LOWER CHOLESTEROL LEVELS ASSOCIATED WITH USE OF ORAL RINSE IN HEALTHY GINGIVITIS PATIENTS

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BACKGROUND

A novel iodine-based oral rinse is being developed as a once-daily treatment for gingivitis. The oral rinse has demonstrated broad-spectrum antimicrobial, antifungal and antiviral activity in vitro, and safety in animal and human clinical trials. Ongoing clinical studies continue to assess its safety, efficacy and potential impact on biomarkers of inflammation.

OBJECTIVE

The purpose of this study was to evaluate a novel iodine-based oral rinse for safety and for use in reducing gingivitis and biological markers of inflammation in otherwise healthy human subjects.

METHODS

All subjects received dental prophylaxis at the beginning of the study. Study participants were randomized to receive either a placebo rinse or a once-daily, 30 second iodine-based oral rinse. Subjects were evaluated four times over a three month period and dental assessment indices for gingivitis, plaque, and bleeding scores were collected. Blood tests were performed to assess safety and to determine the effects of the oral rinse on relative levels of biological markers of inflammation and low-density lipoprotein cholesterol (LDL-C). Statistical analysis was performed using the Student's t-test and the nonparametric Mann-Whitney U-test.

RESULTS

No treatment-related adverse events were observed. Results showed that after three months of treatment, LDL-C in the iodine-based oral rinse treatment group was significantly ($p<.05$) lower compared to the Placebo group.

CONCLUSIONS

The novel iodine-based oral rinse was shown to be safe in the study. The use of this iodine-based oral rinse may be associated with lower LDL-C. Additional studies are needed to further define the efficacy of the once-daily iodine rinse and evaluate its effect on biological markers of inflammation.

FUTURE DIRECTION

A new 6-month placebo controlled trial (n= 76) is underway at the Center for Oral Health Research at The University of Kentucky. Study endpoints include safety, efficacy against gingivitis, and impact on biomarkers of inflammation including: a full lipid panel, endotoxin, interleukin-1 beta, interleukin-6, C-reactive protein, acute phase proteins and cardiovascular disease analytes, prostaglandin E2 and isoprostane.

BACKGROUND/PREVIOUS RESULTS

Chemistry Liberates I_2

Removes and kills biofilm
Inactivates endotoxin (LPS)
Effective against gingivitis and plaque
Antimicrobial
No known microbial resistance
Non-sensitizing/Non-irritating/Non-staining
Refreshing taste

In Vitro Activity – Oral Pathogens

Actinomyces naeslundii
Actinomyces actinomycetemcomitans
Lactobacillus paracasei
Porphyromonas gingivalis
Porphyromonas intermedia
Streptococcus mutans
Streptococcus oralis
Treponema denticola

Broad Spectrum Activity

Property	Assay	Organism	Results
Hard Surface Disinfectant	AOAC	Pseudomonas aeruginosa, Staphylococcus aureus, Salmonella choleraesuis	100% kill of all bacterial species
Fungicidal	AOAC	T. mentagrophytes	100% kill of fungi
Yeast Biofilm	XTT Reduction Assay	C. albicans and C. glabrata biofilm	Dose Response, up to 100% kill
Virucidal	AOAC	Herpes Simplex Type 1	>99.99% reduction in less than 15 minutes
Virucidal	AOAC	Polio Virus Type 1	>99.9% reduction in less than 15 minutes
Tuberculocidal	AOAC	Mycobacterium bovis BGC	>99.999% reduction
Biofilm	Center for Biofilm Engineering	Mixed Biofilm	>99.999% kill
Endotoxin	Center for Biofilm Engineering	Mixed Gram-negative bacteria	62 to 68% reduction

*AOAC: Association of Official Analytical Chemists International

Safety / Toxicology Background

Study	Results
ISO Agar Diffusion Cytotoxicity Test	Acceptable
Acute Inhalation Toxicity	Non toxic/Non irritating
Primary Eye Irritation	Non toxic/Non irritating
Primary Skin Irritation	Non toxic/Non irritating
Acute Dermal Toxicity	Non toxic/Non irritating
Acute Oral Toxicity	Non toxic

Study	Results
Guinea Pig Sensitization	Non-sensitizing
30 Day Human Clinical Trial (dose: twice per day)	Safe – no adverse events Transient changes in TSH
90 Day Human Clinical Trial (dose: twice per day)	Safe – no adverse events Transient changes in TSH
90 Day Human Clinical Trial (dose: once per day)	Safe – no adverse events No significant changes in TSH

RESULTS OF MOST RECENT STUDY

Gingivitis / Bleeding

Gingival Index			Bleeding Index		
Treatment Group	Mean % Reduction Gingival Index	Difference vs. Placebo	Treatment Group	Mean % Reduction Bleeding	Difference vs. Placebo
Placebo	21.67	–	Placebo	35.98	–
Iodine Rinse	38.39	16.72	Iodine Rinse	52.41	16.43

While the FDA Guidance Document for Gingivitis Oral Rinses calls for a ≥15% reduction in Gingival Index over placebo which was achieved, differences were not statistically significant primarily due to the small sample size and a much greater reduction in gingival index in the placebo group than was anticipated (the literature indicates that typical reduction in gingival index for placebo rinses is 0-14%).

Safety

No irritation/alterations in taste perception
No treatment related adverse events
No significant differences in thyroid function tests

Cholesterol – LDL-C

No significant differences in LDL-C between placebo and treatment group at baseline
LDL-C significantly ($p<0.05$) lower in treatment group vs. placebo at day 90

BIOMEDICAL DEVELOPMENT CORPORATION

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