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Review

# Clinical Evaluation of A 5% Potassium Nitrate Containing Mouthrinse in Relieving Dentine Hypersensitivity (DH)

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## Abstract

Potassium nitrate dentifrices ($KNO_3$) have been used to treat the symptoms of dentine hypersensitivity (DH), however relatively few mouthrinse studies have been published.

### Aim

The aim of this study was to compare a 5% $KNO_3$ mouthrinse to a placebo control in an 8-week double-blind placebo-controlled study.

### Materials and Methods

Male and female subjects aged 18 to 65 years in good health and a history of Dentine Hypersensitivity were recruited for the study. Subjects were randomised and allocated into the test and control groups and instructed to use the mouthrinse twice a day after brushing with a regular family toothpaste using a small head soft toothbrush. The clinical evaluation of Dentine Hypersensitivity included 1) Subjective Sensitivity (Perception of overal sensitivity) using aVAS score, 2) Thermal Sensitivity response from a one second air blast from a dental air syringe using VAS Scores, 3) Tactile Sensitivity Threshold Scores on the selected test teeth using a controlled force probe (gm. weight) and 4) Tactile Sensitivity at a Fixed Force of 40 gm. weight evaluating the remaining teeth to determine the existence of dentine sensitivity based on a simple yes/no response. Subjects were evaluated at baseline, four and eight weeks.

### Results

The 104 subjects recruited for the study, 103 subjects (35M; 68F mean age 34.6 years) completed the study. The results indicated that the tactile response demonstrated the clearest difference between the $KNO_3$ mouth rinse and placebo. Both the $KNO_3$ and placebo mouth rinse showed an increase in the tactile sensitivity threshold (i.e. less sensitivity) at both evaluation time points with the increase in the tactile sensitivity threshold twice as high at Week 8 than at Week 4. The increase in sensitivity threshold using $KNO_3$ was twice as large as the increase with Placebo at both time points (6.79 g for $KNO_3$ compared to 3.60g for Placebo at Week 4 and 11.80 g for $KNO_3$ compared to 6.58 g for Placebo at Week 8) with a statistically significant difference ($p = 0.031$) at Week 8. Moreover, the efficacy of the $KNO_3$ treatment was more apparent in subjects with a more severe condition of dentine hypersensitivity, as measured by the number of threshold sensitive teeth at baseline. Among the 75 subjects with ≥ three tactile sensitive teeth, the active treatment was statistically significantly superior to placebo ($p < 0.01$) at both the Week 4 and Week 8 evaluation points.

### Conclusion

These results therefore confirm the results of Gillam et al. ~~(1996)~~ by demonstrating that a 5% $KNO_3$ mouthwash significantly reduced dentine hypersensitivity as measured by tactile stimulation.

**Key Words:** Dentine Hypersensitivity; Potassium Nitrate Mouthrinse; Placebo Controlled, Randomised Double Blind; Tactile Evaluation

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## Introduction

Potassium nitrate ($KNO_3$) has been used previously in a dentifrice or gel to treat the symptoms of dentine hypersensitivity (DH). There have been relative few published studies on the use of potassium containing mouthrinses. Of these published studies Gillam et al. [1] and Pereira & Chava [2] compared a 3% $KNO_3$ mouthrinse to a control and suggested that $KNO_3$ mouthrinses appear to have therapeutic potential to alleviate DH. Efficacy for $KNO_3$ rinses in reducing DH was also demonstrated in subjects following periodontal treatment (Martinez and Loscos [3] and Oteo et al. [4]. A study by Yates et al. [5] Comparing a 2% Potassium citrate mouthrinse with a base rinse minus actives placebo control also reported highly significant reductions in DH for both groups although due to the magnitude of the placebo response (30-40%) there were no significant differences between the two groups.

## Aim

The aim of this clinical study was to compare a 5% $KNO_3$ mouthrinse to a placebo control in an 8-week double-blind placebo-controlled study.

