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Clinical Reductions of Gingivitis and Plaque Accumulation by the Use of an Oral Rinse Containing Copper Bisglycinate

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ABSTRACT

Metal ions of copper, tin, and zinc have demonstrated plaque inhibition when used for oral hygiene. Copper bisglycinate is a unique stable complex of copper suitable for oral use. Oral rinses containing copper levels of 250 ppm or 500 ppm (as bisglycinate) were examined for plaque (Turesky PI) and gingival inflammation/bleeding (Löe-Silness GI) efficacy, dental staining (Meckel), and oral-soft tissue in a blinded, parallel group study. Results were compared to placebo and a 0.12% chlorhexidine gluconate oral rinse (Peridex®) as controls. Following baseline examinations, subjects (188) were stratified into four balanced groups based on plaque and gingivitis scores, and then randomly assigned a treatment product. Subjects received an oral prophylaxis and began twice daily brushing with a commercially available fluoride containing dentifrice followed by rinsing for 30 seconds with 15 ml of the assigned oral rinse. After eight weeks of the study regimen, subjects (179) were examined for plaque, gingivitis, dental staining, and oral-soft tissue. Percent reductions were determined relative to placebo. The 500 ppm copper oral rinse gave a 22.6% gingivitis reduction, 55.1% reduction in gingival bleeding, and 52.2% plaque accumulation reduction, which were all significantly different ($p < 0.05$) from placebo. These reductions were similar to the observed 26.6% gingivitis reduction, 56% gingival bleeding reduction, and 58.4% plaque reduction for the 0.12% chlorhexidine gluconate oral rinse. However, dental staining was about 70% less for the 500 ppm copper rinse compared to the 0.12% chlorhexidine gluconate rinse. The 250 ppm copper rinse demonstrated reductions for gingival bleeding (25.4%) and plaque (41.1%) significantly different from placebo. Reductions for gingivitis (7.3%) and dental staining were not statistically different from placebo. Oral-soft tissue results were equivalent for all treatment groups. **Copper bisglycinate has clinically significant efficacy similar to 0.12% chlorhexidine gluconate regarding plaque, gingivitis, and gingival bleeding with 70% less observed staining.**

INTRODUCTION

Copper is an essential dietary ingredient with a recommended daily allowance of 2-3 mg. Previous reports have demonstrated that cupric ion is retained in the oral cavity (Afseth et al., Scan. *J. Dent. Res*. 91, 42-45, 1983) and shows efficacy regarding plaque and gingivitis (Waerhaug et al., *J. Clin. Periodont*. 11, 176-180, 1984). Although clearly efficacious for oral hygiene, cupric ion, and other metal salts of zinc and tin, have a problem with stability in an aqueous environment. We have developed a cupric bisglycinate complex as a stabilized form of cupric ion. This complex can be formulated in a wide range of aqueous rinse or dentifrice compositions. The following eight-week human clinical study was conducted to demonstrate the effects of the copper bisglycinate complex on plaque, gingivitis, gingival bleeding, and dental staining.

MATERIALS AND METHODS

All subjects were given a commercially available fluoride containing dentifrice (Advanced Formula Crest® (0.243% NaF); Procter & Gamble Company) and a toothbrush. Mouthrinse formulations were:

- 0.12% chlorhexidine gluconate oral rinse (Peridex®)
- 250 or 500 ppm cupric ion (as bisglycinate) containing water, ethanol (16.25%), glycerin, polysorbate 80, flavor, sodium saccharin, and sodium hydroxide.
- Copper placebo containing water, ethanol (16.25%), glycerin, polysorbate 80, flavor, glycine, Na saccharin, Na benzoate, benzoic acid, and FD&C Blue #1.

Study Design & Examinations

188 male subjects (17-43 yrs) were recruited from the Seminario Mayor de la Asunciòn, Guatemala. The study was a randomized, blinded, parallel design with a matched placebo control and a positive control (0.12% chlorhexidine gluconate).

