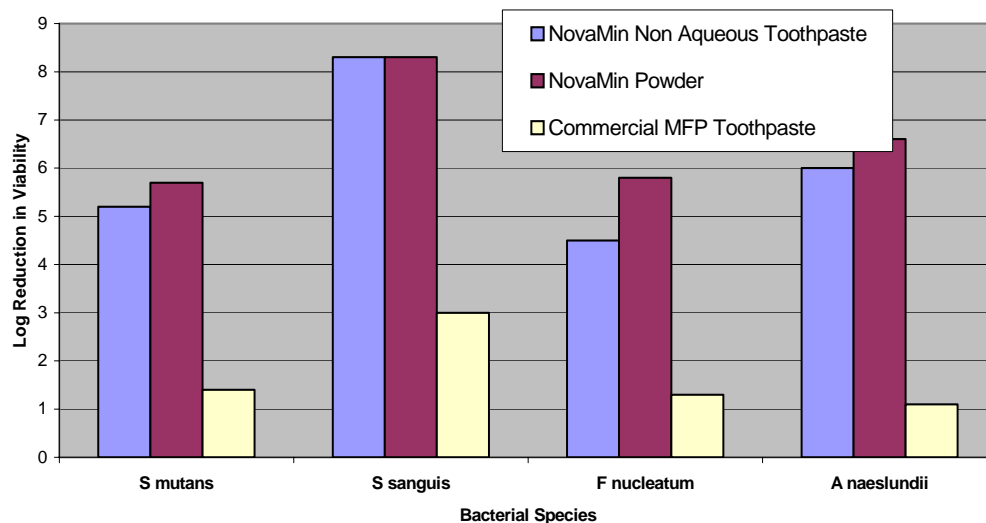
This study demonstrated that a dentifrice containing NovaMin® could significantly improve in oral health as measured by a reduction in gingival bleeding and reduction in supra-gingival plaque compared with negative dentifrice over the 6-weeks study period.

NovaMin® In-Vitro Study Results

In-Vitro Anti-Microbial Data:

In conjunction with our SBIR grant, we conducted in vitro anti-microbial experiments to determine effectiveness of NovaMin® at controlling key oral bacteria. The work compared pure NovaMin®; a 3.5 wt.% NovaMin toothpaste; and commercially available toothpaste against key oral bacteria associated with tooth decay and other oral diseases. Results shown below demonstrate a high kill rate for the NovaMin® and NovaMin® containing toothpaste. These kill rates are comparable to antibiotic rinses currently in use to treat gingivitis and other oral pathologies:

Log Reduction in Microbial CFU's - 2 Minute Exposure to 1:3 Dilution



In-Vitro Remineralization Data:



Paper #59549

In Vitro Human Enamel Remineralization Using Bioactive Glass Containing Dentifrice

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Objectives: To determine early caries remineralization capability of NovaMin® (bioactive glass) containing dentifrice compared to commercial dentifrice on human enamel in vitro using confocal laser scanning microscopy (CLSM).

Methods: Eighteen human molars were sterilized and sectioned into quadrants along mesiodistal and buccolingual planes. Each section was mounted in epoxy resin then mechanically polished to expose 3 mm diameter treatment windows. Three sections of each tooth were uniformly demineralized to create 100 µm lesions, the fourth section held as a control. Two lesionous sections were then further treated under pH cycling regimen for 20 days (at 37° C) with daily ~23 hours synthetic saliva, 1 hour acid challenge and 6 minutes dentifrice treatment (NovaMin® dentifrice or Colgate® Regular). All sections were then cross-sectioned through the treatment window for confocal microscopic analysis.

Results: CLSM analysis was performed with modified Nikon microscope with Odyssey confocal capability and Metamorph 4.1.6 software. All four sections of 18 teeth were analyzed to determine remineralization based upon two imaging parameters, Lesion Area and Total Gray Value (fluorescence), which have previously correlated well with transverse microradiography (TMR), a direct measure of mineral density. For 16 of 18 teeth, NovaMin® treated tooth sections remineralized lesions more than Colgate® for both parameters. Single tailed T-test for treatment groups yielded significant difference ($p < 0.001$). NovaMin® dentifrice treatment reduced lesion area an average 41.9%, while Colgate® averaged 24.9%. NovaMin® sections also exhibited an average 70.5% decrease in total gray value (reduced porosity) compared to 48.1% for Colgate®. Two-way ANOVA testing of three tooth sections (original lesion, NovaMin® treatment, Colgate® treatment) for both parameters found significant difference ($p < 0.0001$). Duncan multiple range testing found these three sections statistically different at significance level 0.01.

Conclusions: A NovaMin® dentifrice exhibits further remineralization of early caries lesions in human enamel compared to Colgate® Regular in vitro.