## Materials and Methods

Subjects who gave their oral and written informed consent and satisified both inclusion and exclusion criteria were entered into the study, which had local Joint Research and Ethics Committee (JREC [IRB]) approval. The study was conducted according to the guidelines for good clinical practice (GCP). All subjects were given an oral examination (DGG) to determine their suitability for the study. The clinical assessments were performed by DGG/AA who were trained and calibrated in these assessments prior to the commencement of the study.

### Inclusion and Exclusion Criteria

Male and female subjects aged 18 to 65 years selected for the study had to be in good health, and report sensitivity on the subjective, tactile and thermal scales, as described below. Among the exclusion criteria for subjects were: (1) Chronic disease associated with intermittent or constant daily pain; (2) Regular use of a desensitizing dentifrice within 2 months before the start of the study; (3) A dental prophylaxis within 2 weeks of the projected start of the study; (4) Daily doses of certain medications, including analgesics, anticonvulsants, antihistamines, sedatives, tranquilizers, mood-altering drugs or antiinflammatory drugs; (5) Demonstration of gross oral neglect or the need for extensive dental therapy.

Subjects in the study were instructed to use the mouthrinse twice a day after brushing with a regular family toothpaste (Colgate Great Regular

Flavour), using a small head soft toothbrush.

Four clinical evaluations of sensitivity were used:

### Subjective Sensitivity

Subjects were asked to evaluate their typical perceived pain level due to dentine hypersensitivity using a 100 mm Visual Analog Scale (VAS).

**Thermal Sensitivity:** Each sensitive tooth was subjected to a one second application of cold air from a standard dental air syringe at 40-65 p.s.i. at a temperature of 19°C+ 3°C and the intensity of pain evoked was marked by the subject on a 100 mm Visual Analogue Scale (VAS).

**Tactile Sensitivity Threshold:** Each sensitive tooth was subjected to a variable force in grams using the Yeaple probe (Vine Valley Research, Middlesex, New York, USA) and the pain sensitivity threshold was recorded.

**Tactile Sensitivity at a Fixed Force of 40 grams:** All additional teeth were subject to a fixed force of 40 grams using the Yeaple probe and the existence of sensitivity was recorded as a yes/no variable. All subjects reporting an overall hypersensitivity score in the range of 30-80 mm on a 100 mm VAS at both the qualifying and baseline visit were eligible for the study.

Tactile sensitive teeth were those with a positive response to a fixed force of 40 grams followed by a Yeaple probe threshold score in the range of 15-50 grams. Thermal sensitive teeth were those which displayed a response from 30-80 mm on the 100 mm VAS. Selected subjects were to have at least one tactile sensitive tooth and a minimum of two thermal sensitive teeth.

Information on all adverse experiences or other on-going conditions occuring during the course of the study was collected, whether or not they were associated with the study product. At each visit, subjects were questioned regarding the occurrence of side effects in such a way as to not lead or bias the subject's response.

Sensitivity assessments were conducted at Baseline and at 4 and 8 weeks. Each subject received a diary to record the number of times they brushed their teeth during the study; this was to monitor their compliance during the study.

## Statistical Methods

### Analysis of Non-incisors

Statistical results for both thermal and tactile efficacy were based on teeth other than incisors. This was supported by suggestion in the literature that efficacy was difficult to demonstrate in incisor teeth, perhaps because of the bilateral innervation confounds the results [6].

Analyses of the primary efficacy measures based on the teeth were performed utilizing mixed linear models (implemented with SAS, PROC MIXED). In these analyses the unit of analysis was the tooth within the subject and multiple teeth within the same subject were adjusted for. This was particularly important for the tactile measure in which a widely varying number of teeth were evaluated in different subjects (Table 1),

and therefore the analysis based on subject averages was not appropriate.

The t-statistic reported for the three efficacy measures in (Tables 3-5) was the ratio of the mean change from baseline divided by its standard error and reported from the mixed linear model. The significance level associated with the t-statistic represents the statistical significance of the change from baseline.

## Results

One hundred and four subjects were randomised and 103 subjects were considered intent-to-treat evaluable and included in the analyses. Of the 103 subjects (35M; 68F mean age 34.6 years) who completed the study, 31 subjects (30%) were smokers. The two treatment groups were comparable for all the demographic characteristics (Table 2).