At baseline subjects were evaluated for Löe-Silness Gingival Index, Turesky Plaque Index, Meckel Stain, and Oral Soft-Tissue as previously described (Perlich et al., *J. Clin. Dent*. 6(Sp Is) 54-58, 1995). Subjects received an oral prophylaxis, were stratified per baseline gingivitis & plaque scores, and randomly assigned to a treatment group. Each subject rinsed for 30 seconds with 15 ml the assigned mouthrinse after brushing with common toothbrush and NaF dentifrice. Examinations were repeated after eight-weeks of assigned treatment.

Statistical Analysis

Statistical calculations were by one-way analysis of covariance performed for each examiner using the initial score as the covariant. Significant differences between each of the treatment groups were determined using Student-Newman-Keuls test. All statements of significance were based on $p < 0.05$, two-tailed test, and all percent reductions were calculated versus the placebo rinse control.

RESULTS

Safety Results

There were no significant differences in the (i) number of subjects with comments; (ii) number of subjects with a specific comment; or (iii) reporting of adverse events for any of the test groups compared to placebo.

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Table 1. Balance of Baseline Scores for Subjects Completing Eight Week Examinations

Group	Treatment	Gingival Index	# Gingival Bleeding Sites	Turesky Plaque
A (N = 44)	Placebo	1.1642 (0.018)[a]	27.27 (2.749)[a]	2.01 (0.088)[a]
B (N = 45)	250 ppm Cu^{+2}	1.1987 (0.026)	33.22 (4.181)	2.01 (0.103)
C (N = 45)	500 ppm Cu^{+2}	1.1836 (0.025)	31.42 (3.979)	1.94 (0.120)
D (N = 45)	0.12% CHX[c]	1.1900 (0.026)	32.29 (4.315)	2.05 (0.094)

Table 2. Covariance -Adjusted Eight-Week Gingival Index Results

Group	Treatment	Gingival Index	% Reduction
A (N = 44)	Placebo	0.8938 (CD)[b]	———
B (N = 45)	250 ppm Cu^{+2}	0.8289 (CD)	7.3%
C (N = 45)	500 ppm Cu^{+2}	0.6918 (AB)	22.6%
D (N = 45)	0.12% CHX[c]	0.6559 (AB)	26.6%

Table 3. Covariance-Adjusted Eight-Week Gingival Bleeding Results

Group	Treatment	# Gingival Bleeding Sites	% Reduction
A (N = 44)	Placebo	18.09 (BCD)[b]	———
B (N = 45)	250 ppm Cu^{+2}	13.50 (ACD)	25.4%
C (N = 45)	500 ppm Cu^{+2}	8.12 (AB)	55.1%
D (N = 45)	0.12% CHX[c]	7.96 (AB)	56.0%

Table 4. Covariance-Adjusted Eight-Week Turesky Plaque and Meckel Stain Results

Group	Treatment	Plaque Score	% Reduction Plaque	Meckel Stain
A (N = 44)	Placebo	2.09 (BCD)[b]	———	0.76 (CD)[b]
B (N = 45)	250 ppm Cu^{+2}	1.23 (AD)	41.1%	1.73 (D)
C (N = 45)	500 ppm Cu^{+2}	1.00 (A)	52.2%	3.59 (D)
D (N = 45)	0.12% CHX[c]	0.87 (AB)	58.4%	11.36 (ABC)

[a] Standard Error of the Mean enclosed in parentheses.
[b] Letters denote significant differences vs. indicated treatment groups for $p < 0.05$ as determined by two-tailed Student-Newman-Keuls test.
[c] CHX - chlorhexidine gluconate.

CONCLUSION

-The 500 ppm copper bisglycinate oral rinse provided clinically significant reductions in plaque (58.4%), gingival inflammation (26.6%), and gingival bleeding (56.0%). This efficacy was equivalent to that observed for 0.12% chlorhexidine with 70% less dental staining.

-The 250 ppm copper bisglycinate oral rinse provided clinically significant reductions in plaque (41.1%) and gingival bleeding (25.4%). Reductions for gingival inflammation (7.3%) and dental staining were not statistically different from placebo.

-Copper bisglycinate is a unique stable complex of cupric ion suitable for use in oral care products for the prevention of oral disease.

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