### Subjective Response

For both treatment groups, the decrease in sensitivity from baseline was observed to be statistically significant at both Week 4 and Week 8. However, the subjective assessment of hypersensitivity did not show a difference between the two treatments at either Week 4 or Week 8 (Table 3).

### Thermal Response

Baseline levels of thermal sensitivity were comparable between the two treatment groups. For both treatment groups, the decrease in sensitivity from baseline was observed to be statistically significant at both Week 4 and Week 8. Thermally sensitive teeth in subjects using the $KNO_3$ rinse exhibited a greater reduction in thermal sensitivity at Week 4 than with Placebo whereas the reverse was true at Week 8. Neither difference was statistically significant.

### Tactile Response – Teeth Qualifying For Threshold Testing

At baseline, the teeth exposed to the $KNO_3$ mouth rinse were numerically more sensitive than ~~were~~ the teeth exposed to the placebo (19.06 g versus 20.21 g, p=.055). The post-baseline comparisons were adjusted for this baseline difference. For both treatment groups, the decrease in sensitivity from baseline was observed to be statistically significant at both Week 4 and Week 8. Both $KNO_3$ and Placebo showed an increase in the tactile sensitivity threshold (i.e. reduction in sensitivity) at both time points with the increase in the tactile sensitivity threshold being twice as high at Week 8 as at Week 4. The increase in the sensitivity threshold with $KNO_3$ was twice as large as the increase with Placebo at both time points (6.79 g for $KNO_3$ compared to 3.60g for Placebo at Week 4 and 11.80 g for $KNO_3$ compared to 6.58 g for Placebo at Week 8) with the difference at Week 8 being statistically significant (p=.031). Moreover, as shown in (Table 6) the efficacy of the active treatment was more apparent in subjects with a more severe condition of dentine hypersensitivity, as measured by the number of threshold sensitive teeth at baseline. For the 75 subjects with at least three tactile sensitive teeth, the active treatment was statistically significantly superior to placebo ($p < 0.01$) at both the Week 4 and Week 8 evaluation points.

### Safety

There were 5 events reported in 5 subjects, during the 8 weeks of the study. Only one event, a mouth ulcer considered to be mild and unrelated to the product, was reported in the $KNO_3$ group; the other 4 reported events were in the placebo group.

## Discussion

According to Orchardson & Gillam [7] formulations containing potassium salts (either in toothpaste, gels, solutions and mouthrinses) have been widely used for treating DH although the effectiveness of these formulations (in toothpaste form) in reducing DH has been questioned [8]. The regular use of a pre- or post-rinse mouthrinse following routine toothbrushing with a fluoride toothpaste may be more acceptable to consumers and it is feasible that a formulation containing potassium and fluoride may be beneficial not only for reducing symptoms of DH but also help prevent root caries in an adult population [1,9]. The question of whether a pre-rinse or a post-rinse desensitising mouthrinse would be more effective was not addressed in this study and this may need to be resolved in further studies.

Evaluation of the pain response in clinical trials designed to assess the efficacy of desensitizing products, however, is problematic for the clinical assessor. This was due in part to the highly subjective nature of the problem as well as the influence of Hawthorne and placebo effects throughout the duration of the trial. The study by Yates et al. ~~(5)~~ highlighted this problem of the magnitude of the placebo response which has also been reported by other investigators [1, 10-12]. Other factors such as lack of statistical power (small sample size) and lack of standardization of the methodology used in clinical trials to determine treatment outcomes can also influence the results [13].

Efficacy for $KNO_3$ rinses in reducing DH has been previously demonstrated in subjects following periodontal treatment ~~(3-4)~~ as well as in subjects with a history of DH ~~(1-2)~~. Both Gillam et al. (1) and Pereira & Chava ~~(2)~~ evalauted a 3% $KNO_3$ mouthrinse using similar methodology with the exception of the tactile evaluation over 6-8 weeks product use. In the Gillam et al. study ~~(1)~~ the clearest difference between the two treatments was demonstrated on the tactile scale, whereas Pereira & Chava ~~(2)~~ demonstrated significant differences in both the Overall sensitivity and Thermal scales. The present study appeared to confirm the findings of the Gillam et al. study ~~(1)~~ in that the tactile response demonstrated the clearest difference between the $KNO_3$ mouthrinse and placebo. Both $KNO_3$ and placebo showed an increase in the tactile sensitivity threshold (i.e. less sensitivity) at both evaluation time points with the increase in the tactile sensitivity threshold twice as high at Week 8 than at Week 4. The increase in sensitivity threshold using $KNO_3$ was twice as large as the increase with Placebo at both time points (6.79 g for $KNO_3$ compared to

3.60g for Placebo at Week 4 and 11.80 g for $KNO_3$ compared to 6.58 g for Placebo at Week 8) with a statistically significant difference ($p = 0.031$) at Week 8

Moreover, the efficacy of the $KNO_3$ treatment was more apparent in subjects with a more severe condition of dentine hypersensitivity, as measured by the number of threshold sensitive teeth at baseline. Among the 75 subjects with at least three tactile sensitive teeth, the active treatment was statistically significantly superior to placebo ($p < 0.01$) at both the Week 4 and Week 8 evaluation points.

## Conclusions

The results from the present 8-week clinical study appear to demonstrate that rinsing with a 5% $KNO_3$ mouthrinse following toothbrushing may alleviate DH, particularly in those individuals with more severe DH. Furthermore, the results confirmed the results of Gillam et al. ~~(1)~~ by demonstrating that the 5% $KNO_3$ mouthrinse significantly reduced DH as measured by tactile stimuli.

**Table 1:** Number of Threshold Sensitive Teeth (Non-incisors) per Subject

| Teeth per Subject | % of Subjects |
|---|---|
| 1 | 16% |
| 2 | 22% |
| 3 | 22% |
| 4-5 | 22% |
| 6-7 | 12% |
| 8-12 | 7% |

**Table 2:** Demographic Characteristics of the Study Population

| Characteristics | $KNO_3$ Rinse | Placebo | TOTAL | P-Value |
|---|---|---|---|---|
| | n = 51 | n = 52 | n = 103 | |
| **Age (years)** | | | | |
| N | 51 | 52 | 103 | |
| Mean | 33.66 | 35.49 | 34.59 | 0.387 |
| Std. Err | 1.43 | 1.54 | 1.05 | |
| Minimum | 18.78 | 19.15 | 18.78 | |
| Maximum | 61.52 | 62.80 | 62.80 | |
| **Sex** | | | | |
| Male | 14 ( 27.5%) | 21 ( 40.4%) | 35 ( 34.0%) | |
| female | 37 ( 72.5%) | 31 ( 59.6%) | 68 ( 66.0%) | 0.213 |
| **Race** | | | | |
| Caucasian | 39 ( 76.5%) | 38 ( 73.1%) | 77 ( 74.8%) | |
| Black (Non-Hispanic) | 6 ( 11.8%) | 3 ( 5.8%) | 9 ( 8.7%) | 0.597 |
| Hispanic | 2 ( 3.9%) | 4 ( 7.7%) | 6 ( 5.8%) | |
| Asian/Pacific | 4 ( 7.8%) | 6 ( 11.5%) | 10 ( 9.7%) | |
| Other | 0 ( 0.0%) | 1 ( 1.9%) | 1 ( 1.0%) | |
| **Smoker** | | | | |
| No | 35 ( 68.6%) | 37 ( 71.2%) | 72 ( 69.9%) | 0.832 |
| Yes | 16 ( 31.4%) | 15 ( 28.8%) | 31 ( 30.1%) | |

Age P-value from the ANOVA model with treatment as a factor. All other P-values were from the Fisher's Exact Test.

**Table 3:** Subjective Assessment at Baseline and Post-Baseline: Reduction in Sensitivity

| Period | $KNO_3$ Rinse | Placebo | P-value |
|---|---|---|---|
| | | | |
| **Baseline** | | | 0.479 |
| LS Mean | 44.49 | 42.00 | |
| LS Std Err | 2.50 | 2.45 | |
| | | | |
| **Week 4** | | | 0.701 |
| LS Mean | -8.91 | -10.34 | |
| LS Std Err | 2.65 | 2.60 | |
| t-statistic | 3.36 $^{+}$ | 3.98$^{+}$ | |
| | | | |
| **Week 8** | | | 0.895 |
| LS Mean | -13.99 | -13.49 | |
| LS Std Err | 2.70 | 2.62 | |
| t-statistic | 5.18$^{+}$ | 5.14$^{+}$ | |

(+) p< 0.001

Sensitivity was measured on a 100 mm visual analogue scale anchored at "no pain" to "intense pain". Analysis was based on subject averages; P-values and least squares means from ANOVA model with treatment as a factor. Post-baseline P-values and least squares means were adjusted for the baseline scores.

**Table 4:** Thermal Assessment at Baseline and Post-Baseline Reduction in Thermal Sensitivity

| Period | $KNO_3$ Rinse | Placebo | P-value |
|---|---|---|---|
| | | | |
| **Baseline** | | | .506 |
| LS Mean | 54.60 | 53.09 | |
| LS Std Err | 1.59 | 1.60 | |
| | | | |
| **Week 4** | | | .419 |
| LS Mean | -14.15 | -11.08 | |
| LS Std Err | 2.66 | 2.69 | |
| t-statistic | -5.32$^{+}$ | -4.11$^{+}$ | |
| | | | |
| **Week 8** | | | .628 |
| LS Mean | -17.15 | -19.11 | |
| LS Std Err | 2.81 | 2.89 | |
| t-statistic | -6.10$^{+}$ | -6.62$^{+}$ | |

(+) p< 0.001

Sensitivity was measured on a 100 mm visual analogue scale anchored at "no pain" to "intense pain".

P-values and ~~lest~~ squares means were from a mixed linear model analysis with treatment as a factor.

Post-baseline P-values and least squares means were adjusted for the baseline scores.

**Table 5:** Tactile Assessment at Baseline and Post-Baseline Differences: Increase in Tactile Sensitivity Threshold (gm)

| Period | $KNO_3$ Rinse | Placebo | P-value |
|---|---|---|---|
| | | | |
| **Baseline** | | | .055 |
| LS Mean | 19.06 | 20.21 | |
| LS Std Err | .41 | .42 | |
| | | | |
| **Week 4** | | | .113 |
| LS Mean | 6.79 | 3.60 | |
| LS Std Err | 1.39 | 1.42 | |
| t-statistic | 4.88$^{+}$ | 2.54$^{*}$ | |
| | | | |
| **Week 8** | | | .031$^{*}$ |
| LS Mean | 11.80 | 6.58 | |
| LS Std Err | 1.66 | 1.71 | |
| t-statistic | 7.12$^{+}$ | 3.85$^{+}$ | |
| | | | |

(+) p<.001

(*) p<.05

Sensitivity threshold was measured in grams. P-values and least squares means were from a mixed linear model analysis of the non-incisor teeth with treatment as a factor. Post-baseline P-values and least squares means were adjusted for the baseline scores.

**Table 6:** Tactile Assessment at Baseline and Post-Baseline Differences: Increase in Tactile Sensitivity Threshold (g) (for Subjects with at Least 3 Threshold –Sensitive Teeth at Baseline - n = 75)

| Period | $KNO_3$ Rinse | Placebo | P-value |
|---|---|---|---|
| | | | |
| **Baseline** | | | .047 * |
| LS Mean | 18.85 | 20.12 | |
| LS Std Err | .44 | .44 | |
| | | | |
| **Week 4** | | | .009 * |
| LS Mean | 6.51 | 1.40 | |
| LS Std Err | 1.33 | 1.34 | |
| | | | |
| **Week 8** | | | .008 * |
| LS Mean | 11.74 | 4.81 | |
| LS Std Err | 1.76 | 1.80 | |
| | | | |

(*)p<.05

Sensitivity measured in grams. P-values and least squares means were from a mixed linear model analysis of the non-incisor teeth with treatment as a factor. Post-baseline P-values and least squares means were adjusted for the baseline scores.

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### In Memoriam

This previously unpublished paper is in recognition of the major input that Professor Frederick (Rick) Curro had in the Dental Community both in Industry and in Academia.

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